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The Pathophysiology of Injuries and Deaths Managed in Emergency Departments After Earthquake Disasters: A Narrative Review

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Review Article

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Abstract

Earthquakes cause devastating effects, resulting in the deaths of thousands of people each year. Understanding the full range of impacts, including fatalities, and the pathophysiological mechanisms underlying these effects is crucial for mitigating the aftermath of earthquakes. Therefore, this review aims to: delineate the critical golden time periods following earthquakes and identify the most effective responses and resilience factors during these periods; accurately define the terminology for injuries sustained post-earthquake; elucidate the basic pathophysiology of CRUSH injury-induced myopathy, one of the most significant pathologies in post-earthquake patient management; explore the role of nitric oxide (NO) mechanisms in crush injuries, which are believed to be fundamental to the "smiling death phenomenon" and represent the unseen part of the iceberg; and highlight the importance of the 3 main phenomena responsible for mortality—acidosis, coagulopathy, and hypothermia—during disasters. This comprehensive review, based on the latest literature, encompasses search and rescue, pre-hospital processes, emergency department procedures, and subsequent internal and surgical management algorithms.

Major earthquakes are among the most devastating natural disasters, and the epidemiology of injuries and deaths related to earthquakes is unique for these disasters.[1] When assessing injuries related to earthquakes, they predominantly result from blunt, penetrating, and crush traumas due to building collapses. Additionally, secondary disasters following earthquakes continue to exert adverse effects on human metabolism.[2-5] Many survivors of injuries from earthquakes experience complications leading to additional morbidity and mortality. Direct injuries to vital organs such as the head and heart following building collapses, as well as major vascular injuries, are significant causes of death. Additionally, crush injuries resulting from prolonged pressure of collapsed buildings on the body are also important contributors to mortality. However, following a catastrophic earthquake, clinicians attempt to manage patients under faster and more challenging conditions with diagnostic and treatment tools than they would in routine periods before the disaster.[6] Therefore, having a good understanding of the pathophysiology of injuries not only helps identify critical conditions in triage and management algorithms for the injured but also facilitates practical solutions and rapid intervention methods in the very nature of disasters.[7,8] This review is prepared with the aim of understanding basic pathophysiological mechanisms to comprehend the management of injured individuals trapped in collapsed buildings and their clinical conditions in disaster settings. It also aims to lead researchers in understanding clinical conditions that affect mortality of the injured in pre-hospital and emergency department settings, as well as to pioneer research into still unknown conditions.

Variations in Earthquake Protective Positions Based on Country Income Levels

Earthquake preparedness and response strategies vary significantly according to the income level of countries and communities. High-income countries have more resources to invest in resilient buildings, advanced infrastructure, early warning systems, and comprehensive disaster response plans. This serves as a crucial indicator of resilience against transforming an earthquake into a mass casualty incident (MCI) or a catastrophic disaster. Low-income levels, on the other hand, lead to poor construction quality and a lack of earthquake preparedness. The magnitude and severity of earthquakes are significant factors that influence the human toll across different regions.

In the preparedness phase for earthquakes, drills and simulations are conducted to raise awareness in communities. During these drills, it is recommended that people adopt specific anatomical positions in certain areas to protect themselves during an earthquake. Currently,

there are 2well-known positions for personal protection during a quake: the "Drop, Cover, and Hold On" and the "Fetal Position in the Triangle of Life."

Many organizations, including the Occupational Safety and Health Administration (OSHA), the American Red Cross, and the Federal Emergency Management Agency (FEMA), have long recommended "Drop, Cover, and Hold On" as the course of action during an earthquake.[9-11] Therefore, regardless of income level, many countries such as the United States, Japan, Chile, Turkey, India, Indonesia, Guatemala, Papua New Guinea, and China agree that "Drop, Cover, and Hold On" is the most appropriate measure to take during an earthquake and incorporate it into their national drills. However, in earthquakes of similar magnitude and intensity, the pattern of destruction and the number of collapsed buildings vary significantly among these countries.[12,13]

The main goal in protecting against crush injuries, which are among the most common injuries in earthquakes, is to minimize one's target size to increase survival chances and reduce injury risk. Therefore, it is debatable how effective Drop, Cover, and Hold On would be in protecting individuals inside pancake-collapsed buildings, especially in low-income countries. In a recent expert consensus study conducted with experienced medical search and rescue teams, it was agreed that the Fetal Position in the Triangle of Life could be more beneficial than Drop, Cover, and Hold On in collapsed buildings.[14] The consensus highlighted that the Fetal Position in the Triangle of Life offers less body surface area, reduces the likelihood of crush injuries, protects a larger part of the body from injury, provides better protection against hypothermia, and better sustains basal metabolism. Consequently, the appropriate protective position during the onset of an earthquake may vary based on a country's income level. As a result, each country and community may determine different protective positions during the preparedness phase according to the safety of their structures.

Golden Time Periods Influencing Mortality in Earthquakes

The trauma and golden hours hypothesis, though not widely used, can facilitate learning by discussing earthquake patients. Following collapses after earthquakes, the golden hours begin, and as time passes, the mortality of the injured increases. This information applies to trauma patients we manage during non-disaster periods. However, to describe mortality and time in earthquakes, it may be appropriate to start with the earthquake itself and then proceed sequentially with 4 golden time periods (Table 1).

- **First Period:** In this period, it may be more appropriate to express events in seconds. As seen in severe traumas, the early death of critically injured individuals with extensive damage occurs after structures collapse, and this time frame exhibits the highest mortality rates during earthquakes.[15] Considering rescue times in earthquakes, patients are particularly lost under collapses due to the initial collapse in cases of severe injuries, such as heart, brain, respiratory system damage, and massive bleeding. In these initial mortalities, the quality of building stock and the type of collapses are more effective than search and rescue and health interventions.
- **Second Period:** In this period, events occur within minutes. It refers to the mortality of survivors with severe injuries such as massive bleeding or respiratory distress after the collapse of structures. In the second period, victims may still be unreached under the rubble. The speed and experience of local search and rescue teams are crucial in these mortality rates.[16]
- **Third Period:** This period occurs within hours and encompasses the process starting from the detection of injured individuals trapped under rubble after a collapse. It involves their transfer to hospital emergency departments, where necessary interventions such as hydration, electrolyte management, and management of crush syndrome, as well as surgical procedures for crush injuries, are undertaken (hours).[17] If hours pass and the injured person remains undetected under the rubble, dehydration and electrolyte disturbances can become significant factors contributing to mortality during this time frame.[5] During this period, regional and national search and rescue efforts, as well as the medical management of disasters, focus on preparation. It is the crucial time frame in which the concept of golden hours applies in disasters. Key dynamics include national and international preparedness processes for disasters, resilient medical plans,

Table 1. Golden Time Periods influencing mortality in earthquakes

Time Period	Events	Description	Key Factors in Mortality Mitigation
First Period (Seconds)	Early death of critically injured individuals after structure collapses	Immediately after structure collapse, high mortality rates are observed following severe injuries such as heart, brain, respiratory system damage, and massive bleeding.	Resilient structures and building codes play a critical role in mitigating initial casualties.
Second Period (Minutes)	Mortality of severely injured survivors under rubble	Immediate rescue of individuals still trapped under rubble post-collapse is crucial. The speed of local search and rescue teams is critical during this period.	Rapid and organized local search and rescue teams are essential for reducing mortality rates.
Third Period (Hours)	Extraction of injured from rubble and transfer to hospital emergency departments	Detection and extraction of injured individuals trapped under rubble, followed by transfer to emergency departments for hydration, electrolyte management, crush syndrome management, and surgical interventions.	National preparedness for medical disaster resilience is crucial in this period. Preparation includes medical plans, early management algorithms, and coordinated response efforts.
Fourth Period (Days, Weeks, Months)	Mortality process due to intensive care and surgical complications	Long-term period involving intensive care and surgical complications after initial treatments for rescued individuals from collapsed structures. This phase is crucial where medical resilience plays a decisive role.	Continued medical resilience and capacity building are essential for managing prolonged medical complications and ensuring long-term survival outcomes.

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and early management algorithms for patient care. These efforts aim to facilitate rapid responses in the early stages of disasters, emphasizing the importance of preparedness focused on regional and national levels.

- **Fourth Period:** This period can be expressed in terms of days, weeks, and months. It pertains to the mortality process that emerges after early-stage treatments are provided to patients rescued from under the rubble, involving intensive care and surgical complications (days, weeks, months).[18] This phase is crucial in disasters where medical resilience plays a decisive role.

In earthquakes, the collapse of buildings and the entrapment of injured individuals under debris do not necessarily mean that every trapped person is squeezed. Entrapment in collapsed buildings refers to any body part being stuck between 2hard objects, initiating mortal pathophysiological mechanisms in the tissue. Therefore, assuming similarity in every trapped individual after each building collapse and establishing a relationship between extraction time and mortality independent of injury mechanisms can lead to incomplete and incorrect conclusions, undermining post-earthquake intervention efforts. It should also be remembered in the 4-period post-earthquake mortality process that medical interventions and treatments conducted days after the earthquake may still impact post-earthquake patient mortality.

Correct Terminology

Following early trauma-related mortalities due to building collapses in earthquakes, the next concern is deaths related to crush injuries from being trapped under debris, which cause damage to organs and systems of the injured. The impact of crushing on cells and its rapid manifestation on unaffected systems begins immediately after the trauma-related first period deaths. There are 4distinct terminologies that describe the damage caused by collapsed building materials, particularly to extremities, in earthquakes: CRUSH injury, CRUSH syndrome, Compression syndrome, and Compartment syndrome.[19] The assumption that "acute kidney injury during earthquakes" terminology refers to crush syndrome is a misconception.[20] Table 2 provides some definitions. Understanding the correct terminology and diseases hinges on understanding how collapsed building materials affect the body during earthquakes. If building debris exerts severe pressure on a part of the body, it can result in fractures in bones, soft tissue damage, and trauma-related consequences in the affected area.

Awareness in Earthquake Triage

In the aftermath of earthquakes, triage is essential at every stage of the response to the resulting damage. This is because, even in the twenty-first century, earthquakes continue to be one of the most impactful disasters on societies, causing significant deaths, injuries, and property losses.[21] Therefore, for earthquake-related injuries, accurate, effective, and dynamic triage is conducted at every point of medical contact (repeated based on the ratio of patient volume to triage team until the patient receives primary treatment and is discharged from the hospital).

The triage algorithm required at each point of medical contact during earthquakes varies. Sequentially, triage involves the rescue of patients trapped under debris, the basic assessment of injury severity, rapid implementation of necessary interventions, and transportation to the hospital (*primary triage*); upon the patient's admission to the emergency department, the determination of injury severity, and the allocation of the treatment area (*secondary triage*); and finally, the completion of the emergency department (ED) process, including surgical treatment, intensive care transfer, and transfer to other treatment centers (*tertiary triage*). Table 3 summarizes the characteristics of the triage algorithms used in patient management during disasters.

Table 2. Muscle injuries and syndromes

Injuries and Syndromes	Description
Crush injury	Injury resulting from the direct physical compression of muscles by a heavy object.
Crush syndrome	Also known as rhabdomyolysis, it involves a series of metabolic changes produced by an injury severe enough to disrupt the cellular integrity of skeletal muscles and release their contents into the circulation.
Compression syndrome	An indirect muscle injury caused by the simple, slow compression of a group of muscles, leading to ischemic damage and the subsequent release of crush substances into the bloodstream.
Compartment syndrome	Localized rapid increase in tension within a muscle compartment, inevitably leading to metabolic disturbances like rhabdomyolysis.

Primary Triage

In *primary triage*, which is conducted by Emergency Medical Services (EMS) personnel or Medical Search and Rescue Team in the field, the most commonly used triage models are START (Simple Triage and Rapid Treatment) and SALT (Sort, Assess, Life-Saving Interventions, and Triage/Treatment) for adult casualties (patients above the age of 8 years), while JumpSTART, a modification of START, is used for children.[22] The SALT triage system was developed to combine the deficiencies of internationally widely used triage systems like START with national triage standards.

In disasters, the most important feature of these triage models commonly used in the field is that, as their names suggest, they prioritize and classify casualties according to color codes while also incorporating short (calculated in less than 60 seconds) and simple (the patient's respiration, circulation, and consciousness are assessed using simple methods), quick interventions/treatments and rapid transport for patients with high mortality rates. Another issue is the confusion in some sources today regarding the last "T" in the START acronym, whether it stands for 'treatment' or 'transport'.[22,23] Similarly, in SALT, although the "T" is known to stand for triage, it also includes treatment. Considering that these triage systems are conducted in the field, both must encompass triage, treatment, and transport. Because field triage naturally prioritizes patients, it also inherently determines transport. Therefore, in field triage, the "T" in START and SALT essentially stands for Triage, Treatment, and Transport (Figure 1).

Currently, START remains the most widely used triage algorithm in MCIs in the United States.[24] However, the performance of existing triage systems, in terms of accurately prioritizing casualties and other performance indices, is still not at the desired level.[25] Therefore, to improve the performance and accuracy of triage systems, there is a need for new models and research that take into

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Table 3. Triage systems used in patient management during disasters

Localization	Level	Point	Provider	System	Focus
Disaster field	*Primary*	Field	• EMS personnel • mSAR Team	• START • SALT • Jump START • Others	• Simple triage • Rapid treatment • Rapid transport
ED	*Secondary*	Admission	ED triage team	WHO's MCI preparedness and response in emergency units triage recommendation	• Day-to-day emergencies: The greatest good for each individual patient • MCI: The greatest good for those who can most benefit from medical interventions (focus on the red patients) • Large Scale disasters: The greatest good for the greatest number of potential survivors (focus on the yellow and green patients)
	Tertiary	Outcome	Specialists • Emergency Medicine • Intensive Care • Surgeons, • Nephrologists • Burn • Pediatricians • Other physicians	SAVE algorithms: • MESS, • BTS • GCS • SAFE-QUAKE	• Treatment Priority • Hospital Organization • Operating Room • Organization • Drainage of injured patients • Transport to Another Hospital

EMS: Emergency Medical Services; mSAR: Medical Search and Rescue Team; START: Simple Triage and Rapid Treatment; SALT: Sort, Assess, Lifesaving Interventions, Treatment/Transport; Jump START: Pediatric Triage Algorithm for Children; ED: Emergency Department; WHO: World Health Organization; MCIs: Mass Casualty Incidents; MESS: Mangled Extremity Severity Score; BTS: Burn Triage Score; GCS: Glasgow Coma Scale.

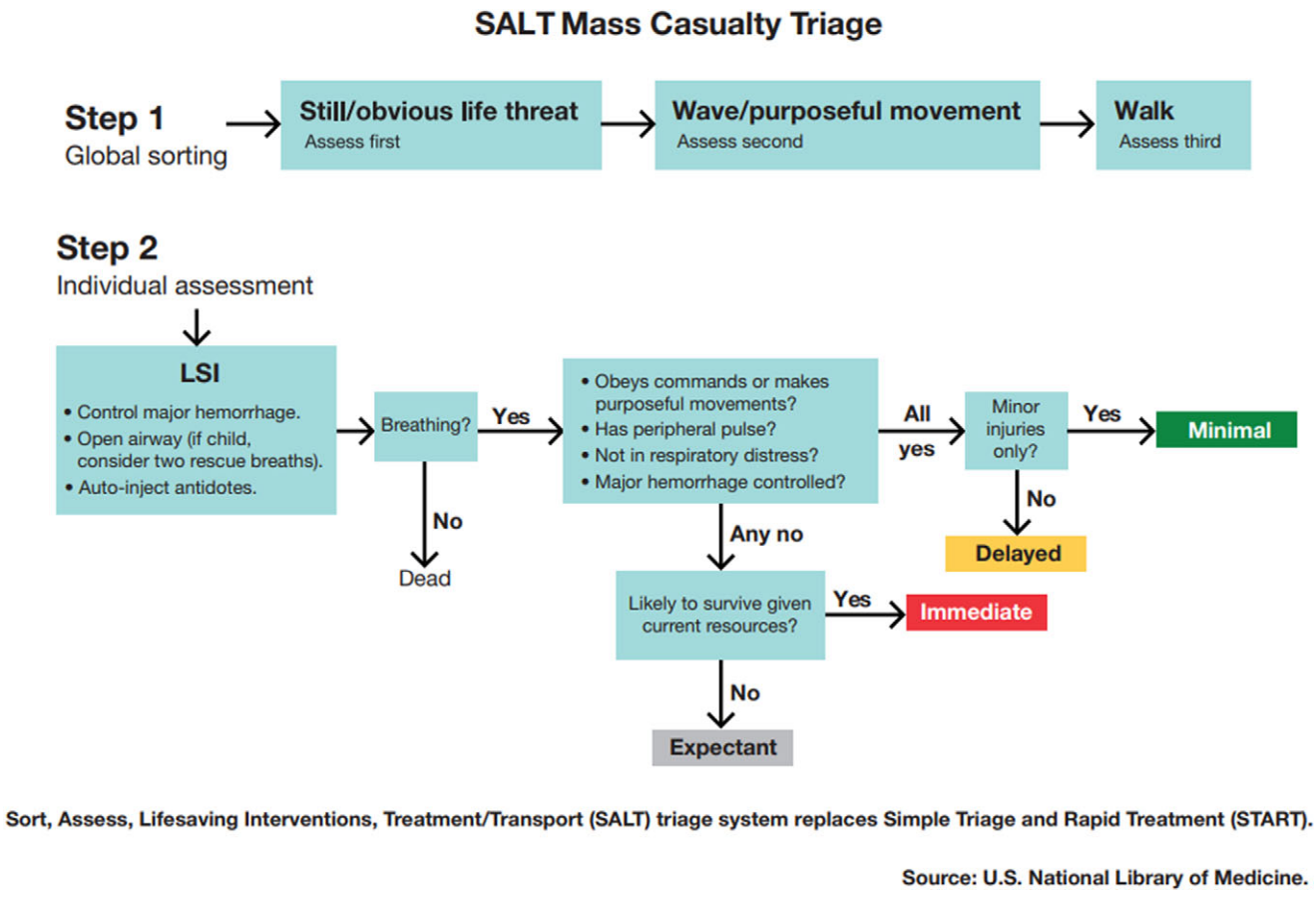

Figure 1. Sort, Assess, Lifesaving Interventions, Treatment/Transport (SALT) triage system replaces Simple Triage and Rapid Treatment (START).

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account national conditions and identify other influential factors affecting the accuracy of triage systems.

Secondary Triage

After the transfer of patients to the ED, earthquake-related casualties are subjected to 2 separate triage processes in the ED: *secondary triage*, which determines the treatment area based on injury severity upon admission, and tertiary triage, which occurs at the conclusion of the ED process. The triage conducted upon admission to the ED is often confused with field triage. Triage systems such as START and SALT should be used for triaging casualties in the field. However, triage systems used in disasters can be revised by practitioners depending on the nature and scale of the incidents. For example, during the February 6 Kahramanmaraş earthquakes in Turkey, the catastrophic number of injured people rendered the pre-hospital system inoperative, with many victims reaching EDs by their own means. In such situations, EDs returned to the field, and in post-earthquake publications, it was suggested that in catastrophic scenarios, the distinction between EDs and the field could disappear, allowing the use of field triage systems like START in EDs as well.[6]

In addition to these, the Emergency Severity Index (ESI) Triage Algorithm, the Australasian Triage Scale, the Canadian Triage System, the Chinese 4-level and 3District Triage Standard, and the Manchester Triage System are also recommended for use in emergency departments during earthquakes and other disasters.[26-28] The World Health Organization's (WHO) 2022 guideline, "*Mass Casualty Preparedness and Response in Emergency Units*," recommends initially classifying casualties in the triage area based on their ability to walk (green for those who can walk; red, blue, and yellow for those who cannot, based on their clinical condition; and black for those with non-survivable injuries) (Figure 2).[23,29,30] They are then directed to the designated color-coded area within the ED. This 5-color triage model recommended by WHO, which should be implemented at the first point of contact in the ED, has a simpler algorithm compared to SALT and aims to determine the area in the ED where the patient will be monitored based on the severity of their injuries. The WHO guideline includes an important detail not found in many other algorithms: it specifies the areas of focus based on the scale of the disaster. For MCI, the focus is on providing the greatest good for those who can most benefit from medical interventions, which means prioritizing red patients. In the case of large-scale disasters, the focus shifts to providing the greatest good for the greatest number of potential survivors, thereby prioritizing yellow and green patients.

Tertiary Triage

In the ED, patients whose injury severity is classified by color coding require a dynamic triage process like field triage. After the rapid initial treatment in the ED, these patients need to be prioritized (tertiary triage) for surgical intervention, intensive care, or transfer to another facility. Recommendations for tertiary triage in the literature are limited. However, there are studies that suggest the use of the Secondary Assessment of Victim Endpoint (SAVE)

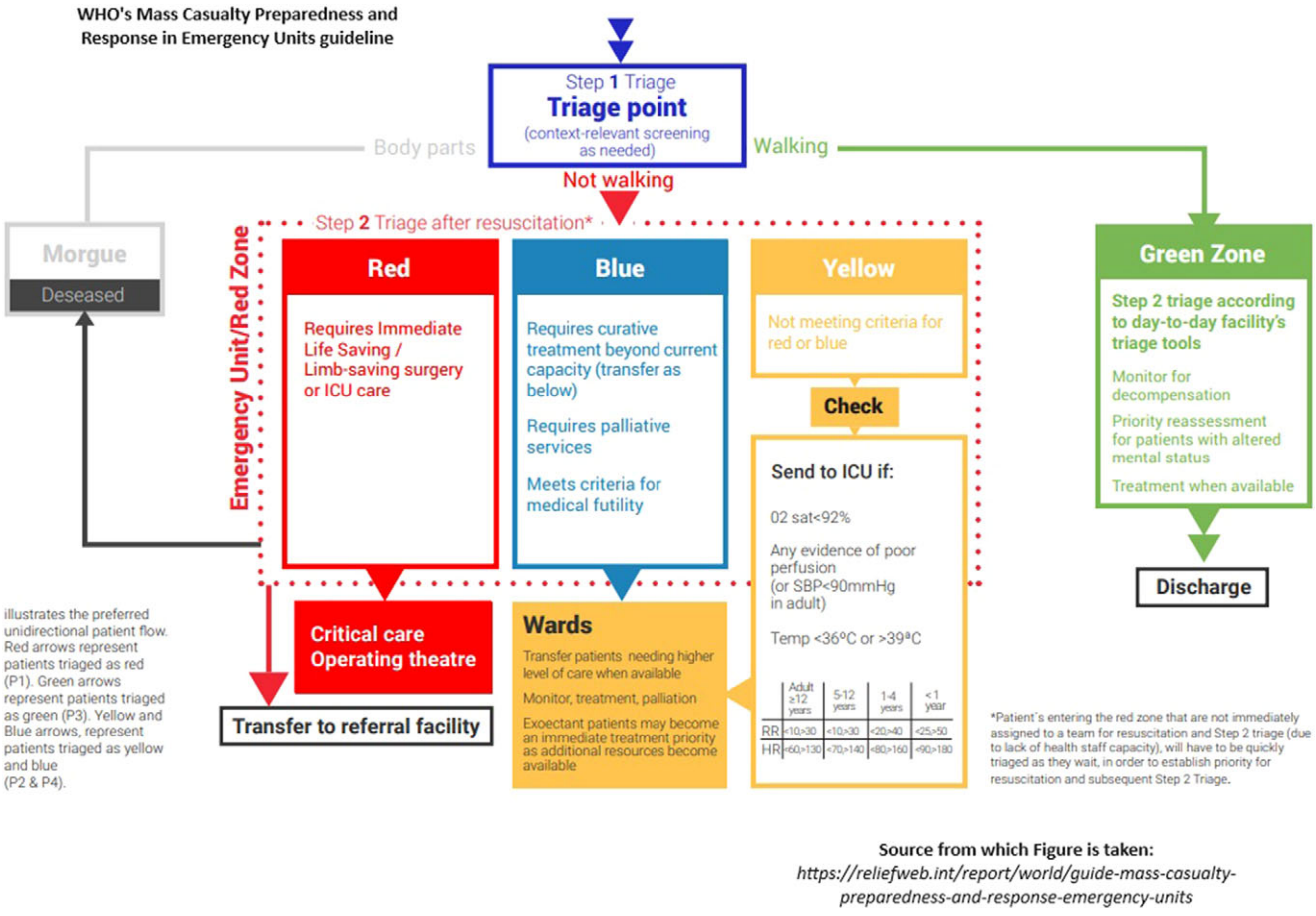

Figure 2. The triage model recommended by WHO in Mass Casualty Preparedness and Response in Emergency Units.

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triage, proposed by Koening and colleagues, in situations where the number of casualties in the field far exceeds available resources, for tertiary triage in the ED.[6,31] SAVE aimed to identify patients with more severe injuries, i.e., those with higher mortality, by using the Glasgow Coma Scale (GCS), Mangled Extremity Severity Score (MESS), and Burn Triage Score (BTS) based on the region of severe injury. It sought to redirect the limited available resources from these patients to those with a higher likelihood of survival. This led to the consideration that SAVE has algorithms capable of identifying severely injured patients.

In the wake of the February 6 Kahramanmaraş earthquakes in Turkey, where 53 000 people died and thousands were injured, researchers examined the use of MESS, one of SAVE's algorithms, for extremity injuries and triaging surgeries. Additionally, they highlighted an important situation not included in SAVE: the development of CRUSH syndrome in earthquake victims, which would limit dialysis units. To address the need for dialysis in transferred patients, they proposed the SAFE-QUAKE Scoring System.[3,4] One of the major points in managing the crowding of ED after earthquakes is ensuring patient flow. Therefore, tertiary triage holds a crucial position in the dynamics of ED during earthquakes.

Crush-Related Myopathy

The mechanism of myopathy in crush injuries is not entirely clear. Traditionally, crush myopathy has been attributed to ischemia resulting from reduced blood flow to the injured muscle. However, this approach fails to explain the relatively short period between the mechanical pressure and the onset of symptoms.[32] Therefore, as commonly applied in orthopedic surgery, muscles typically tolerate total ischemia for 3-4 hours well. Another suggestion is that during muscle crush, the tension applied to the sarcolemma may activate channels sensitive to non-selective stretching. Pressure on muscle tissue results in 2primary outcomes.[33] Firstly, it leads to depletion of adenosine triphosphate (ATP), the cellular energy source, and/or direct injury and rupture of the plasma membrane. This process causes an increase in intracellular free ionized cytoplasmic and mitochondrial calcium (Ca). Secondly, ATP depletion disrupts sodium (Na) function, which is essential for maintaining the integrity of Na^+/K^+-ATPase and Ca^{2+}-myosin ATPase pumps. This depletion also contributes to myocyte damage and the release of intracellular muscle components such as creatine kinase (CK), other muscle enzymes, myoglobin, and various electrolytes.

As a result, considering the physiological mechanism occurring in muscle cells during CRUSH injuries, the crushing and tearing of muscle cells lead to the release of myoglobin, as well as enzymes such as potassium, magnesium, phosphate, acids, creatine phosphokinase (CKMM), and lactate dehydrogenase (LDH), from the intracellular space into circulation due to the disrupted cellular structure. While essential for cellular function, when released in large quantities into circulation, these substances can become toxic. They can cause significant damage to various tissues, particularly the kidneys, reaching life-threatening levels of harm.

Following crushing injuries, regional ischemia occurs due to micro and macro circulation obstruction in muscles, resulting in the release of Na^+, calcium (Ca^{2+}), and fluids that increase muscle volume and tension. CK and ATP are depleted. The nitric oxide system (NOS) is activated, contributing to muscle vasodilation and exacerbating hypotension.[34]

While reading about these mechanisms, I anticipate you're wondering about the duration of pressure required to initiate these reactions.[3] Although there are varying claims in the literature regarding this timeframe, Li and colleagues' study during the 2008 Wenchuan earthquake in China demonstrated that even 1hour of pressure on body parts is sufficient to trigger Crush syndrome.[35]

Emergency physicians primarily combat the toxic effects of released myoglobin and intracellular electrolytes when dealing with patients extracted from under debris.[36] This is because once the weight is lifted off a trapped limb, cellular debris containing all toxic substances due to cell damage enters the systemic circulation via venous circulation, affecting all parts of the body. Crush injuries are commonly associated with acute kidney injury, which is true. However, the entry of numerous electrolytes and intracellular mediators with toxic effects from the crushed tissue into the system threatens the patient's life not only affecting the kidney but also potentially impacting other systems such as the heart (e.g., arrhythmias due to electrolyte disturbances) and the central nervous system. As a result, crush injury trauma often complicates into resistant and severe hemodynamic shock, electrolyte disturbances (hyperkalemia, hypocalcemia, and acidosis), and myoglobinuric kidney failure.

Release of Nitric Oxide and Its Mechanisms of Action Following Crush Injury

Following rhabdomyolysis, we will address and electrolyte disturbances in the appropriate section. However, it is crucial to discuss Nitric Oxide (NO) here, as it emerges as one of the pivotal systems activated early post-crush injury, significantly impacting mortality during rescue, pre-hospital, and early emergency department admissions.

To understand the NO mechanism, it is necessary to examine its sub-isoforms. Studies conducted on rats have generally identified 3different nitric oxide synthase (NOS) isoforms:[37] the first is Neuronal NOS (nNOS), primarily found in the sarcolemma and fast (type II) muscle fibers; the second is Endothelial NOS (eNOS), detected in the vascular endothelium of all mammals, as well as in the cytoplasm and mitochondria of mitochondria-rich fibers in rat skeletal muscle; and the third, isoform, Inducible NOS (iNOS), induces the production of mRNA and protein in macrophages following endotoxin application in mice, indicating iNOS activity. NOS activity in rat skeletal muscle is associated with the density of type II muscle fibers and is inversely related to muscle strength development; NO synthesis in active muscles opposes contraction strength. Another significant effect of NO is its regulation of vessel diameter and blood flow. Therefore, increased NO production in skeletal muscle can affect vascular tone and blood flow, as well as contraction characteristics. By examining the distribution of the NOS system in tissues, the physiopathological effects that will arise from the system's activation can be predicted. Consequently, in injured individuals trapped under collapsed structures following earthquakes, especially in the early period (during rescue from under the rubble and pre-hospital care), the changes in blood flow caused by NO can have a significant impact on muscle function and systemic circulation. This can lead to hemodynamic-hypovolemic shock, a characteristic feature of CRUSH syndrome in humans. Increased NO production (induced by iNOS) can also cause destructive damage in muscle tissue and exacerbate rhabdomyolysis. In the 1990s, Rubinstein and colleagues investigated the clinical impact of NO as a new regulator of skeletal muscle function, particularly following muscle crush injuries.[34] This study demonstrated increased

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blood flow in crushed tissues due to NO, indicating systemic vasodilation and resistance shock, and argued that it increased damage caused by myoglobin in kidney tubules. The systemic toxic effects of the NO system and intracellular mediators are critically important during the rescue process from under rubble, pre-hospital care, and initial presentation to the emergency department. In patients arriving at the emergency department, the management and mortality factors of the deadly triad paradigm—acidosis, coagulopathy, and hypothermia—must be addressed. In earthquake-related emergency department admissions, the management of these 3lethal conditions must be closely monitored.

The Mortality Triad in Earthquake-related Injuries: Acidosis, Coagulopathy, and Hypothermia

Acidosis

Blood pH is maintained within a narrow range for optimal physiological function. Acid-base balance is typically achieved within the pH range of 7.35 to 7.45. Blood pH distinguishes between acidemia (pH below 7.35) and alkalemia (pH above 7.45).[38] In earthquake-related injuries, there are several reasons why a patient brought to the emergency department may exhibit conditions leading to acidosis. Particularly, the inclusion of intracellular hydrogen (H) into the bloodstream and damage to the body's major acid-base regulator, the kidneys, are primary factors contributing to the cause and progression of this acidosis. Except for trauma conditions in the respiratory tract without trauma or obstruction causing ventilation and perfusion disturbances in the lungs due to earthquakes, generally, the acidosis observed in the blood is metabolic acidosis.

Metabolic acidosis occurs due to an increase in weak acids or a reduction in the strong ion difference (SID).[39] Serum proteins, albumin, and inorganic phosphate are considered weak acids. Strong ions like Na^+, K^+, $CA^{2+,}$ Mg^{2+}, and Cl^-, are fully ionized in body fluids.[40] SID refers to the excess of strong cations over strong anions, with a normal plasma value of 42 mEq/L.[41] The method of measuring metabolic acidosis using SID and weak acids was introduced by Stewart in the 1980s and still sparks debate in clinical practice. Plasma base excess is commonly used in clinical practice to identify the metabolic component of acidosis. The base excess approach has been shown to be equivalent to Stewart's SID approach in measuring acid-base status in critically ill patients.[42] Metabolic acidosis is classified into acute and chronic categories. Acute metabolic acidosis typically develops over a few days. Chronic acidosis, on the other hand, is a condition that can persist for weeks to years, although the exact timeframe for chronicity is not precisely defined. Maintaining a narrow range of 7.35-7.45 is crucial for cellular enzyme activities and the integrity of cell membranes. Due to its strong affinity to proteins, when free, H^+ ions bind to proteins, disrupting their functions. This primarily intensifies glucose metabolism and impairs central nervous system functions. As the concentration of H^+ ions exceed 45, acidosis (pH <7.35) may occur, while dropping below 35 can lead to alkalosis (>7.45). Life-threatening thresholds for blood pH are defined as <6.80 and >7.70.[43] Understanding acid-base disturbances in patients presenting to the emergency department due to earthquake-related injuries is crucial. We know that these disturbances can impact many factors, from etiology to diagnosis, treatment, and management decisions. In cases of metabolic acidosis, a commonly used method to identify the etiology is to calculate the anion gap.

Considering the factors that cause acidosis, along with the numerous factors draining into the compressed system, the damage caused by acute kidney injury can itself lead to acidosis. For example, in diabetic ketoacidosis, increased acid production results in a high anion gap. Similarly, in crush injuries, the acid load from damaged tissues contributes to acidemia in the circulatory system. The development of AKI due to the deposition of toxic substances in the renal tubules can lead to metabolic acidosis. Insufficiency in acid excretion, termed acute uremic acidosis, can also contribute to high anion gap levels. This creates a cycle where the clinical manifestation of AKI exacerbates the high anion gap. An interesting question arises: Can the presence and amount of anion gap upon admission to the emergency department for earthquake-related injuries provide insights into the prognosis of patients? New research is needed to answer this question.

Acidosis-induced electrolyte imbalances can have a fatal impact on earthquake-related injuries. Therefore, determining the etiology is crucial for selecting the appropriate treatment methods for the injured, such as fluids, dialysis, or bicarbonate therapy. Here, it is worth mentioning a critical point. Consider a patient being extricated from under rubble. It is known that intravenous access should be established, and a bolus of fluid should be administered even before the patient is fully rescued. However, in our daily practice, the most used fluid by ambulances is 0.9% NaCl. Patients with severe injuries from earthquakes typically require more fluids, up to 6 liters, while older patients with less severe injuries may only need 3 liters. However, administering a bolus of 0.9% NaCl can expose the patient to severe acidosis due to the fluid's pH range of 4.5 to 7.

This becomes a mistake during rescue operations, pre-hospital care in ambulances, and in the emergency department. Following the Bingöl earthquake, a study involving Professor Mehmet Sever, who has conducted valuable research on this topic in our country, advocated for the addition of 50 mmol of bicarbonate per liter of isotonic saline.[44]

Coagulopathy

In coagulation studies, pigs are chosen as experimental models because their cardiovascular systems closely resemble those of humans.[45] Because they are large enough to be easily instrumented and allow for repeated blood sampling. However, coagulation and bleeding models in pigs are based on concepts and procedures previously developed in other animals, particularly dogs. Despite this, they are superior to dog models because they are more applicable to human physiological events and clinical issues.[46]

When searching the literature for coagulopathy related to earthquake-induced injuries, direct results may not readily appear. Indeed, information on injuries caused by earthquakes is more commonly derived from data collected during actual earthquake events rather than from simulations. Despite extensive research on this topic, I have not found direct studies or opinions. However, by approaching the issue indirectly, we can uncover some insights into the pathophysiology of coagulopathy. Firstly, if you attempt to interpret coagulopathy in this patient group through the lens of decreased renal function due to CRUSH syndrome, you will primarily encounter studies on coagulopathy in patients with chronic kidney disease. In these patients, due to the impairment of platelet function by uremia, you will come across the concept of "bleeding tendency in uremia."[47] Research on chronic kidney disease (CKD) has indicated that even in its early clinical stages, CKD increases the risk of early atherothrombotic manifestations of cardiovascular diseases by 25-30%. This has been identified as the most common

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clinical outcome in end-stage renal disease patients on dialysis, accounting for approximately 40% of all deaths.[48] Here, it may be beneficial to revisit the effects of NO. NO, released by platelets and the endothelium, prevents platelets from adhering to the vessel wall and provides a negative feedback mechanism for the propagation of thrombus formation. In essence, NO acts as a thrombo-regulator and has a negative impact on clot formation.

Like NO, another system that negatively impacts coagulation through platelets is antioxidants. Many antioxidants can indirectly inhibit platelets by influencing the metabolism of reactive oxygen species, which alter platelet function. The hypothesis, advocated by some albeit not yet thoroughly supported in the literature, suggests that antioxidant therapy could be beneficial for prognosis in earthquake-related injuries, particularly in Crush injuries. However, this hypothesis loses its validity when considering the negative impact of antioxidants on platelet function. Two other factors that significantly impact coagulopathy are acidosis and hypothermia, which can develop in the body due to environmental conditions. In an animal study conducted by Martini et al., the independent and combined effects of hypothermia and acidosis on thrombin generation kinetics were investigated using a pig model that included 15 animal groups (control, hypothermia, acidosis, and combined hypothermia and acidosis).[49] In this study, hypothermia at 32°C was induced using a cold water blanket containing 4°C circulating water, and acidosis with a pH of 7.1 was induced through the infusion of 0.2 mol/L hydrochloric acid. Once the target pH and/or temperature were reached and stabilized for 15 minutes in these animals, blood samples were taken to analyze thrombin generation kinetics. The data from this study demonstrated that both hypothermia and acidosis impaired thrombin production. Additionally, it is argued that hypothermia and acidosis have distinct inhibitory effects on thrombin production.[50] In Martini's research, hypothermia at 32°C primarily caused a delay in the initiation of thrombin production, without significantly affecting the propagation phase of thrombin generation. This suggests that the inhibitory effect of hypothermia is primarily on the FVIIa/tissue factor pathway. Interestingly, acidosis with a pH of 7.1 moderately inhibited thrombin formation during the initiation phase. However, thrombin production in the propagation phase was persistently and dramatically inhibited by acidosis. This indicates a severe inhibition of FV, FVIII, FIX, FX activation, and the formation of the FXa and prothrombinase complexes due to acidosis.

In conclusion, based on all this information, it is thought that patients with earthquake-induced injuries are more prone to bleeding rather than thrombosis. However, it should also be considered that the venous and arterial systems in a crushed extremity can become dysfunctional for a certain period, which may influence the tendency towards thrombosis.

Hypothermia

In recent years, during the February 6 Kahramanmaraş earthquakes in Turkey, temperatures around the epicenter in southern Turkey dropped to approximately 2.7°C in the hours following the 7.8 magnitude earthquake.[51] On the day of the earthquake, a cold rainstorm occurred, and in the following days, temperatures dropped below freezing and remained there. In events like earthquakes, the condition of hypothermia in patients is often referenced from the "Accidental Hypothermia" literature. Core body temperature, which is the internal temperature, is measured using thermometers with rectal, intravesical, or esophageal probes and is typically defined as a core temperature below 35°C (95°F).[52] Accidental hypothermia is classified based on its severity. Mild hypothermia is defined as a core body temperature between 32°C and 35°C. Moderate hypothermia occurs when the core temperature ranges from 28°C to less than 32°C. Severe hypothermia is diagnosed when the core body temperature falls below 28°C.[53]

Thermoregulation involves a dynamic balance between heat production and heat loss to maintain a constant core temperature. This balance is achieved partly by adjusting central thermogenesis and partly by maintaining a differential temperature gradient between the body core and the environments directly exposed to the external environment. The amount of heat gained from or lost to the environment is closely and rapidly regulated in response to changing conditions. There are 2types of cutaneous receptors: cold and warm. Exposure to cold increases the activity in afferent fibers from cold receptors, which stimulate the preoptic nucleus of the anterior hypothalamus. This leads to direct reflex vasoconstriction, reducing blood flow to the cooling skin, and cooler blood reaches the temperature-sensitive neurons in the hypothalamus. The hypothalamus then initiates various responses: rapid responses via the autonomic nervous system, delayed responses via the endocrine system, adaptive behavioral responses, extrapyramidal skeletal muscle stimulation, and shivering. These responses aim to either increase heat production or decrease heat loss.[54] it is crucial to closely monitor and manage hypothermia in patients trapped under rubble due to an earthquake. The interlinked relationship between acidosis, coagulopathy, and hypothermia, all of which can lead to increased mortality, should be kept in mind.

Highlights

Earthquake Preparedness and Response

The strategies for earthquake preparedness and response vary significantly based on a country's income level. High-income countries have more resources to invest in resilient buildings, advanced infrastructure, early warning systems, and comprehensive disaster response plans, making them more resilient to transforming an earthquake into an MCI or a catastrophic disaster. In contrast, low-income countries often face poor construction quality and lack of preparedness, increasing the risk of severe damage and casualties.

Golden Time Periods Influencing Mortality

- **First Period (Seconds)**: Early deaths of critically injured individuals occur immediately after the collapse due to severe trauma to vital organs. The quality of building stock and type of collapses play a crucial role in these initial mortalities.
- **Second Period (Minutes)**: Mortality of survivors with severe injuries such as massive bleeding or respiratory distress. The speed and experience of local search and rescue teams are critical.
- **Third Period (Hours)**: Involves the transfer of injured individuals to hospitals and necessary interventions. This period is crucial for hydration, electrolyte management, and surgical procedures.
- **Fourth Period (Days, Weeks, Months)**: Post-rescue, this period focuses on intensive care and surgical complications. Medical resilience plays a decisive role.

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Crush-Related Myopathy

Crush injuries lead to the release of myoglobin and other intracellular components, causing significant damage, particularly to the kidneys. Emergency physicians must manage the toxic effects of these substances, which can affect multiple body systems.

Nitric Oxide Release

The release of nitric oxide (NO) following crush injuries significantly impacts mortality due to its role in vasodilation and muscle damage. NO affects blood flow, contributing to hemodynamic-hypovolemic shock, a characteristic feature of CRUSH syndrome.

The Mortality Triad

- **Acidosis**: Earthquake-related injuries often lead to metabolic acidosis due to the release of intracellular hydrogen and kidney damage. Understanding the acid-base disturbances is crucial for effective treatment.
- **Coagulopathy**: Hypothermia and acidosis impair thrombin production, leading to bleeding tendencies. The role of NO and antioxidants in coagulation is significant.
- **Hypothermia**: Hypothermia is a critical concern in earthquake victims, especially in cold weather conditions. It is essential to monitor and manage hypothermia to prevent increased mortality.

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