6 The Relevance of Traumatic Shock and Its Treatment on the Epidemiology of Multiple Organ Failure

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6.1 Shock: Overview

Shock was first described by Hippocrates of Kos around 2400 years ago [1]. The word shock, medically speaking, is the English transliteration of the French *choquer* (to clash, offend, hurt) and was first used by the French military surgeon Henri Francois Le Dran in 1737 to describe the physiologic events that led to the death of soldiers after being shot on the battlefield [2]. More poetically, in 1872 Samuel Gross stated that shock is the "rude unhinging of the machinery of life"; and, in 1895, John Collins Warren referred to it as "a momentary pause in the act of death" [3].

In the modern, technical sense, shock is the culminating clinical manifestations of circulatory failure as a consequence of circulatory deficits and resultant decreased cellular oxygenation and tissue hypoperfusion [4]. The diagnosis of shock is based upon three criteria: clinical presentation, hemodynamics, and biochemical signs. Clinically, there are several manifestations of hypoperfusion, to include: (1) cold and clammy skin, (2) cyanosis, (3) urine output of less than 0.5 mL per kilogram of body weight per hour, and/or altered mental status. Hemodynamically, shock presents with systemic arterial hypotension defined by a systolic arterial pressure less than 90 mm Hg or mean arterial pressure less than 70 mm Hg with associated tachycardia [4]. Biochemically, it is often associated with a metabolic acidosis as a result of anaerobic metabolism leading to hyperlactatemia and a so-called base deficit [4].

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6.2 Mechanisms of Shock

There are four well-established pathophysiologic mechanisms of shock: (1) hypovolemic/hemorrhagic, (2) cardiogenic, (3) obstructive, and (4) distributive. Patients can often present with a combination of the above mechanisms. For example, consider a trauma patient with a tension pneumothorax (obstructive) with a concomitant blunt cardiac injury (cardiogenic) and splenic hilar avulsion (hemorrhagic). Therefore, it is imperative to identify the etiology(ies) of a patient in shock to more accurately guide therapy as the treatment for one type of shock may have deleterious effects if given for a patient with shock due to a different cause (e.g., giving a large volume resuscitation to someone with cardiogenic shock).

Hypovolemic shock is characterized by low cardiac output, resulting in depleted intravascular volume, inadequate oxygen transport, and hypoperfusion of vital organs. This is the most common type of shock in children and is frequently seen secondary to diarrheal illnesses in developing regions [5]. Hemorrhagic shock is a subtype of the broader hypovolemic variety. It most commonly results from a traumatic injury and is the leading cause of preventable death in this population [5]. A thorough history is generally sufficient for the diagnosis of hypovolemic shock and is more sensitive and specific than the physical exam. Multiple laboratory values are typically deranged in hypovolemic shock. An elevation of BUN and creatinine secondary to prerenal kidney injury is often present. Sodium and potassium may be either elevated or depressed depending on the etiology of hypovolemia (e.g., blood loss vs. excessive emesis due to a gastric outlet obstruction). Lactic acidosis may also be present. Of note, if the source of volume loss is from the stomach patients may become alkalotic instead of acidotic [5]. Additionally, patients may present with a normal, or even elevated, hemoglobin and hematocrit secondary to a reduction in plasma volume and hemoconcentration [5].

Up to 81% of cardiogenic shock arises due to acute myocardial infarction. Cardiogenic shock may also result from inadequate cardiac contractility in cases such as end-stage cardiomyopathy, advanced valvular heart disease, myocarditis, or cardiac arrhythmias [6]. In cardiogenic shock, initial hypotension triggers a release of vasoconstrictors to re-establish normal blood pressure. However, despite the restoration of normal mean arterial blood pressure, myocardial oxygenation remains low [7]. Clinically, cardiogenic shock presents as hypotension refractory to volume resuscitation, in contrast to hypovolemic shock which is responsive to volume [8].

Obstructive shock is defined as a disorder involving impaired diastolic filling and reduced cardiac preload including vena cava compression, pulmonary embolism, cardiac tamponade, or tension pneumothorax [9]. Patho-physiologically it is classified according to the location of obstruction. It presents as a rapid, massive drop in cardiac output and blood pressure. However, unlike cardiogenic shock, the decrease in cardiac output is not related to dysfunction of the myocardium. Rather, it is related to a factor extrinsic to the heart itself. Subsequent reduced blood flow in the great vessels, or cardiac outflow with a critical drop in cardiac output, and global oxygen supply ultimately result in tissue hypoxia throughout all organ systems [9].

In distributive shock, also known as vasodilatory shock, there is a characteristic loss of regulation of vascular tone and/or disordered permeability of the vascular system [9]. The most common causes are sepsis and anaphylaxis. In sepsis, there is a massive vasodilatory response to inflammatory cytokines. A similar pathophysiologic mechanism can also be seen in patients with pancreatitis and significant burns. However, in anaphylaxis vasodilation is secondary to IgE-mediated release of histamine from mast cells and basophils [10].

In traumatic injury, the most common cause of distributive shock is neurogenic. Neurogenic shock results from injury to the spinal cord at the cervical and high thoracic levels. Shock results from autonomic dysregulation from a sudden loss of sympathetic tone with preservation of parasympathetic function [11]. The clinical manifestations of this dysregulation are hypotension with bradyarrhythmia. In the trauma patient, neurogenic shock is a diagnosis of exclusion as hemorrhagic shock is by far more common. Nonetheless, the incidence of neurogenic shock in trauma is noteworthy—approximately 19.3% in the patient with cervical cord injuries and 7% in those with thoracic injuries [12].

6.3 Approach to Shock

Although treatments to reverse of each form of shock differ (e.g., antibiotics for sepsis versus embolectomy for massive pulmonary embolism), there are general principles that guide resuscitation of the patient in shock. Most commonly is the "**VIP** rule," an approach published first in 1969 by Weil and Shubin: **V**entilate, **I**nfuse (fluids), and **P**ump (for example, vasoactive agents) [4, 13]. Despite an evolved understanding of the mechanisms of shock, and significant advances in pharmacological and mechanical techniques, these general principles have not changed much over the years.

Using the "**VIP** rule," the first step is to **V**entilate. Upon presentation with feeble or greatly labored thoracic excursion and decreased breath sounds, a clinician may reasonably suspect ventilatory failure. Measurement of pH, carbon dioxide content, and oxygen saturation on blood obtained via arterial puncture provides specific, quantitative information for identifying deficiencies in gas exchange. If respiratory acidosis is present, mechanical assistance of ventilation is usually needed. After the oxygen content of arterial blood reaches a normal level, hypoxic injury to organs and other vital tissues is reduced.

The next focus of attention is to **I**nfuse. This is of particular importance in the trauma patient with hemorrhagic shock. Fluid therapy to improve microvascular blood flow and increase cardiac output is essential. Various modalities to quantify a patient's volume status and need for repletion are currently employed. These modalities include the non-invasive (e.g., passive leg raise, 500 mL "volume challenge," and inferior vena cava diameter assessment by bedside ultrasonography) as well as more invasive techniques that require the placement of intravascular lines (e.g.,

pulse contour analysis/stroke volume variation, impedance cardiography, central venous pressure (CVP), etc.). Each of these provide a practical and near instantaneous guide for fluid repletion. If overloading the heart is of immediate concern, CVP is a reliable indication of the heart's capacity for additional volume. The third aspect in the "**VIP** rule" is the competency of the heart to serve as an effective **P**ump. In persistent severe hypotension, the use of vasopressors, typically an adrenergic agonist, is indicated.

6.4 Shock in the Intensive Care Unit

In the trauma patient, the most common form of shock is hypovolemic, specifically hemorrhagic. This differs from the medical ICU patient in which the most common form of shock is septic in nature [14]. If hemorrhagic shock is suspected, the early use of blood products over crystalloid resuscitation has been shown to result in decreased mortality and improved outcomes [5]. The preferred ratio of red cells, plasma, and platelets remains a topic of active research. Two prospective studies and a systematic review suggest a 1:1:1 transfusion ratio may reduce short-term mortality. However, this is specific to hemorrhage secondary to trauma [15–18]. In patients with hypovolemia not due to bleeding, crystalloid resuscitation is preferred over colloid [15, 19, 20].

An additional important note is that, in contrast to distributive shock (particularly septic), vasopressors are largely contraindicated. Vascular tone in hemorrhagic/hypovolemic shock is increased, and use of pressors may further reduce tissue perfusion, leading to acceleration of organ failure. Of note, an exception to this avoidance of vasopressors in hemorrhagic shock may be emerging in the form of physiologic vasopressin infusion. Recent studies have shown that autogenous vasopressin levels are diminished in hemorrhagic shock [21]. Repletion at physiologic doses appears to reduce the overall amount of transfusion required and possibly improve mortality [22].

6.5 The Epidemiology of Shock

The management of shock has changed drastically over time and there are seemingly constant advances in research and approaches. In the past few decades, there have been marked decreases in mortality with the use of aggressive, early intervention. For example, a recent temporal analysis of patients with STEMI and cardiogenic shock demonstrated a decrease in mortality from 44.6% to 33.8% over a recent 8-year period [23]. In trauma, approximately 30% of deaths are from hemorrhage, with an estimated 49,440 deaths per year in the United States alone [15]. Literature suggests that there are fewer deaths in potentially salvageable patients with the implementation of various trauma protocols, such as damage control resuscitation [24]. Other studies confirm this trend. A single center analysis showed that among patients with severe injury, mortality improved significantly over time [25] (Fig. 6.1).

Table 1. Estimated Hemorrhage-Related Deaths per Year and Years of Life Lost in the United States and Worldwide, According to the Cause of Hemorrhage.

Cause of Hemorrhage	Deaths from Hemorrhage*	U.S. Cases of Hemorrhage		Global Cases of Hemorrhage	
		No. of Deaths per Yr	Yr of Life Lost	No. of Deaths per Yr	Yr of Life Lost
	percent				
Abdominal aortic aneurysm	100	9,988†	65,273‡	191,700§	2,881,760¶
Maternal disorder	23§	138‖	7,572**	69,690‖	4,298,240**
Peptic ulcer disease	60††	1,860‖	38,597**	141,000‖	3,903,600**
Trauma	30‡‡	49,440‖	1,931,786**	1,481,700‖	74,568,000**
Total		61,426	2,043,228	1,884,090	85,651,600

* This column lists the best estimates of deaths from hemorrhage as a percentage of all deaths from the given diagnosis (e.g., all deaths from abdominal aortic aneurysm are ultimately related to hemorrhage).
† Information is from Leading Causes of Death Reports, 1981-2015, Centers for Disease Control and Prevention, 2017 (https://webappa.cdc.gov/sasweb/ncipc/leadcause.html).
‡ Data are from Years of Potential Life Lost (YPLL) Reports, 1999-2015, Centers for Disease Control and Prevention, 2017 (https://webappa.cdc.gov/sasweb/ncipc/ypll10.html).
§ Data are from Lozano et al.[5]
¶ Data are from Global Health Data Exchange, 2016 (http://ghdx.healthdata.org/gbd-results-tool).
‖ Data are from Global Health Estimates 2015: Global Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015. World Health Organization, 2016 (www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html).
** Data are from Global Health Estimates 2015: Global Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015. World Health Organization, 2016 (www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html).
†† Information is from Christensen et al.[6]
‡‡ Information is from Kauvar et al.[7]

Fig. 6.1 Deaths from Hemorrhage. From Cannon et al. [15]

6.6 Multiple Organ Failure: Overview

As previously described, the major consequence in all forms of shock is decreased perfusion to vital organs. Multiple organ failure (MOF) is the most used term for describing this clinical sequelae. The occurrence of organ failure is a considerable cause of mortality in the trauma patient. However, there is no single clinical definition of MOF. Since it was first described in 1977, there have been many scoring systems proposed, but no gold standard has yet to be established [26, 27]. Each of these scoring systems aim to predict outcomes in the trauma patient, including: mortality, length of stay, and time on mechanical ventilation. The most applied scoring systems include the Multiple Organ Dysfunction Score (MODS), Denver Postinjury Multiple Organ Failure Score, and the Sequential Organ Failure Assessment (SOFA) [27].

The MODS was developed in a two-stage process. First, a literature review that evaluated previous measures of organ dysfunction was conducted. From this a list of characteristics of the ideal descriptor for organ dysfunction was developed [27]. Second, a database of surgical admissions was split into development and validation sets and used to calibrate candidate measures of organ dysfunction against mortality. The MODS includes seven organ systems—respiratory, renal, hepatic, cardiac, hematological, neurologic, and gastrointestinal [27]. A cut-off total value greater than five has been widely used to denote MOF with the MODS [27].

The Denver score was developed by trauma experts in 1991, initially including eight organ systems [27]. In the mid-1990s, a modification was made reducing the number of systems to four—respiratory, renal, hepatic, and cardiac. This system was designed to predict outcomes for adult trauma patients with an injury severity score greater than 15 who survived more than 48 hours from injury. Each organ system is scored from zero to three, with a total score greater than three denoting post-trauma MOF. This cut-off value has been validated in prediction of trauma outcomes.

All of the other scoring systems were similarly developed and validated. Beyond prediction of outcomes, these scoring systems have been used to classify categories of MOF. This has motivated research and resulted in significant advances into understanding of the unique pathophysiology behind each subtype. Previous clinical understanding suggested that MOF presented as either early or late onset, a bimodal peak. This has been challenged with emerging research [28, 29]. Using the SOFA score as a clinical marker of MOF, prolonged MOF was identified as a common and unique clinical entity associated with worse outcomes in trauma patients. It has also been called the Persistent Immunosuppression and protein Catabolism Syndrome (PICS) [29–31]. This state is associated with higher mortality and infection rates, as well as higher rates of hepatic and renal dysfunction.

Of particular interest, a recent study describes three distinct forms of MOF based on severity and subsequent recovery [29]. Shepard et al. shows that our contemporary understanding of MOF has changed dramatically. The authors characterized MOF by respiratory, cardiovascular, and hemodynamic dysfunction, with the two former systems found to be dysfunctional in nearly all modern MOF [29]. This contrasts with prior studies in which respiratory and cardiovascular involvement accounted for approximately 50% of cases. The reason for this is likely multifactorial, but may be related to improved management, early identification, and rapid response to patients at risk of MOF as well as lung-protective strategies becoming the standard-of-care.

6.7 The Epidemiology of Multiple Organ Failure

Despite a decrease in the incidence of postinjury MOF over the past decade, there has not been shown to be an improvement in outcomes over time once it occurs [32]. One possible explanation for this trend is given by Sauaia et al., who suggest that high adherence to early resuscitation standards, such as standard operating procedures, has improved outcomes of the initial insult that may have provoked MOF, thus reducing the incidence of MOF [32]. However, adherence to these guidelines does not impact reversal of MOF, and therefore for those patients that develop MOF, outcomes have remained unchanged.

The advent of damage control resuscitation (DCR) is one of the largest innovations in the care of the traumatically injured patient and has yielded an improved overall survival rate. The DCR concept is designed to address the early coagulopathy in trauma by avoiding large crystalloid resuscitation, focusing instead on

replacement of that which was lost—whole blood (or blood products in a balanced ratio) [33]. It applies particularly to those trauma patients with hypothermia, acidosis, and/or significant coagulopathy [33]. DCR may be related to the decreased incidence of MOF in trauma. However, since DCR largely serves to prevent the development of MOF, it may not substantially impact the prognosis once a patent enters MOF. This may also help explain the epidemiological findings of the past decade mentioned above.

6.8 Multiple Organ Failure and Shock

There is an important correlation of MOF and the systemic inflammatory response syndrome (SIRS). In an observational study of 200 patients, 80.1% of those with SIRS on admission developed MOF compared to a 45.5% in patients without SIRS [34]. Therefore, the onset of MOF appears related to the massive release of acute-phase reactants, cytokine storm, and an inflammatory cascade seen in SIRS [35]. Various authors have described cascades that begin with SIRS and end with MOF. For many patients the association between SIRS and MOF may be a continuum of a single pathology [35]. Specifically, one hypothesized mechanism relates alteration of the coagulation pathway in SIRS related to IL-1 and TNF-α with widespread microvascular thrombosis, increased capillary permeability, and impaired tissue perfusion [35].

Additionally, a recent study by Dharap et al. showed that post-trauma inflammation and organ dysfunction were highly correlated. Patients with the above had an overall mortality of 19.5% [34]. Among their cohort, 78% developed SIRS and 72.5% MOF. Mortality was significantly associated with higher SIRS or MOF scores [34]. They found that over 54% of patients with severe MODS had evidence of SIRS. Only 13% of patients with MOF did not appear to have SIRS [34]. In addition, mortality in patients with both SIRS and MOF was significantly linked to increased mean SIRS and MOF scores [34].

6.9 Conclusion

Despite being described for millennia, there have been significant advances in management of shock and MOF in recent years. MOF rarely occurs in insolation and is closely related to SIRS—both of which are common in the traumatically injured patient. Epidemiological data suggests that the decreased incidence of shock and MOF may be due to the widespread implementation of standard practices of rapid intervention to help prevent the development of shock. However, the mortality of MOF remains largely unchanged. This suggests that future research should focus on interventions for the patient once MOF has occurred. As our understanding of the pathophysiological mechanisms behind MOF improves, the future of MOF treatment may progress to more targeted treatments with the goal of reduced mortality.

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