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Critical Care for the Patient With Multiple Trauma

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Abstract

Trauma remains the leading cause of death worldwide and the leading cause of death in those less than 44 years old in the United States. Admission to a verified trauma center has been shown to decrease mortality following a major injury. This decrease in mortality has been a direct result of improvements in the initial evaluation and resuscitation from injury as well as continued advances in critical care. As such, it is vital that intensive care practitioners be familiar with various types of injuries and their associated treatment strategies as well as their potential complications in order to minimize the morbidity and mortality frequently seen in this patient population.

Keywords

trauma, injury, critical care

Introduction

Trauma-associated death is the leading cause of death worldwide and the leading cause of death in those younger than 44 years old in the United States.[1] Because of this, death following injury is responsible for the greatest number of potential lives lost from any single cause. Over the last 20 years, trauma systems have evolved and have been shown to significantly lessen mortality following injury.[2-4] This has been due to improvements in transportation time from the point of injury to verified trauma centers, methodologies in the initial approach to evaluation and resuscitation from injury, and ongoing critical care techniques that allow time for the patient to recover. As such, it is vital that intensive care practitioners be familiar with the approach to various types of severe injuries as well as their potential complications and expected hospital course. Although an exhaustive review of these topics is beyond the scope of this article, we seek to provide an overview of these topics with an emphasis on potential complications that are especially germane to the critical care practitioner. Due to space restrictions, this article concentrates on the medical management of injuries and does not address the role of surgery per se. Herein, we present a case scenario and discuss treatment strategies with the supporting evidence that are relevant to the intensivist.

Case Scenario

A 25-year-old female is admitted to the intensive care unit (ICU) after falling 20 ft off of a bridge. On initial presentation, she was found to have a Glasgow Coma Score (GCS) of 9 and was intubated and sedated. Her injuries include skull fracture with a subdural and subarachnoid hemorrhage, large left pneumothorax with multiple broken ribs and a flail chest, grade III splenic laceration without contrast extravasation or hemoperitoneum on computed tomography (CT) scan, and an open right femur fracture. Trauma surgery, neurological surgery, orthopedic surgery, and possibly interventional radiology, in addition to the intensivist, are involved in this patient's care, and coordination of the care plan is pivotal to the patient's survival.

Airway

Intubation and Ventilation

Initial evaluation and resuscitation of the patient with trauma in the emergency department traditionally follows the "ABCD" approach—assessment of the airway, breathing, circulation, and gross neurologic disability.[5] In the above-mentioned case, the patient has a GCS of 9 and also has a number of severe injuries

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with possible impending shock and resultant metabolic acidosis. She needs to be closely monitored for the need for intubation both to protect the airway and/or to help defend the pH.

Were she to be intubated, short-acting sedatives should be used to allow for ongoing assessment of the patient's neurologic status. Initially, the ventilator should be adjusted to maintain a mild respiratory alkalosis (ie, P_{CO_2} 33-35) to help lower intracranial pressure. Importantly, analgesic agents should be administered empirically both to treat the patient's pain and suffering and to minimize the associated catecholamine surge and increased intracranial pressure associated with pain.

Breathing

The patient has a chest tube that was placed in the left hemithorax and is draining 50 mL/h of blood with a small air leak. Despite adequate sedation and pain control, she remains tachycardic and normotensive with intermittent premature ventricular contractions.

Thoracic Trauma, Pulmonary Contusion, and Blunt Cardiac Injury

Blunt thoracic trauma, including pulmonary contusion, rib fracture, and flail chest, accounts for nearly 25% of mortalities secondary to blunt trauma.[6,7] Independent contributors to mortality following severe chest wall and lung injury include inadequate pain control with resultant inability to extubate or poor pulmonary hygiene, excessive fluid resuscitation (particularly crystalloid-based), and possibly failure to intervene with operative repair of the flail segment fractures in a timely fashion although the last point remains controversial.

Pulmonary contusion typically occurs in high-energy trauma, most commonly motor vehicle collisions, and is associated with complex chest wall abnormalities. Management challenges are derived from the complex local and systemic physiologic effects of this trauma, including reduction in ventilation secondary to poor compliance, increased pulmonary vascular resistance, and impairment of diffusion, and local and systemic inflammatory effects.[8]

Pneumo- and hemothorax are usually treated with a tube thoracostomy following injury. Exceptions to this include unintubated hemodynamically stable patients with occult or radiographically small lesions. Positive pressure ventilation is a significant risk factor for worsening pneumothorax and usually necessitates placement of a thoracostomy drain.[9] The patient in question has multisytem injury, including most notably brain injury. Her propensity to become unstable due to hemorrhage will obfuscate decision making in the absence of a chest tube. Additionally, placement of a chest tube can effectively rule out an area of potential hemorrhage that would require operative intervention. Furthermore, any hemodynamic derangement, as may occur with a tension pneumothorax, will significantly increase morbidity related to her brain injury. Thus, immediate placement of a chest tube in the trauma bay is warranted. To minimize secondary infection, the chest tube should be removed as soon as the patient's medical condition has stabilized, with low-volume output and resolution of the air leak while the system is off suction.[10]

Traditionally, mechanical ventilation has been aggressively used in patients with significant thoracic trauma; however, current practice recommends selective ventilation only to correct significant defects in gas exchange.[11] There are no clear recommendations regarding the ventilator mode most optimal in this patient population, but it is generally asserted that positive end-expiratory pressure or continuous positive airway pressure should be included in patients' ventilator settings with extubation at the earliest possible time.[8] Should the patient develop acute respiratory distress syndrome, standard low-stretch, low-pressure ventilator settings should be prescribed. Although some centers utilize airway pressure release ventilation, there is no convincing evidence that this mode is either equal or superior to the aforementioned strategy in terms of mortality.

Fluid management in patient's with pulmonary contusion requires maintaining euvolemia and avoiding hypervolemia.[6] As in any other critically ill population, assessing volume status in this population can be challenging, and the authors espouse a multimodality approach to this problem. The physical examination, urine output, chest X-ray, basic metabolic panel, hemoglobin concentration, serum lactate, mixed venous oxygen saturation, and measurement of the stroke or pulse pressure variation should be used in combination to assess intravascular volume status as best as possible.

Blunt cardiac injury (BCI) includes a number of injury patterns to the heart following a direct blow to the chest. The spectrum includes contusions to the myocardium, rupture of a chamber (classically the right atrium), and, rarely, injuries to a valve or coronary artery.[12] Incidence of BCI varies from less than 1% in clinical studies to over 30% in autopsy studies.[13]

The biggest risk factors for BCI involve significant blunt thoracic trauma, classically following rapid acceleration/deceleration mechanism or compression to the heart, most commonly a motor vehicle collision.[14,15] Injury patterns of flail chest, fractured sternum, fractured scapula, or first rib fracture can generate enough force to cause BCI. Some patients may not have structural injuries prompting an evaluation for cardiac injury but may present with a new, persistent dysrhythmia (most commonly sinus tachycardia) not attributable to hypovolemia, pain, or anxiety.[14] Any new dysrhythmia following trauma, most importantly thoracic trauma, warrants investigation. Additionally, it is important to differentiate between a primary cardiac event that led to the trauma and a traumatic event to the myocardium.

Patients at risk of BCI require an electrocardiogram (ECG) and serum cardiac enzyme measurement on admission.[16] Both a normal ECG and normal troponin I can be used to rule out BCI with a near 100% negative predictive value.[16,17] Patients with an abnormal ECG, elevated troponin I, persistent arrhythmia, or unexplained hemodynamic instability should receive a transthoracic or tranesophageal echocardiogram and continuous cardiac monitoring.[16,18]

The treatment of BCI involves continuous cardiac monitoring and supportive therapy for 24 to 48 hours. Although the presence of any dysrhythmia, including sinus tachycardia, is

a risk factor for subsequent arrhythmias, such as ventricular tachycardia or fibrillation, there is no role for prophylactic pharmacologic intervention. Should a serious or potentially fatal arrhythmia occur, standard advanced cardiac life support-based resuscitation should be implemented. All acute coronary syndromes should follow advance cardiac life support guidelines and catheterization when indicated.[19]

Flail Chest

The management of patients with flail chest has evolved significantly over the previous decade; however, there is little controversy about the importance of adequate pain control and chest physiotherapy in these patients. Because delayed and inadequate pain control can result in atelectasis, pneumonia, and the need for ventilatory support, early aggressive pain control should be managed by a dedicated pain service. The pain service should utilize regional analgesia that has been found to provide more effective pain relief with fewer side effects and improved outcomes relative to intravenous (IV) narcotic administration.[12] These effects are likely due to decreased central nervous system depression with improved pulmonary toilet.[20]

Regional anesthetics include epidural catheters, intercostal and intrapleural blocks, and paravertebral blocks. Each method allows the delivery of local anesthetic, most commonly bupivacaine, through either bolus or continuous injection, to allow significant pain control without sedation and respiratory depression. Limited literature exists comparing regional techniques; however, specific patient considerations can guide choice of technique. The most extensive body of literature supports the use of epidural analgesia for significant improvement in subjective pain score and pulmonary function tests when compared to IV opioid analgesia alone. Epidural analgesia has been shown to decrease hospital length of stay, total ventilator days, and ICU stays.[21-23] Direct head-to-head comparisons with narcotic regimens reveal superior outcomes in patients with epidural anesthesia when compared to IV narcotic use. These trials also found that epidural analgesia is associated with decreased mortality and fewer pulmonary complications in the elderly individuals, thus suggesting a decrease in requirements for tracheostomy.[24,25] Paravertebral blocks allow the direct administration of analgesic to the affected ribs in a unilateral or bilateral fashion and have the advantage that they can be performed safely in sedated patients due to the low risk of spinal cord injury and hypotension.[26,27] Paravertebral blocks also have the benefit of allowing continued neurologic assessment of the lower extremities and decreased urinary retention when compared to epidural analgesia. Uniquely among the catheter-based analgesic techniques, paravertebral block may be continued beyond hospitalization, hence, we use them extensively in our practice.[28]

Although not widely available, surgical stabilization of rib fractures (also known as rib plating) has a growing body of literature demonstrating decreased ventilator days, decreased incidence of pneumonia, and shorter ICU length of stay.[6,29,30] It should be noted that this technique is most useful in patients without respiratory failure due to underlying pulmonary contusion and probably is best reserved for patients who fail medical management of their pain.[31] The role of rib plating for chest wall stabilization in patients who do not have impaired ventilation remains controversial.

Circulation

The patient is noted to have ongoing oozing of blood from her open femur fracture. Her internationsl normalized ratio (INR) is 1.9 and her temperature is 35°C. She does not take any anticoagulants. She is aggressively warmed by noninvasive means. She continues to receive plasma, is given 2 g of tranexamic acid, and has serial measures of her coagulation parameters and hemoglobin level.

The orthopedic service asks whether the patient is sufficiently stable to undergo repair of the femur fracture on the day of admission. Because her traumatic brain injury (TBI) is still evolving and may result in intracranial hypertension and also because she has a moderate-grade splenic laceration, she is potentially too unstable to undergo formal internal fixation (ie, ''open reduction, internal fixation'') of the fracture. A ''damage control'' strategy consisting of operative lavage of the wound, external fixation of the fractured segments, and closure of the skin defect is implemented to minimize the chances of fat embolism, osteomyelitis, and the duration of operation. General anesthesia will inhibit the ability for neuromonitoring, thus the neurosurgical service places an intracranial pressure monitoring device.

Approximately 12 hours after her damage control orthopedic operation, she is noted to be hypotensive and her hemoglobin has decreased to 6 g/dL from its previous 10 g/dL. Bedsides, focused assessment with sonography in trauma (FAST) done by the intensivist is now positive in the perisplenic window. Massive transfusion protocol is activated, and she is taken emergently to the operating room where she is found to have bleeding from the spleen necessitating a splenectomy. The abdomen is left open and covered with a commercially available temporary abdominal wall closure device to allow for ongoing resuscitation with mitigation of the risk of abdominal compartment syndrome. She has undergone a ''damage control laparotomy.''

Hemostasis and Component (Also Known as "Balanced" or "Hemostatic" or "Damage Control") Resuscitation

The 2 foremost tenets of trauma are that a patient with hypotension is bleeding until proven otherwise, and the largest cause of preventable traumatic death is the lack of early recognition and correction of hemorrhage and coagulopathy. These tenets have led to the intensive study of coagulopathy in trauma and seminal studies such as Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH-2), Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) and MATTERs II, Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT),

and the Efficacy and Safety of Recombinant Activated Factor VII I the Management of Refractory Traumatic Hemorrhage (CONTROL) trials.

Much of what we understand today about the exsanguinating patient with trauma comes from combat experiences and data gathered over the past two decades. These data have been translated and verified in the civilian population and multiple studies now support the use of a packed red blood cell (PRBC)–fresh frozen plasma (FFP)–platelet (ie, 1:1:1) balanced transfusion ratio for the resuscitation of a bleeding patients with trauma. It should be noted, however, that the use of a 1:1:1 transfusion strategy rests heavily on the extrapolation of data from case series and prospective cohort studies; a well-designed randomized controlled trial has yet to be reported. Regardless of the exact ratio of blood products administered, however, studies have shown that excessive crystalloid fluids should be avoided. The findings of these studies cannot be overemphasized and should also dispel the use of isolated or low ratio of plasma or platelets to PRBC transfusions. For example, the PROMMTT study analyzed the likelihood of in-hospital mortality to early transfusion of plasma and platelets in the civilian population. This study found that higher plasma and platelet to red blood cell ratios in patients receiving at least 3 units PRBCs were associated with a decreased mortality.[32,33] Furthermore, multiple studies now support the use of fibrinogen (in the form of cryoprecipitate) during massive transfusions as well. Thus, a balanced resuscitation strategy should include the use of cryoprecipitate, usually as one 10-unit bag (containing 2.5 g of fibrinogen) for every 10 units of PRBCs. The feasibility of the early/hyperacute use of cryoprecipitate is currently being evaluated in a multicenter, randomized fashion via Early Cryoprecipitate for Severe Trauma Haemorrhage Trial (CRYOSTAT).[34] The results of this study and future studies will add yet further guidance to the resuscitation of patients with traumatic injury.

Other studies have intensified the investigation of pharmaceutical therapies for the resuscitation of the coagulopathic patients with traumatic injury. The CONTROL trial evaluated the efficacy and safety of recombinant activated Factory VII (rFVIIa) in cases of refractory traumatic hemorrhage. This study was terminated after only approximately a third of the patients were enrolled secondary to a low mortality as determined by a futility analysis. In the study group, rFVIIa reduced blood product use but did not affect mortality compared to placebo. Thus, we recommend the avoidance of rFVII in all but the most refractory bleeding episodes due to lack of proven efficacy, possible harm, and cost. Contrarily, the CRASH 2, MATTERs, and MATTERs II trials investigated the use of the low-cost antifibrinolytic agent, tranexmic acid (TXA). The TXA is a plasminogen inhibitor, thus impairing the interaction of plasminogen and fibrin that would normally result in clot dissolution. The results of this colossal study (over 20 000 patients from 274 hospitals) show that there was a 1.5% reduction in all-cause mortality with a number needed to treat of 67 patients when given to patients with signs of bleeding (systolic blood pressure less than 90 mmHg, heart rate greater than 110 beats/min).[35,36] There was no increase in thrombotic complications in the treatment arm. Based on post hoc analysis, TXA's initial administration after 3 hours or more following injury may be associated with increased risk of death. Further evidence supporting the use TXA in trauma is supported by the findings of the MATTERs and MATTERs II trials. Both studies are military-based, retrospective, observational studies that examined the use of TXA to no TXA (MATTERs) and TXA with cryoprecipitate to TXA alone, cryoprecipitate alone, or neither intervention (MATTERs II). MATTERs showed that patients receiving TXA had a lower mortality than those not receiving TXA (17.4% vs 23.9%; $P = 0.03$), and this benefit was greatest in patients receiving more than 10 units of blood (14.4% vs 28.1%l $P < .001$).[37] MATTERs II showed that mortality was least in groups treated with the combination of cryoprecipitate and TXA versus treatment with TXA alone, cryoprecipitate alone, or neither intervention (11.6%, 18.2%, 21.4%, and 23.6%, respectively). MATTERs II supports the use of cryoprecipitate in patients with trauma as it may add to the survival benefit independent of TXA.

A relatively new medication now being used for the treatment of the antivitamin K-based anticoagulated patient with trauma is prothrombin complex concentrate (PCC). Available under a variety of trade names (Beriplex, Ocplex, and Kcentra), the medication provides a concentrated source of the vitamin K-dependent coagulation factors. The PCCs are available as 3-factor or 4-factor formulations. The difference between the 2 formulations resides on the amount of factor VII in the drug. The seminal study supporting the use of 3-factor PCC examined 43 patients with an INR greater than 2 experiencing acute bleeding. At 30 minutes after administration of PCC, INR decreased to less than 1.3 through 48 hours. This was achieved using a fraction of the volume that would be required should FFP need to be administered. There is currently little data specifically in the patient with trauma or data showing the superiority of 4-factor PCC when compared to 3-factor PCC. Furthermore, it is unknown whether there is benefit in reversing other, newer, anticoagulants by administration of PCC.

There is now interest in use of vesicoelastic testing to assess for coagulopathy in patients with trauma. The 2 commonly used platforms are thrombelastography (Haemonetics Corp, Braintree, Massachusetts) and thrombelastometry (Tem International GmbH, Munich, Germany). These technologies provide a real-time graphical representation of clot formation and strength as well as clot lysis. Although not definitely proven, they may eliminate the need for multiple fragmented blood tests such as prothrombin time, partial thromboplastin time, INR, and fibrinogen. Additionally, these technologies allow trauma surgeons and intensivists to respond quicker to changes in a patients' coagulation state. Although current studies are promising and we support its use, there is yet to be published data showing a mortality benefit.

Damage Control Surgery

The surgical management of patients with trauma has morphed significantly over the last 2 decades with introduction of damage control surgery (DCS) for the unstable patient. Rotondo and Schwab first described a 3-phase procedure, including initial control of hemorrhage and gross contamination followed by resuscitation in the ICU before definitive operative management and abdominal closure. The objectives of the first operation are to treat only the immediate life-threatening injuries so as to prevent or quickly correct the ''lethal triad'' of hypothermia, acidosis, and coagulopathy. Since the introduction of damage control laparotomy, the principles of DCS have expanded to include external fixation of long bone fractures when the potential for infection, extremity edema, or the patient's overall stability preclude definitive internal fixation (damage control orthopedics), decompressive craniectomy when the degree of cerebral edema or the patient's overall condition preclude replacement of the skull flap (damage control neurosurgery), and shunting of arteries in lieu of formal repair when the patient's condition does not allow time for creation of a formal bypass (vascular damage control).

The decision to perform DCS is ideally made prior to the start of operation, based on the patient's hemodynamics and degree of injury. It can be utilized in both blunt and penetrating trauma with the surgeon packing open cavities or ligating bleeding vessels to control hemorrhage and stapling off injured bowel to avoid ongoing spillage. Where a blood vessel cannot be ligated, such as an end artery, a plastic shunt is used to maintain distal blood flow. No attempts are made to anastomose the bowel or injured blood vessel or to create an ostomy at the time of initial surgery. To determine whether DCS is needed, the surgeon will use parameters such as base deficit, lactate level, body temperature, and need for blood transfusion but will also look for signs of nonsurgical bleeding indicative of a profound coagulopathy.[38,39] Patients who undergo DCS often arrive at the ICU in extremis, requiring continued massive transfusion, active rewarming, and correction of acidosis. Following laparotomy, a temporary abdominal wall closure device will be in place. A variety of these are commercially available, but the surgeon can also use towels covered by plastic (also known as Barker Dressing) or sterilized plastic IV bags that are sutured to the skin or abdominal fascia.

The intensivist should try to return the patient to his or her normal physiology as quickly as possible, but it may require 24 to 48 hours of continued resuscitation. Rewarming should commence immediately by preheating the ICU suite, using a fluid warmer for all IV fluids, including blood products, and increasing the heat delivered through the heat and moisture exchanger on the ventilator. Intravascular warming catheters, pleural lavage, and bladder irrigation are rarely used but are options if needed. Sodium bicarbonate rarely needs to be administered unless the pH is persistently less than 7.2, as this may inhibit the effect of vasoactive agents and clotting factors.[40]

The intensivist must always keep in mind that deterioration in clinical status may necessitate a return to the operating room for exploration and further treatment. The patient may have a missed bowel injury that can lead to an inflammatory state or a persistent surgical hemorrhage requiring new packing or definitive control. The patient may develop signs of compartment syndrome, despite having a temporary abdominal closure, and in such cases, the device can be removed at the bedside by the surgical team. Surgical versus nonsurgical bleeding must be distinguished as diffuse coagulopathy may be worsened by early return to the operating room. Minimizing the risks of ongoing nonsurgical bleeding is of utmost importance as it allows for more definitive surgical decision making. The intensivist must also firmly understand the nature of injuries and involve the interventional radiologist as needed to assist with hemorrhage control using transcatheter techniques. Ultimately, direct communication between the surgeon and the intensivist is critical when assessing for causes of ongoing physiologic instability or sudden deterioration.

Barring any reason to operate earlier following laparotomy, the surgeon should plan for a return to the operating room within 36 to 48 hours to create any necessary anastomoses or ostomy and consider definitive abdominal closure. If the patient has received massive resuscitation, there is often significant bowel wall edema that limits fascial closure at this stage and may necessitate diuresis. Early definitive closure is the goal as the prolonged open abdomen is associated with enterocutaneous fistulae, abscesses, infection, and multiorgan system failure. With that in mind, some patients are not stable for early definitive closure and will require multiple returns to the operating room for graduated abdominal closure. Studies have shown that patients who received less blood product, had a lower lactate level upon arrival at the ICU, and who had a vacuum-assisted closure device were more likely to be closed at their initial take back.[41]

In some patients, primary fascial closure cannot be achieved. These patients are managed in a variety of ways, depending on the patient's clinical presentation, including split thickness skin grafts, placement of mesh, creation of myofascial advancement flaps or a combination of these options. Once the patient's abdomen is closed, the intensivist must watch for signs of a developing abdominal compartment syndrome, including decreased urine output, high ventilator peak pressure, and elevated bladder pressures. In addition, patients may develop intra-abdominal sepsis, bowel obstructions, bleeding, or fascial dehiscence.

Although treatment of the open abdomen following DCS can be complex, treatment of damage control orthopedic, neurosurgical, or vascular surgery is often more straightforward. The timing for conversion of an external fixture to an internal device will vary based on the nature of the fracture. Following placement of a temporary arterial shunt, the trauma or vascular surgeon will return to the operating room within 12 to 36 hours for creation of a bypass.[42,43] During this time, the limb or organ distal to the shunt must be monitored closely for signs of ischemia that may occur should the shunt clot. In this instance, emergency surgery is needed to reestablish blood flow.

Disability

Twenty-four hours after arriving at the ICU, the patient develops acute elevations in her intracranial pressure which are treated with boluses of 23% hypertonic saline and increased sedation. Serial CT scans shows stabilization of the patient's subarachnoid hemorrhage and subdural hemorrhages.

One week following admission to the ICU, the patient remains obtunded. The patient has had recurrent fevers for several days, and the fevers are frequently accompanied by tachycardia to 120 beats/min, hypertension, and rigors. All cultures are negative and the chest X-ray only shows a pulmonary contusion on the left. All intravascular catheters have been changed empirically with no effect.

Traumatic Brain Injury

Traumatic brain injuries have an annual incidence of approximately 2.5 million cases or 824 cases per 100 000 persons. Moreover, the overall incidence of TBI has been steadily rising since 2001, although the incidence of TBI-related death has remained constant. Standard treatment for patients with established TBI includes neurosurgical evaluation, serial neurologic examination with liberal use of CT scanning, seizure prophylaxis for 7 days, and reversal of coagulopathy. It is recommended that all salvageable patients with a GCS less than 9 and an abnormal CT scan of the head have continuous intracranial pressure monitoring (ICP). Patients with possible TBI who require emergency operation of any sort and therefore will not be able to undergo serial neurologic examination for an extended duration may also benefit from ICP monitoring. In the above-mentioned case scenario, use of an ICP monitor is critical for the aforementioned reasons. The patient has a depressed mental status making the neurologic examination unreliable. Furthermore, she is at risk of recurrent intracranial hemorrhage or cerebral edema, either of which could raise the ICP and further injure the brain. Recurrent intracranial bleeding may necessitate operative intervention, and a rise in the ICP may serve as an early sentinel for intracranial hemorrhage. Finally, any operative intervention will necessitate general anesthesia with inability to clinically monitor the patient's neurologic status for the duration of the operation and shortly thereafter.

In addition to use of intraparenchymal or intraventricular monitors to measure ICP, jugular blood oxygen saturation or intraparenchymal oxygen monitors can also be used to assess oxygen delivery to the brain globally or regionally. Important parameters for management of the TBI patient include maintenance of ICP less than 20 mm Hg, cerebral perfusion pressures greater than 60 mm Hg, brain partial pressure oxygen (P_bO_2) greater than 15 to 20 mm Hg, avoidance of systemic hypoxia and hypercapnea, and the maintenance of normothermia. These parameters are designed to optimize adequate perfusion and oxygenation and to minimize secondary injury and cerebral edema. Although various studies have found each individual parameter to be associated with outcome, no parameter has been consistently noted to be better than another either as a single modality or as part of a bundle. Noninvasive cortical oxygen and blood flow monitors, which use near-infrared spectroscopy and ultrasound, are also available but have not been shown to correlate well with invasive monitors, which are presumed to be the gold standard.

Following injury, elevated ICP should be treated in an aggressive manner beginning with early intubation. Appropriate analgesia and sedation should be utilized to minimize increases in ICP caused by pain and agitation. Despite limited evidence in the literature, propofol and fentanyl are most commonly utilized for their rapid onset and short duration, with avoidance of benzodiazepines due to long duration of action, neurodepressant effects, and a possible causative association with delirium. However, other agents such as dexmedetomidine or ketamine can also be used.[44,45] Historical concerns regarding a causative association between ketamine and increases in ICP are increasingly being discounted as clinically inconsequential. High-dose barbiturate therapy may be utilized as a salvage therapy when all other medical and surgical therapies have failed; however, it should be noted that meta-analysis have found no clear benefit or improved outcomes.[46]

Recurrent or sustained elevations in ICP can also be treated with hyperosmolar agents, such as mannitol and hypertonic saline, once the possibility of cerebral hemorrhage has been ruled out. Mannitol, dosed at 0.25 to 1 g/kg with a target serum osmolarity of approximately 320 mosm/L, may be used to decrease ICP in the acute period and may have a lingering antioxidant effects to further protect the brain from inflammation and edema. Hypertonic saline functions to decrease cerebral edema by osmotic mobilization of water across the blood–brain barrier and may also have beneficial effects by inhibiting neutrophil margination and transmigration into brain parenchyma.[47] Hypertonic saline has shown efficacy in decreasing ICP acutely with the utilization of bolus doses of 23% normal saline as well as by utilization of continuous infusion of 3% to 5% saline.[48,49] Several small studies suggest superiority of hypertonic saline over mannitol in overall mortality.[50] Although the upper limit for serum sodium has not yet been determined, additional doses of hypertonic saline to push the serum sodium beyond 160 meq/L are unlikely to affect ICP as this degree of hypernatremia corresponds to a serum osmolarity greater than 320 mosm/L.

The utilization of steroids has been historically controversial in patients with brain and spinal cord injury. However, the pivotal Corticosteroid Randomization after Significant Head Injury trial and subsequent consensus statements now firmly recommend against their use following TBI.[50,51]

Moderate, brief hypothermia to 33°C to 35°C for 48 hours has also been debated as a neuroprotective agent in TBI.[52,53] Hypothermia is effective in controlling ICP following TBI and stroke; however, no clear evidence finds an association between hypothermia and reduction in mortality in these patients. A study done by Clifton et al involving 392 patients found no benefit in the treatment of TBI with hypothermia when induced within 8 h.[54] Confirming these findings, a large

multinational study found no utility in hypothermia as a primary neuroprotective strategy and was terminated for futility.[55] Post hoc analysis of this and another trial suggests that patients undergoing craniotomy for evacuation of a hematoma following TBI may benefit from early hypothermia,[56] but this finding still needs to be corroborated via properly designed studies.

Patients with TBI have a 4% to 25% risk of seizures within the first week following injury.[57,58] Administration of prophylaxis does not impact the incidence of delayed (greater than 7 days from injury) seizures. Thus prophylactic administration of antiseizure medication for 7 days following TBI is a standard of care.[59] The 2 most commonly used agents are phenytoin and levetiracetam. There is no uniform practice regarding phenytoin dose adjustment based on serum levels versus prescribing a fixed dose for 7 days and not monitoring levels. A recent, adequately powered, prospective, observational study found no difference in seizure control or adverse reactions between the 2 agents.[60] Two other studies found that a course of phenytoin is significantly less expensive, with a possible savings as high as US$343 per course or US$19 per quality-adjusted life-year, despite the need for testing of serum drug levels.[61,62]

Although not validated in prospective studies, retrospective studies suggest a survival benefit from administration of β-blockade in patients with severe TBI.[63,64] It is thought that this may be due to a hyperadrenergic state with resultant myocardial ischemia and cardiopulmonary dysfunction.[65] However, the exact population of patients who may benefit from this intervention, medication to be used, dose to be given, and duration of therapy have yet to be determined. Although some investigators suggest the use of a nonselective agent that crosses the blood–brain barrier easily, such as propranolol, others suggest agents with α- and β-blocking properties, such as labetolol, or selective blocking agents, such as metoprolol, may also be beneficial. Future studies are being planned in order to better define the efficacy of this treatment.

Neurological Fever and Paroxysmal Sympathetic Hyperactivity in Trauma

Critically ill patients develop fevers for both infectious and noninfectious reasons, especially when having multiple traumatic injuries.[59] Several poorly understood mechanisms, including changes in neurotransmission with a reset of thermoregulation in the hypothalamus, predispose patients with TBI for fever.[66,67] Fever in conjunction with symptoms of sympathetic hyperactivity is a syndrome referred to as paroxysmal sympathetic hyperactivity (PSH), dysautonomia, neurostorming, and sympathetic storming.[68,69] Although known by many names, the process of increased or unopposed sympathetic and motor activity remains the same.[69,70] In addition to fever, patients with PSH may exhibit tachycardia, diaphoresis, hypertension, tachypnea, contractures, extension posturing, and spasticity.[68-70]

The onset of persistent fever or any of the above-mentioned signs in TBI should prompt an evaluation for an infectious source with necessary culturing and imaging after fully considering the patient's clinical findings, history, and other potential sources of fever. Many processes, such a neuroleptic malignant syndrome or serotonin syndrome, may mimic PSH and should be considered before instituting treatment.[65,69] While awaiting results, efforts to maintain normothermia should be instituted, as fever can cause secondary brain injury.[66,71,72] Fever in TBI is a well-documented contributor to elevations in ICP and worsening injury.[66,70,71,73] Once other fever sources have been ruled out, treatment strategies to control PSH should commence.

Although much remains to be learned regarding the management of PSH, a multimodal approach is often indicated. Cooling devices to maintain normothermia, IV fluids to maintain euvolemia, as well as appropriate pharmacotherapy should all be instituted. Several medications are available for the treatment of PSH, and, often, multiple agents are applied to assist in symptom management as well as sympathetic control.[74-76]

The administration of morphine will assist in regulating sympathetic activity. Propranolol, which crosses the blood–brain barrier more readily than other nonselective beta-blockers, is believed to play a role in catecholamine and metabolic control. Bromocriptine serves as a dopamine agonist and can also be used. Many other pharmaceutical options exist, including clonidine, baclofen, benzodiazepines, and gabapentin, but no agent or regimen has been shown to be superior to another. These alternative medications for the treatment of PSH all have a role in either downregulating sympathetic activity, decreasing muscle spasms, or working on GABA channels.[75,76] However, there are no prospective, controlled studies evaluating use of any of these medications for PSH. The DASH after TBI trial is an ongoing randomized study whose goal is to assess the feasibility and safety of propranolol and clonidine in this cohort.[77]

Other Critical Care Issues in the Patient With Multipe Trauma

Once the patient has been stabilized and is no longer being actively resuscitated, enteral nutrition is started. The patient continues to have an open abdomen with a temporary closure device in place, but the trauma service concurs that the patient can be fed enterally. However, 48 hours following admission, she is noted to have a rising creatinine and blood urea nitrogen.

Acute Kidney Injury in Trauma

Acute kidney injury (AKI) has historically been an underrecognized yet highly morbid complication of traumatic injury, associated with significantly increased hospital costs and length of stay. Studies have shown a 6% to 36.8% incidence of AKI in the critically ill patient with trauma as defined by the Acute Kidney Injury Network or Risk, Injury, Failure, Loss, and End-stage renal disease criteria.[78-82] Its presence is also associated with higher rates of multiple organ failure and multiple studies have shown that AKI of any degree is associated with an increased risk of mortality.[83]

Multiple risk factors for the development of AKI following trauma have been identified, including age, presence of comorbidities, blunt mechanism of injury, and administration of IV contrast. Higher injury severity score and need for blood product transfusion are also associated with an increased risk of developing AKI. In order to prevent renal injury, all efforts should be made to resuscitate the patient and avoid episodes of hypotension. There has been much debate over the years regarding the appropriate fluid for resuscitation of the patient with traumatic injury . Despite initial enthusiasm for hetastarch and hypertonic saline, clinical studies have shown a variety of adverse outcomes ranging from acidosis to bleeding and death.[84,85] Recently, there has been an interest in minimizing iatrogenically induced hyperchloremic acidosis using balanced electrolyte solutions and avoiding normal saline.[86,87] However, these studies are still in their infancy, and more durable evaluations need to be undertaken before definitive recommendations are made.

Much concern has also been raised about the use of intravenous contrast and its nephrotoxic effects in the setting of trauma. The CT scans have become routine in the workup of injured patients, and, in addition, many interventions are now able to be performed endovascularly. There are little data regarding the amount of contrast required to cause AKI. In fact, Matsushima et al found that the dose of IV contrast is not an independent risk factor for the development of AKI.[88,89] It is important to always weigh the potential benefit of a study or procedure against the risk of contrast-induced AKI.

Despite ongoing attempts to identify the ideal modality, timing, and dosing of renal replacement therapy for severe AKI, no studies have found a significant difference between intermittent dialysis and continuous renal replacement therapy.[90] However, CRRT may better allow the maintenance of electrolytes and the removal of fluid without the large fluctuations in blood pressure that can be seen with intermittent hemodialysis. This is especially important in the patient with traumatic brain injury, as autoregulation of cerebral blood flow is disrupted and cerebral perfusion pressure becomes more directly associated with systemic blood pressure.

Antibiotic Coverage in Trauma

The above-mentioned patient has an open fracture. This necessitates initiation of empiric antibiotic coverage until the orthopedic service has irrigated the wound and closed the skin defect in the operating room.

Patients presenting with multiple injuries prompting critical care management often require antibiotics to prevent complications from infection. Multiple injuries alone, however, do not always warrant antimicrobial coverage. The existing policies regarding antibiotic coverage for other critically ill patients apply when caring for the acutely injured patient in terms of empiric, targeted, or prophylactic use. Newly febrile patients should be thoroughly evaluated with cultures and potential sources of infection from instrumentation.[91] If symptomatic or at a risk of severe infection, appropriate empiric antibiotics are to be administered.[92]

Areas of controversy in antibiotic management of trauma-related injuries include gunshot-induced fractures, hemo- or pneumothoraces, and lacerations, to name a few. Fractures from gunshot wounds are open fractures; however, they may be treated as closed fractures and do not require empiric antibiotic therapy when due to a medium velocity weapon (eg, hand gun) and managed nonoperatively.[93] Higher velocity gunshot wounds are at greater risk of infection. Therefore, a short course of antimicrobial coverage is recommended.[93] When administered, gram-positive coverage should be selected. The addition of gram-negative coverage should be considered in fractures associated with a laceration that is 2 cm or more in size (Gustillo type II) due to higher probability of infection. Penicillin coverage should also be added in very large (more than 10-cm laceration) open fractures, those with concomitant vascular injury, and those where there is a concern for fecal or clostridial exposure (Gustillo type III).[94]

Use of prophylactic antibiotics for tube thoracostomy remains more controversial than antibiotic management in fractures due to numerous studies with conflicting data. Due to the degree of conflicting evidence, the Eastern Association for the Surgery of Trauma Practice Management Guidelines Committee was not able to render a recommendation supporting or refuting this practice.[95] Presently, antibiotic administration for tube thoracostomy in trauma should be patient specific as opposed to an all or nothing approach until more data are available.

Lacerations, abrasions, and other wounds without signs of infection or organ and bone involvement do not warrant routine antibiotics when managed nonoperatively. In certain populations, such as those with immunocompromised states or multiple chronic medical problems, antibiotics may be considered due to impaired wound healing. Ultimately, the decision to administer antibiotics in critically ill patients with trauma is a conscious one with specific indications due to the known risks of unnecessary antibiotic exposure. If initiated, antibiotic spectrum should be narrowed and discontinued as soon as possible to prevent complications.

Nutritional Support

As with the care of most critically ill patients, adequate caloric nutrition is paramount to the recovery of the patient with trauma. Unique to this population is the likely need for multiple operative interventions from various teams combined with multifaceted injuries often including bowel injuries with possibly multiple anastomoses, need for an open abdomen, or paralytic ileus—all of which hinder the delivery of adequate nutrition early following injury. Additionally, the need for recurrent operations and irregular scheduling makes frequent, prolonged bouts of NPO status the norm rather than the exception, further hindering nutritional support. Complicating the issue for intensivists is that there currently are no clear recommendations regarding preprocedural fasting in the intubated critically ill patient. Oftentimes, the American Society of Anesthesiologists practice guideline for preprocedural fasting

in healthy patients undergoing elective (often times outpatient) procedures is extrapolated to be used for intubated, critically ill, multiply traumatized patients. These guidelines state patients should be NPO for 6 h and 8 h following a light or fatty meal, respectively. However, the guidelines do not classify tube feeds, do not address the rationale for NPO status in patients who are already sedated and intubated, and do not differentiate between pre- and postpyloric feeds.

Despite that mentioned earlier, due to the allowance of clear liquids, some advocate for the use of a clear carbohydrate-rich oral solution 2 to 3 h preoperatively to simulate the fed state. The use of such solutions has been shown to modulate the inflammatory immune response to surgery and may decrease the amount of postoperative immunosuppression, thus potentially reducing postoperative infectious complications. Additionally, prolonged preoperative fasting may be associated with other complications such as hypoglycemia, dehydration, and electrolyte abnormalities; however, these were found in studies only evaluating healthy patients. A single small study consisting of 75 intubated patients with trauma evaluated the use of a reduced fasting protocol (cessation of feeds 45 minutes prior to a procedure for gastric delivery and immediately prior to a procedure for postpyloric delivery) and found that there was no increase in complications (death, urinary tract infections, catheter-associated blood-borne infections, and ventilator-assisted pneumonia) as compared with a control group whose feeds were stopped the midnight of the intervention. Their data also showed a trend toward improved delivery of prescribed calories in the intervention arm. Regardless, the lack of durable, large, randomized studies and established dogma have resulted in widely variant practice with no difference in outcome.[96]

Constant interruption of enteral nutrition has proven to be one of the foremost challenges to adequate nutritional delivery.[97,98] Contributing to this interruption is the still very routine practice of measuring gastric residual volumes and holding tube feeds based on an arbitrary volume to prevent aspiration and ventilator-associated pneumonia. Evidence to support this routine practice is lacking, despite its broad-based use. Multiple studies examining the effectiveness of holding tube feeds based on a gastric residual volume have been conducted in the past decade. A recent nonblinded randomized study by Williams et al compared gastric tube aspiration frequency of every 4 hours with a more liberal regimen of every 8 hours (once the target feed volume had been established and maintained for greater than 4 hours) with a gastric residual volume cutoff of 300 mL. They found that patients in the intervention group had a slightly higher occurrence of vomiting. No other differences in complications, including ventilator-associated pneumonia, were found. A meta-analysis of 6 randomized control trials and 6 prospective observational studies found that there was no association between complication rates and the gastric residual volume in medical patients. The same study did find that the incidence of aspiration increased among surgical patients if gastric residual volumes were greater than 200 mL; however, this was only found in one study. Perhaps the most convincing study of the nonutility of measuring gastric residual volumes was conducted by Reignier and colleagues. Their study was a multicenter, randomized, open-label trial consisting of nine ICUs in France. A total of 449 patients took part in the study with the interventional arm not having residual volumes measured and intolerance to enteral feeds solely based on regurgitation and vomiting. The control arm used a gastric volume greater than 250 mL measured every 6 h as a cutoff for holding enteral nutrition. They found that a significantly higher proportion of patients in the intervention group received 100% of their prescribed nutrition with no increase in the incidence of ventilator-associated pneumonia, mechanical ventilator duration, mortality, infectious complications, and ICU length of stay.[99]

Given that only 52% of critically ill patients reach their nutritional goal, bolus feeds is a viable option and may prove a more manageable method of feeding over traditional continuous infusion.[97,100] MacLeod et al compared an intermittent bolus feeding regimen to a continuous drip feeding regimen in mechanically ventilated patients with trauma in a prospective randomized fashion consisting of 164 patients. They found that there were no differences in complications between the two groups and that intermittently fed patients reached their goal caloric intake quicker than patients who were fed by continuous drip.

Due to the complexity associated with these patients, many feel that simply starting parenteral nutrition is adequate and greatly simplifies the clinical decision-making process. There have now been a plethora of studies showing the benefits of enteral nutrition over parenteral nutrition and guidelines from the Society of Critical Care Medicine, the American Society for Parenteral and Enteral Nutrition, the Canadian Critical Care Clinical Practice Guidelines Committee, and the European Society for Clinical Nutrition and Metabolism all have consensus statements preferring enteral nutrition whenever feasible. We strongly support the recommendations from the American Society for Parenteral and Enteral Nutrition in that the use of parenteral nutrition should be strictly reserved for those previously healthy patients having an absolute contraindication for enteral nutrition and who will continue to have that contraindication for at least 7 days after admission. The vast majority of patients with trauma do not meet these criteria and thus parenteral nutrition should be withheld.

The use of supplemental parenteral (defined as the use of parenteral nutrition in conjunction with enteral nutrition to help patients meet their caloric intake goal) nutrition is more controversial with varying interpretations of the Enteral Nutrition in Adult Critically Ill Patients (EPaNIC) trial and a randomized controlled trial by Heidegger and colleagues. These trials have conflicting results, and it is unclear how the results of these studies apply to traumatically injured patients. We believe that further study must be done on this population subgroup before initiating supplemental parenteral nutrition to meet caloric goals.

Conclusion

Care of the multisystem or severely injured patient requires coordination of a care plan among numerous specialists. As such, it is imperative that all intensivists be familiar with how

to prioritize treatment of injury, identify ongoing or evolving injury, and understand the vernacular and approach of the trauma surgeon so as to be able to appropriately intervene and coordinate the overall management of these patients.

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References

1. WISQARS—US Injury Statistics. 2013. http://www.cdc.gov/injury/wisqars/facts.html. Accessed February 15, 2013.
2. MacKenzie EJ, Rivara FP, Jurkovich GJ, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med*. 2006;354(4):366-378.
3. Nathens AB, Jurkovich GJ, Cummings P, Rivara FP, Maier RV. The effect of organized systems of trauma care on motor vehicle crash mortality. *JAMA*. 2000;283(15):1990-1994.
4. Shafi S, Nathens AB, Elliott AC, Gentilello L. Effect of trauma systems on motor vehicle occupant mortality: a comparison between states with and without a formal system. *J Trauma*. 2006;61(6):1374-1378; discussion 8-9.
5. Committee on Trauma. *Advanced Trauma Life Support for Doctors*. Chicago, IL: American College of Surgeons; 2008:61.
6. Vana PG, Neubauer DC, Luchette FA. Contemporary management of flail chest. *Am Surg*. 2014;80(6):527-535.
7. Allen GS, Coates NE. Pulmonary contusion: a collective review. *Am Surg*. 1996;62(11):895-900.
8. Simon B, Ebert J, Bokhari F, et al. Management of pulmonary contusion and flail chest: an Eastern Association for the Surgery of Trauma Practice Management guideline. *J Trauma Acute Care Surg*. 2012;73(5 suppl 4):S351-S361.
9. Richter T, Ragaller M. Ventilation in chest trauma. *J Emerg Trauma Shock*. 2011;4(2):251-259.
10. Adrales G, Huynh T, Broering B, et al. A thoracostomy tube guideline improves management efficiency in trauma patients. *J Trauma*. 2002;52(2):210-214; discussion 4-6.
11. Shackford SR, Virgilio RW, Peters RM. Selective use of ventilator therapy in flail chest injury. *J Thorac Cardiovasc Surg*. 1981;81(2):194-201.
12. Schultz JM, Trunkey DD. Blunt cardiac injury. *Crit Care Clin*. 2004;20(1):57-70.
13. Teixeira PG, Georgiou C, Inaba K, et al. Blunt cardiac trauma: lessons learned from the medical examiner. *J Trauma*. 2009;67(6):1259-1264.
14. Bock JS, Benitez RM. Blunt cardiac injury. *Cardiol Clin*. 2012;30(4):545-555.
15. Elie MC. Blunt cardiac injury. *Mt Sinai J Med*. 2006;73(2):542-552.
16. Clancy K, Velopulos C, Bilaniuk JW, et al. Screening for blunt cardiac injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73(5 suppl 4):S301-S306.
17. Rajan GP, Zellweger R. Cardiac troponin I as a predictor of arrhythmia and ventricular dysfunction in trauma patients with myocardial contusion. *J Trauma*. 2004;57(4):801-808; discussion 8.
18. Restrepo CS, Gutierrez FR, Marmol-Velez JA, Ocazionez D, Martinez-Jimenez S. Imaging patients with cardiac trauma. *Radiographics*. 2012;32(3):633-649.
19. El-Menyar A, Al Thani H, Zarour A, Latifi R. Understanding traumatic blunt cardiac injury. *Ann Card Anaesth*. 2012;15(4):287-295.
20. Ho AM, Karmakar MK, Critchley LA. Acute pain management of patients with multiple fractured ribs: a focus on regional techniques. *Curr Opin Crit Care*. 2011;17(4):323-327.
21. Luchette FA, Radafshar SM, Kaiser R, Flynn W, Hassett JM. Prospective evaluation of epidural versus intrapleural catheters for analgesia in chest wall trauma. *J Trauma*. 1994;36(6):865-869; discussion 9-70.
22. Mackersie RC, Karagianes TG, Hoyt DB, Davis JW. Prospective evaluation of epidural and intravenous administration of fentanyl for pain control and restoration of ventilatory function following multiple rib fractures. *J Trauma*. 1991;31(4):443-449; discussion 9-51.
23. Moon MR, Luchette FA, Gibson SW, et al. Prospective, randomized comparison of epidural versus parenteral opioid analgesia in thoracic trauma. *Ann Surg*. 1999;229(5):684-691; discussion 91-92.
24. Ullman DA, Fortune JB, Greenhouse BB, Wimpy RE, Kennedy TM. The treatment of patients with multiple rib fractures using continuous thoracic epidural narcotic infusion. *Reg Anesth*. 1989;14(1):43-47.
25. Wisner DH. A stepwise logistic regression analysis of factors affecting morbidity and mortality after thoracic trauma: effect of epidural analgesia. *J Trauma*. 1990;30(7):799-804; discussion 5.
26. Lonnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. *Anaesthesia*. 1995;50(9):813-815.
27. Karmakar MK. Thoracic paravertebral block. *Anesthesiology*. 2001;95(3):771-780.
28. Karmakar MK, Chui PT, Joynt GM, Ho AM. Thoracic paravertebral block for management of pain associated with multiple fractured ribs in patients with concomitant lumbar spinal trauma. *Reg Anesth Pain Med*. 2001;26(2):169-173.
29. Tanaka H, Yukioka T, Yamaguti Y, et al. Surgical stabilization of internal pneumatic stabilization? *A prospective randomized study of management of severe flail chest patients. J Trauma*. 2002;52(4):727-732; discussion 32.
30. Nirula R, Allen B, Layman R, Falimirsk ME, Somberg LB. Rib fracture stabilization in patients sustaining blunt chest injury. *Am Surg*. 2006;72(4):307-309.
31. Voggenreiter G, Neudeck F, Aufmkolk M, Obertacke U, Schmit-Neuerburg KP. Operative chest wall stabilization in flail chest—outcomes of patients with or without pulmonary contusion. *J Am Coll Surg*. 1998;187(2):130-138.
32. Holcomb JB, Fox EE, Wade CE, Group PS. The prospective observational multicenter major trauma transfusion (PROMMTT) study. *J Trauma Acute Care Surg*. 2013;75(1 suppl 1):S1-S2.
33. Holcomb JB, del Junco DJ, Fox EE, et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT)

study: comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg*. 2013;148(2):127-136.
34. International Standard Randomised Controlled Trials Number. CRYOSTAT Study: To determine whether early administration of cryoprecipitate in bleeding trauma patients is possible. London: Current Controlled Trials, c/o BioMed Central 2014. Identifier ISRCTN55509212. http://www.controlled-trials.com/ISRCTN55509212. Accessed December 15, 2014.
35. Perel P, Al-Shahi Salman R, Kawahara T, et al. CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage) intracranial bleeding study: the effect of tranexamic acid in traumatic brain injury—a nested randomised, placebo-controlled trial. *Health Technol Assess*. 2012;16(13): iii-xii, 1-54.
36. Roberts I, Shakur H, Coats T, et al. The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. *Health Technol Assess*. 2013;17(10):1-79.
37. Morrison JJ, Dubose JJ, Rasmussen TE, Midwinter MJ. Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study. *Arch Surg*. 2012;147(2):113-119.
38. Diaz JJ, Cullinane DC, Dutton WD, et al. The management of the open abdomen in trauma and emergency general surgery: part 1-damage control. *J Trauma*. 2010;68(6):1425-1438.
39. Weber DG, Bendinelli C, Balogh ZJ. Damage control surgery for abdominal emergencies. *Br J Surg*. 2013;101(1):e109-e2118.
40. Sagraves SG, Toschlog EA, Rotondo MF. Damage control surgery—the intensivist's role. *J Intensive Care Medicine*. 2006;21(1):5-16.
41. Hatch QM, Osterhout LM, Ashraf A, et al. Current use of damage-control laparotomy, closure rates, and predictors of early fascial closure at the first take-back. *J Trauma*. 2011; 70(6):1429-1436.
42. Bechara C, Huynh TT, Lin PH. Management of lower extremity arterial injuries. *J Cardiovasc Surg (Torino)*. 2007;48(5): 567-579.
43. Feliciano DV. Management of peripheral arterial injury. *Curr Opin Crit Care*. 2010;16(6):602-608.
44. James ML, Olson DM, Graffagnino C. A pilot study of cerebral and haemodynamic physiological changes during sedation with dexmedetomidine or propofol in patients with acute brain injury. *Anaesthesia Intensive Care*. 2012;40(6):949-957.
45. Chang LC, Raty SR, Ortiz J, Bailard NS, Mathew SJ. The emerging use of ketamine for anesthesia and sedation in traumatic brain injuries. *CNS Neurosci Ther*. 2013;19(6):390-395.
46. Roberts I, Sydenham E. Barbiturates for acute traumatic brain injury. *Cochrane Database Syst Rev*. 2012;12:CD000033.
47. Pascual JL, Ferri LE, Seely AJ, et al. Hypertonic saline resuscitation of hemorrhagic shock diminishes neutrophil rolling and adherence to endothelium and reduces in vivo vascular leakage. *Ann Surg*. 2002;236(5):634-642.
48. Gantner D, Moore EM, Cooper DJ. Intravenous fluids in traumatic brain injury: what's the solution? *Curr Opin Crit Care*. 2014;20(4):385-389.
49. Wakai A, McCabe A, Roberts I, Schierhout G. Mannitol for acute traumatic brain injury. *Cochrane Database Syst Rev*. 2013;8: CD001049.
50. Bratton SL, Chestnut RM, Ghajar J, et al. Guidelines for the management of severe traumatic brain injury. XV. Steroids. *J Neurotrauma*. 2007;24(suppl 1): S91-S95.
51. Hurlbert RJ, Hadley MN, Walters BC, et al. Pharmacological therapy for acute spinal cord injury. *Neurosurgery*. 2013;72(suppl 2):93-105.
52. Maekawa T, Yamashita S, Nagao S, Hayashi N, Ohashi Y. Prolonged mild therapeutic hypothermia versus fever control with tight hemodynamic monitoring and slow rewarming in patients with severe traumatic brain injury: a randomized controlled trial [published online August 6, 2014]. *J Neurotrauma*. 2014.
53. Kramer C, Freeman WD, Larson JS, et al. Therapeutic hypothermia for severe traumatic brain injury: a critically appraised topic. *Neurologist*. 2012;18(3):173-177.
54. Clifton GL, Miller ER, Choi SC, et al. Lack of effect of induction of hypothermia after acute brain injury. *New Engl J Med*. 2001; 344(8):556-563.
55. Clifton GL, Valadka A, Zygun D, et al. Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial. *Lancet Neurol*. 2011;10(2):131-139.
56. Clifton GL, Coffey CS, Fourwinds S, et al. Early induction of hypothermia for evacuated intracranial hematomas: a post hoc analysis of two clinical trials. *J Neurosurg*. 2012;117(4):714-720.
57. Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma*. 2007;24(suppl 1):S1-S106.
58. Schierhout G, Roberts I. Anti-epileptic drugs for preventing seizures following acute traumatic brain injury. *Cochrane Database Syst Rev*. 2001:CD000173.
59. Rehman T, Deboisblanc BP. Persistent fever in the ICU. *Chest*. 2014;145(1):158-165.
60. Inaba K, Menaker J, Branco BC, et al. A prospective multicenter comparison of levetiracetam versus phenytoin for early posttraumatic seizure prophylaxis. *J Trauma Acute Care Surg*. 2013; 74(3):766-71; discussion 71-73.
61. Cotton BA, Kao LS, Kozar R, Holcomb JB. Cost-utility analysis of levetiracetam and phenytoin for posttraumatic seizure prophylaxis. *J Trauma*. 2011;71(2):375-379.
62. Pieracci FM, Moore EE, Beauchamp K, et al. A cost-minimization analysis of phenytoin versus levetiracetam for early seizure pharmacoprophylaxis after traumatic brain injury. *J Trauma Acute Care Surg*. 2012;72(1):276-281.
63. Mohseni S, Talving P, Wallin G, Ljungqvist O, Riddez L. Preinjury beta-blockade is protective in isolated severe traumatic brain injury. *J Trauma Acute Care Surg*. 2014;76(3): 804-808.
64. Schroeppel TJ, Fischer PE, Zarzaur BL, et al. Beta-adrenergic blockade and traumatic brain injury: protective? *J Trauma*. 2010;69(4):776-782.
65. Cotton BA, Snodgrass KB, Fleming SB, et al. Beta-blocker exposure is associated with improved survival after severe traumatic brain injury. *J Trauma*. 2007;62(1):26-33; discussion 5.
66. Badjatia N. Hyperthermia and fever control in brain injury. *Crit Care Med*. 2009;37(7 suppl):S250-S257.

67. Mrozek S, Vardon F, Geeraerts T. Brain temperature: physiology and pathophysiology after brain injury. *Anesthesiol Res Pract*. 2012;2012:989487.
68. Hughes JD, Rabinstein AA. Early diagnosis of paroxysmal sympathetic hyperactivity in the ICU. *Neurocrit Care*. 2013;20(3): 454-459.
69. Perkes IE, Menon DK, Nott MT, Baguley IJ. Paroxysmal sympathetic hyperactivity after acquired brain injury: a review of diagnostic criteria. *Brain Inj*. 2011;25(10):925-932.
70. Perkes I, Baguley IJ, Nott MT, Menon DK. A review of paroxysmal sympathetic hyperactivity after acquired brain injury. *Ann Neurol*. 2010;68(2):126-135.
71. Bao L, Chen D, Ding L, Ling W, Xu F. Fever burden is an independent predictor for prognosis of traumatic brain injury. *PloS One*. 2014;9(3):e90956.
72. Cairns CJ, Andrews PJ. Management of hyperthermia in traumatic brain injury. *Curr Opin Crit Care*. 2002;8(2):106-110.
73. Thompson HJ, Tkacs NC, Saatman KE, Raghupathi R, McIntosh TK. Hyperthermia following traumatic brain injury: a critical evaluation. *Neurobiol Dis*. 2003;12(3):163-173.
74. Rabinstein AA, Benarroch EE. Treatment of paroxysmal sympathetic hyperactivity. *Curr Treat Options Neurol*. 2008;10(2): 151-157.
75. Hinson HE, Sheth KN. Manifestations of the hyperadrenergic state after acute brain injury. *Curr Opin Crit Care*. 2012;18(2): 139-145.
76. Choi HA, Jeon SB, Samuel S, Allison T, Lee K. Paroxysmal sympathetic hyperactivity after acute brain injury. *Curr Neurol Neurosci Rep*. 2013;13(8):370.
77. Patel MB, McKenna JW, Alvarez JM, et al. Decreasing adrenergic or sympathetic hyperactivity after severe traumatic brain injury using propranolol and clonidine (DASH After TBI Study): study protocol for a randomized controlled trial. *Trials*. 2012;13:177.
78. Podoll AS, Kozar R, Holcomb JB, KFinkel KW. Incidence and outcome of early acute kidney injury in critically ill trauma patients. *PloS One*. 2013;8(10):1-5.
79. Constantini TW, Fraga G, Fortlage D, et al. Redefining renal dysfunction in trauma: implementation of the Acute Kidney Injury Network staging system. *J Trauma*. 2009;67(2):283-288.
80. Skinner DL, Hardcastle TC, Rodseth RN, Muckart DJJ. The incidence and outcomes of acute kidney injury amongst patients admitted to a level I trauma unit. *Injury*. 2014;45(1):259-264.
81. Shashaty M, Meyer N, Localio AR, et al. African American race, obesity, and blood product transfusion are risk factors for acute kidney injury in critically ill trauma patients. *J Crit Care*. 2012; 27(5):496-504.
82. Bagshaw SM, George C, Gibney RTN, Bellomo R. A multi-center evaluation of early acute kidney injury in critically ill trauma patients. *Ren Fail*. 2008;30(6):581-589.
83. Wohlauer MV, Sauaia A, Moore EE, Burlew CC, Banerjee A, Johnson J. Acute kidney injury and posttraumatic multiple organ failure: the canary in the coal mine. *J Trauma*. 2012;72(2):373-380.
84. Duchesne JC, McSwain NE, Cotton BA, et al. Damage control resuscitation: the new face of damage control. *J Trauma*. 2010; 69(4):976-90.
85. Lissauer ME, Chi A, Kramer ME, Scalea TM, Johnson SB. Association of 6% hetastarch resuscitation with adverse outcomes in critically ill trauma patients. *Am J Surg*. 2011; 202(1):53-58.
86. Lehmann L, Bendel S, Uehlinger DE, et al. Randomized, double-blind trial of the effect of fluid composition on electrolyte, acid-base, and fluid homeostasis in patients early after subarachnoid hemorrhage. *Neurocrit Care*. 2013;18(1):5-12.
87. Young JB, Utter GH, Schermer CR, et al. Saline versus Plasma-Lyte A in initial resuscitation of trauma patients: a randomized trial. *Ann Surg*. 2014;259(2):255-262.
88. Matsushima K, Peng M, Schaefer EW, Pruitt JH, Kashuk JL, Frankel HL. Posttraumatic contrast-induced acute kidney injury: minimal consequences or significant threat. *J Trauma*. 2011; 70(2):415-420.
89. Kim DY, Kobayashi L, Constantini TW, et al. Is contrast exposure safe among the highest risk trauma patients? *J Trauma*. 2012;72(1):61-67.
90. NIH/VA Renal Failure Trial Network, Palevsky PM, Zhang JH, et al. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med*. 2008;359(1):7-20.
91. O'Grady NP, Barie PS, Bartlett JG, et al. Guidelines for evaluation of new fever in critically ill adult patients: 2008 update from the American College of Critical Care Medicine and the Infectious Diseases Society of America. *Crit Care Med*. 2008; 36(4):1330-1349.
92. Deresinski S. Principles of antibiotic therapy in severe infections: optimizing the therapeutic approach by use of laboratory and clinical data. *Clin Infect Dis*. 2007;45(suppl 3):S177-S183.
93. Holtom PD. Antibiotic prophylaxis: current recommendations. *J Am Acad Orthop Surg*. 2006;14(10 spec no.):S98-S100.
94. Hoff WS, Bonadies JA, Cachecho R, Dorlac WC. East Practice Management Guidelines Work Group: update to practice management guidelines for prophylactic antibiotic use in open fractures. *J Trauma*. 2011;70(3):751-754.
95. Moore FO, Duane TM, Hu CK, et al. Presumptive antibiotic use in tube thoracostomy for traumatic hemopneumothorax: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73(5 suppl 4): S341-S344.
96. Schneider JA, Lee YJ, Grubb WR, Denny J, Hunter C. Institutional practices of withholding enteral feeding from intubated patients. *Crit Care Med*. 2009;37(7):2299-2302.
97. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Crit Care Med*. 1999;27(7):1252-1256.
98. Sudenis T, Hall K, Cartotto R. Enteral Nutrition: What the dietitian prescribes is not what the burn patient gets [published online April 9, 2014]! *J Burn Care Res*. 2014.
99. Reignier J, Mercier E, Le Gouge A, et al. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA*. 2013;309(3):249-256.
100. MacLeod JB, Lefton J, Houghton D, et al. Prospective randomized control trial of intermittent versus continuous gastric feeds for critically ill trauma patients. *J Trauma*. 2007;63(1):57-61.