

Advancing Boundaries In the Care of the Trauma Patient

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Trauma victims have benefited from the development of trauma systems and pre-hospital provision of care, improved abilities to diagnose injuries, advances in non-invasive management of life-threatening injuries, better **Intensive Care Units (ICU)s** and critical care medicine and advances in our understanding of the physiologic effects of trauma and how to correct these deviations.

IMAGING STUDIES

Gone are the days of the plain film radiology as the only means of diagnosing injury. Advances in **computed tomography (CT)** have allowed trauma surgeons to detect many more injuries at earlier stages, with less risk to the patient. Godfrey Hounsfield invented the first commercially available CT scanning machine at EMI laboratories in 1971, work that culminated in a Nobel Prize in medicine.¹ Legend states that money from the success of The Beatles enabled EMI to undertake the CT scan research. This original machine was incredibly slow by today's standards: a CT brain took 4 minutes for each slice, and a processing time of 2.5 hours, with poor resolution of images.

Current generations of CT machines have multiple capabilities including: observing dynamic processes such as blood flow in the heart or brain (Dynamic Volume CT); rotating images to view them from any plane to better understand the relationship of the injury to the surrounding organs (Multislice CT); rapid acquisition time – with chest, abdomen and pelvis imaging performed in 20 to 30 seconds thus moving patients out of radiology and into the operating room or ICU faster (Helical or Spiral CT); 3-dimensional reconstruction – which allows for better imaging of possible spinal trauma (MPR – Multiplanar reconstruction). A practical limitation is the hospital-to-hospital variation in both machines and processing software. To address this limitation, the American College of Surgeons is trying to cull the software into one central location, so that all CT images can be uploaded via the internet from any institution and thus si-

multaneously viewed via another, distant institution. CT scans have become so advanced that many institutions have obviated the need for MRI imaging of the cervical spine if the 3-D reconstructed Multislice CT is negative for injury.

Magnetic Resonance Imaging (MRI) has long been used for diagnosis in neurologic trauma including **diffuse axonal injury (DAI)** of the brain, as well as for ligamentous injury of the cervical spine. However, the MRI may now have a new role in the trauma patient. In the poly-trauma patient, the diagnosis of cardiac contusion at times may be difficult, especially in older patients with cardiac disease and those at risk of peri-traumatic myocardial infarction. Recent data have suggested that Cardiac MRI may be able to detect, with great accuracy, areas of cardiac contusion obviating the need for cardiac catheterization. However, this technology is in its infancy.

Ultrasound has advanced the care in the trauma bay. Previously, an unstable trauma patient with multiple possible etiologies for shock would have undergone either a laparotomy or a **diagnostic peritoneal lavage (DPL)**. Neither is without potential for complications, and the DPL can be overly sensitive for some clinically insignificant injuries. The ultrasound probe can detect intra-abdominal bleeding and help delineate whether the hypotension is due to an abdominal source requiring emergent operative intervention, or not. **FAST (Focused Abdominal Sonography for Trauma)** is safe, rapid and repeatable, even in the ICU, for the unstable patient.

ANGIOEMBOLISATION RATHER THAN OPERATE

CT scan imaging can localize the source of bleeding. Evidence of active bleeding was, previously, an almost absolute indication to operate. Earlier detection of this ongoing bleeding, and early intervention would prevent patients from exhibiting the clinical and physiological manifestations of shock. Older generations of CT scans had too much width between images to delineate smaller ac-

tive hemorrhages. However, modern multislice scanners can detect this bleeding as denoted by a blush of IV contrast. Today's **Interventional Radiology (IR)** has been able to treat many injuries that would otherwise have required operative intervention.

Ring and Athanasoulis in 1973 first described a case managed by interventional radiologic therapy when they described control of ongoing pelvic bleeding,² thus expanding the role of Angiography from diagnostic to therapeutic. Using intravascular wires and catheters, one can locate the actively bleeding vessel, and deploy one of a variety of devices or agents to stop, or embolize the bleeding vessel. The biggest impact has been seen in the management of pelvic fractures and splenic injuries. Ongoing bleeding from pelvic fractures are extremely difficult to manage operatively. Attempted packing, either intra-peritoneally or extra-peritoneally is associated with significant morbidity and mortality from the release of the tamponade effect with a laparotomy. One is often reduced to mass ligation rather than individual vessel ligation, which can lead to gluteal ischemia and impotence. Active arterial pelvic bleeding could be life-threatening; however, with the assistance of IR, the bleeding can be stopped, and the trauma physiology and coagulopathy corrected. Splenic injuries with evidence of ongoing bleeding (a blush on CT scan) have the potential to lead to exsanguination. Much literature has been published on the success of IR to embolize splenic trauma with both splenic preservation and obviating the need for a laparotomy. This technology has also been successfully extended to liver injuries with evidence of active hemorrhage.

CHANGES IN AORTIC INJURIES

Nowhere are the changes to management more evident than in the management of blunt aortic injuries.³ An injury that once was destined for major operative intervention with an ensuing high mortality and a significant risk of paraplegia from an aortic cross-clamp is now largely managed with endovascular

placement of an aortic stent. Fabian et al in 1997 attempted to document the natural history, treatments and outcomes of aortic injuries. At that stage, the only operative treatment was an open procedure via a left thoracotomy, associated with significant complications including ARDS, a significant ICU length of stay, worsening of other injuries and most notably, a very high rate of paraplegia. The worsening of other injuries was most common with bleeding from intra-peritoneal solid organ injuries and worsening intracranial hemorrhage from the systemic heparin that was administered. Paraplegia was noted with aortic cross-clamp times greater than 30 minutes.

Endovascular aortic surgery was first described for abdominal aortic aneurysms. Subsequently, many traumatic vascular injuries have been shown to be amenable to this minimally invasive approach. The paradigm in the management of aortic injuries has shifted: clinicians make liberal use of CT angiography for both screening and diagnosis, rather than chest X-ray; conventional angiography has almost disappeared; beta-blockers are widely used to control the heart rate and blood pressure; there is planned delayed operative repair predominantly with endovascular stent grafts, and, in select cases, non-operative management of aortic injuries. Whereas in 1997 immediate repair was the dictum, by 2008 our understanding of the nature of aortic injuries has defined patient populations in whom delayed operative repair is better than immediate operation. In 1997 all patients were managed with open repair; by 2008 almost 65% of aortic injuries were managed with endovascular stents, introduced via small cut downs in the groin that gains access to the bilateral femoral arteries. Using real time radiology in specially designed operating rooms, the surgeon positions the stent across the traumatic pseudoaneurysm. The dose of systemic heparin is considerably lower, thus reducing the risk of worsening other injuries. This approach, which avoids a thoracotomy, is best suited in patients with intracranial injuries and those with significant thoracic trauma, as are seen in many trauma patients. Mortality rates have fallen from 22% to 13%; the rate of paraplegia, from 8.7% to 1.6%.

DAMAGE CONTROL LAPAROTOMY

Multiply injured trauma patients are just as likely to die from their intra-operative metabolic and physiological derangements as from their injuries. **Damage Control Laparotomy (DCL)** has emerged in the last 20 years.⁴ The principles of DCL defy the traditional principles of definitive (elective) operative intervention. Stone et al first described the staged approach to the severely injured patient, based on observations that patients who survived the operating room often died from severe metabolic and physiologic derangements, associated with severe exsanguinating injuries. Profound shock with blood loss initiates the “Deadly Triad” of hypothermia, acidosis and coagulopathy. A fourth component is often added, first coined by Asensio et al, notably dysrhythmia, which usually heralds death. The onset of this deadly triad is most noted in patients who undergo prolonged operative management of their injuries. Severe hemorrhage leads to tissue hypoperfusion and diminished tissue oxygenation, leading to reduced heat generation in the setting of accelerated loss of body heat. Hypothermia can lead to cardiac dysrhythmia, decreased cardiac output, left shift of the oxygen-hemoglobin dissociation curve, induction of coagulopathy by inhibiting the coagulation cascade, and impairment of the immunological response and function. Coagulopathy occurs due to a combination of hypothermia, activation of fibrinolytic system, hemodilution and transfusion of packed red cells without transfusion of clotting factors. This coagulopathy makes any surgical attempt at blood loss control extremely difficult. When the body is under-perfused due to hypotension and blood loss, anerobic metabolism ensues with the production of lactic acid. Acidosis worsens cardiac contractility and cardiac output. Thus blood loss, hypotension, acidosis and coagulopathy create a negative feedback loop that quickly spirals out of control, leading to the exsanguination of the patient.

The physiological guidelines that can predict the need for DCL include the following: Hypothermia with $T \leq 34^{\circ}\text{C}$, Acidosis with $\text{pH} \leq 7.2$, Serum bicarbonate of $\geq 15\text{mEq/L}$, Transfusion of $\geq 4\text{L}$ packed red cells, Transfusion of $\geq 5\text{L}$ blood and blood products, Intra-operative volume replacement $\geq 12\text{L}$, and clinical evidence

of intra-operative coagulopathy. In the operating room, DCL implies immediate operative control of life-threatening hemorrhage, control of gastrointestinal contamination with rapid resection or closures and forgoing the restoration of intestinal continuity, the use of intra-vascular shunts rather than repairs and the judicious use of abdominal packing and temporary abdominal closures. Once DCL is undertaken, the next stage begins as rapidly as possible in the ICU with correction of the metabolic acidosis, coagulopathy and hypothermia. Following correction of these, the patient is returned to the operating room for conclusion and possible definitive repair of any remaining injuries. In extreme cases, it may take two or three days of intense resuscitative efforts until the patient is stabilized sufficiently to undergo the second operation. The advent of DCL and the expanse in our understanding of the “Deadly Triad” and “Lethal Quartet” has indeed improved mortality and has resulted in a dramatic increase in survival of the most seriously injured patients.

ACTIVATED RECOMBINANT FACTOR VII

Coagulopathy in certain patients can progress to a point almost incompatible with life. In extreme coagulopathy which results from massive blood loss, which is replaced with intravenous crystalloid solutions and packed red cells, often without other blood products, coupled with hypothermia and acidosis compounded by prolonged operative interventions, results in a bleeding tendency that is unable to be corrected with conventional replacement of blood and blood products⁵. Recombinant Factor VIIa (NovoSevenTM) was originally licensed for use in haemophilic patients with inhibitors of clotting factors. Given our advancing understanding of the coagulopathy that ensues in trauma patients, it was felt that these patients suffered from non-surgical, traumatic coagulopathy. Factor VIIa was thought to bypass much of the coagulation cascade and induce clotting in these patients, in the setting of profound hypothermia and thrombocytopenia.

In 1999 Kenet et al published the first account of the use of Factor VIIa in trauma, in a soldier with traumatic coagulopathy following a gunshot wound to the Inferior Vena Cava. Factor VIIa, an

initiator of thrombin generation, acts via two pathways to activate Factor Xa. One pathway is at the site of tissue injury complexed with Tissue Factor. Tissue Factor is present in the sub-endothelial layer of the vascular wall that is exposed following trauma. The second mechanism of action is via the surface of platelets. Factor VIIa activates factors IX and X on the platelet membrane which then progress to thrombin and fibrin formation (the Thrombin Burst). Most of the literature comes from the experience seen with the Israeli army, which relates good results in patients with severe hemorrhage and traumatic coagulopathy. The largest US experience is from the Maryland Shock Trauma Institute. While the population was mixed and the results not conclusive, the indication was that Factor VIIa might indeed be useful in patients with traumatic coagulopathy,⁶ specifically with an apparent reduction in the incidence of Multiple Organ Failure and ARDS. While Factor VIIa has been shown to work despite profound hypothermia and thrombocytopenia, it is largely ineffective in face of severe acidosis; thus it is not the panacea that it was initially thought to be. Currently, a world wide clinical trial for Factor VIIa in trauma is addressing its role and indications.

TREATING THE COMPLEX COMPLICATIONS; SEPSIS ARDS AND THE NEED FOR IMPROVED MONITORING

The hallmark of **Acute Respiratory Distress Syndrome (ARDS)** is an inability to oxygenate the patient. Mortality rates exceeded 50% in much of the original literature. ARDS affects both trauma and non-trauma patients and may be seen following prolonged abdominal operations, pancreatitis or major vascular surgical cases. Akin to other complications, there has been a rise in long term complications in trauma patients who are now surviving their initial trauma who would otherwise have previously died. We have expanded our understanding of both the pathophysiology that leads to ARDS as well as the treatment strategies. A considerable amount of resources are dedicated to explaining the cytokine, hormonal and inflammatory cascade behind ARDS, some of which is being undertaken at Rhode Island Hospital Department of Surgery. RIH has shown that an exaggerated pro-

inflammatory response is seen in the ARDS lungs. Early concepts for the management of ARDS evoked the maxim that if some is good, then more must be better. However, unfortunately over-distention of the alveoli and "Supra-Physiologic" ventilation was proven to be detrimental to the lungs. Treatment strategies, as defined in the **ARDS Research Network (ARDSnet)** protocols are directed at limiting the ongoing insult to the lungs, by decreasing tidal volumes and decreasing alveolar stretch injury due to the ventilator. This has decreased both the incidence of ARDS and the morbidity and mortality from ARDS across the country.

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Sepsis remains a significant cause of mortality in ICU patients: mortality ranges from 25 to 50%. As our care improves to allow more patients survive the initial phases of the trauma, we are seeing increasing rates of sepsis. A collaborative, the "Surviving Sepsis Campaign," was launched in Barcelona in 2002. This begins with early aggressive care in the Emergency Department, continues through the Operating Rooms with damage control laparotomy and control of abdominal contamination, into the ICU with Medical Algorithms, or "Bundles" of evidence-based patient care guidelines.

Above this, research advances have led to the introduction of Activated Protein C (Drotrecogin Alfa (Xigris). Whilst the indications are limited to the extremely ill, Xigris has contributed to improved survival following sepsis. Unfortunately, recent operative intervention, within 48 hours, is a contra-indication to the usage of Xigris. Furthermore, Xigris has increased our understanding of the role of the coagulation system in critically ill patients. Protein C is the source of **Activated Protein C (APC)**, a naturally occurring protein in the body

that helps to regulate blood flow and control inflammation on the microvascular level. In patients with severe sepsis, Protein C levels are low and, partly due to damage to blood vessels, cannot be converted in sufficient quantities to the activated form, APC. Thereby, clotting and inflammation of the small blood vessels go out of balance which may lead to multiple organ failure and death.

There have been many tremendous advances in monitoring systems for these critically ill patient, both invasive (Swann-Ganz catheters) and minimally invasive (LiDCO and PiCCO) which can give accurate, minute-to-minute records of a patient's cardiac function, vascular resistance, tissue oxygenation and tissue oxygen debt, and intra-vascular volume status. Coupled with advances in our understanding of the mechanisms of action of inotropes and vasopressors, we continue to improve our ability to detect and correct derangements in physiology induced by trauma, shock and sepsis. Current research focuses on non-invasive, transdermal measurements of cardiac function, oxygen delivery/debt, as well as trans-dermal measurement of blood chemistry and hematology. Hopefully, this will minimize the phenomenon of ICU anemia, iatrogenically induced from repeated, necessary and unnecessary phlebotomy. The promise of the future ICU is that the labs of a patient will be available in a fashion akin to obtaining a pulse oximetry.

BASIC SCIENCE AND ANTI-INFLAMMATION

Many advances have been made in our understanding of the immunological dysregulation that ensues following traumatic critical illness. The trauma patient who survives the early causes of death still risks **Systemic Inflammatory Response Syndrome (SIRS)**, which can ultimately lead to **Multi-Organ Dysfunction Syndrome (MODS)** with its extremely high rate of death. A well recognized immune burst follows trauma. This immuno-inflammatory response is characterized by elaboration of cytokines acting as acute phase reactants and hormones, such as Interleukin-1 (IL-1), IL-2, IL-6, IL-12, tumor necrosis factor (TNF) and Interferon-Gamma (IFN). Cytokines play a critical role for signal-

ing intracellular substances that initiate, amplify and perpetuate inflammatory response both locally and systemically. Significant portions of this work have been undertaken at Rhode Island Hospital Department of Surgery.^{7, 8} IL-6 is regarded as being the most accurate prognostic marker regarding outcome of trauma patients with SIRS, sepsis or MODS. Sex hormones, specifically estrogen, have been shown to modulate this cytokine burst. There is a growing body of evidence linking the inflammatory dysfunction of trauma with the pituitary-adrenal axis suppression following trauma and critical illness. Several investigators have attempted to track cytokine level changes to determine the best time to operate in the semi-elective setting in the multiply injured patient. It is believed that if one attempts to stabilize orthopedic injuries while the patient is still acutely and severely inflamed, the patient has a significantly higher risk for MODS and death. Thus, waiting for the severe inflammatory burst to resolve may improve outcomes. In essence, certain authors have documented better sensitivity for cytokines rather than clinical parameters. This is truly translational research in practice whereby clinical entities are studied in the basic science laboratory, determinations are made, and the knowledge is brought back to the patient's bedside.

CONCLUSIONS

Trauma patient care requires well honed clinical skills, rapid diagnostic tests and studies and immediate operative intervention. These patients benefit from improved diagnosis, treatment of bleeding through minimally invasive procedures, better understanding of the physiological and coagulopathic changes induced by trauma, quick and accurate operative strategies, and improved post-operative critical care.

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The authors have no financial interests to disclose.

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