

## Advances in the Management of Bleeding Trauma Patients

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### DAMAGE CONTROL RESUSCITATION (DCR)

Management of traumatic hemorrhage has progressed over the past century. With better understanding of the pathophysiology of hemorrhage and adverse effects of previous practices, resuscitation has shifted to replace lost blood with blood components instead of crystalloids. The resuscitation of injured and bleeding patients is complex and requires a “multi-modal” strategy, now termed damage control resuscitation (DCR).<sup>1</sup>

Damage control resuscitation has three pillars: early surgical control of bleeding, permissive hypotension, and blood product transfusions while avoiding crystalloids. Identifying patients at risk of severe hemorrhage who would benefit from DCR is crucial. Early initiation of these practices in prehospital settings could prevent or minimize physiologic complications such as organ failure and mortality, while avoiding excessive use of blood products.

### Permissive hypotension

Permissive hypotension is a management strategy in which resuscitation is withheld in patients until surgical control of bleeding is obtained. In order to prevent disruption of local hemostasis at the site of injury, providers administer blood or fluids to maintain a systolic blood pressure of about 80 mmHg or to a level that results in an adequate mental status and tissue perfusion.<sup>2</sup> Additionally, permissive hypotension may decrease post-operative coagulopathy and lessen non-surgical bleeding. While several studies have been unable to definitively demonstrate a survival benefit, trends do suggest decreased mortality in both the first 24 hours of care, as well as in-hospital mortality.<sup>3,4</sup>

### Blood Resuscitation

Current guidelines indicate that bleeding patients should be resuscitated with blood products instead of crystalloid fluids. Traditional administration of large amount of crystalloid increase the risk of outcomes, such as abdominal compartment syndrome, acute respiratory distress syndrome, dilutional coagulopathy and hyperchloremic metabolic acidosis.<sup>5</sup> Simply put, if a patient loses blood, it should be replaced with blood.

Advantages of blood components resuscitation come from their inherent properties – oxygen carrying capacity, presence of coagulation factors and platelets, and avoidance of

some of the negative sequelae of saline containing fluid. Using whole blood for resuscitation appears to be the logical choice since it contains the ideal amounts of hemoglobin, platelets and clotting factors. Military protocols have made this a practical element of damage control resuscitation in combat and military personnel are often thought of as “walking blood banks”. However, due to storage and other logistical limitations, whole blood cannot be widely used as a resuscitative fluid. On the contrary, in civilian centers, blood is separated into its components – packed red blood cells (PRBC), plasma, and platelets – to prolong storage duration and availability.

The PROPPR and PROMIT trials examined the ideal ratios of blood components during massive transfusion.<sup>6,7</sup> A balanced resuscitation that is as close to 1:1:1 of plasma:platelet:PRBC appears to be the most beneficial. This represents a significant departure from past practices where blood components were ordered in response to lab value-detected deficiencies and plasma was not transfused until after 4 or more units of blood were administered. Ensuring early balanced blood resuscitation also appears to improve survival in hemorrhaging trauma patients compared to the common practice of transfusing PRBC first and then catching up with other components later in the resuscitation.<sup>8</sup>

The benefit of adding plasma and platelets (*plus fibrinogen*) early in resuscitation is due to their role in halting and correcting trauma-induced coagulopathy. The COMBAT and PAMPer trials evaluated whether administering plasma in prehospital settings en route to trauma centers offered any advantage.<sup>9,10</sup> These studies were designed to simulate rapid and slow transport to a trauma center, respectively. Prehospital plasma administration appears to have the advantage in settings with longer transport times, but not in cases where there is rapid transport to a definitive care setting. Additionally, there are logistical issues to consider. Fresh frozen plasma requires cold storage and then thawing prior to administration which renders it extremely difficult to use in the prehospital setting. Pre-thawed plasma will resolve the storage and thawing limitations; however, it has a short shelf life (<5 days), which leads to increased waste in areas with infrequent rates of use. Never-frozen plasma has a longer lifetime and is possibly the best option in the pre-hospital settings. Freeze-dried plasma has been tested and appears to have similar coagulation parameters with the advantage of

easy storage and transport.<sup>11,12</sup> Shelf life is about 2 years and reconstitution only requires mixture with distilled water prior to administration, but this product is not yet approved by the Food and Drug Administration.

### Hemorrhage Control

Early management of hemorrhage depends on rapid control of the bleeding site. Traumatic hemorrhage can be divided into two categories – compressible and non-compressible. For compressible hemorrhage, pre-hospital interventions have proven to be extremely beneficial. The easiest and fastest method of controlling compressible hemorrhage is direct pressure to the bleeding site. Tourniquets applied by pre-hospital providers, police officers, or bystanders can reduce blood loss from injured extremities significantly, improving survival rates.<sup>13,14</sup> Hemostatic dressings were developed to simultaneously provide direct pressure as well as initiate thrombotic reaction resulting in cessation of bleeding

Non-compressible hemorrhage occurs in a cavity where direct pressure or tourniquet use is not possible, such as the thoracic cavity, the abdomen, or the pelvis. Traditionally, once a non-compressible hemorrhage is identified, the patient is transported immediately to the operating room or the interventional radiology suite for control of the source of hemorrhage. Occasionally, in patients with impending traumatic cardiac arrest or those who lose vital signs due to hemorrhage, an emergency department thoracotomy (EDT) is performed to provide manual control of the source of hemorrhage in the chest or clamp the descending aorta in order to halt bleeding in the abdomen or the pelvis. Recently, a minimally invasive approach has gained acceptance in the trauma community to provide early and temporary control of bleeding in the abdomen or the pelvis. The resuscitative endovascular occlusion of the aorta (REBOA) technology borrows from skills commonly used in vascular surgery to deploy a balloon in the descending aorta, like aortic clamping performed in EDT. Advances in this technology have shortened time to access and correct placement of the balloon in the aorta. The aorta is divided into three zones of balloon placement. Zone 1 is in the thoracic descending aorta above the celiac artery and equates with the xiphoid process. The balloon is deployed in zone 1 when intra-abdominal hemorrhage is suspected. Zone 3 lies between the renal arteries and the bifurcation of the aorta. The provider inflates the balloon in zone 3 only if pelvic bleeding is suspected due to presence of pelvic fractures while abdominal sources of bleeding are ruled out. Zone 2 extends from the celiac artery to the renal arteries. The balloon should not be inflated in zone 2 under any circumstances, to prevent ischemic insult to the kidneys and viscera.<sup>15</sup>

Several centers have implemented REBOA in their damage control resuscitation protocols and have begun reporting their results. Early data supports its use; however, these studies have been critiqued due to lack of an appropriate

comparison group.<sup>16</sup> Joseph et al compared REBOA to a control group using propensity score matching and placement of REBOA resulted in higher mortality and morbidity.<sup>17</sup> These results should not be interpreted as lack of evidence of benefit. Instead, they should lead to further assessment to identify the injured and bleeding population that could benefit the most from this approach. Pre-hospital application should not be initiated or discussed until more solid data on REBOA's safety and efficacy has been established.

### Experimental Approach – ResQFoam

For non-compressible hemorrhage, presently there is no quick option for applying direct pressure at the bleeding site. Immediate surgical control is the only intervention most of the time, with REBOA being an occasional temporary choice *en route* to the OR. Recently, an experimental technology for abdominal hemorrhage was approved for a clinical trial (*Clinicaltrials.gov: NCT02880163*). This product uses an expandable polyurethane foam that is injected into the peritoneal cavity to create a tamponade effect in the abdomen to stop or slow bleeding as an adjunct to other damage control resuscitation components.<sup>18,19</sup> Foam is administered into the abdomen within 30 minutes of arrival to the emergency department with definitive surgical intervention to be carried out within 3 hours from foam deployment. Fortunately, this foam does not adhere to vital structures or organs which facilitates its prompt removal once the peritoneal cavity is opened.

### Correcting Coagulopathy

Bleeding in injured patients can be complicated by the development of trauma-coagulopathy. Resuscitation with blood components, plasma, platelets, and fibrinogen, replace lost and consumed clotting factors. Hemostasis and clotting are tightly coupled to fibrinolysis and dissolution of clots, lest the entire circulatory system would thrombose once clotting was initiated. Injured patients are at risk for excessive fibrinolysis which promotes bleeding and the development of the lethal triad. Tranexamic acid (TXA) is a lysine analogue that results in reversal of thrombolysis. The widespread pre-hospital use of TXA is based on the CRASH 2 trial, which showed a mortality benefit in patients who were suspected of hemorrhage and received TXA.<sup>20</sup> However, there were several study design issues and the treatment effect size was small, reducing mortality due to severe hemorrhage from 5.6% to 4.8%. This meant that 125 patients needed to be treated with tranexamic acid to prevent one death. The MATTERS study, a retrospective study of TXA in military settings, showed a mortality benefit due to administration of TXA.<sup>21</sup> As a result of these two studies, tranexamic acid has become widely used in massive transfusion protocols nationally and internationally. Pre-hospital use has also increased, although there are not enough robust studies to support its prehospital use. The Department of Health in

Rhode Island recommends administering TXA for injured patients with hypotension, tachycardia, or if the prehospital provider determines that the patient is at risk of hemorrhage. When we examined local TXA practices we identified a high rate of administration without clear indication when given by EMS. We believe that TXA should be administered cautiously, ideally in patients with hemorrhage and evidence of fibrinolysis. Data from University of Pittsburgh showed a 3-fold increase in the rate of VTE events, thus further studies are needed to establish appropriate criteria to guide pre-hospital providers to administer such an important medication.<sup>22</sup>

Traditionally, evaluation of trauma coagulopathy has relied on tests such as PT, PTT, and INR. The results of these tests are delayed and do not reflect the actual coagulation status of an injured, hypothermic and actively bleeding patient. Additionally, these standard clinical tests are normalized and run at 37°C, while nearly half of all bleeding trauma patients arrive at the hospital hypothermic. Fortunately, there is a technology that provides an assessment of the entire coagulation and thrombolysis status of the patient. This technology, thromboelastogram (TEG), assesses the time to bleeding, the strength of the formed clot, as well as the dissolution of the clot or thrombolysis. Advances in this technology have allowed trauma surgeons to obtain timely and early assessments of the coagulopathy in trauma patients. Therefore, a tailored resuscitation with blood products and choice of pharmacological resources can be given to an injured trauma patient resulting in less products utilization and rapid correction of coagulopathy.

### STOP THE BLEED CAMPAIGN

Resuscitation and control of traumatic hemorrhage has evolved. Management commences with arrival of prehospital providers where control of compressible hemorrhage is performed, and blood product resuscitation is initiated. Rapid transport to a trauma center within a mature trauma system network ensures timely expert surgical management for these patients – continued resuscitation, correction of coagulopathy and surgical control. However, in cases where prehospital care is delayed due to mass casualty, an active shooter, or logistical factors, some interventions that could be provided by bystanders may prove to be lifesaving. The Stop The Bleed initiative by the American College of Surgeons’ Committee on Trauma and the Hartford Consensus aims to educate lay people on the proper use of tourniquets and hemostatic dressings applications, among other first aid measures, prior to arrival of EMS providers.<sup>23</sup> In neighboring Connecticut (CT), kits containing essential tools for early hemorrhage control (pressure bandages, hemostatic dressings, tourniquets, and personal protective gloves) are placed alongside every automatic external defibrillators in public places. This strategy was mandated by legislation in

CT aiming to reduce preventable deaths due to compressible hemorrhage. Bleeding control or “B-con” courses are educational seminars that are routinely provided to large groups such as schools, civic groups, sporting events, etc. The short classes consist of a formal presentation and hands-on practice of bleeding control. In two years since its official launch in February 2017, more than 40,000 classes have been conducted in 77 countries with over 600,000 attendees trained in bystander hemorrhage control methods. Participation, especially when hands-on training is provided, improved laypersons’ willingness to use a tourniquet in an emergency.<sup>24</sup> Community education to raise awareness regarding the importance of participation in early bleeding control and engaging in B-Con courses continues to be an important public health matter.<sup>25</sup>

### CONCLUSION

Improved understanding of the pathophysiology of hemorrhage, coagulopathy, and resuscitation, along with technical advances and innovations, have improved outcomes of bleeding trauma patients. but there continues to be a need for early hemorrhage control. Involving bystanders appears to be a promising approach toward improving outcomes. Ongoing research and support by academic and government institutions is a crucial factor in combating mortality from traumatic hemorrhage – a serious public health problem.

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