Western Trauma Association critical decisions in trauma: Damage-control resuscitation

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Hemorrhage is one of the leading causes of preventable trauma deaths worldwide. Since the recognition of the lethal triad of hypothermia, acidosis, and coagulopathy, damage-control surgery (DCS) has become a tenet of trauma care. A natural sequala of DCS has been the reconsideration of hemorrhagic shock resuscitation. Now known as damage-control resuscitation (DCR), a term coined by Holcomb et al. in 2007 following observations during Operations Iraqi Freedom and Enduring Freedom, DCR represents a paradigm shift in the management of hemorrhagic shock.[1,2] Prior to DCR, volume restoration was obtained using large volume crystalloid-based resuscitation. This proved deleterious, and in the last two decades, crystalloid resuscitation has been replaced by whole blood, balanced component resuscitation, or both. The article and its associated algorithm (Fig. 1) aim to provide a stepwise approach to the initial management of hemorrhagic shock resuscitation based on the most current evidence-based recommendations and expert opinion. The letter designations within the algorithm represent decision points and correspond to lettered headings in this article, which elaborate on the thought processes and evidence for the current recommendations, as well as notable caveats during DCR. This algorithm is intended to be used in conjunction with DCS during the initial phases of trauma care.

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ALGORITHM

Prehospital Care

The methods and means by which prehospital care is provided vary widely and depend on state and local protocols. The WTA has published a decision algorithm specifically targeting prehospital care.[3] A main component of prehospital care is the appropriate initial triage for risk of hemorrhage and initiating goal-directed resuscitation based on suspected injuries. Key concepts during prehospital care include obtaining IV access, implementing hemorrhage control techniques, and rapidly restoring circulating blood volume. In ideal settings, prehospital resuscitation should include transfusion of whole blood, if available, or packed red blood cells and plasma.[4] In the absence of blood products, judicious use of crystalloid fluids is reasonable. If active hemorrhage is suspected, tranexamic acid (TA) should be administered in the prehospital setting, if consistent with local protocols. In patients without suspected traumatic brain injury (TBI) permissive hypotension resuscitation to a systolic blood pressure (SBP) 90 mm Hg, should be implemented. However, in patients with

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known or suspected TBI, SBP should be maintained at or above 110 mm Hg, if possible, as even short episodes of hypotension may result in increased TBI-associated morbidity and mortality, albeit at the possible expense of increased truncal hemorrhage.[5–7]

Recognition of Patients Requiring DCR and Initial Hemorrhage Control

The American College of Surgeons Advanced Trauma Life Support (ATLS) classifies hemorrhagic shock based on a combination of the amount of blood loss and associated clinical findings, including heart rate, blood pressure, and Glasgow Coma Scale.[8] While this is a practical and simplistic method for defining hemorrhagic shock, recent literature questions the accuracy of this classification and the associated clinical findings. While the most basic definition of a shock state is end-organ hypoperfusion, this may not always be accompanied by hypotension. Historically, SBP of less than 90 mm Hg has been the threshold of hemorrhagic shock. However, geriatric and pregnant patients may not exhibit the same physiologic response to shock and may, in fact, present with shock despite SBP being significantly higher than 100 mm Hg. In addition, medications, such as beta-blockers, may alter the physiologic response to significant blood loss. Therefore, SBP and heart rate alone should not be the only defining parameters when identifying candidates for DCR.[9] Evidence of active external hemorrhage or suspected noncompressible hemorrhage, based on the mechanism of injury, should raise suspicion for progression to life-threatening hemorrhagic shock requiring DCR. In addition, a base deficit (BD) of ≤5.0 mmol/L, shock index (SI) ≥ 1, or need for prehospital blood transfusion have all been validated as indicators for needing DCR.[10–14] Once active hemorrhage is identified, hemorrhage control techniques must be implemented expeditiously. Depending on the known or suspected source of hemorrhage, these techniques may include compression dressings, placement of a tourniquet, placement of a pelvic binder, or performing resuscitative endovascular balloon occlusion of the aorta (REBOA)/resuscitative thoracotomy (RT). In addition to these maneuvers, adequate IV access must be obtained, if not already performed. Options for vascular access include two large-bore IVs, intraosseous catheter placement, or large-bore central venous lines. Blood samples should be drawn for a type and crossmatch, to assess hemoglobin levels, BD, coagulation parameters (PT/PTT/INR, rapid thromboelastography [TEG]/rotational thromboelastometry [ROTEM if available), ionized calcium (iCa) and fibrinogen levels.

Blood Product Administration

The next vital component of DCR is the restoration of circulating blood volume.[15] Similar to the prehospital phase of care, variability exists in blood resuscitation protocols based on resource availability. Historically, crystalloids were the resuscitation fluid of choice. High-volume crystalloid infusion has

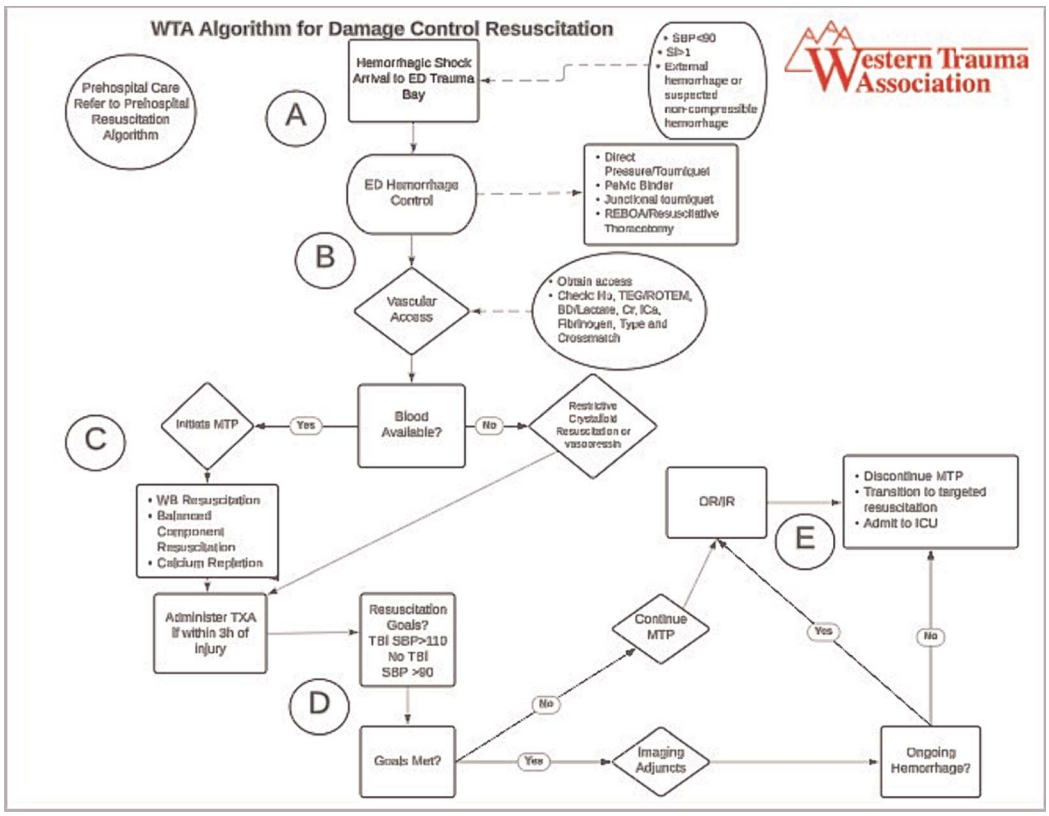

Figure 1. A Western Trauma Association critical decisions algorithm for DCR of patients presenting in hemorrhagic shock. ED, emergency department; SI, shock index; Hb, hemoglobin; Cr, creatinine; OR, operating room; IR, interventional radiology; ICU, intensive care unit.

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been shown to worsen acid-base balance, increase the inflammatory response, induce hypothermia and endothelial membrane instability, and is associated with decreased tissue oxygenation and worsening of hemorrhagic coagulopathy, among other effects.[16–20] Therefore, we recommend limited or sparing use of crystalloid fluids during DCR. Current military and supporting civilian trauma literature recommend low-titer type O whole blood (LTOWB) as the initial resuscitative blood product of choice as warm fresh whole blood is not logistically available in civilian trauma centers and not yet approved by the Food and Drug Administration (FDA).[21–23] Low-titer type O whole blood improves the oxygen-carrying capacity and coagulation profile compared with blood component therapy.[24] Currently, the duration of cold storage of LTOWB ranges from 21 to 35 days, depending on the preservation process utilized, considerably increasing its availability and decreasing wasted resources.[25] The use of LTOWB decreases mortality risk and bleeding complications when compared with blood component therapy.[23,26] In one study, patients receiving whole blood had a significant reduction in the incidence of ARDS, duration of mechanical ventilation, need for massive transfusion protocol (MTP) activation, and transfusion volumes.[27] However, no difference in survival rates was found when comparing blood component therapy with whole blood.[28] Conversely, a recent meta-analysis of 24 studies, including 58,717 subjects, suggests hemostatic resuscitation with LTOWB may confer improved early and late survival compared with component therapy alone.[29] Nonetheless, LTOWB, if available at all, is often accessible in limited quantities, necessitating the utilization of a balanced component transfusion strategy. Aware of the limitation of resources and variability between trauma centers, an MTP should be promptly initiated. Civilian studies have shown that balanced component resuscitation for massive replacement of blood loss with thawed plasma, packed red blood cells and platelets is a successful strategy to minimize mortality from traumatic coagulopathy. Current literature recommends a ratio of 1:1:1 (plasma/platelets/pRBC) between components as the optimal resuscitative strategy; however, this ideal situation may not be feasible.[30] As such, a ratio of 1:1:2 is an acceptable; although not ideal, alternative.[21,28,30–34]

Fibrinogen deficiency has been identified in patients requiring massive transfusion due to hemorrhage. Early treatment and replacement as part of MTP has been recommended to decrease transfusion rates and mortality in trauma patients in hemorrhagic shock. In the United States, cryoprecipitate infusion is the standard replacement therapy which, along with FFP, corrects hypofibrinogenemia more efficiently.[35,36] In Europe, fibrinogen concentrates are readily available and have been shown to improve low fibrinogen levels due to the coagulopathy of trauma.[37] While acute fibrinogen deficiency can be treated with cryoprecitate, the CRYOSTAT-2 randomized trial suggests that early, empiric high-dose (≥5 pooled units) cryoprecipitate does not improve clinical outcomes nor improve mortality.[38] One pooled unit of cryoprecipitate (100 mL, 2 g fibrinogen equivalent) per 7 to 8 units of pRBC transfused is the appropriate dose that provides a significant survival benefit while limiting the total amount of blood components transfused.[39] As such, it is recommended that every round of MTP (6 units of PRBCs) should include one unit of pooled cryoprecipitate. The geriatric population is a group that requires special consideration, as many of these patients may be prescribed direct oral anticoagulants (DOACs). The management hemorrhagic shock in these patients is controversial as no current guidelines are established, and their reversal are determined by the treating physician based on the clinical picture at the time of the resuscitation and the indication for the use of DOACs. Regardless of the indication for DOAC, in general, reversal should be done expeditiously in patients presenting with hemorrhagic shock.

A high-normal iCa level should be maintained to counteract the citrate content of stored blood products, correct patient calcium deficiency prior to the trauma, and remedy homeostasis alterations during the shock state.[40,41] Hypocalcemia should be prevented in patients with hemorrhagic shock as it exacerbates the acidosis and coagulopathy associated with the coexisting hypoperfusion, as calcium is critical in several essential physiologic roles.[42] Ionized calcium levels should be monitored closely during resuscitation and calcium replacement therapy of 1–2 g calcium chloride or 3–6 g calcium gluconate per each MTP round should be administered promptly, without delay while obtaining laboratory values. Abnormal calcium levels during trauma resuscitation could be associated with increased mortality and use of blood products.[43,44]

Tranexamic acid should be given to patients at risk of hemorrhagic shock who have not already received a dose during the prehospital phase. Studies have shown reduced mortality in trauma patients receiving TXA despite their increased injury severity and transfusion requirements. The patient should only receive the initial TXA dose if administered within 3 hours of injury. When given >3 hours postinjury, TXA increases the risk of mortality.[45–47] This mortality data was not analyzed in patients with hyperfibrinolysis, as documented by viscoelastic testing (ROTEM or TEG). However, documented hyperfibrinolysis in the setting of ongoing hemorrhage should be treated according to clinical judgment.[48] Historically, for eligible patients (see section above titled Recognition of Patients Requiring DCR), TXA was given as a 1-g bolus over 10 minutes followed by 1-g intravenous infusion over 8 hours. This often resulted in the infusion being delayed or, in some cases, inadvertently omitted altogether. As such, it is now recommended that TXA be administered IV or IO as a 2-g bolus, negating the need for the infusion dose.[49] It should be noted that rapid infusion of TXA has been infrequently associated with transient hypotension.

Women of childbearing age require special consideration. Historically, Rhesus factor (Rh)-negative blood has been recommended for women of childbearing age as the administration of Rh-positive blood products to a Rh-negative woman of childbearing age may induce alloimmunization that may cause hemolytic reactions to subsequent transfusions or, more concerning, risks inducing hemolytic disease of the fetus and newborn in subsequent pregnancies. However, most MTPs utilize Rh-positive blood products as most blood donor centers use male donors to reduce the risk of transfusion-related acute lung injury. Current studies have shown that the risk of a woman developing alloimmunization, surviving hemorrhagic shock, producing anti-Rh antibodies, and subsequently getting pregnant with an Rh-positive fetus is exceedingly low and the benefits of Rh-positive transfusion far outweigh the risks. A recent survey among female respondents suggests that most would accept

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lifesaving transfusion of Rh-positive blood products even with the potential low risk of future fetal harm.[50] The overall risk of alloimmunization for Rh-negative female patients in hemorrhagic shock exposed to Rh-positive blood is low varying from 3% to 20%.[51] As such, women of childbearing age in shock can receive Rh-positive blood, but conversion to Rh-negative blood should be undertaken once available. Current practices in obstetrics have introduced LTOWB as part of their transfusion strategies. Furthermore, Rh-immunoglobulin (Rhogam) should be administered to Rh-negative women, when feasible, if Rh-positive blood is utilized.

Although the classic principle in the management of bleeding is prompt resuscitation with blood products and definitive hemorrhage control, patients may present to facilities without blood component availability or surgical expertise. In this setting, recent literature recommends the use of low-dose vasopressin to counteract the refractory vasodilatation during transfer to definitive care.[52] It has been proposed that the use of vasopressin during acute resuscitation decreases blood product requirements and the risk of developing deep venous thrombosis.[53] It has been shown that supplementing exogenous vasopressin during resuscitation improves blood pressure, preserves renal mitochondrial function, and mitigates acute kidney injury.[54] Norepinephrine and phenylephrine use at this early stage of resuscitation has not been proven to be of benefit and is related to detrimental outcomes.[55] For institutions with no blood products available, we currently recommend the use of vasopressin and the judicious limited use of crystalloid fluid for resuscitation in patients in hemorrhagic shock awaiting transfer to an established trauma center.

Resuscitation Goals

As previously mentioned, blood pressure goals differ based on the presence or absence of a TBI. In patients with known or suspected TBI, maintaining SBP ≥ 100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 years or older than 70 years should be the goal for decreasing mortality and improving outcomes.[56] The goal is to prevent a secondary brain injury by maintaining an adequate cerebral perfusion pressure, which has been shown to have beneficial effects on the penumbra.[56,57] Several recent studies have demonstrated that whole blood transfusion was associated with decreased overall mortality, as well as TBI-related mortality among patients with concomitant hemorrhagic shock and TBI.[58–60] While vasopressors, specifically norepinephrine, have historically been used to maintain CPP, their use should be limited in the initial resuscitation phase and not be used until adequate volume repletion has been achieved. If TBI is not suspected, permissive hypotension (SBP ~ 90 mm Hg) should be attempted. A useful adjunct to assessing resuscitation goals is the serial measurement of either lactate or BD. Although both measurements are a gauge of end-organ perfusion, they can be affected by other metabolic and physiologic factors, such as acute drug/alcohol intoxication, underlying hepatic disease, and chronic renal failure. As such, lactate or BD trends should be followed as an indicator of adequate resuscitation, rather than relying on a single measurement.

Hypothermia should be monitored and treated throughout the resuscitative efforts as profound hypothermia has been shown to affect hemodynamics, as well as the clotting cascade. Active warming may be achieved via warm IV fluids, warm humidified ventilator circuitry, and passive warming of the environment.

Transition to Targeted Therapy

If the patient is a responder to resuscitative measures, consider performing adjunct imaging studies to further identify the injuries and the source of hemorrhage, if still unknown. If there are radiographic signs of ongoing hemorrhage or injuries requiring surgical intervention, the patient should be promptly transported to the operating room. For nonresponders or transient-responders, those that demonstrate continued physiologic deterioration despite volume repletion, DCR utilizing the massive transfusion protocol should continue in conjunction with immediate transfer to the operating room or interventional radiology suite for definitive hemorrhage control. Once active bleeding control is achieved, the patient should be considered for transitioning from a massive transfusion protocol to a targeted resuscitation strategy based on hemodynamics and viscoelastic testing.[61]

CONCLUSION

Prompt and definitive hemorrhage control is the main goal in the management of the actively bleeding patient. Damage-control resuscitation is the current mainstay in improving survival in this group of patients. Whole blood and/or balanced component therapy resuscitation and TXA should be initiated in the prehospital setting and adjuncts, such as early administration of fibrinogen (cryoprecipitate) and calcium repletion, should be started immediately upon arrival to the trauma bay as part of the DCR. Strategies, such as hypotensive resuscitation, limited use of crystalloids, and DCS, should be utilized, if necessary, as part of the definitive management of the bleeding patient. Even as significant advances in resuscitative strategies have been developed over the last five decades, further investigations into the optimal management of hemorrhagic shock continues.

AUTHORSHIP

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