

Exsanguination Shock: The Next Frontier in Prevention of Battlefield Mortality

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Heretofore, those wounded in combat who arrived at a deployed medical treatment facility with signs of life and subsequently died have been designated as having died of wounds, with the vast majority classified as dying due to “hemorrhage” from nondescript hemorrhagic shock.^{1–4} In the future, the development and use of new technology may offer the greatest potential for decreasing mortality among these patients in the deployed setting. A subset of patients who pose a particularly vexing challenge to combat medics, emergency physicians, and surgeons are those who are severely hypotensive and/or pulseless on arrival, but who are able to be resuscitated to the point of clinical hemostasis and seemingly viable physiology only to eventually regress to cardiovascular collapse and death. These patients for all intent and purposes meet the definition of “exsanguination,”^{5,6} and to improve survival, their condition must be more fully described and better understood. The objective of this commentary is to re-introduce the term “exsanguination shock” and to provide a rudimentary characterization of this condition in combat casualty care.

Clinical Context

The injury illustrated in Figure 1 occurred in 2010 following detonation of an explosive device. The injuries included a traumatic right above-the-knee amputation with complex femoral, inguinal, and pelvic wounds as well as a traumatic left below-the-knee amputation. In addition, there was a grade IV spleen injury with hemoperitoneum. There were no chest, neck, or head wounds in this case. The soldier arrived 42 minutes after injury with tourniquets in place

having been applied to both lower extremities during tactical combat casualty care. In addition, a topical hemostatic agent (combat gauze [Combat Medical Systems, Fayetteville, NC]) had been applied in the field to the right inguinal region with manual pressure maintained during casualty evacuation. Despite hemorrhage control maneuvers and rapid evacuation, on admission to the combat casualty care facility the injured individual had a temperature 36.1°C, hemoglobin of 6.2 g/dL, and a pH of 6.91. The left femoral pulse was weakly palpable and this patient went directly to the operating room; after a FAST examination revealed hemoperitoneum, a laparotomy with splenectomy was performed. Despite aggressive resuscitation (16 units packed red blood cells, 14 units of plasma, and 13 units of platelets), surgical hemostasis, and apparent physiologic improvement, cardiovascular collapse and death ensued on the operating room table. This patient died as a result of near exsanguination but died with adequate circulating blood volume and indicators of improving physiology.

The death in this scenario highlights a clinical course of demise which, while not new to trauma surgery, warrants a reappraisal given the burden of injury following nearly 10 years of war in Iraq and Afghanistan. During this time, the US Military has made strides in reducing the death rate from combat wounds⁷ through a combination of improvements in protective equipment and dedication to data-driven process improvement with an aim to optimize all aspects of combat casualty care.^{8,9} Together, these advances, as well as rapid medical evacuation and positioning of forward surgical capability, have resulted in relatively high numbers of high-acuity patients reaching military surgeons soon after the time of injury.

Although gains have been made, additional room for improvement remains. To help direct these efforts, studies of those killed in combat have been completed; and they consistently identify hemorrhage as the leading cause of potentially survivable death on the battlefield.^{2,3} Efforts to address these deaths due to hemorrhage continue with research to optimize the use of blood products for resuscitation. In addition, efforts are underway to improve prehospital resuscitation, apply mechanical hemostasis to sites of groin and axial hemorrhage, and to further accelerate evacuation of patients and improve interventions during evacuation.^{10–12} In aggregate, these advances have the potential to increase the number of casualties arriving to surgical treatment facilities with severe hemorrhage able to be initially resuscitated but at high risk for clinical demise similar to the previous case

Submitted for publication March 30, 2011.

Accepted for publication April 22, 2011.

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DOI: 10.1097/TA.0b013e3182211286

Report Documentation Page

Form Approved
OMB No. 0704-0188

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1. REPORT DATE 01 JUL 2011		2. REPORT TYPE N/A		3. DATES COVERED -	
4. TITLE AND SUBTITLE Exsanguination shock: the next frontier in prevention of battlefield mortality				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Blackbourne L. H., Baer D. G., Cestero, R. F., Inaba K., Rasmussen T. E.,				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX				8. PERFORMING ORGANIZATION REPORT NUMBER	
				10. SPONSOR/MONITOR'S ACRONYM(S)	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 3	19a. NAME OF RESPONSIBLE PERSON
a REPORT unclassified	b ABSTRACT unclassified	c THIS PAGE unclassified			

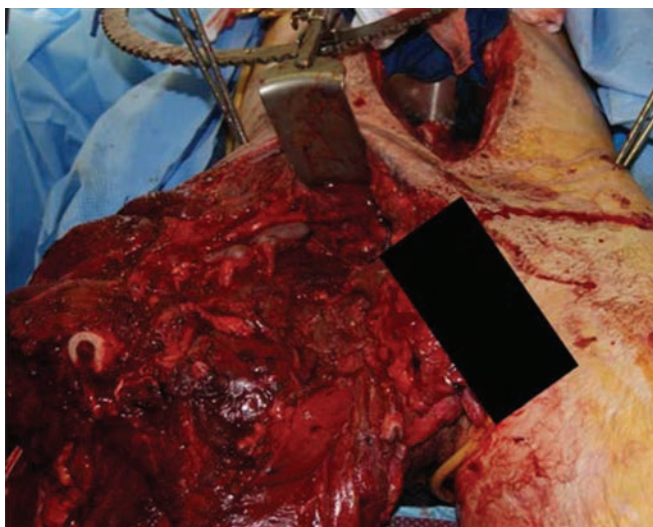


Figure 1. This patient died as a result of near exsanguination but expired with adequate circulating blood volume and indicators of improving physiology.

scenario. Although these cases are similar to the infrequent patient requiring resuscitative thoracotomy in civilian trauma centers, the relatively high volume of these patients at deployed combat medical facilities has brought this clinical problem to the forefront.

Patients who enter the medical evacuation chain with at least signs of life and hypovolemic cardiac arrest are the subject of a recent report by Edens et al.¹³ investigating outcomes after emergency thoracotomy at combat support hospitals. Of the 101 patients described in this report, 34% died either in the operating room or in the intensive care unit, indicating that they survived long enough to receive resuscitative care. Undoubtedly, in some cases surgical hemostasis was never obtained; however, for others, bleeding was controlled and patients still died despite the use of modern balanced transfusion and resuscitation practices. In fact, non-survivors received an average of over 13 units of red blood cells and 5 units of plasma, perhaps indicative of the phenomenon of “exsanguination shock.” Data from a review by Eastridge et al. in this publication indicates that the population in whom resuscitation ultimately fails may be significant, as more than 50% of those classified as died of wounds received cardiopulmonary resuscitation during evacuation or at admission to a surgical facility.

The physiologic derangement that leads to death in patients in whom surgical hemostasis has been obtained and blood volume restored is not known. The lethal mechanism may be the result of a process put in place by the primary insult itself (i.e., exsanguination and ischemia) or it may be related to restoration of blood volume and oxygen carrying capacity (i.e., reperfusion). Evidence from the animal literature suggests that the failure of one or more vital organs, such as the heart, lungs, or small intestine, may be a root cause. In fact, in swine models of severe hemorrhage and tissue injury, studied by Sondeen and others in this issue, death in resuscitation failures is often precipitated by respiratory arrest, not

hypovolemia. Hypotheses regarding primary and secondary lesions abound and include the following:

- Oxygen debt that is not repaid rapidly enough.
- Inflammatory storm secondary to ischemia.
- Depletion of cellular metabolites (e.g., oxygen and adenosine triphosphate).
- Intracellular ion dysregulation.
- Coagulation system derangement (microthrombi, acute coagulopathy, and consumptive coagulopathy).
- Central nervous system/neuroendocrine system dysfunction.¹⁴
- Endothelium dysfunction.
- Cell membrane dysfunction.
- Vascular smooth muscle dysfunction.¹⁵
- Ischemia-reperfusion/free radical formation.¹⁶
- Capillary plugging by activated neutrophils.¹⁷
- Vasopressin deficiency.¹⁸

As with all complex problems, the underlying pathophysiology is likely multifactorial and interrelated and likely varies among individual patients. The list summarized above almost certainly fails to include items that will prove vital to impacting death from exsanguination shock. However, the summary suggests several potential therapeutic approaches, some of which are currently being explored. These approaches include improving our understanding of blood product use in trauma resuscitation, inflammatory modulation, development of asanguineous resuscitation fluids to meet metabolic demand, cytokine clearance, hypothermia, better assessment of the coagulation system and interactions of coagulation system and the inflammatory response, deployment of endothelial/cell membrane stabilizers, and various forms of organ support such as extracorporeal membrane oxygenation/continuous renal replacement therapy.^{19–23}

Given this population of patients who fail to resuscitate after trauma and hemorrhage, we have an unprecedented opportunity to refine practice with knowledge and new technologies. Although current efforts are focused on innovation in the prehospital arena to mitigate hemorrhage and improve resuscitation, improved interventions after surgical hemostasis will be required to make maximal impact on reducing these deaths in those suffering from extensive hemorrhage.

A more thorough understanding of the pathophysiology involved derived from relevant animal models and observational studies of trauma patients followed by hypothesis-driven research to evaluate interventions are clearly the path forward. Advances in this area will allow us to replace “irreversible shock” with “exsanguination shock” in the trauma lexicon.

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