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# Revisiting early postinjury mortality: Are they bleeding because they are dying or dying because they are bleeding? $^{ imes}$

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#### ABSTRACT

*Background*: Intense debate continues in the search of the optimal ratio of blood components to deliver preemptively in the critically injured patient anticipated to require a massive transfusion. A major challenge is distinguishing patients with refractory coagulopathy versus those with overwhelming injuries who will perish irrespective of blood component administration. The hypothesis of this clinical study is that a predominant number of early deaths from hemorrhage are irretrievable despite an aggressive transfusion policy.

Materials and methods: During the 7-y period ending in December 2009, there were 772 inhospital trauma deaths. Each of these deaths had been assigned a cause of death via concurrent review by the multidisciplinary hospital trauma quality improvement committee. Emergency department deaths and patients arriving from outside facilities were excluded from this study.

Results: Of the 382 patients (49.5% of total) who died secondary to acute blood loss, 84 (22.0%) survived beyond the ED; of these 84, 68 (81%) were male, mean age was 31 y, and 30 (36%) sustained blunt trauma. Cause of death was determined to be exsanguination in 63 (75%), coagulopathy in 13 (15%), metabolic failure in 5 (6%), and indeterminate in 3 patients (4%).

*Conclusion*: These data indicate that 75% of patients who succumb to postinjury acute blood loss are bleeding because they are dying rather than dying because they are bleeding. Conversely, only 13 (2%) of the hospital deaths were attributed to refractory coagulopathy. These critical facts need to be considered in designing studies to determine optimal massive transfusion protocols.

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#### 1. Introduction

Trauma continues to be the leading cause of death for those under the age of 45 y in the United States [1]. Hemorrhage requiring massive transfusion is recognized as the leading cause of preventable deaths in trauma patients [2]. A recent trial on hemoglobin-based oxygen carriers at our institution identified evidence of coagulopathy in nearly one-third of severely injured patients within 15 min of injury [3], consistent with previous reports [4,5]. While resuscitation with massive transfusion of red blood cell (RBC) products improves survival, it can also hasten the onset of the lethal triad of coagulopathy, hypothermia, and acidosis [6]. Consequently, there has been intense debate in the search for optimal ratios of blood components to deliver preemptively in the critically injured patient anticipated to require massive transfusion [7]. The primary focus has been on the ratio of fresh frozen plasma (FFP) to RBC, but recently has included platelets.

A major challenge in defining optimal component ratios is distinguishing patients with refractory coagulopathy *versus* those with overwhelming injuries who will perish irrespective of blood component administration. A recent report revealed that greater than 50% of patients receiving FFP for trauma did not have an identified coagulopathy [8]. Thus, the acute coagulopathy of trauma is not well delineated, and its prevalence in trauma patients remains unclear. We hypothesized that a predominant number of early deaths are due to uncontrollable hemorrhage, not coagulopathy, and are irretrievable despite an aggressive transfusion policy.

#### 2. Methods

All in-hospital trauma deaths at the Rocky Mountain Regional Trauma Center at Denver Health (DHMC) from 2002-2009 were reviewed. DHMC is a state-designated level I trauma center verified by the American College of Surgeons Committee on Trauma and the academic trauma center for the University of Colorado Denver. Our massive transfusion protocol (MTP) was established in 1981, when our studies indicated the optimal FFP-to-RBC ratio is 1:2 [9]. After an initial 4 units of RBC and 2 units of FFP, additional blood component administration is guided by laboratory testing. In 2003 we adopted thromboelastography for this purpose. The data collection and storage processes were in compliance with the Health Insurance Portability and Accountability Act and approved by our institutional review board (COMIRB Protocol 10-0477). During the 7-y period ending in December 2009, there were 772 in-hospital traumatic deaths. Patient data were compiled in Excel spreadsheet format and categorized into groups based on injury type and location of death. All patients with major central nervous system ("Head/Neck" injury severity score [ISS] of 5 with no other ISS >3) injuries were excluded, as were patients that expired in the emergency department (ED) within 30 min of arrival or who came to Denver Health via transfer from an outreach facility. Other exclusions included cirrhotic patients and those who died of multiple organ failure or burn injuries. The remaining patients' records were then examined to determine the cause

of death. Information was taken from the electronic records system including the trauma history and physical, operative report, anesthesia operative records, and coroner's report. Patients with a hemorrhagic cause of death were identified, and the hospital multidisciplinary trauma quality improvement committee (three trauma surgeons, one neurosurgeon, and one orthopedic surgeon) reviewed these deaths to determine whether the cause of death was exsanguination or coagulopathy. The committee definition of exsanguination included all deaths in the operating room (OR) due to uncontrollable hemorrhage.

The ISS is derived from the Trauma Registry, calculated at the time of patient discharge by a trauma coordinator. The international normalized ratio (INR), activated partial thromboplastin time, and base deficit (BD) were performed in our central laboratory. The data are reported as mean  $\pm$  SEM. Transfusion data were derived from the previously mentioned electronic records as well as blood bank records.

#### 3. Results

During the study period, 772 patient deaths at DHMC were attributed to injury. A total of 382 patients (49.5%) died of hemorrhage, and, of these, only 84 (22.0%) survived beyond the ED. It is these patients, who survived beyond the ED while eventually succumbing to acute blood loss, that were the focus of this review. Of the 84 patients studied, 67 patients died in the OR, 16 in the ICU, and 1 in interventional radiology, as shown in Fig. 1. Sixty-eight (81%) were male, mean age was 31 y, and 30 (36%) sustained blunt trauma. Cause of death was determined to be exsanguination in 63 patients (75%), coagulopathy in 13 (15%), metabolic failure in 5 (6%), and indeterminate in 3 patients (4%), as shown in Fig. 2. The patients who died of metabolic failure and whose deaths were indeterminate are described here and not in the remainder of the results section.

Hemorrhagic deaths attributed to acute blood loss were stratified by time until death from arrival to the ED, as shown in Fig. 3. Early deaths were virtually always due to exsanguination. Deaths resulting from refractory coagulopathy occurred later, with peaks at 4 and 8 h after arrival.



Fig. 1 – Location of death due to acute blood loss from 2003–2009. Of the 84 patients in the study, 67 patients died in the OR, 16 in the ICU, and 1 in interventional radiology.

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