Improvements in Early Mortality and Coagulopathy are Sustained Better in Patients With Blunt Trauma After Institution of a Massive Transfusion Protocol in a Civilian Level I Trauma Center

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Introduction: Transfusion practices across the country are changing with aggressive use of plasma (fresh-frozen plasma [FFP]) and platelets during massive transfusion with current military recommendations to use component therapy at a 1:1:1 ratio of packed red blood cells to FFP to platelets.

Methods: A massive transfusion protocol (MTP) was designed to achieve a packed red blood cell:FFP:platelet ratio of 1:1:1. We prospectively gathered demographic, transfusion, and patient outcome data during the first year of the MTP and compared this with a similar cohort of injured patients (pre-MTP) receiving ≥10 red blood cell (RBC) in the first 24 hours of hospitalization before instituting the MTP.

Results: One hundred sixteen MTP activations occurred. Twelve non-trauma patients and 31 who did not receive 10 RBC (15 deaths, 16 early bleeding controls) were excluded. Seventy-three MTP patients were compared with 84 patients with pre-MTP who had similar demographics and injury severity score (29 vs. 29, p = 0.99). MTP patients received an average of 23.7 RBC and 15.6 FFP transfusions compared with 22.8 RBC (p = 0.67) and 7.6 FFP (p < 0.001) transfusions in pre-MTP patients. Early crystalloid usage dropped from 9.4 L (pre-MTP) to 6.9 L (MTP) (p = 0.006). Overall patient mortality was markedly improved at 24 hours, from 36% in the pre-MTP group to 17% in the MTP group (p = 0.008) and at 30 days (34% mortality MTP group vs. 55% mortality in pre-MTP group, p = 0.04). Blunt trauma survival improvements were more marked and more sustained than victims of penetrating trauma. Early deaths from coagulopathic bleeding occurred in 4 of 13 patients in the MTP group vs. 21 of 31 patients in the pre-MTP group (p = 0.023).

Conclusions: In the civilian setting, aggressive use of FFP and platelets drastically reduces 24-hour mortality and early coagulopathy in patients with trauma. Reduction in 30 day mortality was only seen after blunt trauma in this small subset.

Key Words: Massive transfusion, Protocol, Component therapy, Mortality, Coagulopathy after trauma.


Exsanguination is a leading cause of mortality after severe trauma, second only to central nervous system injury. Although effective therapy for significant traumatic brain injury remains elusive, impacting mortality after hemorrhagic shock is an area under intense investigation. In the early 1990s, abbreviated laparotomy was popularized and the term “damage control surgery” became part of mainstream surgical thought process. Indeed, the main component of the “bloody vicious cycle” is trauma-induced coagulopathy. Classically, this coagulopathy was felt to be related to hypothermia, acidosis, and dilution, and although these factors play a large role in many patients, recent studies have documented that a significant minority of patients arrive to the trauma center coagulopathic before the institution of any form of therapy. In these patients, the civilian practice of transfusion of packed red blood cells (PRBCs) without adequate repletion of clotting factors is likely inadequate.

A multitude of studies have been published by the US military based on their experience in recent conflicts. They espouse the use of whole blood, or in its absence, aggressive repletion of clotting factors in the form of fresh-frozen plasma (FFP), cryoprecipitate and platelets in patients who require massive transfusion. Indeed, recent military recommendations for component therapy include attempts to maintain a transfusion ratio of units of PRBC to units of FFP to units of platelets of 1:1:1. This practice is part of a philosophy of “damage control resuscitation,” which also consists of permissive hypotension, minimization of crystalloid resuscitation, control of hypothermia, and prevention of acidosis.
In civilian centers, where whole blood is unavailable and aggressive component therapy is resource intensive, implementing these transfusion ratios is difficult outside of a well-designed protocol. Surprisingly, a recent review of the world’s experience with massive transfusion led to the discovery of fewer than 10 such protocols in use around the world. As a busy, urban level I trauma center, we are often presented with one and, not infrequently, more than one patient who is exsanguinating. Because of difficulties involved with rapidly obtaining FFP and recombinant factor VIIa (rFVIIa), our group led a multidisciplinary effort to create a massive transfusion protocol (MTP), which was instituted on February 1, 2007. We hypothesized that the institution of such a protocol would lead to improvements in patient physiology and overall outcome after massive transfusion in our center.

**PATIENTS AND METHODS**

A prospective study of patients with trauma requiring massive transfusion was undertaken. Massive transfusion was defined as transfusion of \( \geq 10 \) units of PRBCs in any 24-hour period during their hospital stay. Although the protocol was designed to be used by all services across the institution, non-trauma patients were excluded from this data set. The study took place at Grady Memorial hospital, a state of Georgia, urban level I trauma center and was approved by the institutional review board of Emory University.

Patients were cared for by a group of nine general and trauma surgeons, all double boarded in surgery and surgical critical care. No faculty turnover occurred during the two time frames studied (historic controls, prospective trial) and, outside of the institution of the MTP, resuscitation philosophies remained constant. However, aside from this protocol, resuscitation was not based on a specific algorithm and a variety of endpoints of resuscitation were used based on the clinical scenario and attending surgeon discretion. The general practice pattern of our group is to use serial base deficit measurements, obtained from arterial blood gases, in the initial resuscitation phase, with other markers, such as lactate measurements, obtained from arterial blood gases, in the clinical scenario and attending surgeon discretion.

The protocol dictates performing coagulation parameters, obtained from arterial blood gases, in the initial resuscitation phase, with other markers, such as lactate level and invasive measurements of preload, used once the initial resuscitation is complete. Although the protocol, as described later, dictated transfusion ratios during the initial hemorrhagic insult in the prospective aspect of the trial, no specific hemoglobin concentration was used as a transfusion trigger, in either the historic or prospective aspect of the trial, once the initial hemorrhage was controlled and the protocol was terminated.

**Protocol Development**

In the fall of 2006, a multidisciplinary group of physicians, led by trauma surgeons, convened and, over a series of face to face meetings, designed a MTP. This protocol was based heavily on military recommendations, with some modifications based on local resources. Clinical areas included in the work group included: departments of trauma/general surgery, emergency medicine, pathology and laboratory medicine, anesthesiology, pulmonology/medical intensive care, emergency department nursing, intensive care unit (ICU) nursing, blood bank management, laboratory services, and operating room services. Every effort was made to be inclusive in the design of the protocol, with the end result approved by the Grady Health System Medical Executive Committee. To guarantee blood product availability, the blood bank redesigned their blood release forms, updated their computer software as well as purchased and installed two additional component thawers. In addition, thorough in-services were performed across departments by the trauma surgeons (operating room personnel, ICU, and emergency department nursing), anesthesiology (anesthesia personnel), and the blood bank medical director (hospital-wide nursing, laboratory services, blood bank personnel).

**Protocol Design**

In brief, the protocol is designed to ensure immediate availability of aggressive and early component therapy and is activated with a phone call to the blood bank. Activation of the protocol is restricted to an attending or fellow from surgery, anesthesia, emergency medicine, or critical care. Efforts are made by clinical personnel to obtain and deliver a sample of the patient’s blood to the blood bank for blood typing. The blood bank responds to the call for protocol activation by immediately placing six units of group O or type-specific PRBC and six units of group AB FFP in a cooler as the “initiation package.” For this purpose, the blood bank maintains an adequate inventory of thawed plasma products for immediate distribution. Blood bank then continues to prepare predesignated “packages” of components to be picked up every 30 minutes with a goal ratio of PRBC:FFP: platelets of 1:1:1 (Table 1). The blood bank continues to issue group O PRBC, but will issue ABO type compatible FFP once the patient’s blood type is known, because of limited group AB plasma inventory. If requested, the blood bank is able to “double up” the protocol to allow for 12 units of PRBC and 12 units of FFP to be delivered every 30 minutes. In addition, if bleeding is uncontrolled, the clinical service can request a 3.6 mg dose of rFVIIa after package 2 (e.g., 18 units of PRBCs) with an identical second dose, if needed, distributed 30 minutes later.

The charge nurse in the area of resuscitation is responsible to designate a “runner,” whose job it is to arrive at the blood bank immediately and every 30 minutes to pick up the cooler, return used coolers, and deliver blood products to the patient area. In addition to hemorrhage control, the attending physician in charge of the resuscitation is responsible for the decision to start and stop the protocol as well as for the decision to use rFVIIa.

The protocol dictates performing coagulation parameters and blood gases at least every other hour to monitor response to therapy. The blood bank medical director, through the transfusion committee of the hospital, reviews the MTP qual-
Protocol Implementation

The hospital-wide protocol was instituted on February 1, 2007 after approval by the medical executive committee and after all in-training was accomplished. This implementation required several modifications to our routine blood bank practices and an extensive effort by our blood bank medical director to implement significant changes within the blood bank to meet the demands of the MTP. This protocol would be difficult, if not impossible, to run in a smaller blood bank with fewer resources. Fortunately, the plasma usage in our busy level I trauma center allows for routine storage of six units of thawed plasma with minimal wastage. This is clearly not feasible in all civilian centers.

Despite the in-service training, the first several weeks had several protocol failures with relatively high PRBC:FFP ratios, and this prompted a second round of in-services. Thereafter, the protocol ran smoothly and effectively, with occasional protocol violations related to shortages or unavailability of components, most notably platelets. A second cluster of protocol violations occurred in the month of July, likely related to a large amount of personnel turnover. Routine in-services in July, as well as with any protocol modifications, are now planned institution wide.

During the first 12 months of the protocol, 116 MTP activations occurred. Non-trauma patients accounted for 12 activations (10%) and 31 patients did not receive 10 units of PRBCs in the first 24 hours. This included 15 patients (13%) who died before 10 units being transfused and 16 patients (14%) who had bleeding controlled before requiring 10 transfusions. These 43 patients were excluded leaving 73 patients in the study group.

Table 1 Massive Transfusion Protocol: Package Contents*

<table>
<thead>
<tr>
<th>Package</th>
<th>PRBCs</th>
<th>Plasma</th>
<th>Platelets</th>
<th>Cryoprecipitate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation</td>
<td>6 units (UD/TS)</td>
<td>6 units (UD)</td>
<td>1 apheresis**</td>
<td>20 units</td>
</tr>
<tr>
<td>1 (0.5 h)</td>
<td>6 units (UD/TS)</td>
<td>6 units (UD)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
</tr>
<tr>
<td>2 (1 h)</td>
<td>6 units (UD/TS)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
<td>10 units</td>
</tr>
<tr>
<td>3 (1.5 h) $</td>
<td>6 units (UD/TS)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
<td>10 units</td>
</tr>
<tr>
<td>4 (2 h)</td>
<td>6 units (UD/TS)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
<td>10 units</td>
</tr>
<tr>
<td>5 (2.5 h)</td>
<td>6 units (UD/TS)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
<td>10 units</td>
</tr>
<tr>
<td>6 (3 h) $$</td>
<td>6 units (UD/TS)</td>
<td>6 units (TS)</td>
<td>1 apheresis**</td>
<td>20 units</td>
</tr>
</tbody>
</table>

PRBCs = Packed Red Blood Cells; UD = Universal Donor; TS = Type-Specific.
* PRBCs and Plasma can be doubled to 12 units each per cycle by request.
** 1 apheresis unit of platelets considered to equal 8–10 standard units.
$ Recombinant Factor VIII may be used at attending physician discretion (Dose: 3.6 mg, one repeat dose as needed in 30 min).
$$ If protocol still active, alternate packages identical to packages 5 and 6 until protocol terminated.

Data Collection

Clinical and blood bank data on all MTPs were collected prospectively from February 1, 2007 to January 31, 2008. Data collected are listed in Table 2.

A comparative group was created by querying the trauma registry and identifying all patients in the 2 years before the institution of the protocol (February 1, 2005–January 31, 2007) who received ≥10 units of PRBC in the first 24 hours of their hospital stay and retrospectively, through intensive chart review and review of blood banking records, recording the same data points above. The prospective and comparative groups were well matched in terms of age (35 years vs. 37 years, \( p = 0.42 \)), gender (84% vs. 82% male, \( p = 0.81 \)), percentage blunt trauma (60% vs. 58%, \( p = 0.71 \)), Injury Severity Score (ISS) (29 vs. 29, \( p = 0.99 \)) and initial base deficit (−13.6 vs. −12.8, \( p = 0.54 \)).

Statistical Analysis

Statistical analysis was performed using SPSS software (SPSS, Chicago, IL). Continuous data are presented as means ± standard error of the mean, and categorical data are presented as proportions. Comparisons between groups for continuous data were done using Student’s \( t \) test, and comparisons for categorical data were performed using \( \chi^2 \) analysis. Significance was set at \( p \leq 0.05 \).

RESULTS

Demographics and Overall Outcome

Between February 1, 2007 and January 31, 2008, 116 MTP activations occurred. Forty three (37%) previously described patients were excluded with 73 (63%) patients serving as the study group. Demographic information for the remaining 73 patients is included as Table 3. No patient had any documented pre-existing use of anticoagulants in this group.

As evidenced by the high mean ISS score, this was a critically injured population. Overall mortality was 17.6% at 24 hours and 38.4% at 30 days and at hospital discharge. Mean hospital length of stay was 25.5 ± 2.9 days with mean...
Plasma, Platelets, Cyroprecipitate). No whole blood was used.

Hospital stay were quantified (Packed Red Blood Cells, Fresh Frozen activated Partial Thromboplastin Time. Prothrombin Time; INR International Naturalized Ratio; ICU Intensive Care Unit.

In the penetrating trauma group, 15 patients (51%) had a single major source of hemorrhage and 14 patients were deemed to have multiple sources, including 2 patients who had abbreviated injury scale grade 4 injuries in both their thoracic and peritoneal cavities. Twenty-four-hour mortality in the single source group was 20%, with all three deaths requiring resuscitative thoracostomies during the initial resuscitation. The highest 24-hour mortality was seen in the patients with multiple sources of hemorrhage after penetrating trauma with a 24-hour mortality rate of 29% (4 of 14 patients). All four early deaths sustained an abdominal vascular injury in combination with a severe solid organ injury.

Table 2 Data Collected

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Outcome data</th>
<th>Laboratory data</th>
<th>Transfusion data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>24 Hour mortality</td>
<td>Emergency department</td>
<td>1st 6 h</td>
</tr>
<tr>
<td>Gender</td>
<td>30 Day mortality</td>
<td>Blood counts (hemoglobin, hematocrit)</td>
<td>1st 24 h</td>
</tr>
<tr>
<td>History of anticoagulant use</td>
<td>Hospital mortality</td>
<td>Platelet counts</td>
<td>Hospital stay</td>
</tr>
<tr>
<td>Mechanism of injury</td>
<td>Hospital length of stay</td>
<td>Coagulation parameters (PT, INR, aPTT)</td>
<td></td>
</tr>
<tr>
<td>Anatomic injury, type and severity</td>
<td>ICU length of stay</td>
<td>Fibrinogen level</td>
<td></td>
</tr>
<tr>
<td>Injury severity score</td>
<td>Ventilator days</td>
<td>ICU admission</td>
<td></td>
</tr>
<tr>
<td>Vital signs on admission</td>
<td></td>
<td>Blood counts (hemoglobin, hematocrit)</td>
<td></td>
</tr>
<tr>
<td>Initial base deficit</td>
<td></td>
<td>Platelet counts</td>
<td></td>
</tr>
<tr>
<td>Time to and length of 1st operation</td>
<td></td>
<td>Coagulation parameters (PT, INR, aPTT)</td>
<td></td>
</tr>
<tr>
<td>Use of damage control procedure</td>
<td></td>
<td>Fibrinogen level</td>
<td></td>
</tr>
<tr>
<td>Crystalloid infusion, 1st 6 and 1st 24 h</td>
<td></td>
<td>ICU admission</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Demographics and Overall Outcome

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35 ± 1.6 yr</td>
</tr>
<tr>
<td>Gender</td>
<td>84% Male</td>
</tr>
<tr>
<td>Mechanism of injury</td>
<td>35 MVC</td>
</tr>
<tr>
<td>ISS</td>
<td>29 ± 1.4</td>
</tr>
<tr>
<td>Initial base deficit</td>
<td>−13.5 ± 0.87</td>
</tr>
<tr>
<td>24 Hour mortality</td>
<td>17.6%</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>38.4%</td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>25.5 ± 2.9 d</td>
</tr>
<tr>
<td>ICU length of stay</td>
<td>16.4 ± 1.8 d</td>
</tr>
<tr>
<td>Ventilator days</td>
<td>12.7 ± 1.4 d</td>
</tr>
</tbody>
</table>

SEM = Standard Error of the Mean; MVC = Motor Vehicle Collision; GSW = Gunshot Wound; SW = Stab Wound; ISS = Injury Severity Score; ICU = Intensive Care Unit.

In the penetrating trauma group, 15 patients (51%) had a single major source of hemorrhage and 14 patients were deemed to have multiple sources, including 2 patients who had abbreviated injury scale grade 4 injuries in both their thoracic and peritoneal cavities. Twenty-four-hour mortality in the single source group was 20%, with all three deaths requiring resuscitative thoracostomies during the initial resuscitation. The highest 24-hour mortality was seen in the patients with multiple sources of hemorrhage after penetrating trauma with a 24-hour mortality rate of 29% (4 of 14 patients). All four early deaths sustained an abdominal vascular injury in combination with a severe solid organ injury.

Protocol Results

The average PRBC:FFP ratio in the 73 patients was 1.9:1, and the average PRBC:platelet ratio was 1.48:1. Twenty-three patients had either a PRBC:FFP or PRBC:platelet ratio higher than 2:1 and were considered protocol failures. Of these patients, 12 had a PRBC:FFP ratio greater than 3:1 and 12 patients had a PRBC:platelet ratio greater than 3:1. Most protocol failures occurred in the first month of the protocol, during the month of July, or were related to hospital shortages in platelets. There was no difference in any demographic information, no difference in ISSs, and no difference in overall outcomes between protocol successes and failures.

Patients whose PRBC:FFP transfusion ratio was between 2:1 and 3:1 had very similar early outcomes when compared with patients whose ratio was between 1:1 and 2:1, with a early mortality rate of 19% in the former group compared with 14% in the latter (p = 0.64). Late mortality (30 days and hospital stay) was also similar between these two groups (31% vs. 36%, p = 0.74). The small number of patients in whom the PRBC:FFP transfusion ratio was >3:1 had a much worse early outcome with an early mortality of 57% (4 of 7 patients, p < 0.001). Late mortality was also worse in the
patients with ratios greater than 3:1 (57% vs. 36%), but this did not reach statistical significance (p = 0.24).

Data for patients whose PRBC:platelet transfusion ratio was >2:1 mirrored that of patients who failed for high PRBC:FFP ratios. Early mortality was highest in the 12 patients whose PRBC:platelet ratio was >3:1 (50% vs. 11%, p = 0.001). Early mortality was similar in patients whose PRBC: platelet transfusion ratio was between 1:1 and 2:1 and those who ratio was between 2:1 and 3:1 (10% and 18%, p = 0.89). Late mortality trended higher in patients with a ratio >3:1 (50% vs. 34%), but this did not reach statistical significance. This data are summarized in Table 4.

### Comparative Analyses

The 73 patients resuscitated with the MTP were compared with 84 historic controls (pre-MTP) who received ≥10 units of PRBCs in the first 24 hours of their hospital stay treated between February 1, 2005 and January 31, 2007. As previously stated, there was no difference in any demographic information or injury severity between the two groups.

### Effect of Protocol on Transfusion Practices and Crystalloid Usage

Patients undergoing transfusion via the MTP had significantly more aggressive early component therapy in the form of increases in FFP, platelet, and cryoprecipitate infusion (Fig. 1, A–C). In the first 6 hours, MTP patients received significantly more FFP (13.7 units vs. 5.5 units), significantly more platelets (14.1 units vs. 9.2 units), and significantly more cryoprecipitate (11.6 units vs. 7.6 units) than pre-MTP patients, despite having similar initial PRBC transfusions (22 units vs. 19.4 units). Patients in the MTP group also required, on average, only 1.7 additional PRBC units between 6 hours and 24 hours after injury compared with 3.4 additional PRBC units during this time period in pre-MTP patients. After 24 hours, MTP patients required a mean of 2.7 units of PRBC versus pre-MTP patients who required a mean of 9.3 units of PRBC (p < 0.0001).

Total hospital PRBC transfusions was not significantly different between groups, although pre-MTP patients required, on average, nearly three more units of PRBC per patient, despite having a lower overall survival (see below). Total hospital FFP transfusion was higher in the MTP patients (18 units vs. 12 units), although total hospital platelet and cryoprecipitate transfusions were similar between groups.

Crystalloid usage in the first 6 hours was significantly less in the MTP group than the pre-MTP group by a mean of 2.3 L (6.9 ± 0.5 L vs. 9.2 ± 0.6 L, p = 0.006). The usage of rFVIIa was unchanged in the two time periods (15% vs. 14.8% of patients) with a 45% mortality rate in the MTP group and a 50% mortality rate in the pre-MTP group.

### Outcomes: Coagulation Parameters and Laboratory Values

Coagulation parameters were measured at three time points: arrival to the emergency department, arrival to the ICU, and 24 hours after arrival to the ICU. Despite having similar emergency department values, MTP patients had significantly lower prothrombin time (PT) and international normalized ratio values (15.1 ± 0.26 and 1.31 ± 0.29 vs. 17.5 ± 1.1 and 1.72 ± 0.17, respectively, p values: 0.04, 0.04) on arrival to the ICU than did pre-MTP patients. Similarly, fibrinogen levels were significantly higher in MTP patients compared with pre-MTP patients (324 ± 19 vs. 255 ± 19, p = 0.01). Although partial thromboplastin time (PTT) values were similar on arrival to

### Table 4 Mortality and Transfusion Ratios

<table>
<thead>
<tr>
<th>PRBC: FFP ratio</th>
<th>1:1–2:1</th>
<th>2:1–3:1</th>
<th>&gt;3:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h mortality</td>
<td>14%</td>
<td>19%</td>
<td>57%*</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>31%</td>
<td>36%</td>
<td>57%</td>
</tr>
</tbody>
</table>

PRBC: Platelet Ratio = Packed Red Blood Cell to Platelet Ratio.
* P < 0.001 vs. Transfusion Ratio < 3:1.
In the ICU, they were significantly lower in MTP patients at 24 hours (32.2 ± 1.3 vs. 48.8 ± 7.7, \( p = 0.04 \)) than in pre-MTP patients. Comparative results are summarized in Figure 2, A–C.

**Outcomes: Mortality**

Overall mortality at 24 hours was markedly decreased in the MTP group over the pre-MTP group (17% vs. 36%, \( p = 0.008 \)) (Fig. 3A). This was especially true for victims of blunt trauma, with 24-hour mortality noted to be 14% (6 of 44) in these patients. Survival to discharge in patients with blunt trauma was also significantly better in the MTP group than in the pre-MTP group (66% vs. 45% survival, \( p = 0.042 \)) (Fig. 3B). Improved survival at 24 hours was also noted in the MTP group for victims of penetrating trauma, although this did not reach statistical significance (24% mortality, MTP vs. 34% mortality, pre-MTP, \( p = 0.38 \)). At 30 days, survival was similar in victims of penetrating trauma in the MTP and pre-MTP group (41% vs. 43% mortality, \( p = 0.91 \)) (Fig. 3C).

On detailed review of the operative notes, early deaths from coagulopathic bleeding occurred in 4 of 13 (31%) patients in the MTP group versus 21 of 31 (68%) patients in the pre-MTP group (\( p = 0.023 \)).

In blunt trauma, early deaths had similar demographics and injury severity with similar incidences of abdominal trauma, need for laparotomy, and transfusion requirement. They had similar transfusion ratios of PRBCs to FFP and platelets. Interestingly, patients who suffered early mortality had worse initial coagulation studies, with a significantly higher PT (20.1 ± 1.5 vs. 16.3 ± 0.6, \( p = 0.03 \)), higher international normalized ratio (1.93 ± 0.2 vs. 1.5 ± 0.1, \( p = 0.03 \)) and higher PTT (41.6 ± 6.7 vs. 35.6 ± 2.4, \( p = 0.05 \)). They also had a trend toward a lower initial fibrinogen level (52 ± 21 vs. 202 ± 15, \( p = 0.10 \)).

In penetrating trauma, early deaths also had similar demographics and injury severity and, in addition, had similar admission physiology, but because of small number of data points, we were unable to conduct a comparative analysis of laboratory data.

**DISCUSSION**

Massive transfusion, as defined by transfusion of 10 or more units of PRBCs in a 24-hour period, is needed in a small
subset of the most critically injured patients. Indeed, massive hemorrhage is the leading cause of death within 48 hours of traumatic injury.7 Component therapy, in the past, has focused on aggressive replacement of red cell mass, with less emphasis on early replacement of coagulation factors. The American Society of Anesthesiologists recommend, in general, component therapy to maintain a platelet count greater than 50,000 platelets/µL, maintenance of a PT less than 15 seconds and maintenance of a PTT less than 40 seconds.10

Classically, trauma-induced coagulopathy has been felt to be a delayed phenomenon, related to acidosis and dilution. However, there is now an increasing body of evidence, which indicates that the sickest patients may develop coagulopathy very early after injury, even before arrival at the receiving facility.11–13 In these patients, early aggressive replacement of clotting factors is likely warranted.

Based on recent clinical data, and a sophisticated computer model,14 the military has recommended a universal transfusion protocol, which would replace blood loss with component therapy at a ratio of 1:1:1 for PRBC, FFP, and platelets when whole blood was unavailable.7 Surprisingly, when searching for existing protocols in use in 2005, they could only document a handful in active use and noted that there are no medical institutional requirements for a MTP.7 The recommendations for aggressive component therapy lay at the heart of the “Damage Control Resuscitation” paradigm, which has been used very successfully in the recent Iraqi conflict.6,8,15–17

Our MTP was designed in accordance with this philosophy of aggressive component therapy, and, indeed, it dramatically altered our transfusion practices. Nearly triple the amount of FFP was given in the first 6 hours of resuscitation compared with pre-MTP patients. The amount of platelets and cryoprecipitate was also significantly increased. Although the amount of PRBC units given in the first 24 hours was not different between the two groups (23.7 units vs. 22.8 units), the mean number of PRBC transfusions given from 24 hours to hospital discharge was three times less in the MTP group (2.7 units vs. 9.3 units). This is nearly seven less PRBC units transfused per patient over their hospital course. It is noted that the MTP group received roughly six extra FFP transfusions per patient during the hospital course, and these extra transfusions were generally universal donor FFP. Because the shelf life of PRBC is significantly shorter than FFP (42 days vs. 12 months), it may be worthwhile to transfuse extra FFP in an effort to limit PRBC transfusion; however, it remains to be seen whether the savings of an equivalent number of crossmatched PRBC transfusions is worth the cost of using extra universal donor FFP.

The decreased need for late transfusions may be related to improvements in the coagulation cascade and significant decreases in postoperative anemia. Indeed, most every coagulation studies were significantly improved on arrival to the ICU in the MTP group, and although more FFP was given in the first 24 hours in the MTP group, the pre-MTP group required more FFP in the period between 24 hours after admission and hospital discharge. Moreover, early deaths from coagulopathic bleeding, which constituted over two thirds of the deaths in the pre-MTP group, dropped significantly after the institution of the MTP.

The proportion of patients receiving rFVIIa did not change with the MTP, occurring in about 15% in both groups. Theoretically, more aggressive replacement of fibrinogen and more efficient resuscitation should allow for rFVIIa to be more effective. Unfortunately, too few patients in this initial experience received this expensive medication to note a difference in transfusion requirement or outcome. Larger studies are needed to address this question.

Finally, the use of aggressive crystalloid administration in the early postinjury phase has been questioned in recent years.18–20 The MTP allowed us to significantly decrease the volume of crystalloid given in the early resuscitation phase. It may be that a decrease in the incidence of secondary abdominal and extremity compartment syndromes, and possibly also a decrease in the incidence of Acute Respiratory Distress Syndrome will follow. Again, further studies, with larger patient numbers, will be required to answer these questions.

The sustained improvement with mortality in patients with blunt trauma seen in our early experience with a MTP has not been previously documented. It is presumed that the majority of military patients treated with their MTPs have been victims of penetrating trauma. A recent study from Cotton et al.21 documented their early experience with a Trauma Exsanguination Protocol. They had marked improvements in overall survival in 94 patients who received transfusion via this protocol over historic controls and the use of the protocol was an independent predictor of survival at 30 days. They had a decrease in early crystalloid usage, and an overall decrease in total 24-hour blood product usage. Although they had nearly twice the proportion of penetrating patients in the protocol group (56% vs. 30%), a penetrating trauma mechanism was not an independent predictor of 30 day mortality in the multivariate model. In our series, the proportion of penetrating trauma was similar between MTP and pre-MTP groups (40% vs. 42%), and while a decrease in 24-hour mortality was noted, it was much more modest than in patients with blunt trauma, and unlike in the patients with blunt trauma, the mortality difference was not sustained to the point of discharge (Fig. 3). The reasons for this difference are not completely clear. Although it generally thought that patients with blunt trauma are more likely to have multiple potential sources for coagulopathic hemorrhage than penetrating trauma patients, who may have a single source of surgical bleeding that is more easily controlled definitively, this was not seen in our series. Indeed patients with blunt trauma were more likely to have a single significant source of hemorrhage than were penetrating trauma patients (61% vs. 51%). Despite this fact, patients with blunt trauma, with either a single source of multiple sources, had lower early mortality rates than their respective penetrating trauma
groups. It may also be the relatively small number of patients suffering penetrating trauma does not yet allow us to show a significant difference in mortality. Because of the small number of patients in each of the subgroups and because of the multiple confounding factors, a larger sample size will be needed to answer this question more definitively.

The 1:1:1 ratio espoused by the military was not achieved in the majority of patients in our series. There is still controversy over the optimal ratio for component therapy in a civilian trauma population. In a recent series, Gunter et al.\textsuperscript{22} from Vanderbilt described a survival advantage for civilian patients receiving a 2:3 FFP:PRBC ratio and a 1:5 platelet:PRBC ratio in a series of 259 trauma resuscitations, with no improvement seen in patients with more aggressive component therapy. This mirrored our experience with patients receiving ratios between 1:1 and 2:1 of PRBC to either FFP or platelets having similar early and late mortality to those who received ratios between 2:1 and 3:1. Only patients who received 3:1 ratios of PRBC to FFP or platelets had higher early mortality. It may be that a 1:1:1 ratio is not necessary in a civilian trauma population to improve survival in patients with evidence of early coagulopathy after trauma. Lower ratios, such as those espoused by the Vanderbilt group, may be adequate. Of course, our protocol, which is designed to provide a 1:1:1 ratio, achieved lower ratios in the majority of patients. It may be these more aggressive goals are necessary in protocol design, with the understanding that the true transfusion ratios will rarely meet the defined goals. Conversely, if a lower PRBC:FFP ratio would still allow for improved patient outcome and fewer total hospital PRBC transfusions, it may be that these lower ratios should be targeted. Until we have a larger experience and until more data are available, however, we have continued to target a 1:1:1 ratio in our MTP.

The three main limitations to this study include the relatively small sample size, the use of historic controls, and the relatively high-protocol failure rate. This data represent our initial experience with a complex, multidisciplinary protocol, and we felt that sharing some of the pitfalls and difficulties we experienced in the design and implementation of the MTP would be helpful to other institutions looking to design similar protocols. We were also impressed with the overall change in 24-hour mortality associated with the change in our transfusion practice, despite the relatively small numbers. Ongoing data collection will allow us to analyze outcomes in some of the subgroups and may allow for a more precise determination of the optimal component therapy ratio.

The use of historic controls, although not an ideal study design, seemed to be the best method of determining the effect of the MTP on our outcomes. Indeed, this protocol is the sole philosophic change in our group’s resuscitation practices over the last 5 years, and we have had no faculty turnover during either the historic or prospective aspects of the trial. We did not feel that randomizing patients to either aggressive component therapy by protocol or less aggressive therapy without a protocol was ethically justified.

Finally, as the institution has accrued experience with the MTP and as all the involved departments have sent the dramatic improvements in patient outcomes, protocol failures have become less common. Although the availability of platelets is an ongoing issue, we feel that more efficient early resuscitations will allow for an overall decrease in coagulopathic bleeding and a decrease in component use during the rest of the patients hospitalization. Besides further outcomes analysis, further directions for research should include efforts to further elucidate the mechanism of early coagulopathy after trauma and further defining factors that puts a patient at risk for requiring massive transfusion in an effort to improve efficiency in the use of this scarce resource.

In summary, we report the design and implementation of a MTP in a busy, urban civilian level I trauma center and we have documented not only significant improvements in survival, especially after blunt trauma, but also decreases in early crystalloid usage and improvements in coagulation parameters. In should be noted, however, that the protocol we adopted is likely not suitable for all institutions, as it requires significant blood banking personnel and equipment resources. Individualized MTPs should be adopted by centers routinely taking care of patients with trauma in an effort to improve the early resuscitations of these critically injured patients.

**REFERENCES**


