

Damage Control Hematology: The Impact of a Trauma Exsanguination Protocol on Survival and Blood Product Utilization

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Background: The importance of early and aggressive management of trauma-related coagulopathy remains poorly understood. We hypothesized that a trauma exsanguination protocol (TEP) that systematically provides specified numbers and types of blood components immediately upon initiation of resuscitation would improve survival and reduce overall blood product consumption among the most severely injured patients.

Methods: We recently implemented a TEP, which involves the immediate and continued release of blood products from the blood bank in a predefined ratio of 10 units of packed red blood cells (PRBC) to 4 units of fresh frozen plasma to 2 units of platelets. All TEP activations from Febru-

ary 1, 2006 to July 31, 2007 were retrospectively evaluated. A comparison cohort (pre-TEP) was selected from all trauma admissions between August 1, 2004 and January 31, 2006 that (1) underwent immediate surgery by the trauma team and (2) received greater than 10 units of PRBC in the first 24 hours. Multivariable analysis was performed to compare mortality and overall blood product consumption between the two groups.

Results: Two hundred eleven patients met inclusion criteria (117 pre-TEP, 94 TEP). Age, sex, and Injury Severity Score were similar between the groups, whereas physiologic severity (by weighted Revised Trauma Score) and predicted survival (by trauma-related Injury Sever-

ity Score, TRISS) were worse in the TEP group (p values of 0.037 and 0.028, respectively). After controlling for age, sex, mechanism of injury, TRISS and 24-hour blood product usage, there was a 74% reduction in the odds of mortality among patients in the TEP group ($p = 0.001$). Overall blood product consumption adjusted for age, sex, mechanism of injury, and TRISS was also significantly reduced in the TEP group ($p = 0.015$).

Conclusions: We have demonstrated that an exsanguination protocol, delivered in an aggressive and predefined manner, significantly reduces the odds of mortality as well as overall blood product consumption.

Key Words: Hemorrhage, Exsanguination, Trauma, Massive transfusion.

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The majority of deaths from trauma occur in the first few hours after injury, with hemorrhage accounting for the largest percentage of deaths within the first hour of arrival at a trauma center.¹⁻³ Hemorrhagic shock and exsanguination account for more than 80% of deaths in the operating room (OR) and nearly 50% of deaths in the first 24 hours after injury.²⁻⁴ Overall, only central nervous system injury is more lethal. Although only a few interventions contribute to improved survival and functional recovery after brain and spinal cord injury, much greater potential remains to develop more effective approaches to prevent or control exsanguination and hemorrhagic coagulopathy that will critically impact overall survival in major trauma.^{2,3}

A growing body of evidence has demonstrated that coagulopathy and thrombocytopenia are frequently present on admission in severely injured patients, and the degree of coagulopathy has been correlated with outcome.⁵⁻⁷ Several authors have suggested earlier use of blood products [including plasma and platelets (PLT)] in severely injured patients and transfusion of these products in ratios similar to that of whole blood.⁸⁻¹¹ Yet most resuscitation efforts are begun solely with packed red blood cells (PRBC) and crystalloid. In subsequent phases, plasma, PLT, and cryoprecipitate are added either by specific requests of the trauma team or because the extent of the PRBC consumption activates a "massive trauma protocol" that delivers a complement of component therapy.

Recently, military physicians have reported that the application of damage control resuscitation has resulted in a significant reduction in combat-related mortalities in both Iraq and Afghanistan.¹² This process involves the early delivery of blood component therapy (PRBC, plasma, and PLT), permissive hypotension, and minimizing crystalloid-based resuscitation.¹²⁻¹⁴ However, experience in the civilian setting would suggest that successful implementation of such a process would require a multidisciplinary approach involving the participation of surgeons, anesthesiologists, Transfusion Medicine specialists, and Blood bank personnel. Given the numerous obstacles, logistical nightmares, and difficulties associated with such an extensive collaboration, it is no

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surprise that trauma exsanguination protocols (TEPs) are an uncommon finding (even in Level I trauma centers). We sought to evaluate whether implementation of an exsanguination protocol (providing immediate and continuous access to PRBC, plasma, and PLT) would improve survival and reduce overall blood product consumption in the most severely injured patients.

MATERIALS AND METHODS

Study Setting

This study was approved by the Vanderbilt University Institutional Review Board. Vanderbilt University Medical Center (VUMC) is an academic, Level I trauma center that provides trauma care for a catchment area of approximately 65,000 miles² of the southeastern United States. The trauma center admits approximately 3,600 acutely injured patients annually with more than 800 being admitted to the trauma intensive care unit (ICU). The 14-bed trauma ICU is located within a 31-bed trauma unit. The non-ICU beds include a seven-bed acute admission area and a 10-bed subacute care unit.

Development of an Exsanguination Protocol

In the spring of 2005, the VUMC Blood Utilization/Transfusion Committee convened a subcommittee to address the problem of rapidly acquiring a large amount of blood products in during the initial management of severely injured patients. Specifically, the group was charged with developing a protocol that would provide blood products to hemodynamically unstable trauma patients in an immediate and sustained manner. Additionally, it was thought that the delivery of these blood products in a predefined ratio would prevent the development or at least decrease the severity of traumatic coagulopathy. This last goal would in theory obviate the need for and dependence on serial coagulation and hematological profiles. Collectively, the committee hoped that these measures would (1) improve access to these products, (2) reduce mortality, and (3) decrease overall blood product utilization. This subcommittee consisted of faculty from the Division of Trauma, the Department of Anesthesiology, the Department of Pathology (Transfusion Medicine), and the Department of Hematology. The resulting protocol was presented and approved by the Division of Trauma, the Blood Utilization/Transfusion Committee, the Main OR Committee, and the Director of the Transfusion Service. Finally, the protocol was presented and approved at the VUMC Perioperative Enterprise Committee, chaired by the Departmental Chiefs of the Section of Surgical Sciences and Anesthesiology.

Implementation and Utilization of the Exsanguination Protocol

The VUMC TEP was implemented on February 1, 2006. The steps and process of the protocol are as follows: upon arrival of a severely injured patient, the attending trauma surgeon determines if the patient, based on physiology or injury complex, will likely warrant a blood bank response beyond routine. The attending activates the TEP by notifying

the blood bank and supplying the blood bank technician with the following information: the attending's name and the patient's "Stat" name, sex, medical record number, and the OR location where blood products are to be delivered. A type and screen are sent immediately to the blood bank through a pneumatic tube system. Upon receipt of phone notification of TEP (by the trauma attending only), the blood bank prepares and dispenses the following blood products as part of the initial response: 10 units of nonirradiated, uncrossed PRBC, 4 units of AB-negative plasma, and 2 units of single donor PLT. The blood bank then notifies the trauma team that initial response products are en route and ascertains whether the TEP should continue or cease. If the blood bank personnel are told to continue, the next round of products is prepared. If the protocol is to continue the following products will be delivered as soon as they are prepared: 6 units of nonirradiated PRBC, 4 units of thawed plasma, and 2 units of single donor PLT. This cycle of dispensing follow-up products will continue until terminated by the attending trauma surgeon in the OR. Cryoprecipitate is made available for all cycles upon physician request. For each new cycle of products generated, the blood bank contacts the OR to notify them that the next round of products is en route and to get the trauma attending's direction as to whether or not to continue the protocol. TEP activation is a Quality Performance Indicator at our institution as mandated by the Perioperative Committee. All cases in which the TEP is activated are reviewed as part of the Blood Utilization Committee Performance Improvement/Quality Improvement (PI/QI) program.

Selection of Participants

We prospectively collected demographic, laboratory, blood product utilization, injury severity, and outcome data on all TEP activations as part of our protocol's mandatory PI initiative. The data on all activations is assessed on a quarterly basis. Between February 1, 2006 and July 31, 2007, there were a total of 94 patients who received initial blood products through the TEP. To develop an 18-month comparison cohort (pre-TEP), we attempted to choose what we thought would be the most comparable group to those who had, in the experience of our PI/QI group, been receiving the TEP in the previous year. These were patients that were (1) taken directly to the OR from the trauma bay, (2) went to the OR with the trauma team, and (3) those receiving at least 10 units of blood. To this end, we then queried the institution's Trauma Registry of the American College of Surgeons for all trauma patients admitted from August 1, 2004 and January 31, 2006 who (1) were admitted directly to the trauma service, (2) went immediately to the OR from the trauma bay, (3) were operated on by the trauma team during this initial operation, and (4) received at least 10 units of PRBC during the initial 24 hours. One hundred seventeen patients met these criteria.

Definitions

We evaluated trauma registry data including age, gender, and mechanism of injury. Injury scores, including initial

Glasgow Coma Scale, weighted Revised Trauma Score (w-RTS), and Injury Severity Score (ISS) were evaluated as well. The w-RTS incorporates the initial Glasgow Coma Scale, systolic blood pressure, and respiratory rate, using coded and weighted values, which range from 4 (normal) to 0 (poor) for each of the physiologic variables (yielding a high of 7.841 and a low of 0). Abbreviated Injury Scale is an anatomic injury scoring system that quantifies injuries in various body regions from a score of 1 (minor injury) to 6 (nonsurvivable). ISS is calculated by summing the squares of the three highest Abbreviated Injury Scale scores in three different body regions (values range from 1 to 75).

The incidences of 24-hour and 30-day mortality were recorded and evaluated. Predicted survival based on previously described trauma-related Injury Severity Score (TRISS) methodology was calculated and evaluated. TRISS is calculated and weighted for the patient's ISS, w-RTS, age, and mechanism of injury. Unexpected survivors were defined as those patients who had a TRISS probability of survival <50% yet survived to discharge from the hospital. Unexpected deaths were defined as those patients who had a TRISS probability of survival >50% yet died before discharge from the hospital. Intraoperative crystalloid administration was defined as all normal saline, lactated Ringer's solution, and plasmalyte received during the course of the operation. Intraoperative blood products (PRBC, plasma, and PLT) were defined as those products initiated while in the OR. Twenty-four hour blood product calculations were defined as the total number of products received 24 hours from time of arrival to the hospital. This included blood in the trauma bay, OR, and postoperatively up to the 24-hour postadmission mark.

Statistical Analysis

Continuous data are presented as means \pm standard deviation with comparisons between groups performed using the Student's *t* test or the Mann-Whitney *U* test, as appropriate. Categorical data are reported as proportions and, where appropriate, tested for significance using χ^2 or Fisher's exact tests. The primary data analysis compared 30-day mortality between the pre-TEP and TEP groups using a multivariable logistic regression model. The variables included in the analysis of 30-day mortality were age, sex, mechanism of injury (i.e., blunt vs. penetrating), TRISS, and total 24-hour blood product utilization [i.e., the number of units of PRBC, fresh frozen plasma (FFP), and PLT transfused]. Secondary analyses comparing overall and individual blood product consumption between the two groups were performed using multivariable linear regression models. To meet the normality of residuals assumption required of linear regression analysis, the values for overall and specific blood component (i.e. PRBC, FFP, and platelet) consumption were log transformed. The variables included in the analyses of both intraoperative and 24-hour individual blood component utilization were age, sex, mechanism of injury, and TRISS. In an effort to minimize the risk of falsely identifying significant results with

multiple comparisons, all multivariate regression models were prespecified and judged a priori to be clinically sound. All statistical tests were two-tailed with $p < 0.05$ set as significant. Statistical software (SPSS, version 15.0; SPSS, Inc., Chicago, IL) was used for analysis.

RESULTS

Study Group

A total of 211 patients met inclusion criteria. These patients were divided into two groups for the purpose of this study: pre-TEP ($n = 117$) and TEP ($n = 94$).

Univariate Analysis

Demographic comparison was made between the two groups. Age, sex, and ISS were similar between the groups. The TEP group demonstrated higher physiologic severity (lower w-RTS) on arrival (3.7 vs. 4.4, $p < 0.05$). In addition, the predicted survival (by TRISS) was significantly lower in the TEP group (40% vs. 50%, respectively; $p < 0.05$). TEP patients had a higher percentage of patients with penetrating injuries (53% vs. 36%, $p = 0.012$). Descriptive data are shown in Table 1.

Primary and secondary outcome measures were then compared (Table 2). Thirty-day mortality was lower in TEP (51% vs. 66%, $p = 0.03$). Using TRISS methodology, the TEP group had a greater percentage of unexpected survivors and fewer unexpected deaths (22% vs. 5% and 9% vs. 22%, respectively; $p < 0.05$). The TEP patients received more intraoperative blood products of all types (PRBC, FFP, and PLT) while receiving less intraoperative crystalloid administration (4.9 vs. 6.7 L, $p = 0.002$). Postoperative blood products requirements up to 24 hours were lower in the TEP group with respect to PRBC (2.8 U vs. 8.7 U, $p < 0.001$), FFP (1.7 U vs. 7.9 U, $p < 0.001$), and PLT (0.9 U vs. 5.7 U, $p < 0.001$). Total 24-hour blood product utilization is represented in Figure 1. Twenty-four-hour PLT transfusion was less for TEP (3.1 vs. 6.8 U, $p < 0.001$). Although total 24-hour transfusions of FFP were lower in the TEP group, this was not statistically significant. There was no difference in 24-hour PRBC transfusions between the groups.

Table 1 Baseline Characteristics and Descriptive Data of the Study Groups

Characteristic	Pre-TEP (n = 117)	TEP (n = 94)	<i>P</i>
Age, yr (\pm SD)	39.3 \pm 17.7	35.5 \pm 15.3	0.176
Male (%)	76	73	0.657
w-RTS (\pm SD)	4.45 \pm 2.6	3.74 \pm 2.8	0.037*
ISS (\pm SD)	29.8 \pm 16.2	32 \pm 16.8	0.217
TRISS (\pm SD)	0.53 \pm 0.38	0.40 \pm 0.39	0.029
Penetrating mechanism (%)	30	56	0.012*

* Statistically significant at $p < 0.05$.

TEP, trauma exsanguination protocol; w-RTS, weighted Revised Trauma Score; ISS, Injury Severity Score; TRISS, trauma-related Injury Severity Score.

Table 2 Univariate Analyses of Primary and Secondary Outcome Measures

Variable	Pre-TEP (n = 117)	TEP (n = 94)	p
30-d mortality (%)	65.8	51.1	0.030*
24-h blood product use (units)	39 ± 28	31.8 ± 19	0.017*
24-h RBC use (units)	19.8 ± 12.8	18.8 ± 11.2	0.695
24-h FFP use (units)	12.4 ± 12.5	9.9 ± 7	0.595
24-h PLT use (units)	6.8 ± 7.2	3.1 ± 3.7	<0.001*
Intraoperative RBC use (units)	11.1 ± 8.5	16 ± 11.4	0.001*
Intraoperative FFP use (units)	4.3 ± 4	8.2 ± 6.8	<0.001*
Intraoperative PLT use (units)	1.1 ± 2.6	2.2 ± 2.3	<0.001*
Intraoperative crystalloid (L)	6.7 ± 4.2	4.9 ± 3.0	0.002*
Unexpected survivors (%)	5.1	22.3	<0.001*
Unexpected deaths (%)	22.2	8.5	0.007*

* Statistically significant at $p < 0.05$.

TEP, trauma exsanguination protocol; RBC, red blood cell; FFP, fresh frozen plasma; PLT, platelets.

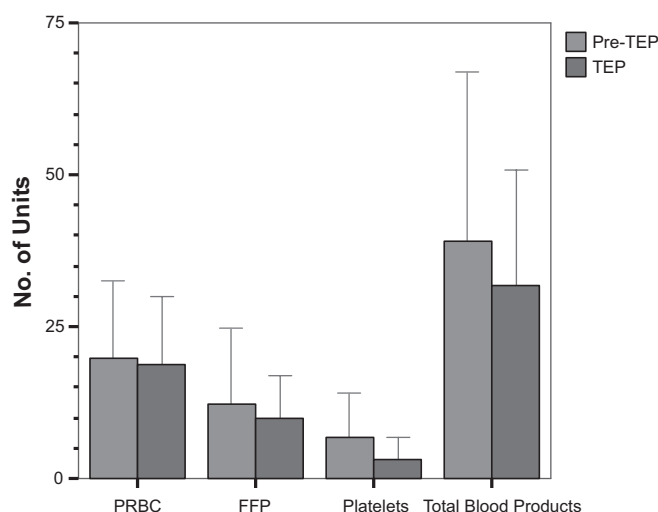


Fig. 1. Unadjusted initial 24-hour blood product utilization before and after implementation of TEP. Each bar corresponds to the mean number of units transfused + standard deviation.

Multivariate Analysis

Using multivariable logistic regression analysis, we sought to identify predictors of mortality (Table 3). Adjustment was made for the following variables: age, gender, mechanism of injury, TRISS, and 24-hour transfusion of PRBC, FFP, and PLT. TEP was found to be a predictor of 30-day mortality (OR 0.26, $p < 0.01$, 95% CI 0.12–0.57).

Multivariate linear regression analysis was then performed to evaluate the impact of TEP on total and individual blood product utilization when controlling for age, gender, mechanism of injury, and TRISS. Implementation of TEP was associated with a decrease in 24-hour total blood products (34.36 vs. 43 U, $p = 0.015$) and a decrease in 24-hour platelet transfusion (4.65 vs. 11.98 U, $p < 0.001$). No difference was seen in 24-hour PRBC and FFP transfusion between PRE-TEP and TEP when controlling for the aforementioned confounding variables.

Table 3 Odds Ratios for 30 Days Mortality in Study Groups

Variable	Odds Ratio (95% CI)	p
Received TEP	0.26 (0.12–0.56)	0.001*
Age	1.02 (0.998–1.042)	0.071
Sex	1.040 (0.489–2.214)	0.919
Penetrating mechanism	1.260 (0.639–2.486)	0.505
24-h RBC utilization	1.074 (1.028–1.121)	0.001*
24-h FFP utilization	1.013 (0.963–1.066)	0.612
24-h PLT utilization	0.914 (0.851–0.981)	0.013*

* Statistically significant at $p < 0.05$.

CI, confidence interval; TEP, trauma exsanguination protocol; RBC, red blood cell; FFP, fresh frozen plasma; PLT, platelets.

DISCUSSION

Despite tremendous efforts and attention directed at implementation of damage control techniques (abbreviated laparotomy, reversal of acidosis, correction of hypothermia), traumatic coagulopathy has been seriously understudied and underappreciated.^{2,12,15} Increasing evidence has demonstrated coagulopathy in the severely injured patient is often present in the field or upon arrival to the trauma center.^{14,16–18} In the absence of a predefined massive transfusion protocol, access to the appropriate volume and ratios of blood products may be significantly delayed. Failure to immediately address and treat this coagulopathy may lead to a worsening of coagulopathy from crystalloid based dilution, a hopeless “chasing” of uncorrectable labs, and an eventual exsanguination from nonsurgical hemorrhage. Our multidisciplinary group has recently designed an exsanguination protocol to address the often overlooked hematological aspects of current damage control strategies. Delivered in an early, aggressive, and predefined manner, the TEP has resulted in a 74% reduction in the odds of mortality at our institution.

Transfusion of blood products, let alone “massive transfusion,” has historically been associated with an increased mortality risk in both elective surgery and trauma patients.^{19–23} However, in the subpopulation of severely injured patients presenting in physiologic extremis, use of blood products in a preemptive and aggressive manner appears to reduce mortality. We demonstrated reduced 30-day mortality with a greater number of unexpected survivors after implementation of the TEP. The mortality reduction was observed in both penetrating and blunt injuries and remained significant after controlling for numerous cofounders (age, sex, mechanism of injury, TRISS, and blood product consumption). Similarly, military experience from Operation Iraqi Freedom and Operation Enduring Freedom has documented improved survival with a similar protocol using PRBC, FFP, and packed PLT in a 1:1:1 fashion.¹²

Through prompt replacement of PRBC and necessary blood components, we thought that we would be able to prevent the almost inevitable coagulopathy seen in these patients. By reducing the incidence and severity of this often overwhelming process, we hoped to reduce the number of blood products consumed. Although the TEP patients re-

ceived more products intraoperatively, we were able to reduce postoperative and overall 24-hour product utilization.

This reduction is not only important from a blood utilization and cost standpoint, but also for a potential reduction in morbidity among survivors. Numerous authors have demonstrated an increase in acute lung injury, acute respiratory distress syndrome, and multiple system organ failure with massive transfusion.^{20,24–26} By minimizing hemorrhage early and decreasing overall blood product use, the incidence and severity of these morbidities may also be reduced.

Increasing evidence has demonstrated that aggressive crystalloid-based resuscitation strategies are associated with cardiac and pulmonary complications, development of abdominal compartment syndrome, coagulation disturbances, and immunologic and inflammatory mediator dysfunction.^{27–30} Particular to coagulation disturbances, increasing crystalloid volumes are associated with platelet dysfunction and coagulopathy. Barak et al. demonstrated that patients who received less than 3 L of crystalloid intraoperatively had significantly less disturbances in their coagulation levels than those patients who received at least 3 L.²⁷ This is consistent with previous investigations demonstrating the clinical significance of “dilutional” coagulopathy after excessive saline administration. In the present study, we were able to reduce the amount of intraoperative crystalloid administration by almost 2 L after controlling for appropriate confounders. Reducing crystalloid use and replacing “what is bled” is also the approach advocated by military data from Iraq using the concept of damage control resuscitation.^{12,14}

Limitations to this study include the relatively small sample size for each cohort and the retrospective design using data collected via a trauma registry database and computerized patient chart. In addition, a notable limitation is the fact that the population is not homogenous and the cohort is not identically matched; however, these issues were addressed with the use of multivariable regression strategies. Additionally, we did not collect data on prehospital fluid and blood product administration. This may have impacted the initial physiologic presentation and triggered trauma faculty to activate the TEP. Both populations also include many individuals that died intraoperatively. Though we speculate that a fairly similar number exists between the two groups, patients who died in the OR would likely skew the data toward increased blood component utilization in the survivors. Finally, we only assessed 30-day survival on these patients and did not evaluate them with regard to long-term follow-up.

CONCLUSIONS

In the absence of a predefined exsanguination protocol, access to appropriate blood components and sufficient quantities of the same may be significantly delayed. As many severely injured trauma patients arrive at the hospital with coagulopathy already present, any delay in the prompt replacement of blood products may result in an exacerbation of the coagulopathy with ongoing consequent hemorrhage and,

ultimately, higher mortality. We implemented an organized policy to address exsanguinating hemorrhage in the most severely injured patients and have shown a 74% reduction in the odds of mortality. The use of an exsanguination protocol, delivered in an aggressive and predefined manner, also increases unexpected survivors and reduces unexpected deaths. Further, patients resuscitated using the TEP required less intraoperative crystalloid and received less blood products overall. Future research should be directed at determining the underlying mechanisms for the mortality reduction associated with using an exsanguination protocol in addition to defining the appropriate blood component ratios needed to optimally treat traumatic coagulopathy.

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DISCUSSION

Dr. Larry J. Butler (Colorado Springs, Colorado): This topic is obviously a very timely one. Over the last 48 hours we've discussed many issues related to coagulopathy in the severely-injured patient.

Gene Moore, yesterday, showed us data suggesting that the optimal FFP to packed red cell ratio was about 2.5 to 1. In the discussion of that, Dr. Lucas reminded us that over 20 years ago he similarly saw an optimal ratio in the 1 to 2 range.

Dr. Holcomb, also in the discussion of that paper, mentioned the military's experience with a 1 to 1 ratio and promised us upcoming data. In fact the next paper to be presented this afternoon deals with the civilian experience in the optimal ratio of FFP to packed red blood cells.

Factor VII's role has also been discussed in decreasing mortality in combat casualties as well as decreasing the time to operative intervention in the brain-injured patient.

So this is obviously a very pertinent topic. This study looks at the institution of a trauma exsanguination protocol. Interestingly enough, this happened just about the same time we introduced our massive transfusion protocol. And I think many of us are doing this.

Questions I have are related primarily to whether these cohorts truly related. I think there is a huge difference in the

mechanism of injury, almost two to one penetrating in the study group compared to the retrospective cohort.

Several things happened then and I wondered if you looked at issues in the differences between the blunt and the penetrating in terms of prehospital time, amount of crystalloid infused, and temperature on presentation.

Also, was the operative management in these different groups of patients, the blunt and the penetrating, different, specifically the percentage use of damage control laparotomy, the use of open abdomen, or the use of embolization or other techniques?

The increase in penetrating injuries also might suggest that there was an increased ability to surgically control bleeding.

The next set of questions I have for you is in regards to the implementation of your protocol and I'd like to know how this really worked. Did you always have four units of FFP thawed?

And if you did, how much waste was there? If you didn't have that four of FFP thawed, how long did it really take you to get it?

What data or decision points did the attending trauma surgeon use to call for the next round of products? Was he getting lab work, hematocrit, INR, platelet count, fibrinogen? Or was he basing this just on clinical parameters?

Were there any breaks in your protocol? Did you have surgeons giving cryoprecipitate? Did you have them giving factor VII? If you did, were these excluded from your study? Were they included? How did you interpret this in your analysis?

Finally, I would ask if you tried to break down the data and look at penetrating versus penetrating and blunt versus blunt in your two cohorts.

Dr. Patrick Reilly (Philadelphia, Pennsylvania): Number 1, will you be very clear to the audience because it's a little unclear in your abstract and the slides, are you using stored, thawed plasma or are you using fresh frozen plasma?

Number 2, is factor VIIa formally built into your protocol or not? And if it was, was there a difference between the number of patients or timing of administration in those who received factor VIIa in your protocol versus the pre-protocol group?

And the third thing, in the conclusions you sort of hinted that the exsanguination protocol enabled more blood to be available for the injured patient quickly when you needed it. In our experience we believe that as well, but we've never been able to really document it because we can't exactly tell when the blood is transfused reviewing the operative record, only that it was transfused sometime during the operation. The only times we have are when the blood was released from the blood bank. How are you coming to the conclusion that the blood is available and it wasn't available before?

Dr. Carl J. Hauser (Boston, Massachusetts): I'd like to know whether you have looked at the incidence of the, of what we have historically called the "abdominal compartment

syndrome” in these two groups but which probably should be called the “abdominal crystalloid syndrome?”

Dr. Matthew J. Wall, Jr. (Houston, Texas): These days a lot of patients are on platelet poisons. Was that one of your indications for you to institute your protocol or should it be?

Dr. Bryan A. Cotton (Nashville, Tennessee): Thank you. Dr. Butler, thank you once again for your questions. With regards to the mismatch in cohorts, there absolutely is.

We tried to pick what we thought would be the most applicable cohort, patients going straight to the OR from the trauma bay, getting at least 10 units of blood which has classically been defined as one definition of trauma, of massive transfusion.

And that was as good as we could get, at least for this part. Once this was chosen, we were actually cautioned by our statistical consultants not to “over-match” with our study group. Taking that into consideration, we did control for the discrepancies in the penetrating mechanism and the RTS differential in our multiple linear regression model.

With regards to blunt versus penetrating, we have evaluated through our PI process and I can tell you that even though the data is not here, the blunt and penetrating appeared to both benefit with regards to people that we would consider saves or not saves with regards to whether their mechanism was blunt or penetrating.

Pre-hospital variables are hit or miss. They are phenomenally collected on the aeromedical side. They are poorly collected on the ground side. So we do not include those in our database but it would probably benefit from including those.

As far as evaluating abdominal compartment syndrome, interventional radiology, implementation to mechanisms, I can tell you that we did not look at those specifically but that the overwhelming number of these are abdominal procedures not extremity procedures, although they have been activated for traumatic amputations of upper and lower extremities and some severe chest trauma.

As far as the products’ availability, they are generally available within a 10 to 20 minute timeframe. And then about every 20 minutes we get a new cycle distributed to us but without much delay.

In fact, if there is one component that is delayed they will send what is ready and then send another carrier with the extra components when those particular components are prepared.

As far as activation, this was 100 percent a clinical call. From the PI process we can show some times where it should have been activated earlier and it was activated in very much what we would consider a delayed fashion on some people and that was part of the learning process of clinical faculty at the second year fellowship level.

I can tell you that otherwise it was pretty much routinely activated from the trauma bay or shortly after arrival in the operating suite.

And it was pretty much a uniform activation criteria. It’s all clinical acumen for the most part. We did not go based on labs or any resuscitation endpoints.

As far as cryo, factor VII, things like that, we do have cryo built into the protocol by request but it is not automatically delivered.

We have discussed that through our PI process about adding that component to one of our cycles, maybe the second or third cycle. But right now it’s on a prn basis if the faculty request that.

As far as VIIa, that was initially in our protocol but no patients received it. On protocol we’ve had two violations. Those were removed. Factor VIIa was removed from the protocol and use by the administration for pretty much anyone unless it was part of an industry sponsored study.

And we have actually had a couple of activations on emergency general surgery patients that were in hemorrhagic shock from other sources, for intra-abdominal processes. And those two EGS patients were removed.

Blunt-blunt, penetrating-penetrating evaluation, we did not do that. With regards to Dr Reilly who recognized this protocol well as it’s very similar to the one that I learned when I was at fellow at Penn, as far as FFP, it is FFP that they’re thawing.

From that point it’s not ready to go, unfortunately. And we’ve had that debate with the blood bank. They think that that would be a waste to have it already thawed.

They don’t think that they go through it enough to use it as a resource, especially with the AB negative process in our population. As far as VIIa, again, it was initially built in but then removed by the administration.

And then availability, it is fairly available within about a 15-minute window once you make that phone call. And at a minimum we get all the blood. Ten units of blood is immediately available. FFP and platelets are about a 10- to 15-minute lag.

With regards to Dr. Hauser’s comments, we did not evaluate the crystalloid assault of the patients and whether or not they ended up as open abdomens.

But we plan on looking at that in the future to see if by the fact that they did have a reduction in crystalloid intra-operatively and post-operatively, if this did lead to less of the abdominal crystalloid syndrome.

And then, finally, to Dr. Wall, we did not look at coagulation status pre-hospital or Plavix use, Coumadin use.

I can tell you one or two patients that may have been on Coumadin that got it but they were going to the operating suite for another process and would have had it activated most likely anyway. However, we did not evaluate that separately. And then, perhaps it should be included.