Published in final edited form as:

Transfus Med. 2014 June ; 24(3): 162–168. doi:10.1111/tme.12096.

Not Only in Trauma Patients: Hospital-wide Implementation of a Massive Transfusion Protocol

Lisa M. Baumann Kreuziger, MD,

University of Minnesota, Department of Hematology, Oncology and Transplant

Colleen T. Morton, MBBCh, MS,

University of Minnesota, Regions Hospital, Department of Hematology, Oncology and Transplant

Amar T. Subramanian, MD,

Regions Hospital, Transfusion Medicine

Christopher P. Anderson, MPH, and

HealthPartners, Institute for Education and Research

David J. Dries, MSE, MD, FACS

University of Minnesota, Regions Hospital, Department of Surgery

Lisa M. Baumann Kreuziger: bauma260@umn.edu; Colleen T. Morton: Colleen.T.Morton@HealthPartners.com; Amar T. Subramanian: Amar.T.Subramanian@HealthPartners.Com; Christopher P. Anderson: Christopher.P.Anderson@HealthPartners.com; David J. Dries: David.J.Dries@HealthPartners.com

Abstract

Objectives—To review outcomes of massive transfusion protocol (MTP) activation and determine the impact of MTP implementation on blood bank use.

Background—MTP has been established to rapidly provide plasma and packed red blood cells in ratios approaching 1:1. Due to availability, MTP has been utilized in non-traumatic hemorrhage despite evidence of benefit in this population. Our hospital wide implementation of MTP was reviewed for propriety, outcomes, and effect on blood bank resources.

Methods—Retrospective cohort study of patients receiving transfusion after MTP activation from October 2009–2011. Underlying medical conditions and baseline medication use were determined. In-hospital and 24-hour mortality were compared with evaluation for confounding by APACHE score and duration of MTP activation. Blood product use before and after MTP implementation was reviewed.

Results—MTP activation occurred in 62 trauma and 63 non-trauma patients. Non-trauma patients were older, had more underlying medical conditions, and higher APACHE scores

Corresponding author: Lisa M. Baumann Kreuziger, MD, University of Minnesota, Mayo Mail Code 480, 420 Delaware St. S.E., Minneapolis, MN, USA 55455, Phone: (612) 624-0123, Fax: (612) 625-6919, Lisa.baumannkreuziger@bcw.edu.

Author Contribution: LBK was involved with study design, data collection, data analysis, data interpretation, writing, and critical revision; CTM was involved in study design, data interpretation, and critical revision; ATS was involved with study design, data collection, and critical revision; CPA was involved with data analysis, data interpretation, writing, and critical revision; DJD was involved with study design, data interpretation, and critical revision.

The authors have no conflicts of interest to report.

Part of the project was presented at the American Society of Hematology 53rd Annual Meeting, Orlando, FL, Dec 9–13, 2011.

compared to trauma patients. 24-hour mortality was higher in trauma compared to non-trauma patients (27.4% vs. 11.1%, $p=0.02$). There was no significant difference of in-hospital mortality. Transfusion ratio did not differ between trauma and non-trauma patients and was not associated with mortality even when MTP activation duration and APACHE score were considered. Hospital-wide blood product use did not change with MTP implementation.

Conclusions—MTP may be successfully used in trauma and non-trauma settings without significantly impacting overall blood product utilization. Inclusion of non-trauma patients into prospective studies of resuscitation with blood products is warranted to ensure benefit in these patients.

Keywords

Massive transfusion; trauma; non-trauma; survival

Background

Hemorrhagic shock accounts for a significant number of deaths despite improvements in Emergency Department management and critical care. Work completed since the 1970s has showed significant morbidity associated with coagulopathy in trauma patients.(Simmons *et al.*, 1969; Counts *et al.*, 1979; Brohi *et al.*, 2003) Data from combat injury, retrospective studies of civilian trauma patients, and prospective observational studies have suggested improved coagulation profiles and mortality in patients who have been transfused with high plasma:packed red blood cell (PRBC) ratios.(Borgman *et al.*, 2007; Phan and Wisner, 2010; Neal *et al.*, 2012; Holcomb *et al.*, 2012) In spite of methodological flaws in non-randomized studies, massive transfusion protocols (MTP) have been adopted on a worldwide basis for injury management.

Many etiologies exist outside of traumatic injury where significant bleeding may occur in hospitalized patients including aneurysm rupture, post-partum hemorrhage and massive gastrointestinal bleeding. While MTPs were not designed with these patient groups in mind, the availability of MTP have led to its utilization in patients with major bleeding from non-traumatic causes. In an effort to standardize the care of bleeding patients, a MTP at our institution was implemented on a hospital-wide basis in 2009. Multiple reports have recently evaluated the impact of MTP activation in non-trauma patients *on blood product utilization and patient mortality*. (Kauvar, Sarfati, Kraiss, 2012; Morse *et al.*, 2012; Saule and Hawkins, 2012; McDaniel, et al. 2013) *A retrospective cohort study by McDaniel and colleagues found faster delivery of blood products using MTP with equal wasting of platelets between trauma and non-trauma patients.(McDaniel, et al. 2013) We compared hospital wide use of blood products before and after MTP institution to evaluate the impact of MTP on resource utilization. In a similar analysis, Sinha and colleagues reported that MTP increased plasma, platelet and cryoprecipitate transfusion per patient, but did not alter the median number of PRBC transfused or hospital mortality.(Sinha, Roxby, Bersten, 2013) Prospective studies in trauma patients have shown that high plasma:PRBC ratios have the highest impact on reducing mortality in the first 6 hours after injury (Holcomb *et al.*, 2012); therefore, mortality differences should be examined at time points prior to hospital discharge to reflect the impact of hemorrhage management instead of other comorbidities.*

Morse and colleagues reported higher 24-hour mortality in non-trauma patients receiving massive transfusion compared to trauma patients.(Morse *et al.*, 2011) However, these non-trauma patients were significantly older and underlying comorbidities and baseline medication use were not examined and could significantly impact outcome. *In this study, we evaluated the impact of medication use, medical comorbidities, and MTP use on 24-hour and in-hospital mortality in trauma and non-trauma patients.*

Methods

Clinical data of patients who received transfusion after activation of the MTP between October 2009 and October 2011 were reviewed. *To determine the effectiveness of MTP implementation*, patients were also identified who received a massive transfusion, defined as >10 units of PRBC in 24 hours, off protocol via blood bank records. Medications, laboratory parameters prior to transfusion, medical conditions affecting bleeding, and amount of blood products administered were evaluated. APACHE score was calculated from hemodynamic and laboratory parameters within 24 hours of initiation of MTP or first transfusion off protocol.(Knaus *et al.*, 1985) Use of additional hemostatic agents such as desmopressin, recombinant factor VIIa (rfVIIa), and anti-fibrinolytic therapy was recorded. Outcomes including 24 hour and in-hospital mortality and incidence of transfusion reactions including transfusion related acute lung injury (TRALI) were assessed from hemodynamic parameters after transfusion, clinical records, and chest x-rays. Transfusion duration was defined as the period in which blood products were released during MTP activation.

Regions Hospital is a large Level I *Adult and Pediatric* Trauma Center located in St. Paul, MN. Figure 1 shows the MTP *developed by our trauma program* which can be activated by any physician for traumatic or non-traumatic indications. During the time of this review, activated Factor VII (rfVIIa, NovoSeven®, Novo Nordisk, Bagsvaerd, Denmark) was part of the MTP. Use of rfVIIa as a part of our MTP has since been discontinued. No specific transfusion trigger was designated for MTP activation. The trauma group was defined as activations of the MTP protocol due to blunt or penetrating injuries. The non-trauma group consisted of MTP activations for other indications which are listed below. The study was approved by the Health Partners Research Foundation IRB.

In order to evaluate the impact of MTP on overall hospital blood product utilization, we reviewed monthly blood product transfusion data aggregated from blood bank administrative sources. The number of blood products transfused per patient receiving blood products was compared between two time periods: the months prior to MTP implementation (Jan-Sept 2009) and the study time period (Oct 2009–2011). A reduction in institutional PRBC transfusion trigger to <8 grams/dl and institution of blood saving practices by the cardiovascular and orthopedic surgery services occurred in July 2010; nine months after hospital-wide implementation of our MTP.

Data Analysis

Demographics, baseline laboratories, products transfused, use of hemostatic agents and were described using means and standard deviations (SD) for continuous variables and frequency counts and percentages for categorical variables. Continuous variables were compared using

Student's t-test whereas categorical variables were compared using Chi-square tests. Component ratio was calculated by dividing the units of plasma transfused by the number of PRBC units transfused. Component ratio was examined as both a continuous and categorical predictor. Wilcoxon tests were used to determine if baseline medication or hemostatic agents use predicted transfusion of blood products. We investigated predictors of 24-hour and in-hospital mortality *including PRBC:FFP ratio* using logistic regression. After analysis of mortality risk factors confirmed that APACHE II scores were not missing at random, we investigated two separate ways of imputing this value for the 21% of patients for whom it could not be calculated. After finding similar performance among both methods for imputing the APACHE II score, we opted to use the less complicated method and assuming the effect of APACHE score upon mortality (OR 1.15 per point) was the same as the original derivation.(Knaus *et al.*, 1985) Multivariate adjustments were made in linear or logistic regression models, depending on the type of outcome data, and standard errors were adjusted if imputed data was used.(Rubin, 1987) All tests were two-sided, with type I error of 0.05. No adjustment for multiple testing was made, because many of the hypotheses under investigation were highly correlated. These analyses were done using the SAS statistical software platform, v9.2 (Cary, NC, USA).

Results

In total, 125 patients received blood products through activation of our MTP over 2 years (62 trauma patients and 63 non-trauma patients). Due to the widespread acceptance of the protocol, only 8 additional patients received a massive transfusion off protocol. Of patients with activation of the MTP, 22/63 (35%) of non-trauma and 28/62 (45%) of trauma patients received 10 units of PRBC during activation. In addition, 31/63 (49%) of non-trauma and 22/62 (36%) of trauma patients received multiple PRBC transfusions (4–9 units). Baseline demographics showed that trauma patients were younger than the non-trauma patients (Table 1, $p<0.01$). *Mean platelet count was statistically higher in the trauma patients.* Mean APACHE II scores in trauma patients were significantly lower than the non-trauma patients (25 vs 29, $p=0.03$). Therefore, underlying physiologic differences in severity of illness were present between the groups.

Table 2 shows the blood products and hemostatic agents used in our cohort. *No significant differences in the number of transfused PRBC, plasma, platelets or cryoprecipitate units were found between the trauma and non-trauma groups.* Indications for activation of MTP are noted in Table 3. Ruptured abdominal or thoracic aortic aneurysms accounted for 83% (19/23) of the vascular catastrophes for which MTP activation occurred. Ruptured arteriovenous malformations and erosion of arteries into adjacent structures were the other vascular ruptures in the non-trauma group. rFVIIa was used in 19% of the non-trauma group and 15% of the trauma group (Table 2).

Use of rFVIIa was associated with higher amounts of PRBC, plasma, platelets and cryoprecipitate transfusion ($p < 0.01$). Aminocaproic acid was used in the non-trauma group in patients undergoing cardiothoracic surgery or who experienced a vascular rupture. Desmopressin was used primarily in the non-trauma group with 83% (5/6 patients) undergoing cardiothoracic surgery. Of the patients who received vitamin K, 29% were

taking warfarin and 46% had a history of liver failure. Only the use of aminocaproic acid and vitamin K were statistically different across the massive transfusion groups.

Baseline medication use and past medical history were examined to determine if the number of transfused products were associated with these underlying patient factors. Baseline use of aspirin was found in 37% of patients in the non-trauma category compared to 6% of the trauma patients ($p < 0.01$). Of the non-trauma patients on aspirin, 30% had vascular event and 39% had cardiothoracic surgery, the majority of which were coronary artery bypass grafting, and 17% had GI bleeding. Patients were likely taking aspirin due to cardiovascular disease associated with surgery or the aspirin may have been related to the GI bleeding. Three non-trauma patients were taking clopidogrel and one patient each was taking eptifibatide and cilostazol. Heparins were used in 48% of the non-trauma patients as these patients were primarily in the hospital during their event or had vascular surgery where heparin was indicated. Baseline comorbidities were higher in patients in the non-trauma group with 22% of patients with history of liver failure, 29% with renal failure, and 11% with solid tumors ($p = 0.01$ comparison across MTP groups). Hematologic malignancies were present in 5% of patients in the non-trauma group and one non-trauma and one trauma patient had a bleeding disorder. Patients with renal failure were transfused 3 units of PBRC fewer than patients without renal failure ($p = 0.02$). Patients who received rFVIIa had increased transfusion amounts by 5.6 units of PRBC, 5.1 units of plasma, and 1.2 units of platelets ($p = 0.01$). Mortality was higher in patients receiving rFVIIa compared to patients who did not receive rFVIIa but the mortality difference did not reach statistical significance (45% vs 33%, $p = 0.32$). None of the other baseline medications or hemostatic agents showed association with the number of blood products transfused. Correction for APACHE II scores did not significantly affect the estimates of the association between medications and blood products transfused. Overall, despite differences in medications and comorbidities in the transfusion groups, transfusion of PRBC was only associated with underlying renal failure and use of rFVIIa.

We then evaluated outcomes associated with MTP use in our patient sample. Transfusion reactions (TR) occurred infrequently with only 2.4% patients experiencing possible transfusion-related acute lung injury (TRALI). *Only one febrile reaction and one delayed hemolytic transfusion reaction were reported to the hospital blood bank.* Of the 44 patients (35.2%) who died prior to hospital discharge, 24 of these deaths (54.5%) occurred in the first 24 hours. The remaining 81 patients (64.8%), including those who suffered TRALI or TR, survived until discharge. Therefore, TRALI and TR were not risk factors for mortality in our cohort. There was no difference in the rate of in-hospital mortality between trauma patients and non-trauma patients (33.9% vs. 36.5%, $p = 0.85$). However, trauma patients were more likely to die in the first 24 hours than were non-trauma patients (27.4% vs. 11.1%, $p = 0.02$). Mortality was not associated with increased PBRC transfusion (OR 1.04 per additional unit, 95% CI: 1.0–1.1), increased plasma use (OR 1.04 per additional unit, 95% CI 0.97–1.10), increased platelet administration (OR 1.13 per additional unit, 95% CI 0.86–1.48) or more cryoprecipitate use (OR 1.12 per additional unit, 95% CI 0.86–1.48). The ratio of plasma to PBRC units administered appeared to have no association with mortality (OR 0.65, 95% CI 0.26–1.62). A categorization of the component ratio also showed no

association with mortality (Table 4); 63% of patients transfused via MTP received transfusion ratios plasma:PRBC >1.2. We investigated the potentially confounding effects of transfusion duration and APACHE score upon in-hospital mortality. No evidence was found that transfusion duration was a confounder, as there was no association between transfusion duration and mortality in this sample (OR 0.94, per hour, 95% CI 0.80 – 1.10), and the median transfusion duration was 1.7 hours in both surviving and non-surviving patients. As expected, mortality was strongly associated with both higher APACHE scores (OR 1.09 per point, 95% CI 1.02 – 1.16, $p=0.009$) and missing APACHE scores (OR 4.06, 95% CI 1.64 – 10.01, $p = 0.002$). No significant association with APACHE score and transfusion ratio category was found. Therefore, the lack of association between component ratio and mortality was not due to confounding from transfusion duration or severity of illness represented by APACHE scores.

In order to evaluate the impact of MTP on overall blood product use, available blood product utilization data prior to MTP implementation was compared to product use after MTP implementation. A similar number of hospital discharges occurred but the number of patients receiving blood products decreased during the interval of our study (Table 5). No significant change in plasma or platelet use was noted despite 1:1 plasma:PRBC ratios provided in MTP. A trend toward decreased PRBC transfused per patient was noted but not statistically significant (Median pre-MTP 3.2 vs 3.0 post-MTP implementation, $p=0.08$). The number of patients receiving transfusion via MTP per month (median 5, range 1–8) was low in comparison to the number of hospitalized patients receiving transfusion (median 218, range 187–252). Overall, the institution of MTP did not impact overall blood product use.

Discussion

Massive transfusion protocols have been established in many hospitals to allow rapid delivery of component therapy in 1:1 ratios of pRBC to plasma units. Our retrospective review of hospital-wide implementation of a MTP suggested widespread acceptance by acute care and trauma surgeons, critical care physicians, and transfusion medicine staff as a limited number of patients received a massive transfusion off-protocol. A majority of patients received transfusion of plasma:PRBC in ratios >1:2 which suggests physicians followed the protocol as intended. No significant difference in overall hospital blood product use was noted after implementation of MTP, which was likely secondary to the limited number of patients receiving transfusion via MTP, compared to all transfused patients. Other initiatives to limit blood product use were implemented during this timeframe which decreased the number of patients who received transfusion. *A recent study has also shown benefit of MTP implementation in non-trauma patients through faster blood product delivery without increased wasting of products.* (McDaniel, et al. 2013) Overall, MTP can be utilized beyond trauma situations to provide efficient delivery of blood products and consistent management of bleeding patients without significantly affecting the entire hospital transfusion practice.

Due to lack of randomized trials, the American Association of Blood Banks does not make recommendations regarding blood component transfusion ratios, but retrospective studies individually suggest a mortality benefit to transfusion of plasma:PRBC ratios of >1:2.

(Roback *et al.*, 2010; Neal *et al.*, 2012) A recent systematic review found significant heterogeneity between studies and methodological flaws that precluded statistical comparison of low to high plasma:PRBC transfusion ratios.(Rajasekhar *et al.*, 2011) We did not find an association between 24 hour or in-hospital mortality and plasma:PRBC ratios, which was not secondary to confounding due to underlying severity of illness *reflected in the APACHE II score; however, our sample size would have limited our ability to detect small associations between plasma:PRBC ratio and mortality. The APACHE II score is infrequently used as a marker of illness severity in trauma patients but was chosen so a common index could be evaluated across trauma and non-trauma patients. Equal transfusion duration was found in survivors and non-survivors, thus duration of transfusion also did not affect the association between transfusion ratio and mortality.* Few massive transfusions occurred off protocol and most activations of the MTP led to transfusion of high plasma:PRBC ratios. These factors prevented a large distribution of plasma:PRBC ratios in our series to determine an association between mortality and transfusion ratio.

Despite activation of the MTP, most patients in our series did not receive a massive transfusion (>10 units of PRBC). Multiple (4–9 units of PRBC) or massive transfusion occurred in 81% of trauma patients and 84% of non-trauma patients *which could viewed as overactivation of the MTP. Our institution does not have triggers for activation of MTP in non-trauma patients and this is an area of needed research.* However, a German registry review suggested a mortality benefit in trauma patients who receive multiple transfusion with a high plasma:PRBC transfusion ratio.(Wafaisade *et al.*, 2011) Sample size precluded sufficient power to examine the influence of transfusion ratio on mortality between trauma and non-trauma patients who received multiple vs. massive transfusion.

Previous work has also suggested that institution of MTP decreases blood product consumption.(Cotton *et al.*, 2008) *If other patient factors remain constant, a decrease in blood product utilization would suggest improved resuscitation and faster cessation of hemorrhage.* After MTP implementation we only saw a trend toward decreased PRBC transfusion. *Despite providing increased access to plasma and platelets through the MTP, similar plasma and platelet transfusions per patient were seen before and after implementation of the MTP.* A prospective randomized study of MTP would be needed to definitively evaluate if MTP reduced blood product requirements in trauma and non-trauma patients.

Limited information is present in the literature regarding the use of MTP for non-trauma patients. A review of MTP activations at Grady Memorial Hospital reported 37 patients in which MTP was completed for non-trauma indications.(Morse *et al.*, 2012) Similar to our series, trauma patients were younger than non-trauma patients. However, Morse and colleagues found higher 24-hour mortality in non-trauma patients compared to trauma patients (59% vs. 35%) whereas non-trauma patients had better 24-hour survival in our series (11.1% vs. 27.4%).(Morse *et al.*, 2012) The mortality differences did not persist as in-hospital mortality in our series and 30-day mortality were equal in the trauma and non-trauma groups. Similarly, when trauma and non-trauma patients were evaluated together, in-hospital mortality did not change after institution of MTP in an Australian series.(Sinha, Roxby, Bersten, 2013) Underlying medical conditions, APACHE scores, and use of aspirin

was higher in our MTP non-trauma group than the MTP trauma group but this did not translate into a mortality difference. Overall, our patients were transfused fewer PRBCs which may indicate less severe injuries to account for the improved mortality in comparison to patients *in other series*.(Morse *et al.*, 2012; McDaniel, et al. 2013)

At the time of this review, rFVIIa was used off-label in an effort to induce hemostasis in exsanguinating patients. Patients who received rFVIIa were transfused significantly more PRBC, plasma, and platelets, confirming the use only in extreme situations. Mortality was higher in patients receiving rFVIIa which was likely a reflection of the severity of the underlying condition or injury. A recent Cochrane review did not show improvement in mortality in patients treated with rFVIIa and showed increased risk of arterial thromboembolic events.(Simpson *et al.*, 2012) Cost-effectiveness analysis has also shown significant incremental cost associated with rFVIIa use in massive transfusion.(Ho and Litton, 2012) These considerations led the Canadian National Advisory Committee on Blood Products to recommend against use of rFVIIa in non-haemophilic bleeding.(Lin, Moltzan, Anderson, 2012) rFVIIa has subsequently been removed from our hospital MTP.

MTP have begun to be utilized in patients bleeding due to non-traumatic etiologies despite evidence of benefit outside of military and other trauma settings. We present a large cohort of MTP activation for non-trauma indications. Underlying medical conditions and severity of illness demonstrated by APACHE score were higher in non-trauma patients, but 24-hour mortality was greater in trauma patients suggesting the presence of other factors that contributed to mortality differences between the groups. *Even though the majority of patients did not receive a massive transfusion after MTP activation, no significant difference in overall hospital blood product use was found after MTP institution at our institution.* Therefore, unrestricted MTP utilization did not significantly impact the hospital transfusion services, but non-trauma patients should be included into prospective studies to ensure benefit of MTP in this population.

Acknowledgments

We appreciate the assistance of Josh Salzman in the IRB application and coordination of data abstraction.

Lisa Baumann Kreuziger's fellowship is supported through an NIH T32 Training Grant.

References

- Borgman M, Spinella P, Perkins J, Grathwohl K, Repine T, Beekley A, Sebesta J, Jenkins D, Wade C, Holcomb J. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *The Journal of Trauma*. 2007; 63(4):805–13. [PubMed: 18090009]
- Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *The Journal of Trauma*. 2003; 54(6):1127–30. [PubMed: 12813333]
- Cotton B, Gunter O, Isbell J, Au B, Robertson A, Morris J, St Jacques P, Young P. Damage control hematology: the impact of a trauma exsanguination protocol on survival and blood product utilization. *The Journal of Trauma*. 2008; 64(5):1177–82. [PubMed: 18469638]
- Counts RB, Haisch C, Simon TL, Maxwell NG, Heimbach DM, Carrico CJ. Hemostasis in massively transfused trauma patients. *Annals of Surgery*. 1979; 190(1):91–9. [PubMed: 464685]

- Ho K, Litton E. Cost-effectiveness of using recombinant activated factor VII as an off-label rescue treatment for critical bleeding requiring massive transfusion. *Transfusion*. 2012; 52(8):1696–702. [PubMed: 22211634]
- Holcomb J, Del Junco D, Fox E, Wade C, Cohen M, Schreiber M, Alarcon L, Bai Y, Brasel K, Bulger E, Cotton B, Matijevic N, Muskat P, Myers J, Phelan H, White C, Zhang J, Rahbar M. The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study: Comparative Effectiveness of a Time-Varying Treatment With Competing Risks. *Archives of Surgery*. 2012:1–10.
- Kauvar D, Sarfati M, Kraiss L. Intraoperative blood product resuscitation and mortality in ruptured abdominal aortic aneurysm. *Journal of Vascular Surgery*. 2012; 55(3):688–92. [PubMed: 22277689]
- Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Critical Care Medicine*. 1985; 13(10):818–29. [PubMed: 3928249]
- Lin Y, Moltzan CJ, Anderson DR. The evidence for the use of recombinant factor VIIa in massive bleeding: revision of the transfusion policy framework. *Transfusion Medicine*. 2012; 22(6):383–94. [PubMed: 22630348]
- Neal, McDaniel Lauren; Sperry, Matthew; Alarcon, Jason; Forsythe, Louis; Triulzi, Raquel; Peitzman, Darrell; Andrew Raval, Jay. Use of a massive transfusion protocol in nontrauma patients: activate away. *Journal of the American College of Surgeons*. 2013; 216(6):1103–9. [PubMed: 23571144]
- Morse B, Dente C, Hodgman E, Shaz B, Winkler A, Nicholas J, Wyrzykowski A, Rozycki G, Feliciano D. Outcomes after massive transfusion in nontrauma patients in the era of damage control resuscitation. *American Surgeon*. 2012; 78(6):679–84. [PubMed: 22643264]
- Morse B, Dente C, Hodgman E, Shaz B, Nicholas J, Wyrzykowski A, Salomone J, Vercruysse G, Rozycki G, Feliciano D. The effects of protocolized use of recombinant factor VIIa within a massive transfusion protocol in a civilian level I trauma center. *American Surgeon*. 2011; 77(8):1043–9. [PubMed: 21944521]
- Neal M, Marsh A, Marino R, Kautza B, Raval J, Forsythe R, Marshall G, Sperry J. Massive transfusion: an evidence-based review of recent developments. *Archives of surgery*. 2012; 147(6):563–71. [PubMed: 22786545]
- Phan HH, Wisner DH. Should we increase the ratio of plasma/platelets to red blood cells in massive transfusion: what is the evidence? *Vox sanguinis*. 2010; 98(3):395–402. [PubMed: 20432517]
- Rajasekhar A, Gowing R, Zarychanski R, Arnold D, Lim W, Crowther M, Lottenberg R. Survival of trauma patients after massive red blood cell transfusion using a high or low red blood cell to plasma transfusion ratio. *Critical Care Medicine*. 2011; 39(6):1507–13. [PubMed: 21336132]
- Roback J, Caldwell S, Carson J, Davenport R, Drew M, Eder A, Fung M, Hamilton M, Hess J, Luban N, Perkins J, Sachais B, Shander A, Silverman T, Snyder E, Tormey C, Waters J, Djulbegovic B. Evidence-based practice guidelines for plasma transfusion. *Transfusion*. 2010; 50(6):1227–39. [PubMed: 20345562]
- Rubin, D. Multiple Imputation in Nonresponse of Surveys. New York: J Wiley & Sons; 1987.
- Saule I, Hawkins N. Transfusion practice in major obstetric haemorrhage: lessons from trauma. *International Journal of Obstetric Anesthesia*. 2012; 21(1):79–83. [PubMed: 22119633]
- Simmons RL, Collins JA, Heisterkamp CA, Mills DE, Andren R, Phillips LL. Coagulation disorders in combat casualties. I. Acute changes after wounding. II. Effects of massive transfusion. 3. Post-resuscitative changes. *Annals of Surgery*. 1969; 169(4):455–82. [PubMed: 5774736]
- Simpson E, Lin Y, Stanworth S, Birchall J, Doree C, Hyde C. Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia. *Cochrane database of systematic reviews*. 2012; 3:CD005011. [PubMed: 22419303]
- Sinha R, Roxby D, Bersten A. Experience with a massive transfusion protocol in the management of massive haemorrhage. *Transfusion Medicine*. 2013; 23(2):108–13. [PubMed: 23521624]
- Wafaisade A, Maegele M, Lefering R, Braun M, Peiniger S, Neugebauer E, Bouillon B. High plasma to red blood cell ratios are associated with lower mortality rates in patients receiving multiple transfusion (4 red blood cell units<10) during acute trauma resuscitation. *The Journal of Trauma*. 2011; 70(1):81–8. [PubMed: 21217485]

Figure 1.
Massive Transfusion Protocol (MTP) Flow Diagram

Table 1

Baseline Demographics

Variable	All (n=133)	Non-Trauma (n=63)	Trauma (n=62)
Age	53 ± 18.6	61 ± 14.2 *	44 ± 18.8 *
Males (%)	68	67	69
INR n=124	1.6 ± 0.8	1.6 ± 0.8	1.6 ± 0.6
aPTT n=90	42 ± 27	39 ± 27	44 ± 28
Fibrinogen n=40	170 ± 85	187 ± 20	47 ± 12
Hemoglobin n=127	10 ± 2.6	9 ± 2.5	11 ± 2.4
Platelet n=120	205 ± 113	184 ± 128 *	231 ± 85 *
Total Bilirubin n=34	1.5 ± 1.8	1.5 ± 1.9	0.6 ± 0.1
AST n=40 median (IQR)	38 (26–68)	39 (26–59)	142 (23–978)
Albumin n=35	2.7 ± 0.7	2.7 ± 0.7	3.1
Creatinine n=126	1.4 ± 1.1	1.6 ± 1.5	1.2 ± 0.4
APACHE n=107	27 ± 8.5	29 ± 8 *	25 ± 9 *

Values are expressed in mean ± standard deviation unless otherwise indicated

* Statistically significant difference (p<0.05)

INR=International Normalized Ratio, aPTT=activated partial thromboplastin time, AST=aspartate aminotransferase, IQR=Intraquartile range

Table 2

Blood product and adjunctive medication usage during activation of the massive transfusion protocol

Variable	All (n=133)	Non-Trauma (n=63)	Trauma (n=62)	p-value
PRBC	9.5 ± 7.4	8.7 ± 7.0	10 ± 8.1	0.47
Plasma	6.5 ± 5.9	6.2 ± 5.7	6.3 ± 6.0	0.91
Platelets	1.4 ± 1.5	1.5 ± 1.3	1.2 ± 1.4	0.14
Cryoprecipitate	0.8 ± 2.1	1.0 ± 2.2	0.6 ± 2.0	0.09
rfVIIa n(%)	23 (17)	12 (19)	9 (15)	0.38
Aminocaproic acid n(%)	16 (12)	14 (22)	0 (0)	<0.01
Vitamin K n(%)	28 (21)	20 (32)	5 (8)	<0.01
Desmopressin n(%)	7 (5)	6 (9.5)	1 (1.6)	0.06

Values for blood products are given as mean ± SD, comparison between non-trauma and trauma groups with *Wilcoxon* test. Values for medications given as n (%) and compared using Chi-Square test. PRBC=packed red blood cells, rfVIIa=recombinant activated Factor VII

Table 3

Indications for Activation of Massive Transfusion Protocol

Non-trauma (n=63)		Trauma (n=62)	
Indication	N (%)	Indication	%
Vascular rupture	23 (37)	MVA	33 (53)
Gastrointestinal bleed	16 (25)	Gun shot or stabbing	22 (36)
Cardiothoracic surgery	11 (17)	Falls	4 (6)
Obstetric bleed	5 (8)	Head Trauma	2 (3)
Thrombosis	2 (3)	Vascular injury	1 (2)
Orthopedic	1 (2)		
Other*	5 (8)		

MVA=motor vehicle accident

* Other include septic shock, splenic rupture, exploratory laparotomy, neurosurgery, liver disease without bleeding identified

Table 4

Comparison of transfusion ratios between patients with activation of the massive transfusion protocol for trauma and non-trauma indications

	Ratio of Plasma:Packed Red Blood Cell Units			
	<1:4	1:4 – 1:2	1:2 – 1:1	>1:1
# Non-Trauma (%)	7 (11.1)	11 (17.5)	37 (58.7)	8 (12.7)
# Trauma (%)	11 (17.7)	17 (27.4)	30 (48.4)	4 (6.5)
All MTP	18 (14.4)	28 (22.4)	67 (53.6)	12 (9.6)
OR In-hospital Mortality	1.12	0.66	0.68	1 (reference)

OR= Odds ratio. Fishers exact test of transfusion ratio by MTP category p=0.246. No statistical significance found in odds of mortality between transfusion ratio groups using >1:1 as reference.

Table 5

Hospital-wide use of blood products before and after massive transfusion protocol (MTP) implementation

	Pre-MTP implementation	Post-MTP implementation	p-value
Monthly Hospital Discharges	2298 (2068–2349)	2273 (2046–2424)	0.92
# Patients receiving Blood Products per month	235 (221–259)	218 (187–252)	0.03
Total Blood Product transfused/#receiving product	5.4 (4.4–6.3)	5.0 (4.1–6.7)	0.92
PRBC/# receiving product	3.2 (2.9–3.5)	3.0 (2.6–3.6)	0.08
Plasma/# receiving product	1.5 (1.2–1.9)	1.5 (1.0–3.0)	0.78
Platelets/# receiving product	0.3 (0.2–0.5)	0.4 (0.2–0.7)	0.65
Cryoprecipitate/# receiving product	0.1 (0–0.7)	0.2 (0–0.6)	0.13

All values are expressed as Median (range). PRBC=packed red blood cells