Impact of Infusion Rates of Fresh Frozen Plasma and Platelets During the First 180 Minutes of Resuscitation

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BACKGROUND: Whether high-ratio resuscitation (HRR) provides patients with survival advantage remains controversial. We hypothesized a direct correlation between HRR infusion rates in the first 180 minutes of resuscitation and survival.

STUDY DESIGN: This was a retrospective analysis of massively transfused trauma patients surviving more than 30 minutes and undergoing surgery at a level 1 trauma center. Mean infusion rates (MIR) of packed red blood cells (PRBC), fresh frozen plasma (FFP), and platelets (Plt) were calculated for length of intervention (emergency department [ED] time + operating room [OR] time). Patients were categorized as HRR (FFP:PRBC > 0.7, and/or Plts: PRBC > 0.7) vs low-ratio resuscitation (LRR). Student's *t*-tests and chi-square tests were used to compare survivors with nonsurvivors. Cox proportional hazards regression models and Kaplan-Meier curves were generated to evaluate the association between MIR for FFP:PRBC and Plt:PRBC and 180-minute survival.

RESULTS: There were 151 patients who met criteria: 121 (80.1%) patients survived 180 minutes (MIR:PRBC 71.9 mL/min, FFP 92.0 mL/min, Plt 3.5 mL/min) vs 30 (19.9%) who did not survive (MIR:PRBC 47.3 mL/min, FFP 33.7 mL/min, Plt 1.1 mL/min), $p = 0.43$, $p < 0.0001$ and $p < 0.011$, respectively. A Cox regression model evaluated PRBC rate, FFP rate, and Plt rate (mL/min) as mortality predictors within 180 minutes to assess if they significantly affected survival (hazard ratios 1.01 [$p = 0.054$], 0.97 [$p < 0.0001$], and 0.75 [$p = 0.01$], respectively). Another model used stepwise Cox regression including PRBC rate, FFP rate, and Plt rate (hazard ratios 1.00 [$p = 0.85$], 0.97 [$p < 0.0001$], and 0.88 [$p = 0.24$], respectively), as well as possible confounding variables.

CONCLUSIONS: This is the first study to examine effects of MIRs on survival. Further studies on the effects of narrow time-interval analysis for blood product resuscitation are warranted. (J Am Coll Surg 2014;219:181−188. © 2014 by the American College of Surgeons)

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Exsanguination remains the leading cause of preventable traumatic death in both military and civilian settings.[1,2] A major cause of early mortality in trauma patients with severe hemorrhage is coagulopathy, along with acidosis and hypothermia.[3] Patients suffering severe traumatic injuries in the presence of tissue hypoperfusion often present to hospitals with acute coagulopathy of trauma (25% of cases) even before resuscitation efforts, with an overall 4-fold increase in mortality.[4,5] Relative to other mortality causes, such as multisystem organ failure and traumatic brain injury, death from hemorrhage occurs early, usually 2 to 6 hours after the traumatic event.[6-9] It has therefore been well recognized that efficacious resuscitation strategies must begin early and be used in conjunction with surgical hemostatic interventions.[10-15]

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Abbreviations and Acronyms

Ed = emergency department
FFP = fresh frozen plasma
HRR = high-ratio resuscitation
LRR = low-ratio resuscitation
MIR = mean infusion rate
MTP = massive transfusion protocol
OR = operating room
Plt = platelets
PRBC = packed red blood cells

The timing and volume of blood product administration in patients with severe hemorrhage from trauma is therefore critical to uncovering a survival benefit associated with such strategies.

From military and civilian experience, increased awareness regarding avoidance of unnecessary crystalloids in bleeding trauma patients has emerged, with attention shifting toward target-directed use of blood and blood products for resuscitation in patients requiring massive transfusion.[16] Damage-control resuscitation has emerged as a balanced resuscitation strategy for combatting injury-associated coagulopathy in both military and civilian settings.[4,17-20] This strategy involves the use of fresh frozen plasma (FFP) as a primary resuscitative fluid in high ratios (1:1 to 1:2) with packed red blood cells (PRBCs). The survival advantage for high-ratio resuscitation (HRR) in exsanguinating patients has also been described for platelets (Plt: PRBC).[21,22] Multiple investigations have shown a survival benefit when patients have received FFP early in resuscitation, and at high ratios.[22-37] The impact of volume and timing of high-ratio resuscitation with respect to its survival benefit in hemorrhaging severely injured patients has not been reported.

Despite these advances in resuscitative survival strategies, controversy remains regarding the temporal relationship between blood product administration and survival, and there have been only a handful of studies critically examining the timing of resuscitation vis-à-vis survival in this population. These studies recognize that the timing of blood product administration affects outcomes.[3,35-37] It has been noted that the apparent survival advantage among patients receiving higher ratios of FFP:PRBC may merely be due to the fact that they lived long enough to receive the higher ratio of products, therefore the concept of survival bias.[3,35] Moore and colleagues[38] recognized that the critical timeframe and focus for research on massive transfusion occurs in the first 3 hours. To date, examining volume infusion rates of FFP, Plt, and PRBCs and their effect on survival advantage in severely hemorrhaging patients undergoing damage control surgery has not been studied.

In this study, we examined mean infusion rates (MIR) of blood products in patients with severe hemorrhage undergoing damage control surgery. We hypothesized a dose-dependent direct correlation between infusion rates (for both FFP:PRBC and Plt:PRBC) early in resuscitation (in the first 180 minutes of hospital time) and survival. Furthermore, we postulated that early, time-sensitive appraisal of blood product infusion rates can reveal whether or not early HRR is actually taking place, diminishing the effects of survival bias in studies examining HRR. We believe that using MIR to examine early resuscitation may help elucidate a better understanding of the true impact of HRR on survival.

METHODS

Between January 2009 and January 2011, all adult trauma patients treated at the Spirit of Charity Hospital in New Orleans, LA, who underwent massive transfusion and proceeded directly to the operating room (OR) from the emergency department (ED), were selected for inclusion in this study. Adults were defined as nonpregnant, nonincarcerated patients 18 years of age or greater, without traumatic brain injury. Massive transfusion was defined as the administration of 10 or more units of PRBC during the first 24 hours of hospitalization. The Spirit of Charity Hospital is the only American College of Surgeons-verified level 1 trauma center in Louisiana.

Demographics, transfusion events, laboratory data, and mortality during the first 180 minutes of hospitalization were retrieved from the electronic medical records in collaboration with our trauma registry. A team of trauma surgeons determined and defined length of intervention as ED + OR treatment time. Quality control for data was performed by a second set of trauma surgeons who compared the times for blood product release from the blood bank with the recorded time of product arrival and administration. No data inconsistencies were noted.

Mean infusion rates (MIR, in mL/min) were calculated for PRBC, FFP, and Plts for the length of intervention by dividing the volume of each blood product given per care phase (ie, ED time or OR time) by the time spent in each care phase. No patient had exclusively ED or OR care phases, and no patient had zero blood product given in either care phase. Additionally, all patients received both PRBC and FFP in each care phase. Preliminary review demonstrated that most significant events occurred within the selected study timeframe of the first 180 minutes of hospitalization, and total length of intervention for patients included in the study was less than or equal to 180 minutes for 116 of 151 patients (76.8%). The ratios FFP:PRBC and Plts:PRBC were calculated in units.