

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended to serve as a general statement regarding appropriate patient care practices based upon the available medical literature and clinical expertise at the time of development. They should not be considered to be accepted protocol or policy, nor are intended to replace clinical judgment or dictate care of individual patients.

Massive Transfusion for Hemorrhagic Shock

SUMMARY

Exsanguination is a leading cause of early death following traumatic injury. Recent studies demonstrate a survival benefit to protocol-driven transfusion strategies that approach a 1:1:1 [Packed Red Blood Cell (PRBC), Fresh Frozen Plasma (FFP), and Platelet (PLT)] ratio in patients who require replacement of their total blood volume or greater in 24 hours or less. This resuscitation strategy improves patient survival, reduces hospital / intensive care unit (ICU) length of stay, decreases ventilator days, and reduces patient care costs.

RECOMMENDATIONS

- **Level 1**
 - **None**
- **Level 2**
 - **In patients expected to require massive transfusion, begin resuscitation with blood products as soon as possible (minimizing crystalloid resuscitation) to prevent dilutional coagulopathy.**
 - **Administer blood products in a ratio of 1 unit PRBC : 1 unit FFP : 1 unit PLT.**
- **Level 3**
 - **Consider implementing the Massive Transfusion Protocol (MTP) if the patient meets the following criteria:**
 - **SBP \leq 90 mmHg**
 - **Heart rate \geq 120 beats per minute (bpm)**
 - **Positive focused sonography for trauma (FAST) exam**
 - **pH \leq 7.24**
 - **Consider MTP implementation if transfusing \geq 4 units of PRBCs over 1 hour or \geq 10 units over 24 hours (more than one total blood volume).**
 - **Maintain platelet counts above 100,000/dL during times of active hemorrhage.**

INTRODUCTION

Patient mortality following traumatic injury has decreased over the past 30 years mainly due to improved damage control procedures. Mortality rates continue to be elevated during the first hours following trauma center arrival, however, among patients with uncontrolled hemorrhage (1). This continued high mortality rate is attributable to ongoing hemorrhagic shock as a result of the self-perpetuating triad of coagulopathy, acidosis, and hypothermia (2). Measures to stop this process have long been a part of trauma resuscitation, including hypothermia management, surgical control of ongoing bleeding, and treatment of coagulopathy with blood products.

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

In the past decade, there has been a progressive trend towards increased use of blood products during trauma resuscitation, including plasma, platelets, and cryoprecipitate, due to the military experience with whole blood resuscitation in soldiers requiring “massive transfusion”. Massive transfusion is universally accepted as the replacement of a patient’s blood volume, or transfusion of ≥ 10 units of PRBCs, over a 24 hour period (3-9). Similar “damage control resuscitation” is required in approximately 2-5% of civilian trauma. Such early intervention has been demonstrated to translate into a significant improvement in patient outcome (5-9). Damage control resuscitation is designed to treat coagulopathy prior to its clinical manifestation, therefore stopping the self-perpetuating loop of coagulopathic hemorrhage or “deadly triad”.

The strategy of utilizing higher PRBCs:plasma:platelets ratios is not new and has been shown to have modest improvements in patient mortality (4-6). Most recently, there has been significant interest in protocolization of this transfusion process. Studies demonstrate improved patient outcome with implementation of a massive transfusion protocol (MTP) when compared to physician/lab driven resuscitation (4,5,8,9). This improved mortality has been attributed to reduced time to first transfusion of products, thus addressing the fundamental problem of coagulopathy. Riskin et al at Stanford University have shown that a protocol-driven process improves communication among departments, improves the availability of and reduces delays in obtaining blood products, and improves patient outcome (5). Additionally, improved outcomes can be attributed to reducing the use of uncrossmatched blood which has been shown to be an independent predictor of mortality (10).

The optimal ratio of blood products has not been identified, but the data suggests that a 1:2 to 1:3 ratio of PRBC to plasma is optimal and associated with the best outcomes (4,5,8,11-13). It is strongly suggested by Holcomb et al that trying to achieve a 1:1:1 ratio is optimal as this will most closely approximate the 1:2 goal given delays in treatment (6). As for platelets, most studies suggest that transfusing platelets at a 1:1 ratio with PRBCs and trying to achieve a platelet count of greater than 100,000/dL is most beneficial in stopping the coagulopathic cycle and increasing clot formation (5,6). There are a few studies addressing the need for cryoprecipitate and some suggest that transfusing with adequate amounts of plasma will obviate the need for cryoprecipitate (Table 1); however, most studies suggest checking the fibrinogen level and maintaining a level greater than 100 mg/dL (5,11).

FIBRINOGEN CONTENT IN VARIOUS BLOOD PRODUCTS (11)

1 10 unit Cryoprecipitate	2500mg/150ml
1 unit of FFP	400mg/250ml
1 unit of PRBC	<100 mg
1 six pack of platelets	480mg
1 unit of apheresis platelets	300mg
1 unit of whole blood	1000mg

Identifying patients at risk early is a key difference between damage control resuscitation and MTP driven resuscitation. Patients who arrive in the resuscitation bay in profound hemorrhagic shock are easy to identify; it is the patients that arrive relatively stable who are more difficult. Nunez et al reviewed 596 patients in whom 12.4% met MTP criteria. The need for MTP implementation was identifiable using simple non-laboratory values. Patients with SBP ≤ 90 mmHg or less, positive FAST exam, and heart rate ≥ 120 bpm were more likely to need massive transfusion (14). Mc Laughlin identified 4 independent factors that were associated with risk for massive transfusion: heart rate > 105 bpm, SBP < 110 mmHg, pH < 7.25 , and hematocrit $< 32\%$ (15). Specific injury patterns that should prompt consideration for implementation of a MTP include liver laceration with hemorrhage, emergent abdominal aortic aneurysm, pelvic fracture with overwhelming blood loss, massive gastrointestinal hemorrhage, and coronary artery bypass grafting.

LITERATURE REVIEW

Holcomb et al retrospectively reviewed 466 MTP trauma patients treated from June 2005 to June 2006 at one of 16 Level 1 trauma centers (6). They identified four groups of patients: (1) high plasma and high platelets, (2) high plasma and low platelets, (3) low plasma and high platelets, and (4) low plasma and low platelets. Survival at six hours, 24 hours, and 30 days was recorded. Survival, ICU stay, ventilator free days, and hospital free days were best amongst the high plasma-high platelet group. The best outcomes were in centers with an active MTP in place. Survival was best in patients with plasma to PRBC ratios >1:2 and with platelet ratios of >1:5 (Class II).

O'Keeffe et al performed a prospective study of patients for two years after MTP implementation compared to patients from the year prior to MTP (4). Improved times to first transfusion were noted. The MTP patients received fewer blood products in the first 24 hours. Most significantly, the evaluation of differences in cost noted a \$200,000 savings despite the more frequent use of factor VIIa as a part of their protocol (Class III).

Riskin et al reviewed their experience two years prior to and post MTP implementation (5). They originally thought they would see a reduction in the ratio of PRBC to plasma, however, the ratios were similar (1:1.8). An increase in survival was noted following MTP implementation. This was attributed to improved communication with the blood bank improving the time to first transfusion of all products. They recommend activation of a MTP for patients with more than four units of PRBCs in one hour or more than 10 units in less than 12 hours. Resuscitation to hemodynamic stability is recommended instead of a particular hemoglobin or hematocrit target (Class III).

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MASSIVE TRANSFUSION PROTOCOL

