Massive Hemorrhage Protocol

A Practical Approach to the Bleeding Trauma Patient

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KEYWORDS

• Damage control resuscitation • Trauma • Massive hemorrhage protocol • Resuscitation

KEY POINTS

- When possible, conduct a team prebriefing to establish a shared mental model for managing a massively hemorrhaging patient.
- Early administration of blood/blood products results in better patient outcomes for bleeding trauma patients.
- No clinical prediction scores are 100% accurate for predicting MHP. A combination of patient factors, clinical course, and response to blood products may be preferrable.
- Regular monitoring of temperature, fibrinogen, and calcium is critical to optimize patient outcomes.
- Massive hemorrhage protocol termination is critical to preserve blood products, and criteria should be established to support this decision.

CASE EXAMPLE

A 57-year-old female involved in a high-speed motor vehicle collision is transported to the emergency department (ED) of a large community hospital in 28 minutes. She is brought into the resuscitation room, and the clinical team begins their assessment and treatment following the principles of Advanced Trauma Life Support. Her vital signs are as follows:

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Respiratory rate 26 breaths/min,
Blood pressure 88/50,
Heart rate 110 beats/min,
Temperature 34.5°C,
Glasgow Coma Scale is 12.

A focused assessment with sonography in trauma examination is positive for free fluid in the right upper quadrant. There is no evidence of pneumothorax on ultrasound. Her pelvis is stable although suspected to be fractured based on pain during the examination. She has no past medical history, takes no medications, and has no drug allergies. At this point, the clinical team is faced with decisions related to blood product administration, the role of the massive hemorrhage protocol (MHP), and establishing definitive hemostasis.

INTRODUCTION

A damage-control resuscitation strategy represents the standard for the care of the hemorrhaging trauma patient.[1] This 2-pronged approach provides early, ratio-based, blood product administration coupled with definitive and rapid hemostasis. Together, when combined and delivered quickly and effectively, these 2 elements provide improved patient outcomes.[1]

These patients frequently require the initiation of a MHP which is the systematic and coordinated delivery of care to bleeding patients. Previously termed massive transfusion protocols, these early protocols focused predominately on the blood and blood component administration. Emerging evidence supports a more comprehensive approach to caring for these patients, hence the now widely and more aptly termed MHP.

The benefits of MHPs in trauma are numerous, including:[2–6]

1. Decreased variability in treatment
2. Reduced blood product wastage
3. Improved interprofessional communication
4. Standardized process evaluation
5. Faster time to transfusion

Despite the clear benefits of MHPs demonstrated through multiple studies, the details related to the decision-making, the logistics, and the nuances of these protocols remain poorly articulated to the emergency medicine (EM) clinician. As a result, our focus will be to bridge the gap between the evidence and the real-world application of a trauma MHP.

We will address how EM clinicians can practically deliver high-quality, evidence-based care to the bleeding trauma patient through 7 clinically relevant questions. These follow the 7 Ts described by the Ontario MHP group (**Fig. 1**).[7]

Triggers: When Should the Massive Hemorrhage Protocol Be Activated?

The question of when to "trigger" or activate an MHP in trauma is of the utmost importance during the early stages of a trauma resuscitation. There is a clear tension that exists between underactivation (risking preventable exsanguination) and overactivation (resulting in unnecessary transfusion and wasted blood components).[7,8] This tension must be navigated by the emergency or trauma physician during the early stages of the resuscitation and may be complicated by early clinical uncertainty related to the patient's injuries.

Early administration of blood products is linked with improved outcomes among bleeding trauma patients. A delay of 1 minute is associated with a 5% increase in

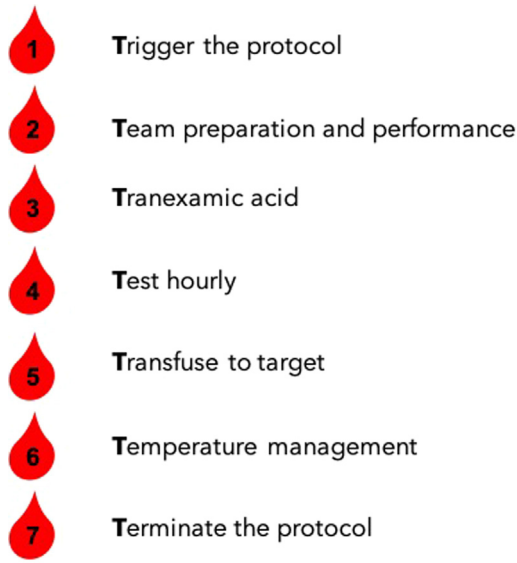

Fig. 1. The 7 Ts of massive hemorrhage protocol

odds of death.[9] Some precise and reliable tactics are needed for clinicians to make an informed, evidence-based decision particularly under stress and high cognitive load.

Historically, most MHP activation criteria are evaluated in the context of the traditional definition of massive transfusion such as 10 units of red blood cells (RBCs) in 24 hours.[10] This definition is challenging as it has little clinical relevance during the early stages of resuscitation (**Fig. 2**).

None of these scores are perfectly 100% sensitive and specific, but they do provide guidance in the decision-making process for MHP activation (**Table 1**).[17] The recently developed RABT score likely offers the greatest utility by combining the shock index (SI), components of the ABC score, and the addition of pelvic fracture.[15]

Many patients with hypotension or hypoperfusion, however, will stabilize following 1 to 2 units of RBCs, and only a subset will require additional blood products.[18] In most cases, our preferred approach to MHP activation is a 2-tiered process whereby the clinician calls for and administers up to 3 units of uncross-matched RBCs (**Fig. 3**). Should this critical administration threshold be surpassed (or predicted to be), then MHP is activated.[16,18]

In our opinion, there are some circumstances under which MHP activation can be considered even before any blood products are administered:

1. The clinician predicts $\geq$3 units of blood products will be required based on the injury mechanism and initial available clinical information[16] (eg, profound prehospital hypotension [systolic blood pressure <60 mm Hg], prehospital traumatic cardiac arrest, hemodynamic instability, and transmediastinal gunshot wound).
2. Institutions whereby the only way to acquire immediate blood products is through MHP activation.
3. The patient is receiving blood products via EMS or at the transferring facility and has ongoing hemodynamic instability.

Finally, based on our collective experience, we consider several high-risk conditions or circumstances that lower our threshold for MHP activation. While evidence is

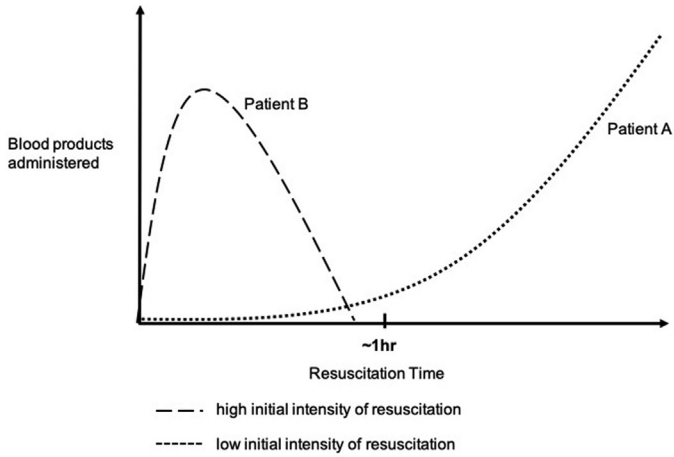

Fig. 2. Patient A who receives 2 units in the emergency department (ED) and 10 units 4 hours later during a trauma laparotomy while considered a "massive transfusion" (MT) by the traditional definition has a more delayed resuscitation trajectory. In contrast, patient B who requires 4 red blood cells (RBCs) and 3 fresh frozen plasma within 60 minutes of ED arrival before stabilizing, while not meeting the typical MT threshold, benefits more from immediate blood products, and hence early massive hemorrhage protocol (MHP) activation. Patients with similar trajectories to patient B are those who the ED clinician wishes to quickly identify for MHP activation.

lacking to provide specific recommendations in such circumstances, we have repeatedly observed rapid clinical deterioration and suggest that the presence of 1 or more of these components lower the threshold to activate the MHP:[19–21]

1. Anticoagulation
2. Prehospital hypotension or shock index $\geq$1.0
3. Geriatric population (typically >65 years).

Team: How Can Team Performance During a Massive Hemorrhage Protocol Be Leveraged to Optimize Patient Outcomes?

An MHP is a specialized, complex yet highly effective strategy to rapidly deliver blood components and coordinate patient care in the setting of traumatic hemorrhage. This protocolized delivery of interventions requires a multidisciplinary (and often ad hoc) team to function seamlessly in a time-sensitive manner. Mini-teams form at the bedside, in the transfusion department, hematology laboratory, and in the transportation of blood products. MHP performance is critical to patient outcomes.

A high-performing team during an MHP is akin to the pit crew in Formula 1.[22] Each individual or mini-team functions semi-autonomously in their defined roles, yet together they strive toward a common goal. For a Formula 1 pit crew, the goal is to prepare the car to head back on the track as fast as possible. During an MHP, the goal is to deliver the necessary blood components and other care interventions as efficiently as possible. To achieve these goals, there are several aspects that lead to a successful MHP team performance:[23–26]

1. Prebriefing and debriefing for each MHP to establish a shared mental model and promote future improvement by tracking quality metrics over time.

Table 1
Massive hemorrhage protocol prediction tools, components, and sensitivity/specificity for massive transfusion (>10U/24 h)

Score/Tool	Components	Sensitivity	Specificity
ABC score[11–14] (≥2 predicts MT)	1. Heart rate (HR) > 120 2. Systolic blood pressure (sBP) < 90 mm Hg 3. Focused abdominal sonography in trauma (FAST) positive 4. Penetrating trauma	47%–90%	67%–90%
Shock Index[14,15] (≥1.0 predicts MT)	HR/sBP	68%	81%
RABT score[15] (≥2 predicts MT)	1. Shock Index ≥ 1.0 2. Pelvic fracture 3. FAST positive 4. Penetrating trauma	78%	91%
Resuscitation intensity (RI)[16]	Total number of products in first 30 min of arrival (eg, 1U RBC, 1U FFP, 1L crystalloid, 500 cc colloid). Typical threshold is ≥4 (RI4)	80%[a]	37%[a]
Critical administration threshold[16]	3U RBC during 1-h period within 24 h after arrival	90%[a]	26%[a]
Narrow pulse pressure[17]	Systolic arterial pressure - diastolic arterial pressure < 30 mm Hg	52.8%	82.7%

Abbreviation: ABC, assessment of blood consumption; FFP, fresh frozen plasma; MT, massive transfusion; RABT, revised assessment of bleeding and transfusion.
[a] Predicting 24-h mortality.

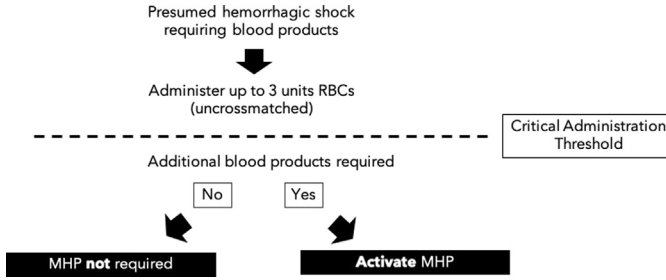

Fig. 3. Two-tiered approach to massive hemorrhage protocol (MHP) activation using the critical administration threshold.

2. Regular practice through case-based education or preferably simulation-based training.
3. Focus on evidence-based communication techniques including closed-loop communication, standardized lexicon of MHP terms, role clarity, and regular situation-assessment updates.

Testing: What Lab Tests Are Needed Initially and Throughout the Process?

Throughout an MHP, laboratory tests are necessary to monitor the adequacy of treatment and evolving complications. High-quality clinical studies are scarce, and there is considerable real-life heterogeneity about which tests are ordered, at what intervals, and how the results impact further management. It remains uncertain whether point-of-care viscoelastic testing such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM) can effectively guide resuscitation of bleeding patients in trauma.[27] Recognizing these limitations, our group recently developed best-practice recommendations on laboratory testing during MHP.[7] These are summarized below:

- Prioritize the collection of samples for ABO/typing and compatibility testing.
- Laboratory testing should include complete blood count, coagulation testing (INR, activated partial thromboplastin time [aPTT], and fibrinogen), electrolytes, calcium (preferably, ionized), arterial or venous blood gas, and lactate.
- TEG or ROTEM represent an alternative for managing coagulopathy; however, these tests lack a clear benefit while increasing the frequency of transfusion.[27]
- A prespecified sequence of sample acquisition eliminates the risk of tube anticoagulant/additive cross-contamination (**Fig. 4**).
- Hourly laboratory testing until the termination of the protocol.
- Required tubes should be assembled into bundles, along with prechecked requisitions, labeled, and attached to the MHP cooler.
- Prioritized results that may have a direct impact on clinical care (eg, hemoglobin, electrolytes).
- Aim for a lab turn-around-time of 20 minutes for all tests.
- Direct communication of laboratory results to clinicians is essential (ie, passive communication such as uploading to a hospital information system, faxing, or emailing is not acceptable during MHP).
- Consider MHP phone attached to the first MHP cooler with a direct line for clinicians to the laboratory.

BLOOD DRAW TOOL

MHP Blood Draw and Testing Protocol

Lab tests[1]		Adult	Pediatric	Baseline	#1	#2	#3	#4	#5
INR, aPTT (baseline only), Fibrinogen	Sodium Citrate (Blue)	2.7mL	1.8 mL	x	x	x	x	x	x
ROTEM/TEG	Sodium Citrate (Blue)	2.7 mL	1.8 mL	x	x	x	x	x	x
Na, K, Cl, Mg, Urea	Serum (Red/Gold)	4.5 mL	2.0 mL	x	x	x	x	x	x
Glucose (baseline only)	Serum (Red/Gold)	NA		x	NA	NA	NA	NA	NA
Ionized Calcium[2]	Serum (Gold)	4.5 mL	2.0 mL	x	x	x	x	x	x
Venous Lactate[2]	Lithium Heparin (Green)	4.5 mL	2.0 mL	x	x	x	x	x	x
G&S (baseline only)[3]	EDTA (Pink)	6.0 mL	1.0 mL[4]	x	NA	NA	NA	NA	NA
CBC	EDTA (Lavender)	4.0 mL	1.0 mL	x	x	x	x	x	x
Venous Lactate	Lithium Heparin (Syringe)	-	-	x	x	x	x	x	x
Arterial Lactate	Lithium Heparin (Syringe)	-	-	x	x	x	x	x	x
Blood gas (pH and base excess)	Lithium Heparin (Syringe)	-	-	x	x	x	x	x	x
Ionized Calcium	Lithium Heparin (Syringe)	-	-	x	x	x	x	x	x
Na, K, Cl	Lithium Heparin (Syringe)	-	-	x	x	x	x	x	x

[1]Lab draws appear in appropriate draw order - Sodium Citrate should always be draw n first.
[2]Can be bundled up (i.e., done together with a blood gas sample, if device/analyzer is available).
[3]Follow facility specific policies regarding ABO confirmation and requirement for second specimen.
[4]500uL for neonates
Prioritize samples as per MHP lead and as available at your facility - vacutainer/microtainers may differ depending on facility and patient population.

Fig. 4. Massive hemorrhage protocol blood draw tool including sequence of sample acquisition (credit ORBCoN).

Tranexamic Acid: What Is the Role of Tranexamic Acid in a Massive Hemorrhage Protocol?

Tranexamic acid (TXA) has been shown in definitive trials to prevent bleeding-related mortality in cases of traumatic injury,[28,29] traumatic brain injury,[30,31] and postpartum hemorrhage.[32] It is most effective in reducing mortality rates if given within 60 minutes of injury or onset of hemorrhage.[28,29,33] An adult total dose of 2 to 3 g appears sufficient[29] and can be given as a single infusion to minimize complexity of care[30] or as 2 intravenous pushes.[34,35] In traumatic injury, prehospital administration of TXA is superior to delaying treatment till hospital arrival,[29,30] has been proven to be logistically possible, is safe, and should be a goal for prehospital transport teams.

In the future, once high-quality bioavailability studies have been performed, intramuscular administration is likely to be an alternative route of administration for patients where intravenous access cannot be secured.[36] In contrast to all other patient groups, TXA is of no benefit in patients with gastrointestinal hemorrhage and increases the risk of thromboembolic complications (in the high doses used in the trial [4 g]).[37] TXA cannot be withheld or its dose cannot be personalized based on currently available laboratory testing, including viscoelastic testing, due to its poor sensitivity.[38] Investigators have put forward analyses from nonrandomized studies suggesting the need to withhold TXA for patients with "fibrinolytic shutdown" (abnormal hypofibrinolysis) due to concerns regarding an increased risk of thromboembolic complications[39]; however, this concern has not been confirmed in other retrospective studies and remains a theoretic concern.[40,41] TXA improves the coagulopathy seen in severely injured trauma patients,[35] for example, when employed before arriving at the hospital, it abrogates trauma-induced coagulopathy.[42] The cost of treatment is minimal (approximately $20 USD per patient), and hence, it is highly cost-effective.[43] The risk of adverse events from a single dose is low, with only an elevated risk of seizures being identified from the randomized trials.[30] Systematic reviews find no increased risk of arterial or venous thromboembolism,[44] with the exception of patients with gastrointestinal hemorrhage receiving high doses (4 g).[37]

Temperature: How Should the Patient's Temperature Be Managed During the Massive Hemorrhage Protocol?

Monitoring and managing temperature is essential for every MHP. In a hypothermic patient, an increase in core temperature of 1°C is associated with a 10% reduction in RBC transfusion.[45] In addition, hypothermia is an independent predictor of mortality

in trauma and causes increased blood loss and higher transfusion requirements.[45,46] Furthermore, the administration of blood components stored at temperatures between 2° C and 6° C can worsen hypothermia if the patient is massively transfused.[47] In this section, we will provide practical recommendations on how to manage temperature in actively bleeding trauma patients focusing on:

1. How to accurately monitor temperature,
2. What techniques to use to maintain or increase temperature, and
3. Practical tips to apply these techniques.

How to monitor the patient's temperature?

The thermal resistor of an intravascular pulmonary catheter is the gold standard for temperature monitoring. However, given the need for specific technical skills for placement and potential complications associated with its use, these catheters are not recommended as a standard tool.[48,49] The use of esophageal, rectal, or bladder thermometer is the technique recommended.[49–52] The selected modality should be informed by the clinical situation and local resources. Thermometers that are accurate at temperatures less than 34° C are recommended to measure the core temperature given the concern for hypothermia during massive hemorrhage resuscitation.[53] Peripheral thermometers (axillary, oral, tympanic membrane, or temporal artery) are less accurate with a margin of error of 2° C, especially at extremes of temperature.[50,51] Based on the best available evidence, we recommend the following:

- The use of a tympanic membrane thermometer until a central monitor is in place.[54,55]
- Initial temperature measurement within 15 minutes of patient arrival or protocol activation.
- Continuous temperature measurement during active rewarming[56] (if not possible, then at least every 30 minutes).

Techniques to maintain or increase a patient's temperature

Prevention of heat loss is important as rewarming hypothermic patients is challenging. Multiple methods should be applied to prevent hypothermia and rewarm the patient, including passive external warming, active external rewarming, and active internal rewarming.[49]

Passive rewarming methods such as removing wet clothing, increasing room temperature, and applying warm blankets should be used to avoid heat loss. However, in isolation, none of these methods are effective to manage significant hypothermia.

Forced-air warmer devices should be used as one of the active external rewarming methods covering a larger area, to be more effective.[57] They are easy and safe to use, decrease heat loss, provide heat to the body, and should be continued in the operating room.[57] Resistive heating devices can increase thermal comfort and maintain the core temperature when physical and logistical challenges limit other methods, such as in prehospital setting and intrahospital transport.[58,59]

Routine use of intravenous fluid warmers should be adopted to avoid worsening of hypothermia due to resuscitation with cold fluids. They should deliver components at normothermia at both low and high flow rates. The temperature should be set ideally at 41.5° C to effectively avoid hypothermia[58]; however, not higher than 43° C to avoid the risk of hemolysis and air embolism.[60]

Intubated patients have a higher risk of heat loss from the airway.[61] Heat and moisture exchange filters should be used to reduce evaporative heat loss from the airway of these patients.

Finally, for patients with temperatures below 32° C who have impaired thermogenesis, the previous cited interventions will possibly be insufficient to raise the core temperature. In these scenarios, clinicians should refer to local guidelines to treat severe hypothermia and investigate other causes aside from massive hemorrhage or transfusion.

Practical tips to apply passive and active rewarming techniques

1. Using shears, as soon as it is safe, remove wet clothing, linens, dressings, and dry the patient thoroughly.[62]
2. Cover the patient with warm blankets
3. The patient's head should also be covered with a warm towel to avoid additional heat loss.[62,63]
4. Forced-air warmer blankets should be in direct contact with the patient, with the perforated side facing the patient, and be secured to avoid it from blowing off the patient as it inflates.

Targets: Once the Massive Hemorrhage Protocol Is Activated, What Resuscitation Targets Should Be Used?

Since bleeding trauma patients may be coagulopathic on arrival and laboratory tests take time, the recommended approach to the transfusion therapy during MHP is ratio-based and is associated with decreased mortality, and faster time to transfusion was associated with better outcomes.[64] The PROPPR trial demonstrated no difference between approaches using 1:1:1 and 1:1:2 ratios.[65] The commonly used and guideline-recommended ratio is 1:1:2 (1 adult dose of platelets (pool of 4 or 1 apheresis unit), 4 units of plasma for every 2 units of RBCs.[66] **Fig. 5** illustrates a prototypical option for configuring MHP packs or coolers. Ratio-based resuscitation may, however, result in inadequate management of coagulopathy, and periodic coagulation tests or viscoelastic assays during MHP is imperative.[67] These tests may allow for a more precise assessment of coagulopathy and enable provision of targeted and personalized hemostatic treatment. The evidence on laboratory targets of transfusion is sparse, with no high-quality clinical trials. Once hemorrhage control is achieved, we recommend to switch to laboratory-based resuscitation.

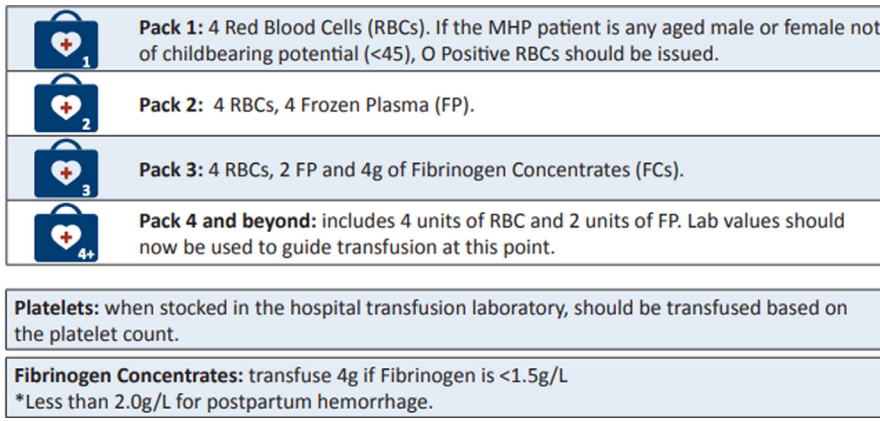

Fig. 5. Example of massive hemorrhage protocol cooler packs composition. (credit ORBCoN).

Thresholds to transfuse red blood cells

RBC transfusion optimizes the oxygen-carrying capacity and provides volume to bleeding patients. In general, numeric thresholds for RBC transfusion are not relevant in the early phases of trauma resuscitation. Rather, we follow the more commonly utilized approach of RBCs when volume is required following the ratios described above.

Thresholds to transfuse platelets

During massive bleeding, platelets usually fall to critical levels only after substantial blood loss and hours of resuscitation (**Fig. 6**). In contrast to the ratio-based approach described above, it may be reasonable to delay platelet transfusion until levels are available. If so, then platelets are transfused when the level is $<100 \times 10^9$/L in patients with intracranial/spinal hemorrhage and less than 50×10^9/L for all other bleeding patients. These thresholds are based on a study from 1972, which demonstrated nearly normal bleeding time at a platelet count of greater than 100×10^9/L and a steep prolongation in bleeding time as platelets fell below 50×10^9/L.[68] These thresholds were widely adopted, and there are no recent high-quality clinical studies to update these recommendations. We recommend platelet transfusion when the level falls below 50×10^9/L rather than following a ratio-based approach for platelets.[7]

Platelet count is only able to assess for quantitative deficiency of platelets. In injured patients, platelet dysfunction may result from injury itself, the use of antiplatelet agents, or congenital defects. If platelet dysfunction is suspected, platelet transfusion may be indicated even in the presence of an adequate platelet count.[69] We strongly recommend consultation with hematology/transfusion medicine regarding an optimal platelet transfusion strategy for complex patients. Viscoelastic assays have an

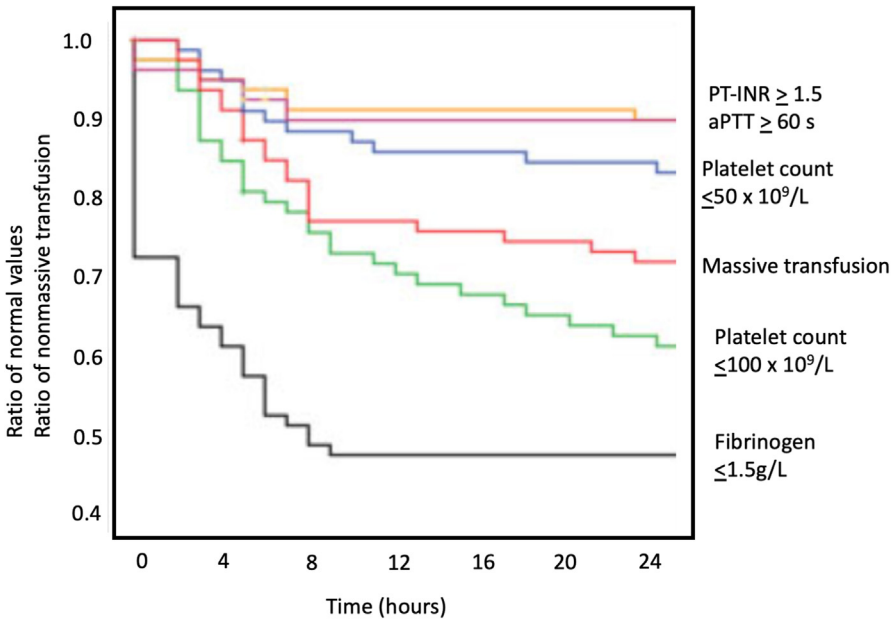

Fig. 6. Kaplan-Meier curves for severely injured trauma patients from emergency department arrival to reaching critical levels of routine coagulation parameters and criteria for massive transfusion (MT) ($\geq$ 10U RBCs). Fibrinogen decreases before platelets, INR, activated partial thromboplastin time (aPTT), and need for MT. (With permission from author).[81]

advantage to assess for the presence of platelet dysfunction.[70] Evidence on how to use their results to guide transfusion therapy is being analyzed. If using ROTEM, reduced EXTEM A10 or MCF (35 mm or below) may signal the need for a platelet transfusion. To correct MCF, in addition to platelets, fibrinogen supplementation may be necessary.[71]

Thresholds to transfuse plasma (or prothrombin complex concentrate)

About 25% of severely injured patients are coagulopathic on admission to ED.[72] Moreover, conventional coagulation tests such as INR are inaccurate to diagnose acute coagulopathy of trauma. More sensitive tests include viscoelastic testing and thrombin generation assays; however, these are not widely available.

It is reasonable to consider plasma transfusion for an INR $\geq$1.8 as it may not be possible to decrease the INR to <1.8 despite large volumes of plasma transfusion.[73,74] Moreover, at INR <1.8, there remain sufficient quantities of clotting factors to effect hemostasis. In the absence of ready availability of plasma, a prothrombin complex concentrate (PCC) may be used.[75,76] The PCC, as compared to plasma, is associated with reduced mortality in bleeding trauma patients and reduced blood loss in bleeding cardiac surgery patients.[76,77]

In some patients, abnormal coagulation tests may also signal the presence of anticoagulant medications or a congenital bleeding disorder. Discussion of these topics is outside the scope of this article. A summary of common drugs that may impair hemostasis and their antidotes is provided in **Table 2**.

Thresholds to transfuse fibrinogen concentrate

Fibrinogen is the first factor to reach critically low levels during massive bleeding.[81] Fibrinogen levels less than 1.5 g/L are associated with increased mortality in massively bleeding trauma patients.[82] Guidelines typically recommend to replace fibrinogen at levels $\leq$1.5 g/L.[66,83] If using rTEG, then a functional fibrinogen (FF)-TEG maximum amplitude less than 20 mm may inform the need for fibrinogen replacement. If using ROTEM, the FIBTEM clot amplitude at 5 min (CA5) may assist with this decision.[71] Evidence-based thresholds have not been established.

Termination: What Factors Should Guide the Clinical Team to Stop the Massive Hemorrhage Protocol?

Similar to the decision to activate the MHP, it is important to have standardized criteria for "stepping down" the protocol. In contrast to the prolific literature on when to activate the MHP, there is very little science to guide the termination of the MHP. Premature termination of the MHP could lead to delays in transfusion, laboratory testing, and transportation. In addition, premature termination can lead to a need to "reactivate" the MHP and to reassemble all team member and leads to confusion within the laboratory as to whether to recommence with pack 1 of blood or continue on from the last pack issued. Similarly, delayed termination can lead to unnecessary transfusions, loss of valuable blood products, continued preparation of blood products by the laboratory staff, and delayed transfusions for other patients within the hospital.

Based on our experience and the best available evidence,[84] it is suggested to consider protocol termination when any of the following occurs:

1. There is definitive hemorrhage control (or a substantial deceleration in blood loss).
2. The patient's hemodynamics and coagulation profile are improving.
3. Inotropes can be reduced or stopped.

At a system level, a protocolized, proactive call from the transfusion laboratory to the clinical team should be integrated into the process if there has been no request

Table 2
Anticoagulant and antiplatelet medications and antidotes

Drug	Antidote	Dosage
Warfarin	PCC IV Vitamin K	INR 1.5 to 2.9–1000 IU INR 3.0 to 5.0–2000 IU INR > 5.0–3000 IU INR unknown – 2000 IU PLUS vitamin K 10 mg IV
Dabigatran (Pradaxa)	Idarucizumab (Praxbind)	5 g IV Repeat at 24 h if PTT up and ongoing bleeding risk
All Xa inhibitors (eg, apixaban [Eliquis], edoxaban [Savaysa], rivaroxaban [Xarelto])[a]	PCC (Note: andexanet not widely available)	2000 IU Repeat at 1 h if ongoing hemorrhage
Low molecular weight heparin (eg, dalteparin, enoxaparin, danaparoid, tinzaparin)	Contact hematology/ transfusion medicine for advice	N/A
ASA	Nothing[b]	N/A
Clopidogrel	Nothing[b] Consider platelet transfusion if ongoing bleeding and other coagulopathies have been corrected	N/A
Ticagrelor	Nothing[b] (Note: bentracimab not yet available)	N/A

Abbreviation: ASA, Acetylsalicylic acid; DOAC, direct acting oral anticoagulants; ICH, intracranial hemorrhage; N/A, not applicable.

[a] Reversal of DOACs is to be considered for a period of 24 h following the last dose.

[b] Clinical studies failed to confirm a benefit of platelet transfusions for ASA/Clopidogrel-treated patients with gastrointestinal bleeding and spontaneous ICH and raised concern regarding harm (use platelet transfusions with caution).[78–80]

for blood within 60 minutes to reaffirm the need to continue the MHP. Failure to terminate the protocol is a common failure point.[85] The MHP almost always commences with formula-based transfusion support and then transitions to laboratory-guided transfusion resuscitation. It remains unknown whether institutions utilizing bedside viscoelastic testing have better clinical outcomes.[27] Some MHPs are designed to be terminated at this transition to lab-based resuscitation; however, we believe that the 2 transitions may not align temporally. Hence, it is acceptable to start lab-guided resuscitation before terminating the MHP. The hospital MHP needs to have a termination protocol to ensure prompt return of blood products, return of the MHP phone or other equipment, safe handover to the intensive care team, and end of protocol blood work. Unnecessary transfusions can occur if this handoff is not structured (ie, failing to communicate that 4 units of RBC were transfused after the last hemoglobin of 6.4 g/dL, leading to additional unnecessary units before a hemoglobin repeat).

An easy, practical, and high-yield tactic to continually improve MHP performance is the integration of a team debrief or huddle to the MHP protocol termination, including a

process of reporting processes that did not go as planned to ensure continuous quality improvement. Finally, to objectively and systematically optimize the MHP, we recommend tracking key process quality indicators including, but not limited to, the following:[7]

1. Proportion of patients receiving TXA within 1 hour of protocol activation.
2. Proportion of patients in whom RBC transfusion is initiated within 15 minutes of protocol activation.
3. Proportion of patients without any blood component wastage.

Case Resolution: Integration of Massive Hemorrhage Protocol Principles

This article provides a detailed review of key MHP principles using the 7T framework. Using the case presented in the introduction of a 57-year-old female involved in a high-speed MVC, we provide a summary for the application of the 7 Ts.

Team: Prior to arrival, the trauma team leader (TTL) conducted a prebriefing "time out" to create a shared mental model, stablish care priorities, and assign tasks. This includes discussion on MHP preactivation, which was not deemed necessary at this point. Instead, the TTL requested 4 units of RBCs to be brought to the trauma bay/ED by a dedicated team member (in case they are not readily and locally available).

Trigger: On arrival, 3 prediction tools were positive (shock index > 1.0, ABC score = 2, and RABT score = 2). However, the team opted to use the critical administration threshold. They transfused 2 units of RBCs while progressing with patient assessment. Two sources of bleeding were identified: (1) intra-abdominal (positive focused assessment with sonography in trauma) and (2) anteroposterior compression fracture of the pelvis on pelvic x-ray. Blood pressure did not improve (90 mm Hg) with the 2 units transfused. The third unit was initiated, and the MHP was activated.

Tranexamic acid: During the prebriefing, the TTL requested TXA (2 g IV bolus), which was prepared and promptly administered following patient's admission. Importantly, the team learned that the patient was using Rivaroxaban for chronic atrial fibrillation. This prompted the administration of PCC (requested urgently and administered while the patient had been taken to the CT scanner suite).

Testing: Following handover from paramedics, the circulating nurse collected blood samples as a new intravenous access was being catheterized prioritizing ABO typing and compatibility testing. Bed-side bundled supplies for minimal laboratory testing were used. Laboratory tests were requested using an established order set, and a team member transported the samples immediately to the laboratory and blood bank. Results with critical values were communicated as they were released by the laboratory staff via phone calls to the trauma bay and operating room (OR) where the patient was transported to following the care provided in the trauma bay/ED. Using a Trauma Resuscitation Checklist to guide postactivation best practices, further blood samples were collected hourly until MHP was called off.

Targets: Following intermittent improvement of the hemodynamic status, the patient was transferred to a hybrid OR for trauma laparotomy, angiography, and possible pelvic angioembolization. At this point, the patient had received the third MHP pack (12 RBCs, 6 plasmas, and 4 g of fibrinogen concentrate [for a fibrinogen level of 1.0 mg/dL]). Platelet level was 157.000/mm^3, and INR was 1.49, not requiring correction. The anesthesiologist switched to a lab-guided strategy by the end of the procedures as the resuscitation moved forward and the patient's hemodynamic status and coagulopathy improved (see Targets section for details).

Temperature: The admission temperature was 34.8°C measured by a tympanic membrane thermometer and at each 30 minutes, subsequently. Two rapid infusers

had been primed prior to patient arrival as part of the prebriefing checklist to infuse blood products at 41.5°C. The patient was promptly exposed with removal of clothes followed by placement of warmed blankets. Following primary and secondary assessments, prior to OR transfer, a forced warm air device was applied. The patient was intubated, warm blankets were placed around the head, and heat and moisture exchange filters were used to reduce further heat loss.

Termination: In the operating room, evacuation of 2 L of blood from the abdominal cavity, splenectomy, liver packing, angiography with embolization, and an external pelvic fixation were performed in a damage-control fashion. By the end of these procedures, the patient's hemodynamic status and coagulopathy had improved considerably, prompting the anesthesiologist to call off the MHP before transfer to the intensive care unit.

SUMMARY

A well-designed MHP is essential in the care of injured and bleeding patients. This article proposes the application of a structured approach using the 7 Ts of MHP to guide this complex process. A successful resuscitation requires a high-performing team following evidence-based metrics. At an institutional level, each MHP requires review to promote areas of success and opportunities for improvement. We believe the 7 Ts of MHP approach is practical, feasible, and customizable across all ED sizes and circumstances. Optimized MHP strategies will inevitably improve outcomes for bleeding trauma patients and reduce the cognitive load for the clinical team.

CLINICS CARE POINTS

- To assist with the decision for MHP activation, the RABT score or critical administration threshold (>3 units/h) is useful.
- When hemorrhage is suspected in a trauma patient, 2 g of TXA should be administered within 3 hours and ideally <1 hour from the injury.
- Upon patient arrival, temperature measurement is essential.
- After the administration of 3 units of RBCs, begin FFP administration to achieve a 2:1 ratio (RBC:FFP).

DISCLOSURE

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