

BLOOD BULLETIN

Futility and Potentially Inappropriate Treatment in Massive Transfusion

Authors: Daniela Hermelin, MD, Chief Medical Officer at ImpactLife; Kirsten Alcorn, MD, Co-Chief Medical Officer at Bloodworks Northwest; Richard Gammon, MD, Chief Medical Officer at Carter BloodCare; Kip Kuttner, DO, Vice President and Medical Director at Miller-Keystone Blood Center; Louis Katz, MD, Chief Medical Officer Emeritus at ImpactLife; Nanci Fredrich, RN, BSN, MM, Transfusion Safety Officer, Versiti Blood Center of Wisconsin; Courtney Hopkins, DO, Senior Medical Officer at Vitalant; Timothy Pancioli, DO, Associate Medical Director at Versiti, Kevin Ha, MD, Associate Medical Director at Versiti; and Theresa Nester, MD, Co-Chief Medical Officer at Bloodworks Northwest.

We extend our tremendous gratitude to the following contributors for their expert guidance and insightful contributions to this *Blood Bulletin*: Jed Gorlin, MD, MBA, Chief Medical Officer of Americas Blood Centers; Walter Dzik, MD, Associate Professor of Pathology, Harvard Medical School; Steven M Frank, MD, Professor, Anesthesiology/Critical Care Medicine, Johns Hopkins Medical Institutions; Diane Calmus, JD, Vice President of Government Affairs of America's Blood Centers; Joel Wu, JD, MPH, MA, HEC, Clinical Ethics Assistant Professor, Center for Bioethics, University of Minnesota; and Debra DeBruin, PhD, Director, Center for Bioethics, University of Minnesota.

The authors disclose no conflicts.



America's Blood Centers®
It's About *Life.*

Futility and Potentially Inappropriate Treatment in Massive Transfusion

KEY POINTS

- There are numerous predictors of potentially inappropriate treatment, but none are fully reliable.
- Prospective discussions and shared decision-making must be routine during ongoing assessment of the massively bleeding patient at regular intervals and should include communication among surgery, anesthesiology, and transfusion medicine specialties.
- Blood suppliers are responsible to many hospitals and patients, and it may be difficult to support one patient's ultramassive transfusion (UMT), especially in times of shortages.

The determination of potentially inappropriate treatment requires a multidisciplinary decision that considers the patient's overall clinical condition, response to resuscitation efforts, and the availability of blood products while possibly considering predetermined time-outs or transfusion volumes.

In these scenarios, prompt surgical intervention, hemostatic agents, and aggressive resuscitative measures beyond transfusion are essential for patient salvage. The availability and feasibility of these resources may influence transfusion support.

INTRODUCTION

Recognition of clinical futility and potentially inappropriate treatment in the context of massive transfusion protocols is a complex and multifaceted concept requiring a pragmatic approach to balance aggressive resuscitation efforts with ethical commitments of beneficence, non-maleficence, responsible blood stewardship and ethical resource allocation.

The term "futile" should only be used in the rare circumstance that "an intervention simply cannot accomplish the intended physiologic goal."¹ Uses of blood that are strictly futile may be withheld or withdrawn solely on standard clinical decision-making and without additional due process requirements.¹

Potentially inappropriate treatments are defined as "treatments that have at least some chance of accomplishing the effect sought by the patient, but clinicians believe competing ethical considerations justify not providing them."¹ In critical care settings, potentially inappropriate treatments are further characterized as treatments "when there is no reasonable expectation that the patient will improve sufficiently to survive outside the acute care setting, or when there is no reasonable expectation that the patient's neurologic function will improve sufficiently to allow the patient to perceive the benefits of treatment."²

A position statement from five critical care societies has recommended that the withdrawal or withholding of potentially inappropriate treatment after a fair decision-making process is ethically defensible.¹

The discussion of the subject is particularly crucial in severe blood shortages, where the judicious use of limited blood products becomes paramount.

When determining potentially inappropriate treatment in massive transfusion, key considerations include:

1. whether the available resources will likely salvage the patient based on injury patterns, physiological derangements, and response to resuscitation;
2. responsible stewardship of the scarce blood product resource, especially during shortages. However, the justification for withholding treatment in cases of potentially inappropriate treatment differs significantly from the rationale for rationing limited resources. Treatment decisions to withhold potentially inappropriate treatment focus on obligations to balance benefits and burdens of treatment for an individual patient, while decisions to withhold treatment from one patient to benefit others in a community are rationing decisions based on justice and population health considerations³; and
3. proactive planning through multidisciplinary discussions, ethical frameworks, and predefined processes rather than reactive decision-making.

An explicit, evidence-based approach balancing patient factors, resource availability, and ethical principles is preferred for these high-stakes decisions.

POSSIBLE INDICATORS OF POTENTIALLY INAPPROPRIATE TREATMENT

Numerous candidate indicators of potentially inappropriate treatment in the setting of massive transfusion have been evaluated including:⁴⁻⁹

1. physiological parameters (e.g., systolic blood pressure,

Futility and Potentially Inappropriate Treatment in Massive Transfusion

heart rate, oxygen saturation, arterial base deficit, peak lactate level, nadir pH, urine output, visible evidence of tissue ischemia (pulseless extremities, visible dead bowel, visible hepatic infarction);

2. cause of critical bleeding (trauma, cardiac surgery, organ transplantation);
3. likelihood of gaining surgical control of bleeding;
4. severity scores (e.g., Glasgow Coma Scale, Injury Severity Score);
5. surgical interventions (e.g., aortic clamping, thoracotomy);
6. patient age;
7. number of red blood cell units (RBCs) transfused; and
8. total blood products transfused and the ratio of different components.

However, no single indicator has been identified as a reliable predictor of futile, or inappropriate treatment. The number of clinical variables, differences in patient management, and other factors make study design challenging. Even the definition of critical bleeding, massive or ultramassive transfusion (UMT) are inconsistent across studies.¹⁰⁻¹²

PREDICTIVE MODELS AND THROMBOELASTOGRAPHY

A variety of proposals have been made for different markers of transfusion futility. These include defining a set number of red blood cell (RBC) units transfused within a certain time period, identification of the 'Death Diamond' pattern through thromboelastography (TEG), and the implementation of STOP Criteria based on arrival lab values, physiology, and rapid TEG.¹³⁻¹⁷ Furthermore, predictors of mortality that have been described include peak lactate above 10 mmol/L, nadir arterial blood gas pH < 7.0, age >65 years, and diagnostic group – with higher mortality in trauma than in cardiac/vascular surgery, with the lowest mortality in transplant surgery.^{12,18} To date, no single approach has proven sufficiently valid to gain wide acceptance.

ETHICAL CONSIDERATION AND DECISION-MAKING PROCESS

Given the complexity of massive transfusion scenarios and the lack of a 'one-size-fits-all' tool to estimate potentially inappropriate treatment, it is essential to develop an explicit decision-making process in which fair and due process elements are incorporated. This process should involve input from hospital ethics committees, multidisciplinary clinical teams, and other stakeholders to ensure the ethical provision of care and responsible resource allocation. Although some

healthcare facilities may have established futility or potentially inappropriate treatment policies, these tend to be time consuming and resource intensive. Developing an expedited fair process decision-making policy must be a priority for real-time decision-making in contingency and crisis conditions.^{1,3}

The goal of prospective discussions and shared decision-making is to reach a local consensus regarding when to reassess prolonging continued emergency care, including ongoing transfusion, of massively bleeding patients. This discussion should incorporate the following factors:^{18,19}

1. clinical markers of critical injury;
 - a. central nervous system (CNS) status and signs of irreversible brain damage (e.g., fixed dilated pupils, extreme anisocoria);
 - b. pressor requirement;
 - c. ventilation mechanics (e.g., FiO₂, lung compliance);
 - d. visible severe ischemia of bowel/liver;
 - e. pulseless cold extremities;
2. current and anticipated ongoing blood loss;
3. number of blood products already transfused;
4. laboratory parameters (e.g., lactate, complete blood count, chemistry, coagulation tests, blood gases, liver function tests); and
5. likelihood of gaining bleeding control.

Ongoing assessment of the massively bleeding patient should occur at regular intervals during resuscitation. Real-time communication with the patient's family or significant others is crucial, focusing on functional outcomes, the patient's wishes, and the possible withdrawal or withholding of treatment deemed inappropriate.

BLOOD SUPPLY CONSIDERATIONS

The number of units of blood provided by the local supplier will depend on available stocks and the needs of other patients. One goal for a massively bleeding patient is to not jeopardize the blood supplier's ability to provide transfusion support for more viable patients who are also in urgent need of the limited supply of blood and components. Multiple casualty situations, such as can occur in mass shootings, are likely to require triage of blood resources to those most likely to survive their injuries.^{5,20}

Blood suppliers may need to pull products from unshipped inventory or request other hospitals to return products to meet a specific patient's needs. These actions can cause shortages at other hospitals, impairing patient care. Blood suppliers face

the difficult task of balancing the needs of one patient at one hospital against those of many patients from many hospitals. This demands effective supplier communication to in these situations.

CONCLUSION

Inappropriate treatment in massive transfusion protocols is a multifaceted issue requiring a pragmatic, multidisciplinary approach. No single factor reliably predicts inappropriate treatment. Decisions should consider the patient's condition, response to resuscitation, blood product availability, and ethical principles. An explicit decision-making process involving ethics committees, multidisciplinary teams, and stakeholders is preferred, incorporating the diagnosis, prognosis, blood loss, laboratory parameters, treatments, and blood supply status. Regular assessments, family communication, responsible stewardship, and ethical resource allocation are essential, especially during times of blood shortages. This collaborative approach ensures judicious blood use while upholding ethical care and navigating the complexities of massive transfusion scenarios. Blood product availability may be improved by assuring blood conservation practices are observed for all transfusions. In addition, consider establishing cooperative blood drives with suppliers. ■

REFERENCES

1. Bosslet GT, Pope TM, Rubenfeld GD, et al. An Official ATS/AACN/ACCP/ESICM/SCCM Policy Statement: Responding to Requests for Potentially Inappropriate Treatments in Intensive Care Units. *Am J Respir Crit Care Med*. Jun 1 2015;191(11):1318-30. doi:10.1164/rccm.201505-0924ST
2. Kon AA, Shepard EK, Sederstrom NO, et al. Defining Futile and Potentially Inappropriate Interventions: A Policy Statement From the Society of Critical Care Medicine Ethics Committee. *Crit Care Med*. Sep 2016;44(9):1769-74. doi:10.1097/CCM.0000000000001965
3. Health MD. Ethical Framework for Transitions Between Conventional, Contingency, and Crisis Conditions in Pervasive or Catastrophic Public Health Events with Medical Surge Implications; Minnesota Crisis Standards Of Care. Accessed May 16, 2024. 2024. https://www.health.state.mn.us/communities/ep/surge/crisis/framework_transitions.pdf
4. Mladinov D, Frank SM. Massive transfusion and severe blood shortages: establishing and implementing predictors of futility. *Br J Anaesth*. Feb 2022;128(2):e71-e74. doi:10.1016/j.bja.2021.10.013
5. Dorken Gallastegi A, Secor JD, Maurer LR, et al. Role of Transfusion Volume and Transfusion Rate as Markers of Futility During Ultramassive Blood Transfusion in Trauma. *J Am Coll Surg*. Sep 1 2022;235(3):468-480. doi:10.1097/XCS.0000000000000268
6. Loudon AM, Rushing AP, Hue JJ, Ziemak A, Sarode AL, Moorman ML. When is enough enough? Odds of survival by unit transfused. *J Trauma Acute Care Surg*. Feb 1 2023;94(2):205-211. doi:10.1097/TA.0000000000003835
7. Liu S, Fujii Q, Serio F, McCague A. Massive Blood Transfusions and Outcomes in Trauma Patients: An Intention to Treat Analysis. *Bull Emerg Trauma*. Jul 2018;6(3):217-220. doi:10.29252/beat-060305
8. Clements TW, Van Gent JM, Lubkin DE, et al. The reports of my death are greatly exaggerated: An evaluation of futility cut points in massive transfusion. *J Trauma Acute Care Surg*. Nov 1 2023;95(5):685-690. doi:10.1097/TA.0000000000003980
9. Katirai A, Landau MJ, Berger JM. The utility of abnormal initial arterial blood gas values in determining clinical futility of trauma cases with severe hemorrhage. *Am J Emerg Med*. Jul 2018;36(7):1253-1256. doi:10.1016/j.ajem.2018.03.063
10. Nunez TC, Young PP, Holcomb JB, Cotton BA. Creation, implementation, and maturation of a massive transfusion protocol for the exsanguinating trauma patient. *J Trauma*. Jun 2010;68(6):1498-505. doi:10.1097/TA.0b013e3181d3cc25
11. O'Keeffe T, Refaai M, Tchorz K, Forestner JE, Sarode R. A massive transfusion protocol to decrease blood component use and costs. *Arch Surg*. Jul 2008;143(7):686-90; discussion 690-1. doi:10.1001/archsurg.143.7.686
12. Dzik WS, Ziman A, Cohn C, et al. Survival after ultramassive transfusion: a review of 1360 cases. *Transfusion*. Mar 2016;56(3):558-63. doi:10.1111/trf.13370
13. Kim JS, Casem CF, Baral E, Inaba K, Kuza CM. Narrative Review: Is There a Transfusion Cutoff Value After Which Nonsurvivability Is Inevitable in Trauma Patients Receiving Ultramassive Transfusion? *Anesth Analg*. Aug 1 2023;137(2):354-364. doi:10.1213/ANE.0000000000006504
14. Farrell MS, Moore EE, Thomas AV, et al. "Death Diamond" Tracing on Thrombelastography as a Marker of Poor Survival After Trauma. *Am Surg*. Jul 2022;88(7):1689-1693. doi:10.1177/0003134821998684
15. Chapman MP, Moore EE, Moore HB, et al. The "Death Diamond": Rapid thrombelastography identifies lethal hyperfibrinolysis. *J Trauma Acute Care Surg*. Dec 2015;79(6):925-9. doi:10.1097/TA.0000000000000871
16. Van Gent JM, Clements TW, Lubkin DT, et al. Predicting Futility in Severely Injured Patients: Using Arrival Lab Values and Physiology to Support Evidence-Based Resource Stewardship. *J Am Coll Surg*. Apr 1 2023;236(4):874-880. doi:10.1097/XCS.0000000000000563
17. Johnson DJ, Scott AV, Barodka VM, et al. Morbidity and Mortality after High-dose Transfusion. *Anesthesiology*. Feb 2016;124(2):387-95. doi:10.1097/ALN.0000000000000945
18. Lo BD, Merkel KR, Dougherty JL, et al. Assessing predictors of futility in patients receiving massive transfusions. *Transfusion*. Jul 2021;61(7):2082-2089. doi:10.1111/trf.16410
19. Morris MC, Niziolek GM, Baker JE, et al. Death by Decade: Establishing a Transfusion Ceiling for Futility in Massive Transfusion. *J Surg Res*. Aug 2020;252:139-146. doi:10.1016/j.jss.2020.03.004
20. Mesar T, Larentzakis A, Dzik W, Chang Y, Velmahos G, Yeh DD. Association Between Ratio of Fresh Frozen Plasma to Red Blood Cells During Massive Transfusion and Survival Among Patients Without Traumatic Injury. *JAMA Surg*. Jun 1 2017;152(6):574-580. doi:10.1001/jamasurg.2017.0098

Blood Bulletin is issued periodically by America's Blood Centers. Publication Editor: Mack Benton. The opinions expressed herein are opinions only and should not be construed as recommendations or standards of ABC, ABC SMT Committee, or its board of directors. Publication Office: 1717 K St. NW, Suite 900, Washington, DC 20006. Tel: (202) 393-5725; Fax: (202) 393-1282; E-mail: memberservices@americasblood.org. Copyright America's Blood Centers, 2024. Reproduction is forbidden unless permission is granted by the publisher. (ABC members need not obtain prior permission if proper credit is given)



America's Blood Centers®
It's About *Life.*