



**MASSIVE BLEEDING AND MASSIVE TRANSFUSION: NARRATIVE REVIEW**

**Juan Diego Montoya Garzon**

MD. Universidad Cooperativa de Colombia

**Silvia del Mar Castellanos Romero**

MD. Universidad del Tolima

**ABSTRACT**

Massive transfusion varies by patient population. Cardiac and vascular surgeries account for about 40% of cases, while trauma, gastrointestinal hemorrhage, and obstetric catastrophes, though important, make up a smaller percentage. Timely assessment and lab tests are crucial for optimal patient care. Historically, massive transfusion meant ten or more units of blood in 24 hours, but it's an arbitrary definition. Alternatives like "ultra-massive transfusion," Critical Administration Threshold for 1 hour (CAT-1), and Resuscitation Intensity (RI) Score provide more context. In volume and blood replacement, crystalloids are suitable for moderate blood loss, but severe trauma favors blood components like plasma, platelets, and packed red blood cells (PRBCs) in a 1:1:1 ratio. Continuous monitoring of hemoglobin, hemostasis, and metabolic parameters is vital. Lab testing helps assess coagulation, but point-of-care platforms provide quicker results.

**KEYWORDS :** Coagulopathy, Hemostasis, Massive Transfusion, Trauma

**INTRODUCTION**

Massive transfusion stands as a vital lifeline in the face of dire medical emergencies, offering a critical means to combat the relentless onslaught of massive hemorrhage. It serves as a life-sustaining bridge, allowing medical professionals the necessary time to address the underlying causes of bleeding, such as surgery, interventional radiology, or other life-saving interventions. Beyond mere survival, massive transfusion steps in as a beacon of hope, replenishing lost blood volume and oxygen transport, aiding the journey towards recovery and healing (1).

The defining threshold of massive transfusion, typically set at the transfusion of ten or more units of whole blood or red blood cells within a mere 24-hour window, serves as a pragmatic approximation of replacing at least one entire blood volume. This threshold serves not only to identify patients across diverse medical domains grappling with profound vascular challenges but also highlights the administrative complexities that may inadvertently impede the swift delivery of essential blood products (2).

**METHODS**

This narrative review involves systematically searching databases such as PubMed and Scopus using strategic keywords like "massive bleeding," "massive transfusion," and related terms. This approach aims to identify relevant studies and critically review and synthesize their findings, providing insight into the current state of knowledge in this vital field of medicine. The process includes assessing study quality, data extraction, and the synthesis of key findings. Fifteen high-quality references have been included to support the narrative. This methodology ensures a comprehensive understanding of managing massive bleeding and transfusion, offering valuable insights into contemporary medical practices.

**Epidemiology**

The need for massive transfusion varies among patient populations. A comprehensive 2016 review spanning 25 years and two countries revealed that cardiac and vascular surgeries accounted for nearly 40 percent of massive transfusions. Gastrointestinal hemorrhage, liver transplants, trauma, and obstetric catastrophes, though classic triggers, were less frequent, constituting only a small percentage. This trend was reaffirmed in a study involving six hospitals across

four countries, which examined 1300 cases of ultra-massive transfusion. Notably, trauma has received significant attention; a 2021 review of a major trauma center indicated that while 18 percent received RBC transfusions, only a fraction required over 10 or 20 units within 24 hours. These insights underscore the importance of timely assessment and early laboratory tests, reducing the necessity for massive transfusions, and optimizing patient care (3,4).

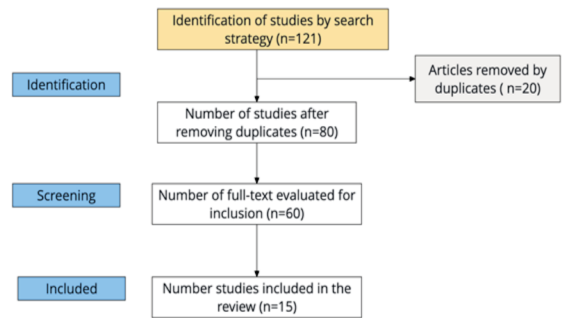


Figure 1. PRISMA.

**Definitions**

Historically, "massive transfusion" was characterized by the transfusion of ten or more units of whole blood or red blood cells within 24 hours, but this definition proved arbitrary, failing to consider patient variables and clinical contexts. The term "ultra-massive transfusion" extends this concept to twenty or more RBC units in 24 or 48 hours, although it's an imperfect predictor of clinical outcomes (5).

Critical Administration Threshold for 1 hour (CAT-1) offers an alternative definition, identifying patients requiring significant blood transfusion by administering three or more RBC units within an hour. Resuscitation Intensity (RI) Score, similar to CAT, assesses transfusion needs based on the number of blood components administered within 30 minutes. Hemorrhage control resuscitation emphasizes early plasma and platelet transfusions, while damage control resuscitation focuses on trauma-induced coagulopathy. The 1:1:1 ratio describes the unit ratios of RBCs, plasma, and platelets in these strategies, but variations exist in component preparation and equivalency. Understanding "coagulopathy" is vital, as it encompasses reduced hemostasis, a common challenge in these scenarios. Mastery of this terminology lays

the foundation for effective patient care and research in the field of massive bleeding and transfusion (6,7).

### Approach to Volume and Blood Replacement

Managing patients in need of massive transfusion necessitates a meticulous consideration of intricate physiological dynamics. The central concerns revolve around sustaining cardiac output, oxygen-carrying capacity, and hemostatic function. No precise hematocrit, platelet count, or coagulation factor deficiency threshold has been established below which blood transfusion becomes futile (8).

### Crystalloid vs. Blood Products:

While crystalloid volume expanders effectively correct blood volume deficits in mildly and moderately ill or injured patients, their use alone in severe trauma with substantial blood loss can result in dilutional coagulopathy and severe tissue swelling, potentially leading to issues like stiff lungs and abdominal compartment syndrome. For more severely injured patients, there's a shift towards using blood components for volume resuscitation, alongside topical hemostatic agents, while avoiding aggressive crystalloid resuscitation (9).

### Component Ratio (1:1:1):

In most patient populations requiring massive transfusion, a common practice is to use a 1:1:1 ratio of plasma to platelets to packed red blood cells (pRBCs). This approach is supported by clinical evidence, as discussed earlier (9).

### Blood Warmer:

To prevent hypothermia, which can exacerbate complications, the use of a blood warmer is essential (9).

### Rationale for Target Hemoglobin:

The American Society of Anesthesiologists recommends avoiding hemoglobin levels below 6 g/dL in healthy individuals. However, older and sicker individuals with cardiovascular disease may benefit from maintaining hemoglobin levels of  $\geq 8$  g/dL. This recommendation is based on supporting data and the physiological rationale that, under certain conditions, oxygen delivery remains sufficient until the hematocrit falls to 10-12 percent. Transfusion strategies aim to optimize this balance while accommodating the delivery of other necessary products such as platelets and cryoprecipitate within the total delivered volume of blood components (10).

### Laboratory Monitoring

Effective management during massive transfusion demands not only initial transfusions with a 1:1:1 ratio but also continuous laboratory monitoring to guide therapy throughout resuscitation (11).

### Hemoglobin and Hemostatic Testing:

Assessing hemoglobin levels and hemostatic capacity is pivotal. Tests include a complete blood count (CBC) with platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen concentration. Although viscoelastic testing (e.g., Thromboelastography - TEG and Rotational thromboelastography - ROTEM) can be substituted for PT, aPTT, and fibrinogen if immediately available, they are slower and costlier. These tests help confirm dilutional effects, guide component ratios, and detect complications like disseminated intravascular coagulation (DIC) (11).

### Challenges with Laboratory-Based Assays:

While widely used, laboratory-based assays may not provide real-time assessment due to the rapid clinical evolution in massive bleeding. To address this, some labs reduce turnaround times by adjusting centrifugation times and fibrinogen monitoring, aiming for a 15-20 minute emergency

hemorrhage panel. Alternatively, point-of-care platforms for coagulation or viscoelastic testing expedite hemostatic evaluation, enhancing blood component usage (11,12).

### Monitoring pH, Blood Gases, Electrolytes, and Metabolites:

Regular measurements of pH, blood gases, electrolytes, and metabolic parameters (e.g., glucose and lactate) yield crucial insights early in critical care and during massive transfusion. Frequent assessments, typically every 20-30 minutes, offer valuable information for effective resuscitation and patient care, whether from arterial or venous blood samples (12).

### Complications

High-volume and rapid transfusions are linked to various hemostatic and metabolic complications that can be mitigated with appropriate blood component selection and consideration of various factors (12,13).

### Hemostatic Abnormalities:

Coagulopathy is prevalent in massive transfusion cases, influenced by clotting factor consumption, tissue trauma, reduced clotting factor activity due to dilution, hypoxia-induced acidosis, hypothermia, or the presence of competitive inhibitors (13).

### Dilutional Coagulopathy:

This condition arises from the dilution of coagulation proteins and platelets due to packed red blood cell (pRBC) transfusions or crystalloid infusions. Gradual dilution prolongs prothrombin time (PT) and activated partial thromboplastin time (aPTT). Platelet concentration decreases with massive transfusion (13).

### Correcting Dilutional Coagulopathy:

Corrective measures include plasma transfusions to restore clotting factors, fibrinogen supplementation using cryoprecipitate, and platelet transfusions when platelet counts drop below 50,000/microL (14).

### Trauma-Associated Coagulopathy:

This condition is characterized by microvascular oozing, prolonged PT and aPTT, thrombocytopenia, low fibrinogen levels, and elevated D-dimer levels. Unlike DIC, it's not truly disseminated or intravascular coagulation. It's effectively treated with antifibrinolytic agents (14).

### Impaired Platelet and Coagulation Factor Function:

Acidosis and hypothermia hinder normal clotting and hemostasis (14,15).

### Hypocalcemia from Citrate Toxicity:

Massive transfusion introduces a large amount of citrate, leading to a decrease in plasma ionized calcium concentration. While most patients don't require calcium administration, it should be considered for symptomatic hypocalcemia (15).

### Hyperkalemia:

High potassium levels in stored blood can be problematic with certain transfusion conditions, but precautions can be taken to minimize the risk (15).

### Hypothermia:

Rapid transfusion of cold blood components can lead to hypothermia, which can exacerbate bleeding and cause other complications. Blood warmers are essential for warming components (15).

### CONCLUSION

The epidemiology of massive transfusion highlights the variability in patient needs across different clinical scenarios. Definitions of massive transfusion have evolved to consider

clinical contexts, emphasizing the importance of early assessment and laboratory monitoring. Managing massive transfusion requires careful consideration of volume replacement strategies and vigilant monitoring to address potential complications, especially coagulopathy and hypothermia.

## REFERENCES

1. Meyer DE, Cotton BA, Fox EE, et al. A comparison of resuscitation intensity and critical administration threshold in predicting early mortality among bleeding patients: A multicenter validation in 680 major transfusion patients. *J Trauma Acute Care Surg* 2018; 85:691.
2. Johansson PI, Stensballe J, Rosenberg I, et al. Proactive administration of platelets and plasma for patients with a ruptured abdominal aortic aneurysm: evaluating a change in transfusion practice. *Transfusion* 2007; 47:593.
3. Delaney M, Stark PC, Suh M, et al. Massive Transfusion in Cardiac Surgery: The Impact of Blood Component Ratios on Clinical Outcomes and Survival. *Anesth Analg* 2017; 124:1777.
4. Ducrocq G, Gonzalez-Juanatey JR, Puymirat E, et al. Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia: The REALITY Randomized Clinical Trial. *JAMA* 2021; 325:552.
5. Liu Z, Ayyagari RC, Martinez Monegro EY, et al. Blood component use and injury characteristics of acute trauma patients arriving from the scene of injury or as transfers to a large, mature US Level 1 trauma center serving a large, geographically diverse region. *Transfusion* 2021; 61:3139.
6. Halmin M, Chiesa F, Vasan SK, et al. Epidemiology of Massive Transfusion: A Binational Study From Sweden and Denmark. *Crit Care Med* 2016; 44:468.
7. Shaz BH, Dente CJ, Nicholas J, et al. Increased number of coagulation products in relationship to red blood cell products transfused improves mortality in trauma patients. *Transfusion* 2010; 50:493.
8. Savage SA, Sumislawski JJ, Zarza BL, et al. The new metric to define large-volume hemorrhage: results of a prospective study of the critical administration threshold. *J Trauma Acute Care Surg* 2015; 78:224.
9. Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; 63:805.
10. Dzik WS, Ziman A, Cohen C, et al. Survival after ultramassive transfusion: a review of 1360 cases. *Transfusion* 2016; 56:558.
11. Kautza BC, Cohen MJ, Cuschieri J, et al. Changes in massive transfusion over time: an early shift in the right direction? *J Trauma Acute Care Surg* 2012; 72:106.
12. Dzik W. Misunderstanding the PROPPR trial. *Transfusion* 2017; 57:2056.
13. Meyer DE, Cotton BA, Fox EE, et al. A comparison of resuscitation intensity and critical administration threshold in predicting early mortality among bleeding patients: A multicenter validation in 680 major transfusion patients. *J Trauma Acute Care Surg* 2018; 85:691.
14. Cotton BA, Au BK, Nunez TC, et al. Predefined massive transfusion protocols are associated with a reduction in organ failure and postinjury complications. *J Trauma* 2009; 66:41.
15. Dorken Gallastegi A, Naar L, Gaitanidis A, et al. Do not forget the platelets: The independent impact of red blood cell to platelet ratio on mortality in massively transfused trauma patients. *J Trauma Acute Care Surg* 2022; 93:21.