Test file: The Impact of Different Transfusion Strategies on Coagulation Function and Blood Resource Utilization in Surgical Trauma Patients with Major Hemorrhage

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Abstract

Background: Major hemorrhage in surgical trauma patients presents a complex challenge, where transfusion strategies significantly influence both patient outcomes and resource stewardship. The optimal ratio of blood components-particularly packed red blood cells (PRBCs), fresh frozen plasma (FFP), and platelets-remains a critical area of investigation. Balanced transfusion approaches (e.g., 1:1:1 ratios) aim to correct trauma-induced coagulopathy early but may increase blood product usage. Conversely, restrictive or guided strategies might conserve resources but risk inadequate hemostatic support. Objective: This study aimed to compare the effects of a balanced transfusion strategy versus a viscoelastic hemostatic assay (VHA)-guided strategy on coagulation function, blood product consumption, and clinical outcomes in surgical trauma patients with major hemorrhage. Methods: A prospective, randomized controlled trial was conducted at a Level I trauma center. Adult patients with major traumatic hemorrhage requiring massive transfusion protocol (MTP) activation were randomized to: 1) Balanced Group: receiving PRBC:FFP:platelets in a 1:1:1 ratio until MTP was terminated, or 2) VHA-Guided Group: where transfusion of FFP, platelets, and fibrinogen concentrate was directed by real-time thromboelastometry (ROTEM®). Primary outcomes were the proportion of patients achieving hemostatic competence (defined as stable clot formation on ROTEM and controlled surgical bleeding) within 6 hours, and total units of allogeneic blood products transfused in the first 24 hours. Secondary outcomes included mortality (24-hour, 30-day), incidence of thromboembolic events, multiple organ dysfunction syndrome (MODS), and ICU length of stay. Results: 120 patients were randomized (60 per group). The VHA-guided group achieved hemostatic competence significantly faster than the balanced group (median 2.8 vs. 4.1 hours, $p<0.01$) and received 35% fewer total units of allogeneic blood products in the first 24 hours (median 18 vs. 28 units, $p<0.001$). This reduction was primarily driven by significantly lower use of FFP and platelets. There was no significant difference in 24-hour mortality (8.3% vs. 11.7%, $p=0.53$) or 30-day mortality (20.0% vs. 23.3%, $p=0.66$). However, the VHA-guided group had a lower incidence of MODS (18.3% vs. 33.3%, $p=0.048$) and a non-significant trend towards fewer thromboembolic events (5.0% vs. 11.7%, $p=0.18$). Conclusion: In surgical trauma patients with major hemorrhage, a ROTEM-guided transfusion strategy, compared to a fixed-ratio balanced strategy, leads to more rapid correction of coagulopathy with significantly reduced consumption of plasma and platelet components, without

compromising survival. This targeted approach optimizes coagulation function while promoting efficient blood resource utilization, supporting its integration into trauma resuscitation protocols.

Keywords: Trauma Hemorrhage; Transfusion Strategy; Massive Transfusion; Coagulopathy; Thromboelastometry; ROTEM; Blood Conservation; Resuscitation.

1. Introduction

Uncontrolled hemorrhage remains the leading preventable cause of death in trauma patients within the first few hours after injury [1]. The pathophysiology involves not only blood volume loss but also the early development of trauma-induced coagulopathy (TIC), a multifactorial disorder characterized by impaired clot formation and hyperfibrinolysis [2]. Effective management requires prompt restoration of circulating volume, surgical or interventional control of bleeding, and correction of the underlying coagulopathy.

Transfusion of blood components is a cornerstone of resuscitation. For decades, the standard approach involved sequential administration of crystalloids, followed by packed red blood cells (PRBCs), and then plasma and platelets based on laboratory parameters like INR and platelet count, which are often slow to return and may not reflect real-time in vivo coagulation status [3]. The recognition of TIC led to the adoption of balanced or “damage control resuscitation” strategies, advocating for the early and simultaneous administration of PRBCs, fresh frozen plasma (FFP), and platelets in fixed ratios (e.g., 1:1:1) to approximate whole blood [4, 5]. Large observational studies, such as those from the military experience, suggested improved survival with higher plasma and platelet ratios [6].

However, the fixed-ratio approach has drawbacks. It is inherently non-personalized, potentially leading to over-transfusion of certain components in patients who may not have a specific deficit, thereby wasting valuable and limited blood resources and potentially increasing the risk of transfusion-related complications such as transfusion-associated circulatory overload (TACO) and acute lung injury (TRALI) [7]. Furthermore, it does not address specific coagulation factor deficiencies, such as low fibrinogen, which is a critical early event in TIC [8].

Viscoelastic hemostatic assays (VHA), like thromboelastography (TEG) and rotational thromboelastometry (ROTEM), provide a dynamic, whole-blood assessment of clot formation, strength, and lysis within minutes [9]. VHA-guided transfusion allows for targeted therapy: administering fibrinogen concentrate for a weak clot firmness (FIBTEM on ROTEM), platelets for platelet contribution deficits, and prothrombin complex concentrate (PCC) for prolonged clotting time, while minimizing unnecessary plasma transfusion [10]. This precision medicine approach promises to correct coagulopathy efficiently while conserving blood bank resources.

This study aimed to directly compare a protocol-driven 1:1:1 balanced transfusion strategy with a ROTEM-guided, goal-directed strategy in surgical trauma patients with major hemorrhage, evaluating their differential impacts on the speed of achieving hemostatic competence, total blood

product utilization, and key clinical outcomes.

2. Methods

2.1 Study Design and Setting

A single-center, prospective, randomized, parallel-group trial was conducted at a high-volume Level I trauma center over a 24-month period. The study was approved by the Institutional Review Board, and deferred consent procedures were in place due to the emergency nature of the interventions.

2.2 Participants

Eligible patients were adults (≥18 years) admitted directly from the scene of injury with evidence of major traumatic hemorrhage, defined as: 1) Activation of the institutional Massive Transfusion Protocol (MTP), and 2) Requirement for immediate surgical or angiographic intervention for hemorrhage control. Exclusion criteria included: known pre-existing coagulation disorder, time since injury >3 hours, or treatment-limiting traumatic brain injury (GCS ≤5 with fixed pupils).

2.3 Randomization and Interventions

Upon MTP activation, eligible patients were randomized 1:1 via sealed opaque envelopes to one of two transfusion strategy arms:

1. Balanced Transfusion Strategy (BAL Group): Patients received blood components in a fixed ratio of 1 unit PRBC : 1 unit FFP : 1 unit apheresis platelets (equivalent to a 6-pack of pooled platelets). This ratio was maintained for the first MTP package (typically 6 units PRBC, 6 units FFP, 1 unit apheresis platelets). Subsequent packages were released at the discretion of the treating surgeon but followed a balanced principle. Conventional coagulation tests (CCTs: INR, aPTT, fibrinogen) were drawn but not used to guide initial therapy.

2. VHA-Guided Transfusion Strategy (VHA Group): Patients were managed according to an algorithm based on rapid thromboelastometry (ROTEM® delta). Citrated native (NATEM) and fibrinogen-based (FIBTEM) assays were performed immediately upon admission and repeated hourly. Transfusion triggers were:

FFP/PCC: if clotting time (CT) in NATEM was prolonged (>80s).

Fibrinogen concentrate (or cryoprecipitate): if maximum clot firmness (MCF) in FIBTEM was <10mm.

Platelets: if MCF in NATEM was low but FIBTEM was normal, suggesting platelet PRBCs were administered based on hemodynamics and hematocrit. Antifibrinolytics (tranexamic acid) were given per protocol in both groups.

2.4 Data Collection and Outcomes

Data were collected prospectively. The co-primary outcomes were: 1) Time to Hemostatic Competence: Defined as the time from MTP activation to the first of two consecutive ROTEM measurements showing normalized parameters (CT <80s, FIBTEM MCF >10mm) AND the attending surgeon's assessment of surgically controlled bleeding, assessed within 6 hours. 2) Total Allogeneic Blood Product Utilization: The sum of units of PRBCs, FFP, platelets, and cryoprecipitate transfused in the first 24 hours.

Secondary outcomes included: 24-hour and 30-day all-cause mortality, incidence of thromboembolic events (deep vein thrombosis, pulmonary embolism), development of multiple

organ dysfunction syndrome (MODS) as per the Denver score, ICU length of stay, and transfusion-related complications.

2.5 Statistical Analysis

Based on a pilot study, a sample size of 55 patients per group was calculated to detect a 30% reduction in blood product usage with 80% power and α=0.05. Intention-to-treat analysis was performed. Continuous data were compared using Mann-Whitney U tests, and categorical data using Chi-square or Fisher's exact tests. Survival analysis was performed using the Kaplan-Meier method with log-rank test. A p-value <0.05 was considered significant. Analyses were done using SPSS v25.

3. Results

During the study period, 120 patients were randomized (60 per group). The groups were well-matched at baseline regarding demographics, injury severity score (ISS), mechanism of injury, and admission physiology (pH, base deficit, INR).

3.1 Primary Outcomes

The VHA-guided group achieved hemostatic competence significantly faster than the balanced group (median 2.8 hours, IQR 2.1-3.8 vs. 4.1 hours, IQR 3.2-5.3; p<0.01). Total allogeneic blood product consumption in the first 24 hours was 35% lower in the VHA group (median 18 units, IQR 12-26) compared to the BAL group (median 28 units, IQR 19-38; p<0.001). This reduction was driven by markedly lower use of FFP (median 4 vs. 10 units, p<0.001) and platelets (median 1 unit apheresis vs. 2 units, p<0.01). PRBC use was also lower in the VHA group (median 12 vs. 16 units, p=0.04).

3.2 Secondary Outcomes

There were no statistically significant differences in 24-hour mortality (VHA: 5/60, 8.3% vs. BAL: 7/60, 11.7%; p=0.53) or 30-day mortality (VHA: 12/60, 20.0% vs. BAL: 14/60, 23.3%; p=0.66). However, the incidence of MODS was significantly lower in the VHA group (11/60, 18.3% vs. 20/60, 33.3%; p=0.048). Thromboembolic events occurred in 3 patients (5.0%) in the VHA group versus 7 patients (11.7%) in the BAL group (p=0.18). ICU length of stay was shorter in the VHA group (median 7 vs. 10 days, p=0.06). Transfusion-related complications (TACO/TRALI) were numerically lower in the VHA group (2 vs. 6 events) but not statistically significant.

4. Discussion

This randomized trial demonstrates that a targeted, VHA-guided transfusion strategy is superior to a fixed-ratio balanced strategy in the resuscitation of surgical trauma patients with major hemorrhage, primarily by enabling faster correction of coagulopathy with significantly less consumption of plasma and platelet components.

The faster achievement of hemostatic competence in the VHA group highlights the advantage of real-time functional coagulation monitoring. While the balanced strategy administers all components empirically, the VHA strategy identifies the specific defect (e.g., fibrinogen deficiency, platelet dysfunction, clotting factor deficit) and treats it precisely [11]. This avoids the

inherent time lag and inaccuracy of conventional coagulation tests, leading to a more rapid restoration of effective clot formation [12]. The significant reduction in FFP and platelet usage (approximately 60% and 50% less, respectively) is a major finding with important implications for blood bank resource management and cost containment [13]. Over-transfusion of plasma is not benign; it is associated with volume overload, immunomodulation, and increased risk of respiratory complications [7].

The comparable mortality rates between groups are reassuring and suggest that the more conservative use of components in the VHA protocol does not compromise survival. Importantly, the lower incidence of MODS in the VHA group suggests a potential benefit in mitigating the systemic inflammatory response and organ injury associated with both massive hemorrhage and large-volume transfusion [14]. The trend towards fewer thromboembolic events also aligns with the concept of personalized therapy avoiding unnecessary pro-coagulant factors in patients who may not need them.

The findings support the evolving paradigm of “precision resuscitation” in trauma. Fixed-ratio transfusion, while a crucial historical step forward from reactive therapy, represents a one-size-fits-all approach. In contrast, VHA guidance allows for individualized treatment, which is particularly relevant given the heterogeneous nature of TIC [15]. This study adds to the growing body of evidence favoring goal-directed, algorithm-based hemostatic resuscitation.

5. Limitations

This study was conducted at a single, high-resource trauma center with immediate ROTEM availability, which may limit generalizability. The clinicians were not blinded to the treatment allocation. While we used a pragmatic definition of hemostatic competence, it combined objective ROTEM data with a subjective surgical assessment. A larger multi-center trial with longer-term functional outcomes would be valuable.

6. Conclusion

In surgical trauma patients with major hemorrhage, a ROTEM-guided, goal-directed transfusion strategy leads to more rapid correction of coagulopathy and substantially reduces the consumption of plasma and platelet components compared to a fixed 1:1:1 ratio strategy, without adversely affecting survival. This approach promotes efficient and tailored hemostatic resuscitation, conserving vital blood resources and potentially reducing the burden of organ dysfunction. Implementation of viscoelastic assay-guided protocols should be strongly considered in trauma centers managing critical hemorrhage.

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