Is thromboelastography (TEG)-based resuscitation better than empirical 1:1 transfusion?

Isaac W Howley,[1] Elliott R Haut,[2] Lenwoth Jacobs,[3] Jonathan J Morrison,[1] Thomas M Scalea[1]

[1]R Adams Cowley Shock Trauma Center, University of Maryland, Baltimore, Maryland, USA
[2]Department of Surgery, The Johns Hopkins University, Baltimore, Maryland, USA
[3]Department of Traumatology and Emergency Medicine, University of Connecticut School of Medicine, Farmington, Connecticut, USA

Correspondence to
Dr Jonathan J Morrison, R Adams Cowley Shock Trauma Center, University of Maryland, Baltimore, MD 21201, USA; jonathan.morrison@umm.edu

ABSTRACT

Thomboelastography (TEG) is a whole blood measure of coagulation which was originally described in the 1950s. However, it has only been in the last few decades that assays have become accessible and viable as a point-of-care test. Following the observation that hemorrhagic shock is associated with an intrinsic coagulopathy, TEG has been used as a method of diagnosing specific coagulation defects in order to direct individualized blood products resuscitation. An alternative transfusion strategy is the administration of fixed ratio products, a paradigm borne out of military experience. It is unknown which strategy is superior and this topic was debated at the 36th Annual Point/Counterpoint Acute Care Surgery Conference. The following article summarizes the discussants points of view along with a summary of the evidence.
Level of evidence Level III.

INTRODUCTION

Hemorrhage constitutes the leading cause of potentially preventable death from traumatic injury.[1] Resuscitation practices prior to the 2000s largely concentrated on the transfusion of packed red blood cells (PRBCs) and synthetic fluid to maintain intravascular volume and tissue oxygen delivery.[2] Limited attention was paid to components such as fresh frozen plasma (FFP), until specific coagulation defects were identified by conventional coagulation tests (CCTs).

This is problematic as CCTs were originally designed for the monitoring of therapeutic anticoagulation in a laboratory setting, rather than the expeditious identification of trauma-related coagulation defects.[3] The timely administration of hemostatic products, like FFP, has acquired a new emphasis following improved understanding of acute trauma coagulopathy (ATC)[4] and the outcomes associated with balanced transfusion strategies.[5]

It has emerged that hemorrhagic shock is associated with an intrinsic coagulopathy that appears to be driven by endothelial hypoxemia, pathological activation of protein C, platelet (PLT) dysfunction and fibrinolytic dysregulation.[6] ATC is separate to the extrinsic coagulopathy observed with dilution and factor depletion from exsanguination. Furthermore, military data have demonstrated that patients receiving a higher ratio of FFP to PRBC were associated with a higher survival than patients who received a lower ratio, referred to as 1:1 resuscitation.[5]

While CCT utility in limited in trauma, viscoelastic assays such as thromboelastography (TEG) may allow for the timely identification of specific coagulation defects, enabling tailored resuscitation.

However, it is unclear whether TEG-guided resuscitation is superior to 1:1 resuscitation. This conference proceeding summarizes the arguments and evidence discussed at the 36th Annual Point/Counterpoint Acute Care Surgery Conference.

TEG-BASED RESUSCITATION IS NOT BETTER THAN 1:1:1 RESUSCITATION (ABRIDGED SUMMARY)

Dr Lenworth Jacobs, MD, Professor of Surgery, University of Connecticut

Coagulopathy is a major complication associated with acute traumatic hemorrhage and is directly linked to hypoperfusion and shock. In order to achieve a successful outcome, the surgeon must optimize coagulation by stopping the hemorrhage, correcting acidosis, warming, restoring cell mass and normalizing the PLT count.

The most effective resuscitation strategy is to transfuse the patients with what is being lost. Whole blood is the optimum resuscitation fluid, but unfortunately it is difficult to acquire in significant volumes. The next best strategy is 1:1:1 resuscitation using blood components which approximate whole blood. The components to transfuse in equal volume are PRBCs, FFP and pooled PLTs.

However, component therapy is not without problems. The longer PRBC units are stored (max. shelf life of 42 days), the greater the storage lesions, which include raised potassium and reduced 2,3-diphosphoglycerate levels. Furthermore, FFP needs to be thawed prior to use, incurring delays, while PLTs have a shelf life of 5 days making them a scarce resource. Despite these shortcomings, reconstituted blood volume with 1:1:1 delivers a hematocrit of around 30%, coagulation factors at around 60–70% of normal plasma and a PLT count of 100×10^9/L.

TEG is a bedside test that is useful in the setting of 'controlled' hemorrhage, such as liver transplant and cardiac surgery. In trauma, bleeding can occur at such a pace that the TEG result may lag behind the clinical situation, leading to delayed and inappropriate therapy. Sometimes it is better to have a continuous supply of all products, rather than some products, delayed.

TEG-BASED RESUSCITATION IS BETTER THAN 1:1:1 RESUSCITATION (ABRIDGED SUMMARY)

Dr Isaac Howley, MD, MPH, Resident in Surgery & Dr Elliot Haut, MD, PhD, Associate Professor of Surgery, Johns Hopkins University

Viscoelastic assays measure the viscosity of blood as it clots under physiological conditions. The two

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most common systems used are TEG (including rapid TEG; rTEG) and rotational thromboelastometry (RoTEM). TEG is most common in North America and will be discussed in this article. The device requires citrated blood to be pipetted into a plastic cuvette, which is loaded onto the analyzer, warmed to the patient's core temperature and slowly oscillates it through an angle of 4°45'. A pin is inserted, which is connected to a torsion wire that generates a trace against time of the clot strength. Specific reagents can be added to allow the assay to assess specific coagulation pathways, identifying coagulation defects.

While the mortality benefits of 1:1:1 are supported by the literature, TEG-guided resuscitation promises 'precision medicine.' TEG has been demonstrated to reliably predict the need for massive transfusion using data that can be generated within 5 min of beginning the assay. However, the real benefit lies in optimizing initial ratio-based transfusion into a tailored transfusion strategy. Several studies, including a randomized trial, have shown that TEG-guided resuscitation reduces overall transfusion requirements and improves mortality.

Furthermore, TEG identifies some defects that cannot be treated with blood products, such as hyperfibrinolysis (HF). This highly lethal coagulopathy requires prompt treatment but is not detected by any CCT.

In summary, ATC is important to identify and treat early. TEG-guided resuscitation represents a comprehensive means of rapidly assessing coagulopathy, although the evidence base is still developing.

EVIDENCE SUMMARY

TEG was originally described as a whole blood assay in 1948 by Professor Hartert.[7] This technique was largely a research tool as it suffered from long assay times and susceptibility to external vibration until the emergence of point-of-care systems in the late 1990s, which increased the use and accessibility of systems. Greatest clinical utility has been seen in the fields of cardiac, vascular and liver surgery, where blood loss is frequently substantial, justifying specialist equipment and training.

The concept that TEG (and other techniques) could aid in the identification and treatment of ATC emerged in the 2000s, with several observational studies. Rugeri et al[8] prospectively analyzed 90 patients with trauma, comparing RoTEM and CCTs. They were able to correlate several rapidly obtained RoTEM parameters, with CCTs, demonstrating RoTEMs diagnostic potential. Several similar studies have been performed which confirm these findings, with the largest originating from Texas.

Holcomb and colleagues examined 1974 consecutive patients with trauma comparing rTEG with CCTs.[9] Several rTEG metrics were predictive of CCT values, for example, alpha angle predicted the need for FFP; maximum amplitude predicted PLT requirements and lysis index 30 documented fibrinolysis (all P<0.001). These investigators also found that the cost of rTEG ($317) was not excessive compared with the CCTs ($286) on the basis that rTEG was available long before CCT results. They concluded that rTEG could replace CCTs entirely.

A major strength also identified at this time was TEG's capacity to diagnose HF. Unlike coagulation defects like hypofibrinogenemia, which can be measured in plasma, there is no reliable CCT to diagnose HF. This is especially important as not only is HF a well-described component of ATC,[10] there is also an effective therapy in the form of tranexamic acid.[11 12] The incidence of HF has been described in TEG studies to be 10–34% of patients undergoing massive transfusion,[13–16] and the mortality in this group is particularly high, 53–76%.[13 14 17]

The first report describing the association of improved mortality with balanced PRBC:FFP ratio was made in 2007 by Borgman et al.[5] Examining 246 patients who underwent a massive transfusion, patients receiving a high ratio of FFP to PRBC had the lowest mortality compared with intermediate and low ratio groups (19% vs 34% vs 65%; P<0.001). This report had a number of methodological issues, specifically survival bias due to the lead time taken to thaw FFP and the problems of missing data; however, the hypothesis has gone on to be tested and confirmed using additional civilian and military data.[18–23]

Importantly, 1:1:1 is one of the few trauma interventions to have undergone a randomized controlled trial. The Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial saw 680 severely injured patients with trauma randomized into two groups: 1:1:1 versus 1:1:2 of FFP:PLT:PRBC.[18] There was no difference in 24-hour and 30-day all-cause mortality, but in the 1:1:1 group more patients achieved hemostasis and fewer hemorrhagic deaths at 24 hours.

Concern has existed over the liberal use of blood products and the potential for transfusion-related reactions such as transfusion-related acute lung injury (TRALI) and transfusion-associated cardiac overload. Despite a single retrospective study suggesting that the incidence of TRALI may be higher,[24] this finding does not seem to be reproducible.[25] Specifically, the incidence of TRALI in the PROPPR study was found to be similar in both groups at 13%.[18]

A reduction in blood product use is desirable for patient safety and also because blood products are a scare and expensive resource. This premise, along with the notion of a tailored resuscitation strategy that targets a specific coagulation defect, has driven interest in a TEG-guided resuscitation.

The Goal-Directed Hemostatic Resuscitation of Trauma-Induced Coagulopathy Trial was a pragmatic randomized clinical trial that enrolled patients requiring massive transfusion protocol activation to either a TEG-guided resuscitation or to a CCT-guided resuscitation.[26] The trial enrolled 111 patients, with 56 undergoing TEG and 55 undergoing CCT-guided transfusion. The study's endpoint was 28-day survival. The trial demonstrated that TEG-guided resuscitation resulted in reduced mortality at 28 days (19.6% vs 36.4%; P=0.032). Furthermore, patients receiving TEG-guided resuscitation required fewer blood products overall and benefitted from more intensive care unit-free and ventilator-free days. The point of survival curve separation was at 6 hours post emergency department admission, where interestingly, the CCT resuscitated group had received more plasma and PLTs. This suggests that more blood products do not necessarily lead to more hemostasis.

Despite these compelling results, a larger trial is underway. The Implementing Treatment Algorithms for the Correction of Trauma-Induced Coagulopathy Trial aims to recruit 400 patients across Europe, randomizing them to a TEG-guided or CCT-guided resuscitation, and is expected to report its findings in late 2019.

CONCLUSION

ATC from hemorrhage results in several defects of the coagulation system. The use of TEG (or similar assays) aids the earlier identification of these defects and can prompt clinicians on the optimum transfusion strategy. The use of a TEG-guided protocol appears to improve survival while reducing overall product use; trials are in progress, which will continue to inform the evidence base.

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