

of tissue trauma and shock. Although we have relatively good early markers of the shock state (base deficit, lactate), there is no biomarker of the extent of tissue trauma, limiting the predictive power of these tools. While a definitive study on the clinical prediction of massive transfusion has yet to be published, it is unlikely that these tools will be useful to activate new coagulation therapies in the future.

Early diagnosis of ATC is therefore required to allow reliable early activation of massive haemorrhage protocols. The routine laboratory coagulation tests in use today are of little value in diagnosing or guiding therapy in these rapidly bleeding patients. The prothrombin time (PT) and partial thromboplastin time (PTT) tests were developed to monitor oral anticoagulant therapy and are not targeted at TIC mechanisms. Usually there is a 45–60 minute delay for results of these tests from the laboratory, by which time the coagulation profile may have changed markedly. Although point-of-care PT measurement is available, again these devices were developed for monitoring oral anticoagulant therapy and have not been validated in trauma haemorrhage.

This has led to a renewed interest in the use of near-patient functional tests of coagulation such as thromboelastometry for the diagnosis of coagulopathy. These devices (Rotational Thromboelastometry - ROTEM, Thromboelastography - TEG) have become robust, reliable tools which may be suitable for the emergency department. These tools are in routine use in some elective surgery settings such as cardiac and liver transplant surgery. Very early work in trauma suggests that they may be able to diagnose TIC and guide therapy [21–23], but much is yet to be learnt about thromboelastometric definitions of ATC/TIC and what the appropriate therapeutic response to abnormal traces should be. ROTEM devices have recently been deployed in Afghanistan as part of a UK Defence Medical Services research project into the early diagnosis of ATC. It is likely that new robust versions of these devices will become routine for the diagnosis, characterisation and treatment of TIC in both civilian and military arenas.

In the absence of a reliable diagnostic test for ATC, many groups are suggesting that blind, empiric protocols for the early administration of plasma and platelet therapies are the only realistic option [24]. Increasingly these regimens are based on the administration of plasma or platelet therapy in proportion to the number of packed red blood cells administered. A retrospective military study investigating the use of plasma therapy in massive transfusion showed a reduction in mortality from 65% to 19% when high-dose regimens approaching 1:1 plasma to red cell ratios were used [25]. Similar effects have been observed in other civilian studies, and with increased platelet and fibrinogen transfusions [26,27]. However there are significant confounders in these studies, particularly relating to survivor bias and the speed of blood loss and the magnitude of effect may be significantly less than described [28]. Some studies have suggested a ceiling effect, beyond which increased plasma administration leads to worse outcomes [29]. Importantly, these are very high dose regimens which, if widely adopted, will put significant pressure on blood resources as well as increase the exposure risk to patients. Further prospective research is needed to understand the optimal timing and dose of blood component therapy in trauma haemorrhage.

In future, it may be possible to move away from blood derivatives in the management of TIC and massive haemorrhage. This is especially important in military and austere settings where the logistics of providing a cold chain and apheresis facilities are extremely demanding. Options on the horizon include lyophilised or freeze-dried plasma [30,31]. Although recent studies evaluating recombinant factor VIIa have been disappointing, the use combinations of recombinant coagulation factors, antifibrinolytics and anticoagulant inhibitors is likely to produce promising results in the future. There are still large gaps in our knowledge of TIC, including an almost complete absence of research on platelet function and in the role of platelet transfusions. Coagulation is a

complex system in itself, but is only a subcomponent of innate immunity. The optimal response to TIC is likely to require specific characterization of the haemostatic derangements at specific time points, and targeted therapy with multiple agents to restore balance to these systems and improve outcomes.

Trauma Induced Coagulopathy is multifactorial in origin and a key determinant of outcomes in trauma. Understanding the mechanisms and drivers of TIC is key to the clinical management of trauma haemorrhage. New damage control resuscitation techniques targeted at ATC may result in significant improvement in survival but there is a significant need for research into new diagnostic tools and therapeutic interventions. With new mechanisms of coagulopathy come new options for therapeutic intervention and drug discovery. Military and civilian research programmes are now building on the work done 40 years ago in Vietnam to save lives in 21st century conflicts.

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