Massive bleeding - Section 3

Management of massive blood loss in trauma and trauma-induced coagulopathy

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Take Home Messages
- Uncontrolled hemorrhage and trauma-induced coagulopathy (TIC) are the major causes for preventable death after trauma and early detection and aggressive management have been associated with improved outcomes.
- Current treatment concepts include the Damage Control Resuscitation (DCR)-concept which advocates the empiric administration of blood products in predefined ratios and the concept of Goal-directed Coagulation Therapy (GDCT) based upon results obtained from early point-of-care (POC) viscoelastic testing.
- GDCT based upon viscoelastic testing allows better characterization of the existing coagulopathy with supplementation of hemostatic agents and blood products according to the individual patient’s needs.
- Implementation and adherence to evidence-based guidelines are essential for improved patient outcomes.

Introduction

Massive blood loss (MBL) and trauma-induced coagulopathy (TIC) remain the major causes for preventable death after trauma.¹,² One out of four severely injured patients admitted to the trauma bay is bleeding with variable degrees of laboratory coagulopathy and early detection and management have been associated with improved outcomes.³ The current understanding of TIC is summarized in Figure 1 but much of the data continues to be rather correlative than causative with robust links still lacking.⁴⁻⁶ Recent surveys confirm heterogeneity in the clinical diagnosis and management of acute trauma hemorrhage and TIC.⁷ In the acute phase, the clinical strategies follow the Damage Control Resuscitation (DCR)-concept which advocates the empiric administration of blood products in predefined ratios.⁸ However, the optimum ratio is still under debate, no universal standard for the composition of these transfusion packages has yet been established and storage time may considerably affect the hemostatic competence of these products.⁹ This approach may also not be adequate to correct hypoperfusion or coagulopathy during the acute phase of trauma hemorrhage.¹⁰ Alternatively, several European but also a few US trauma centers have instituted the concept of Goal-directed Coagulation Therapy (GDCT) based upon results obtained from early point-of-care (POC) viscoelastic testing.¹¹ Viscoelastic tests provide rapid information about the underlying deficiencies with particular focus on the different aspects of hemostasis (initiation, dynamics and stability) thereby allowing targeted coagulation monitoring and therapy according to individual needs. A number of individualized algorithms have been suggested but mostly based upon retrospective registry data or expert opinion.¹²⁻¹⁶ Early viscoelastic variables of clot firmness have been shown to be good predictors for the need of massive transfusion and mortality and a recent Cochrane review provided, apart from known reductions in transfusion requirement, for the first time, a survival benefit with the use of viscoelastic testing in bleeding patients.¹⁷ In the following, the cornerstones of the 2016 updated European guideline for the management of bleeding trauma patients are summarized.¹⁸

Initial resuscitation of the bleeding trauma patient

In severely injured and hypotensive trauma patients, volume replacement should be initiated, at a reduced level, in order to keep the circulation stable at target blood pressure and not exacerbate the bleeding until the bleeding can be controlled (Grade 1B). The fluid of choice is isotonic crystalloid solution (Grade 1A). The “lethal triad of death” should be avoided by controlling against hypoxia, acidosis (Grade 1A) and hypothermia (Grade 1C).

Diagnosis, monitoring and initiation of measures to support coagulation function

Monitoring and measures to support coagulation should be initiated immediately upon hospital admission (Grade 1B) as the time elapsed between injury and bleeding control should be minimized (Grade 1A). The extent of trauma hemorrhage is clinically assessed by using a combination of patient physiology, anatomical injury, mechanism of injury and the individual’s
response to initial resuscitation as outlined in the “Advanced Trauma Life Support”-protocol (Grade 1C). Early and repeated imaging such as computed tomography (CT) and ultrasound (FAST) is recommended to detect extravasal fluid (Grade 1B).

**Laboratory parameters**

Low initial hemoglobin (Hb) is considered indicative for severe bleeding associated with coagulopathy and repeated Hb measurements are recommended (Grade 1B). Laboratory parameters for shock include lactate, ScvO2, hematocrit and base excess. The routine practice should include the early and repeated monitoring of coagulation, using either conventional coagulation assays (CCAs) such as prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet counts and fibrinogen (Grade 1A) and/or viscoelastic tests (Grade 1C). As early variables of clot firmness have been associated with outcome, a rapid and more complete monitoring of the individual’s coagulation profile including fibrinolysis may facilitate a more accurate targeting of therapy as compared to isolated CCAs. In addition, CCAs only monitor clot initiation and only 4% of overall thrombin generation.20 Fibrinogen levels deteriorate first in the early phase of severe trauma and low levels on admission have been associated with poor outcome.21

**Initial coagulation management including massive transfusion**

**Massive transfusion**

The European trauma guideline currently advocates one of the two following strategies for the initial management of patients with bleeding and (expected risk of) massive transfusion: i) plasma (fresh frozen plasma (FFP) versus pathogen-inactivated plasma) in a plasma:packed red blood cell (PRBC) ratio of at least 1:2 (Grade 1B), or ii) fibrinogen concentrate and PRBC according to the individual hemoglobin level (Grade 1C). Further resuscitation measures should be continued using a goal-directed strategy guided by CCAs and/or viscoelastic assays (Grade 1C).

**Plasma-based versus factor-concentrate based strategies**

If a plasma-based coagulation resuscitation strategy is used, plasma (FFP or pathogen-inactivated plasma) should be administered to maintain PT and aPTT < 1.5 times the normal control (Grade 1C) but is to be avoided in the absence of substantial bleeding (Grade 1B). If a factor concentrate-based strategy is executed the treatment with fibrinogen concentrate (or cryoprecipitate) is recommended if significant bleeding is accompanied by viscoelastic signs of a functional fibrinogen deficit or a fib-
Intravenous level < 1.5-2.0 g/l (Grade 1C). A target level for hemoglobin (Hb) of 7-9 g/dl (Grade 1C) is suggested while platelet concentrations should be kept > 50 x 10^9/l (Grade 1C); in patients with TBI and/or ongoing bleeding > 100 x 10^9/l (Grade 2C).

Viscoelastic tests to guide hemostatic therapy

Thromboelastometry is increasingly being used to diagnose, monitor and guide treatment strategies in trauma hemorrhage but currently, no uniformly accepted guidelines exist for how this technology should be integrated into clinical care. Figure 2 summarizes a consensus, which corresponds to a S2k guideline according to the system of the Association of the Scientific Medical Societies in Germany (AWMF) and which informs, for the first time, on specific triggers for individual clinical decision making.22

Hemostatic agents

Based upon CRASH-2 the administration of the antifibrinolytic tranexamic acid (TXA) as early as possible to the trauma patient who is bleeding or at risk of significant hemorrhage is advocated (Grade 1A).23 Insufficient evidence and failure in large clinical trials leaves recombinant activated coagulation factor VII (fresh frozen plasma (FFP) or pathogen-inactivated plasma).

Conflict of interest

Marc Maegle has received honoraria from Astra Zeneca, Bayer, CSL Behring, LFB Biomedicaments France, TEM International/IL-Werfen.

### ROTEM®-based algorithm for the use of hemostatic agents and blood products during early trauma care

| Recommendation | Interpretation |
|----------------|----------------|
| **Consider fibrinogen administration**<br>(fibrinogen concentrate or cryoprecipitate) | **EXTEM**<br>A10 < 45 mm (A5 < 35 mm) or MCF < 55 mm <br>and<br>**FIBTEM**<br>A10 < 10 mm (A5 < 9 mm) or MCF < 12 mm |
| **Consider plasma transfusion**<br>(or prothrombin complex concentrate (PCC))<br>(Note: Low platelets and low fibrinogen may also prolong CT!) | **EXTEM**<br>CT ≥ 80 sec and A10 ≥ 45 mm (A5 ≥ 35 mm) / MCF ≥ 55 mm <br>and<br>**FIBTEM**<br>normal A10 (A5 ≥ 9 mm) or normal MCF |
| **Consider platelet transfusion** | **EXTEM**<br>A10 < 45 mm (A5 < 35 mm) or MCF < 55 mm <br>and<br>**FIBTEM**<br>normal A10 (A5 ≥ 9 mm) or normal MCF |
| **Consider antifibrinolitics** | Any evidence of hyperfibrinolysis in **EXTEM** oder **FIBTEM**! |
| **Consider withholding transfusion** | **EXTEM**<br>Abnormal high A10/MCF |

Figure 2. Thromboelastometry (ROTEM®)-based algorithm for the use of hemostatic agents and blood products during early care for the severely injured with bleeding and TIC.
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