

Simplified treatment algorithm for the management of trauma-induced hemorrhage without viscoelastic testing

Sebastian Casu

Department of Emergency
Medicine, Asklepios Hospital
Wandsbek, Hamburg, Germany

Correspondence to

Dr Sebastian Casu; s.casu@
asklepios.com

Received 26 May 2021

Accepted 2 July 2021

ABSTRACT

Uncontrolled bleeding after major trauma remains a significant cause of death, with up to a third of trauma patients presenting with signs of coagulopathy at hospital admission. Rapid correction of coagulopathy is therefore vital to improve mortality rates and patient outcomes in this population. Early and repeated monitoring of coagulation parameters followed by clear protocols to correct hemostasis is the recommended standard of care for bleeding trauma patients. However, although a number of treatment algorithms are available, these are frequently complex and can rely on the use of viscoelastic testing, which is not available in all treatment centers. We therefore set out to develop a concise and pragmatic algorithm to guide treatment of bleeding trauma patients without the use of point-of-care viscoelastic testing. The algorithm we present here is based on published guidelines and research, includes recommendations regarding treatment and dosing, and is simple and clear enough for even an inexperienced physician to follow. In this way, we have demonstrated that treatment protocols can be developed and adapted to the resources available, to offer clear and relevant guidance to the entire trauma team.

The treatment of hemorrhage after major trauma is a significant challenge in routine clinical practice. Injuries account for over five million deaths each year, with uncontrolled post-traumatic bleeding remaining one of the leading causes of death among these patients.¹⁻³ Additionally, up to a third of trauma patients present with signs of coagulopathy at admission to hospital, and trauma-induced coagulopathy is associated with increased transfusion requirements, complications, and mortality.^{2,4-7} As such, rapid identification and correction of coagulopathy is vital to reduce mortality and improve outcomes for bleeding trauma patients.

Current guidelines recommend early and repeated monitoring of hemostasis in trauma patients, either with viscoelastic testing methods or with standard laboratory tests (SLTs, eg, prothrombin time and Clauss fibrinogen testing).^{2,8,9} As viscoelastic testing is based on assessment of whole blood samples, it is able to provide a more accurate assessment of coagulation defects than SLTs, including measurement of clot strength and detection of hyperfibrinolysis.⁹⁻¹¹ Additionally, viscoelastic testing can be conducted at the point of care, with a turnaround time up to 30–60 minutes shorter than that reported for SLTs.^{2,10,12,13} However, not all treatment centers have

access to viscoelastic testing, and so treatment must be based on the results of SLTs. If these results can be made available in a timely manner, they could be used to guide appropriate hemostasis management in the case of massive bleeding after trauma.

The implementation of goal-directed treatment algorithms can offer a structured approach to bleeding management and can help guide clinicians in appropriate treatment measures.^{2,8,9} A number of algorithms for the management of trauma-related bleeding have previously been published^{9,14,15}; however, these can be complex and often include the use of viscoelastic tests.

We therefore set out to develop a pragmatic and guideline-based treatment algorithm which would support coagulation management in trauma patients in a timely and efficient manner when viscoelastic testing is not available. After a review of current guidelines, an algorithm was based on published evidence, including a viscoelastic testing-based algorithm¹⁵ and parameters for the estimation of plasma fibrinogen levels based on SLTs.¹⁶ As our objective was to develop an algorithm that was simple and clear enough for even an inexperienced physician to follow, we aimed to reduce and simplify each step while providing enough information to guide appropriate patient management. This algorithm was intended to guide treatment and followed steps that were already established and familiar to the treating physician, such as initiating SLTs. Although based on published evidence, this algorithm represents the approach to resuscitation at our center and has not, as yet, been validated.

The final algorithm is presented in [figure 1](#) and is divided into two sections: a checklist to direct the assessment and treatment of the patient with an accompanying decision tree to guide administration of hemostatic agents as needed. This has been designed for easy reproduction on posters to be displayed in the emergency department or on cards for physicians to carry with them for reference. The algorithm is color-coded throughout, according to the bleeding severity and SLT results, to aid with quick reference.

The checklist begins with basic patient management and initial SLTs, followed by obtaining the patient history, with particular reference to potential known bleeding complications such as prescribed oral anticoagulants. A treatment protocol is then detailed, based on initial coagulation factor concentrate administration followed by the potential to escalate treatment to include a massive transfusion

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Casu S. *Trauma Surg Acute Care Open* 2021;**6**:e000779.

<input type="checkbox"/>	Basics	1. Oxygen & fluid management 2. Laboratory blood testing (depending on local protocol) 3. Logistics for further diagnostics, therapy and transport
<input type="checkbox"/>	Maintain!	1. pH >7.2 2. T >35°C 3. Ca. >0.9mmol/L
<input type="checkbox"/>	Medical history	Increased bleeding tendency? Antiplatelet agents? Oral anticoagulation? Antidote therapy possible?
<input type="checkbox"/>	Tranexamic acid	Consider <i>early</i> 1–2 g i.v.
<input type="checkbox"/>	Fibrinogen	2–6 g (30 mg/kg body weight) or in accordance with Base Excess (BE) and hemoglobin (Hb); target range: >150–200 mg/dL (decision tree detailed overleaf)
<input type="checkbox"/>	Prothrombin complex concentrate (PCC)	20–40 IU/kg body weight
<input type="checkbox"/>	In case of massive blood transfusion	Consider early: Fresh Frozen Plasma (FFP):erythrocyte concentrate in 1:1 ratio
<input type="checkbox"/>	Platelets	Target range: >50/mL respectively >100/mL in case of brain injury or upon suspicion of acquired or hereditary failure of platelet function
<input type="checkbox"/>	Ultima ratio	1. Repeat tranexamic acid 2. FXIII (1,250–2,500 IU) 3. rFVIIa (90 micrograms per kg) (off-label use! Pay attention to requirements!)

(A)

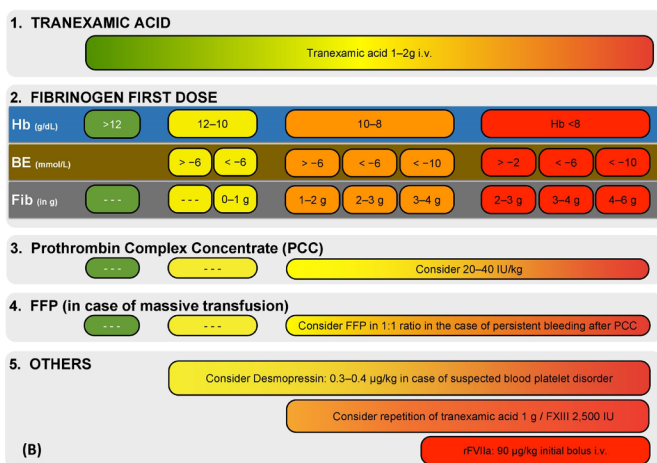


Figure 1 Simplified treatment algorithm for the management of trauma-related bleeding without the use of viscoelastic testing. The algorithm consists of two parts: (A) a checklist to guide assessment and treatment of the patient and (B) a decision tree to guide administration of hemostatic agents.

protocol. Tranexamic acid is suggested for early administration, in line with current treatment guidelines,² followed by fibrinogen administration in line with the publication by Schlimp *et al.*¹⁶ For fibrinogen, dosing can be based on weight, or the decision tree (figure 1B) can be used to guide dosing based on base excess and hemoglobin levels instead of estimating the appropriate dose required. We recommend basing the fibrinogen dose on these parameters as this takes into account the extent of the trauma. Additionally, base excess and hemoglobin levels will have been determined as part of the routine blood gas analysis; as such, results will be available within minutes, and clinicians will be experienced in obtaining and interpreting the results.

Administration of prothrombin complex concentrate (PCC) is proposed as the next step. We recommend PCC as the use of factor concentrates for first-line treatment appears to be superior to fresh frozen plasma (FFP),^{17,18} particularly as PCC can be given immediately compared with the time required to prepare and administer FFP.^{18,19} Additionally, a large volume of FFP is required to significantly increase factor levels, whereas this is not the case for PCC.²⁰ As there is a lack of data regarding the use of base excess and hemoglobin levels to determine the PCC

dose, we have recommended dosing based on body weight. If bleeding persists after PCC administration, a massive transfusion protocol can be initiated. Plasma will only be administered as part of massive transfusion and can be accompanied by platelets if necessary. In severe cases, recommendations are also given for potential further treatment, such as desmopressin, repeated administration of tranexamic acid, and coagulation factors XIII and VIIa. FXIII is known to be an essential contributor to clot strength as it crosslinks and stabilizes fibrin²¹ and, in cases of bleeding and low FXIII activity, the European Society of Anaesthesiology (ESA) guidelines recommend its administration (30 IU/kg),²² hence its inclusion at the end of the algorithm. For rFVIIa, several studies and systematic reviews have demonstrated that rFVIIa administration does not significantly reduce mortality.^{22,23} As such, we only included rFVIIa as ultima ratio if all previous steps were unsuccessful and the requirements for rFVIIa administration were met, in line with the ESA guidelines.²²

It should be noted that this algorithm is only suitable for the initial management of uncontrolled bleeding in the emergency room, particularly after trauma. Later hemostatic management of the patient, for example, in the intensive care unit, will require different treatment guidelines. Additionally, although the administration of fibrinogen according to base excess and hemoglobin levels offers clear and simple guidance on dosing, evidence is currently limited regarding the accuracy of these parameters when used to estimate fibrinogen levels. As such, further research is required to support this guidance.

While many excellent treatment algorithms exist for hemostatic management of trauma-induced bleeding, these are not always practical to administer in day-to-day clinical practice. Treatment recommendations must take into account the available hospital resources, and the knowledge, experience, and time available to clinical staff. As such, simple and clear guidelines can greatly aid clinicians in incorporating up-to-date practices in real-world situations. While viscoelastic testing does appear to offer benefits over SLTs, it must be remembered that this is not available in many treatment centers, and so clear, robust alternatives are vital to ensure patients receive the best possible care. Here we have adapted published guidelines and research to develop a simplified algorithm, adapted to the resources available in our hospital, to guide efficient and appropriate treatment of trauma-induced bleeding. By recommending dosage based on parameters from blood gas analysis, the extent of trauma can be taken into consideration when determining the appropriate dose and the laboratory results can be obtained rapidly. In this way, locally adapted algorithms can be developed, offering clear and relevant guidance for the entire trauma team. Further data and experience will enable refinement of the process and algorithm.

Twitter Sebastian Casu @casusebastian

Contributors SC developed the algorithm and performed writing and critical revision.

Funding This study was funded by CSL Behring.

Competing interests SC has received honoraria for lectures or speakers bureau from CSL Behring; has participated on an advisory board for CSL Behring, MA&S Market Access & Pricing Strategy and Shionogi; and has had a leadership or fiduciary role in other board, society, committee or advocacy groups for AMLS Germany and DBRD Germany. Medical writing support was provided by Claire Crouchley of Meridian HealthComms, Plumley, UK and funded by CSL Behring; there is no grant/award number to report.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which

permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- World Health Organization. Injuries and violence the facts. 2014. https://www.who.int/violence_injury_prevention/media/news/2015/Injury_violence_facts_2014/en/;
- Spahn DR, Bouillon B, Cerny V, Durantau J, Filipescu D, Hunt BJ, Komadina R, Maegele M, Nardi G, Riddez L, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. *Crit Care* 2019;23:98.
- Evans JA, van Wessem KJP, McDougall D, Lee KA, Lyons T, Balogh ZJ. Epidemiology of traumatic deaths: comprehensive population-based assessment. *World J Surg* 2010;34:158–63.
- Fröhlich M, Mutschler M, Caspers M, Nienaber U, Jäcker V, Driessen A, Bouillon B, Maegele M, . TraumaRegister DGU. Trauma-Induced coagulopathy upon emergency room arrival: still a significant problem despite increased awareness and management? *Eur J Trauma Emerg Surg* 2019;45:115–24.
- Chang R, Cardenas JC, Wade CE, Holcomb JB. Advances in the understanding of trauma-induced coagulopathy. *Blood* 2016;128:1043–9.
- Peltan ID, Vande Vusse LK, Maier RV, Watkins TR. An international normalized Ratio-Based definition of acute traumatic coagulopathy is associated with mortality, venous thromboembolism, and multiple organ failure after injury. *Crit Care Med* 2015;43:1429–38.
- Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma* 2003;54:1127–30.
- American College of Surgeons Trauma Quality Improvement Program (TQIP). Massive transfusion in trauma guidelines. 2014. https://www.facs.org/-/media/files/quality-programs/trauma/tqip/transfusion_guidelines.ashx;
- Maegele M. The diagnosis and treatment of acute traumatic bleeding and coagulopathy. *Dtsch Arztebl Int* 2019;116:799–806.
- Whiting P, Al M, Westwood M, Ramos IC, Ryder S, Armstrong N, Misso K, Ross J, Severens J, Kleijnen J. Viscoelastic point-of-care testing to assist with the diagnosis, management and monitoring of haemostasis: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2015;19:1–228.
- Rouillet S, de Maistre E, Ickx B, Blais N, Susen S, Faraoni D, Garrigue D, Bonhomme F, Godier A, Lasne D. Position of the French Working group on perioperative haemostasis (GIHP) on viscoelastic tests: what role for which indication in bleeding situations? *Anaesthesia Critical Care & Pain Medicine* 2019;38:539–48.
- Cotton BA, Faz G, Hatch QM, Radwan ZA, Podbielski J, Wade C, Kozar RA, Holcomb JB. Rapid thrombelastography delivers real-time results that predict transfusion within 1 hour of admission. *J Trauma* 2011;71:407–17.
- Davenport R, Manson J, De'Ath H, Platten S, Coates A, Allard S, Hart D, Pearse R, Pasi KJ, MacCallum P, et al. Functional definition and characterization of acute traumatic coagulopathy. *Crit Care Med* 2011;39:2652–8.
- Carvalho M, Rodrigues A, Gomes M, Carrilho A, Nunes AR, Orfão R, Alves Ângela, Aguiar J, Campos M. Interventional algorithms for the control of coagulopathic bleeding in surgical, trauma, and postpartum settings: recommendations from the share network group. *Clin Appl Thromb Hemost* 2016;22:121–37.
- Schöchl H, Maegele M, Solomon C, Görlinger K, Voelckel W. Early and individualized goal-directed therapy for trauma-induced coagulopathy. *Scand J Trauma Resusc Emerg Med* 2012;20:15.
- Schlimp CJ, Voelckel W, Inaba K, Maegele M, Ponschab M, Schöchl H. Estimation of plasma fibrinogen levels based on hemoglobin, base excess and injury severity score upon emergency room admission. *Crit Care* 2013;17:R137.
- Innerhofer P, Fries D, Mittermayr M, Innerhofer N, von Langen D, Hell T, Gruber G, Schmid S, Friesenecker B, Lorenz IH, et al. Reversal of trauma-induced coagulopathy using first-line coagulation factor concentrates or fresh frozen plasma (RETIC): a single-centre, parallel-group, open-label, randomised trial. *Lancet Haematol* 2017;4:e258–71.
- Steiner T, Poli S, Griebel M, Hüsing J, Hajda J, Freiberger A, Bendszus M, Bösel J, Christensen H, Dohmen C, et al. Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (inch): a randomised trial. *Lancet Neurol* 2016;15:566–73.
- Holcomb JB, del Junco DJ, Fox EE, Wade CE, Cohen MJ, Schreiber MA, Alarcon LH, Bai Y, Brasel KJ, Bulger EM, et al. The prospective, observational, multicenter, major trauma transfusion (PROMTTT) study: comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg* 2013;148:127–36.
- Chowdhury P, Chowdhury P, Saayman AG, Paulus U, Findlay GP, Collins PW. Efficacy of standard dose and 30 ml/kg fresh frozen plasma in correcting laboratory parameters of haemostasis in critically ill patients. *Br J Haematol* 2004;125:69–73.
- Muszbek L, Adány R, Mikkola H. Novel aspects of blood coagulation factor XIII. I. structure, distribution, activation, and function. *Crit Rev Clin Lab Sci* 1996;33:357–421.
- Kozek-Langenecker SA, Ahmed AB, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, De Robertis E, Faraoni D, Filipescu DC, Fries D, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: first update 2016. *Eur J Anaesthesiol* 2017;34:332–95.
- McQuilten ZK, Crighton G, Engelbrecht S, Gotmaker R, Brunskill SJ, Murphy MF, Wood EM. Transfusion interventions in critical bleeding requiring massive transfusion: a systematic review. *Transfus Med Rev* 2015;29:127–37.