Patient Blood Management in Trauma Settings

Summaries of key aspects of PBM which were presented at the

PBM in Trauma Settings

Educational Preceptorship

Some of the recommendations outlined in this document may not be applicable to the local indications for the available products. For country-specific information, please contact your local medical representative.

Guidelines for trauma and perioperative bleeding

In trauma, massive transfusions should be restricted by employing goal-directed, patient-specific management strategies*

Individualization of therapy | **Time to life-saving procedure** | **Improved efficacy**

Transfusion and reoperation for bleeding **independently contribute to postoperative morbidity and mortality**[1]

Goal-directed transfusion strategy

- European bleeding management guidelines recommend **a target Hb level of 70–90 g/L**, where **erythrocyte transfusion** is necessary[2,3]
- For the initial management of massive hemorrhage, one of two strategies are recommended:[3]
  - **Fibrinogen concentrate** or **cryoprecipitate + pRBCs**
  - **FFP** (or pathogen-inactivated FFP) **+ pRBCs** (at least 1:2 ratio)
- Resuscitation measures should be continued using a **goal-directed strategy**, guided by standard laboratory coagulation values and/or VET[3]

FFP

Transfusion of FFP has been associated with an increase in complications, including **increased infection risk** and a **dose-dependent increased risk of ARDS, multiple organ dysfunction syndrome, and pneumonia**[4,5]

Additionally, the RETIC study was terminated early due to an **unacceptably high incidence of treatment failure** and **increased risk for massive transfusion with FFP versus CFC**[6]

European trauma guidelines recommend that **FFP use is avoided** for the correction of hypofibrinogenemia if **fibrinogen concentrate** or **cryoprecipitate** are available[3]

ARDS, acute respiratory distress syndrome; CFC, coagulation factor concentrates; FFP, fresh frozen plasma; FXIII, factor XIII; Hb, hemoglobin; POC, point-of-care; PPH, postpartum hemorrhage; pRBC, packed red blood cell; PT/INR, prothrombin time/international normalized ratio; TXA, tranexamic acid; VET, viscoelastic testing; WHO, World Health Organization.

*Unreferenced claims based on the personal interpretation and expert experience of Dr. Fries.

POC testing

VET to guide hemostatic resuscitation has been associated with a **greater proportion of patients alive and free of massive transfusion at 24 hours**[7]

European trauma guidelines recommend early and repeated hemostatic monitoring using either traditional laboratory determinants, and/or POC PT/INR, **and/or VET**[3]

FXIII

In surgical patients, FXIII levels <60% have been associated with increased postoperative rebleeding and transfusions[8]

European guidelines recommend **monitoring of FXIII and correction of FXIII deficiency in cases of ongoing bleeding**[2,3]

TXA

The WOMAN trial demonstrated that TXA:[9]

- Given within **3 hours** of childbirth
- Reduced the number of women bleeding to death after birth **by >30%**

Even a short delay in treatment with TXA **has been shown to reduce its benefit**[10]

In major trauma patients, **prehospital administration of TXA did not result in a greater number of patients surviving with a favorable functional outcome** at 6 months compared with placebo[11]

Perioperative bleeding guidelines recommend the use of **TXA in PPH as soon as possible within 3 hours**, as well as restrictive administration of TXA in case of fibrinolytic shutdown in critical illness[2]

The most recent WHO guidelines **do not recommend** TXA for **PPH prevention**[12]

1. Vivacqua A, et al. *Ann Thorac Surg* 2011;91(6):1780–1790; 2. Kietaibl S, et al. *Eur J Anaesthesiol* 2023;40(4):226–304; 3. Rossaint R, et al. *Crit Care* 2023;27(1):80; 4. Sarani B, et al. *Crit Care Med* 2008;36(4):1114–1118; 5. Inaba K, et al. *J Am Coll Surg* 2010;210:957–965; 6. Innerhofer P, et al. *Lancet Haematol* 2017;4(6):e258–e271; 7. David JS, et al. *Crit Care* 2023;27(1):141; 8. Kleber C, et al. *Crit Care* 2022;26:69; 9. WOMAN trial collaborators, et al. *Lancet* 2017;389:2105–2116; 10. Gayet-Ageron A, et al. *Lancet* 2018;391(10116):125–132; 11. PATCH-Trauma Investigators and the ANZICS Clinical Trials Group. *N Engl J Med* 2023;389:127–136; 12. WHO. Consolidated guidelines for the prevention, diagnosis and treatment of postpartum haemorrhage. 2025. Available at https://www.who.int/publications/i/item/9789240115637. (Accessed January 2026).

Trauma-induced coagulopathy

What is trauma-induced coagulopathy (TIC)?

TIC refers to abnormal coagulation processes caused by traumatic injury[1]

The German Society for Trauma Surgery notes that **TIC is a distinct clinical condition with a significant impact on survival[2]**

~25–43%
of all severe trauma patients have TIC at hospital admission[3,4]

Early TIC is usually associated with **hypocoagulability**, linked to fibrinogen depletion and hyperfibrinolysis, which may result in uncontrolled hemorrhage[1]

Late TIC is characterized by **hypercoagulability**, which may lead to TEEs and multiple organ failure[1]

TIC is associated with poor patient outcomes

TIC at emergency room admission is associated with:[3]

- Increased rate of **complications**
- High risk of **massive transfusion**
- **x4** **4-fold** higher risk of **mortality**

The pathophysiology of TIC is complex:

- Dysregulation of the hemostatic system results from tissue trauma, shock-related hypoperfusion, endothelial damage, immune system activation, and platelet dysfunction[5]
- Hypothermia and acidosis can further impact hemostatic dysregulation[5]

How is TIC identified?

- Early and repeated monitoring of hemostasis using traditional laboratory tests (PT/INR, Clauss fibrinogen level, platelet count) and/or VET[6]
- Avoid routine use of POC platelet function devices for platelet function monitoring in trauma patients on antiplatelet therapy or with suspected platelet dysfunction[6]

BP, blood pressure; CFC, coagulation factor concentrate; FFP, fresh frozen plasma; MAP, mean arterial pressure; PCC, prothrombin complex concentrate; POC, point-of-care; pRBC, packed red blood cells; PT/INR, prothrombin time/international normalized ratio; TBI, traumatic brain injury; TEE, thromboembolic event; TIC, trauma-induced coagulopathy; TXA, tranexamic acid; VET, viscoelastic testing.

*Unreferenced claims based on the personal interpretation and expert experience of Prof. Schöchl.

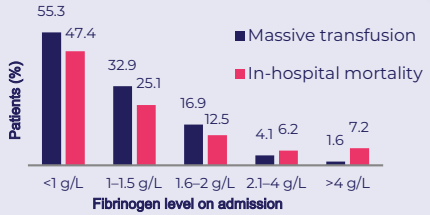
Management of bleeding and coagulopathy following trauma[6]

Damage control resuscitation*

- **Restrictive fluid therapy and permissive hypotension*** → Use of a **restricted volume replacement strategy** with a target MAP of 50–60 mmHg (systolic BP of 80–90 mmHg) until major bleeding has been stopped[6]
- **Temperature management*** → Early application of **measures to reduce heat loss** and warm the hypothermic patient to achieve and maintain normothermia[6]
- **Early and aggressive hemostatic therapy*** → **TXA administration as soon as possible** in trauma patients who are bleeding or are at risk of significant bleeding, if feasible, enroute to the hospital[6]
- **Early and aggressive hemostatic therapy*** → In the initial management of patients with expected massive hemorrhage: **Fibrinogen concentrate/cryoprecipitate and pRBC OR FFP in an FFP/pRBC ratio of at least 1:2 as needed[6]**

CFC treatments can restore hemostasis in trauma patients[7]

Low plasma fibrinogen levels on admission are associated with increased mortality and massive transfusions[8]



Fibrinogen treatment recommendation:

An initial fibrinogen supplementation of 3–4 g (15–20 single donor units of cryoprecipitate or 3–4 g of fibrinogen concentrate). Repeat doses should be guided by VET and laboratory assessment of fibrinogen levels[6]

PCC treatment recommendation:

Provided that fibrinogen levels are normal, PCC is administered to the bleeding patient based on evidence of delayed coagulation initiation using VET[6]

Platelet transfusion recommendation:

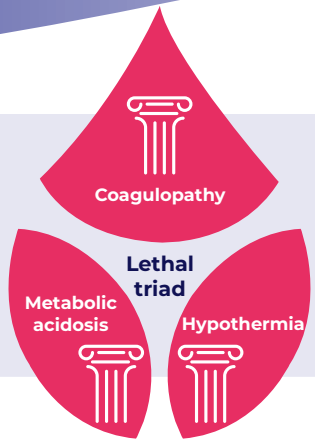
Platelets to be administered to maintain a platelet count >50×10⁹/L in trauma patients with ongoing bleeding and >100×10⁹/L in patients with TBI[6]

1. Moore EE, et al. *Nat Rev Dis Primers* 2021;7(1):30; 2. German Society for Trauma Surgery: S3 Guideline Polytrauma/Severely Injured Patient Treatment. V4.1. 2022. Available at https://www.awmf.org/leitlinien/detail/ll/187-023.html. (Accessed November 2025); 3. Brohi K, et al. *J Trauma* 2003;54:1127–1130; 4. Khan S, et al. *J Trauma Acute Care Surg* 2014;76:561–567; 5. Schöchl H, et al. *Hamostaseologie* 2024;44(1):31–39; 6. Rossaint R, et al. *Crit Care* 2023;27:80; 7. Ponschab M, et al. *Scand J Trauma Resusc Emerg Med* 2015;23:84; 8. McQuilten Z, et al. *Injury* 2017;48:1074–1081.

Fluid resuscitation in trauma

Hypovolemia and acidosis are the key triggers of TIC*

Coagulopathy, metabolic acidosis, and **hypothermia** represent the **three pillars of life-threatening post-injury bleeding**[1]



Fluid therapy should be individualized

EV use after injury[2]

12 hr post-injury → >80% increased mortality

EV use **within first 12 hours** after injury was independently associated with a **>80% higher risk of mortality**

24 hr post-injury → >2-fold increased mortality

EV use was independently associated with a **>2-fold higher risk of mortality within 24 hours**

Aggressive ECR within 12 hours was independently associated **with a 40% reduction in mortality**

EV should be applied cautiously and not in the place of aggressive ECR after severe blunt injury

Fluid volume

Mortality rates have been shown to increase with the amount of plasma transfused[3,4]

A higher volume of plasma transfusion was associated with an increased in-hospital mortality in surgical patients without massive transfusion, and in critically ill patients with sepsis-induced mortality[3,4]

100 mL of FFP → ~5% increased mortality odds

Each **100 mL** increase in **FFP** volume is linked to an **~5% rise** in the odds of **in-hospital mortality**[3]

ECR, early crystalloid resuscitation; EV, early vasopressor; FFP, fresh frozen plasma; ICU, intensive care unit; TIC, trauma-induced coagulopathy.

*Unreferenced claims based on the personal interpretation and expert experience of Dr. Fries.
†Aggressive fluid therapy refers to the rapid administration of large boluses of isotonic crystalloids.

Crystalloids versus colloids for fluid resuscitation

Damage control resuscitation with:[5]

High volumes of crystalloids (>6 L) was associated **with decreased survival**

Low volumes of colloids (median 1 L) was associated **with increased survival**

A meta-analysis concluded that **crystalloids were less efficient than colloids at stabilizing resuscitation in the ICU**[6]

All mortality and **90-day mortality was significantly higher for hydroxyethyl starch than for crystalloids**[6]

However, in the CRISTAL trial, **no significant difference in 28-day mortality was observed with colloids versus crystalloids** among ICU patients with hypovolemia[7]

Key recommendations

Guidelines recommend using **crystalloids for fluid resuscitation** in critically ill patients or those with sepsis[8,9]

In both cases, the use of **starch is not recommended**[8,9]

Gelatin is not recommended for resuscitation in patients with sepsis;[8] however, for critically ill patients in whom acute hypovolemia cannot be adequately treated with crystalloids alone, gelatin and human albumin may be used as adjuncts[9]

ROSE concept

The ROSE concept describes the phases of fluid therapy in septic shock:[10]

- **Resuscitation**
- **Optimization**
- **Stabilization**
- **Evacuation**

During resuscitation and optimization, **aggressive fluid therapy† guided by clinical and hemodynamic parameters is mandatory**[10]

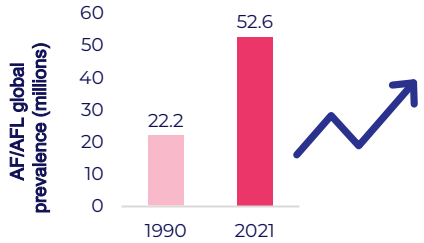
1. Moore EE, et al. *Nat Rev Dis Primers* 2021;7(1):30; 2. Sperry JL, et al. *J Trauma* 2008;64(1):9–14; 3. Xu X, et al. *Front Med (Lausanne)* 2023;10:1130359; 4. Wang R, et al. *Shock* 2023;60(4):545–552; 5. Guidry C, et al. *J Surg Res* 2013;185(1):294–299; 6. Martin GS and Bassett P. *J Crit Care* 2019;50:144–154; 7. Annane D, et al. *JAMA* 2013;310(17):1809–1817; 8. Evans L, et al. *Intensive Care Med* 2021;47(11):1181–1247; 9. German Society for Trauma Surgery: S3 Guideline intravascular volume therapy in adults. V2.0. 2020. Available at https://register.awmf.org/de/leitlinien/detail/001-020. (Accessed January 2026); 10. Willam C and Herbst L. *Med Klin Intensivmed Notfmed* 2024;119(8):634–639.

Management of medication-induced coagulopathy

The global prevalence of atrial fibrillation and atrial flutter is increasing[1]

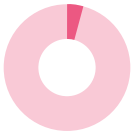
AF/AFL is the most common arrythmia worldwide[1]

The number of patients with AF/AFL more than doubled from 1990 to 2021[1]



The global prevalence of AF/AFL is expected to further increase, driven by aging, hypertension, and obesity[1]

Anticoagulated trauma patients



~3–4%
of all trauma patients are on anticoagulants pre-injury[2]

>20–25%
of hip fracture patients are on anticoagulants pre-injury*

Management of VKA-associated bleeding

Vitamin K can be used to manage bleeds associated with a VKA; however, when used alone, it acts too slowly to correct INR effectively in cases of life-threatening bleeding†

In patients receiving a VKA, a target INR ≤1.4 is considered appropriate in most cases[3]

Key recommendations for managing bleeding related to VKA

- In bleeding patients where **VKA-induced coagulopathy** is considered a contributing factor, we recommend the administration of **4F-PCC plus IV vitamin K**[4]
- **PCC administration in low doses** guided by increased INR, if no VET available, **in the presence of clinically significant bleeding** in patients without fibrinogen deficiency[4]

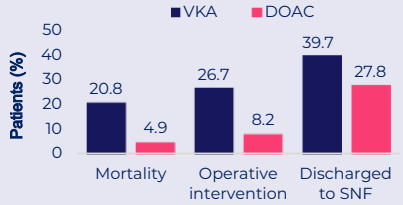
4F-PCC, four-factor prothrombin complex concentrate; AF, atrial fibrillation; AFL, atrial flutter; anti-Xa, anti-activated factor X; BW, body weight; CT, clotting time; DOAC, direct oral anticoagulant; ECA, ecarin; FXa, activated factor X; ICH, intracranial hemorrhage; INR, international normalized ratio; IU, international unit; IV, intravenous; PCC, prothrombin complex concentrate; RVV, Russell's viper venom; SNF, specialized nursing facility; TBI, traumatic brain injury; VET, viscoelastic testing; VKA, vitamin K antagonist.

*Unpublished data provided by Prof. Schöchl. †Statement provided by Prof. Schöchl based on clinical experience or personal interpretation.

CSL

DOACs are associated with lower mortality and improved outcomes compared with VKA

In patients with blunt trauma ICH, use of DOACs led to lower mortality, fewer operative interventions, and fewer discharges to specialized nursing facilities, compared with VKA[5]



When is monitoring of DOACs recommended?

- Major trauma[6]
- Neuro-trauma, including TBI and spinal cord injuries[3,6]
- Acute surgery with high bleeding risk[4]
- Thrombolysis in acute stroke[7]

What options are available for point-of-care monitoring of DOAC plasma levels?

- Point-of-care coagulometer[8]
- ECA-test CT (for dabigatran)[9]
- RVV-test CT (for direct FXa inhibitors)[9]

Strategies for managing DOAC-associated bleeding[10,11]

Non-specific optimization of hemostasis

- Hemoperfusion with porous polymer bead device (for FXa inhibitors)
- Hemodialysis (for dabigatran)

Non-specific DOAC-associated bleed management

- PCC

Specific DOAC-associated bleed management

- Idarucizumab (for dabigatran)
- Andexanet alfa (for FXa inhibitors)

Key recommendations for managing bleeding related to DOACs

- If bleeding is **life-threatening** in those receiving **dabigatran**, treatment with idarucizumab (IV 5 g) is recommended[12]
- If bleeding is **life-threatening** in the presence of an **apixaban or rivaroxaban** effect, especially in patients with TBI, bleeding management with andexanet alfa is recommended[12]
- Alternatively, in bleeding patients treated with anti-Xa agents (**rivaroxaban, apixaban**, and edoxaban), treatment with **PCC** (25 IU/kg BW at first) is recommended by guidelines[4]

1. Tan SCW, et al. *CJC Open* 2025;7:247–258; 2. Wood B, et al. *Scand J Trauma Resusc Emerg Med* 2017;25:76; 3. ACS. Best Practices Guidelines: Traumatic Brain Injury. 2023. Available at https://www.facs.org/media/vgfgjpfk/best-practices-guidelines-traumatic-brain-injury.pdf. (Accessed November 2025); 4. Kietaibl S, et al. *Eur J Anaesthesiol* 2023;40:226–304; 5. Feeney J, et al. *J Trauma Acute Care Surg* 2016;81:843–848; 6. Schöchl H, et al. *Curr Opin Anaesthesiol* 2024;37:93–100; 7. Marsch A, et al. *Cerebrovasc Dis* 2019;48:17–25; 8. Bakhru SH, et al. *Sci Rep* 2025;15:7355; 9. Oberladstätter D, et al. *Anaesthesia* 2021;76:373–380; 10. Rodrigues AR, et al. *J Clin Med* 2024;13:6842; 11. Tomaselli GF, et al. *J Am Coll Cardiol* 2020; 76:594–622; 12. Rossaint R, et al. *Crit Care* 2023;27:80.

Point-of-care monitoring: Interpretation and clinical decision-making

Point-of-care (POC) VET

POC VET (e.g., TEG®, ROTEM®) is increasingly recommended for real-time, targeted management of coagulopathy in trauma and critical care[1,2]

VET-guided hemostatic interventions: Examples from the literature

VET use in trauma settings[3]

- In trauma, **TEG®-guided massive transfusion protocols** have been shown to **improve survival** within 6 hours and **reduce hemorrhagic deaths**
- Compared with CCAs, the use of TEG® also resulted in:
  - **Fewer blood transfusions** without compromising coagulation
  - **More ICU-** and **ventilator-free days**

VET use in cardiac surgery[4]

- In a prospective, randomized, single-center trial, compared with CCAs, POC VET-guided therapy resulted in:
  - **Fewer pRBC, FFP**, and **platelet** transfusions
  - **Reduced costs** of hemostatic therapy
  - **Shorter ventilation time** and **ICU stay**
  - **Lower 6-month mortality rates**

Advantages of test activation in VET[5,6]

Use of activators allows:

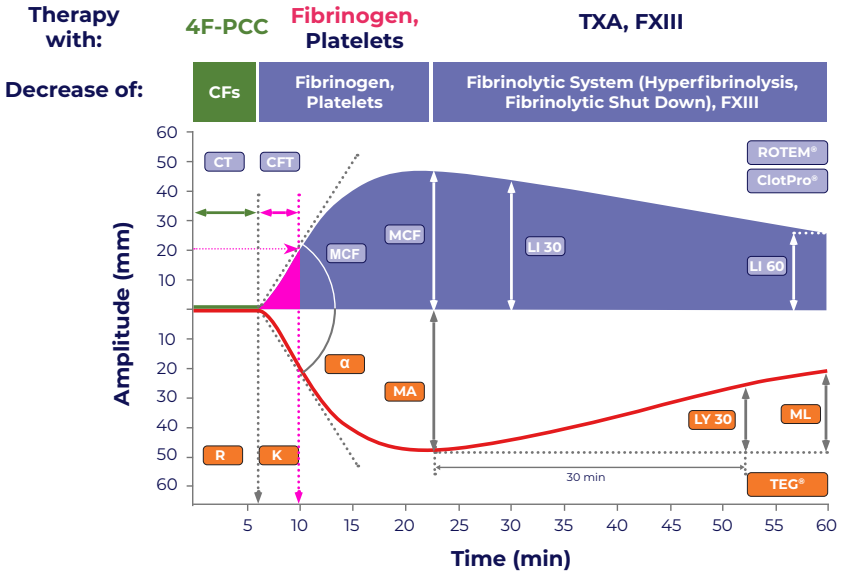
- **Faster** availability of results
- **Improved reproducibility** of measurements

Different assays enable:

- Detection of specific **coagulation factor deficiencies**
- Differentiation between **platelet function** and **fibrinogen contribution**
- Identification of **heparin effect** as a cause of bleeding
- Detection of **hyperfibrinolysis**

4F-PCC, four-factor prothrombin complex concentrate; α, alpha angle; APTEM, aprotinin thromboelastometry; aPTT, activated partial thromboplastin time; CCA, conventional coagulation assay; CFs, coagulation factors; CFT, clot formation time; ClotPro®, elastic motion thromboelastometry; CT, clotting time; EXTEM, extrinsic thromboelastometry; FFP, fresh frozen plasma; FIBTEM, fibrin-based thromboelastometry; FXIII, factor XIII; HEPTEM, heparin-based thromboelastometry; ICU, intensive care unit; INTEM, intrinsic thromboelastometry; K, clot formation time; LI/LY, lysis index; MA, maximum amplitude; MCF, maximum clot firmness; ML, maximum lysis; POC, point-of-care; pRBC, packed red blood cell; PT, prothrombin time; R, reaction time; ROTEM®, rotational thromboelastometry; TEG®, thromboelastography; TXA, tranexamic acid; VET, viscoelastic testing.

Diagnostic and therapeutic capabilities of VET[7]



Functions of ROTEM® assays[5,6]

Assay	Interpretation
EXTEM	Assesses the tissue factor activated pathway (extrinsic pathway) partially measured by PT; assesses clot firmness based on fibrin and platelets
INTEM	Assesses the contact activation pathway (intrinsic pathway) partially measured by aPTT
FIBTEM	Assesses the relative contribution of fibrinogen to clot strength independent of platelets
HEPTEM	Assesses the presence of systemic heparin via comparison with the INTEM assay
APTEM	Verifies the effects of antifibrinolytic drugs

Interpretation of combined assay results[5,6]

The combination of different assays enables a differential diagnosis

- FIBTEM
- EXTEM

Differentiation of platelet and fibrin contribution to clot firmness

- EXTEM
- APTEM

May confirm fibrinolytic activity

- INTEM
- HEPTEM

May indicate the presence of heparin

1. Kietaibl S, et al. *Eur J Anaesthesiol* 2023;40:226–304; 2. Rossaint R, et al. *Crit Care* 2023;27:80; 3. Gonzalez E, et al. *Ann Surg* 2016;263(6):1051–1059; 4. Weber CF, et al. *Anesthesiology* 2012;117(3):531–547; 5. Hartmann J, et al. *Res Pract Thromb Haemost* 2023;7:e100031; 6. Görlinger K, et al. *Korean J Anesthesiol* 2019;72(4):297–322; 7. Lier H and Fries D. *Transfus Med Hemother* 2021;48(6):366–376.

Rational use of blood products and coagulation factor concentrates

Changes in coagulation factor concentrations during blood loss

In major blood loss, coagulation factors do not decrease in concentration at a similar rate[1]

During severe bleeding, **fibrinogen levels decrease to a critical value (<1.5–2 g/L) at an earlier stage** than other hemostatic factors[1,2]

Critical factor levels and predicted blood loss as percentage of blood volume[1]

Hemostatic factor	Critical level	Blood loss % (95% CI)
Fibrinogen	**1 g/L**	**142 (117–169)**
Prothrombin	20%	201 (160–244)
Factor V	25%	229 (167–300)
Factor VII	20%	236 (198–277)
Platelets	$50\times10^3/mm^3$	230 (169–294)

Use of blood products to restore hemostasis

Plasma[3–7]

Pros

- Contains **all** coagulation factors and inhibitors
- Avoids further dilution
- Modulates inflammation

Cons

- Low coagulation factor activity
- Time needed for thawing
- Risk of TACO and TRALI

Low titer O Rh- whole blood[8,9]

Pros

- LTOWB is a universal donor
- Better O_2 transport capacity
- Lower exposure to donors

Cons

- LTOWB contains ~250 mL plasma
- Hemolysis due to Rhesus mismatch
- O Rh- donors rare
- ABO incompatibility

Although plasma is used extensively in the treatment of bleeding patients, there is **no evidence** from RCTs supporting the use of plasma for treating bleeding compared with other interventions[7]

Hemostatic resuscitation with LTOWB is associated with improved early, but not late, survival compared with component therapy (RBCs, plasma, and/or platelets)[10]

4F-PCC, four-factor prothrombin complex concentrate; ABO, A, B, and O blood types; ABP, allogeneic blood product; CI, confidence interval; FXIII, factor XIII; LTOWB, low titer O Rh- whole blood; PCC, prothrombin complex concentrate; RBC, red blood cell; RCT, randomized controlled trial; Rh-, Rhesus negative; TACO, transfusion-associated circulatory overload; TBI, traumatic brain injury; TRALI, transfusion-related acute lung injury.

Use of coagulation factor concentrates to restore hemostasis[11,12]

Advantages

- **Standardized dose**
- **No risk of TACO**
- **No risk of TRALI**
- **ABO matching not required**
- **Rapid administration**
- **Very low risk of viral transmission**

Clinical guideline recommendations for the management of bleeding patients

Treatment of hypofibrinogenemia in bleeding patients is recommended[13]

- An initial **fibrinogen concentrate** dose of 25–50 mg/kg is recommended
- If fibrinogen concentrate is not available, cryoprecipitate can be used (initial dose 4–6 mL/kg)
- Plasma alone is not sufficient to correct hypofibrinogenemia

No recommendation for the use of PCC versus plasma alone in massively bleeding patients[14]

PCC in cardiac surgery

In the management of bleeding during and after cardiac surgery, patients who received 4F-PCC had significantly lower median chest tube drainage and cumulative ABPs given compared with those who received frozen plasma[15]

Units of blood products
40%

Chest tube drainage at 24 h
250 mL

Use of FXIII in trauma

Although FXIII level on admission is associated with number of surgical interventions, blood product transfusions, and coagulation factor administration in trauma patients, FXIII substitution was not associated with improvement in these patient outcomes[16]

Use of platelets to restore hemostasis

Routine use of platelet transfusion is not recommended for patients with hemorrhagic TBI on platelet inhibitors[17]

1. Hiippala ST, et al. *Anesth Analg* 1995;81:360–365; 2. Fries D and Martini WZ. *Br J Anaesth* 2010;105(2):116–121; 3. von Heymann C, et al. *Transfus Med Hemother* 2023;50:107–115; 4. Peng Z, et al. *Shock* 2013;40:195–202; 5. Chowdary P, et al. *Br J Haematol* 2004;125:69–73; 6. Selleng K and Greinacher A. *Transfus Med Hemother* 2021;48:350–356; 7. Levy J, et al. *Anesth Analg* 2017;124:1268–1276; 8. Pahuija S. Glob *J Transfus Med* 2023;8:4–9; 9. Shea SM, et al. *J Thromb Haemost* 2024;22:140–151; 10. Morgan K, et al. *Crit Care Med* 2024;52:e390–e404; 11. Schöchl H, et al. *Curr Opin Anaesthesiol* 2013;26:221–229; 12. Karkouti K, et al. *JAMA* 2025;333:1781–1792; 13. Kozek-Langenecker S, et al. *Eur J Anaesthesiol* 2017;34:332–395; 14. Vlaar A, et al. *Intensive Care Med* 2021;47:1368–1392; 15. Karkouti K, et al. *JAMA Netw Open* 2021;4:e213936; 16. Katzensteiner M, et al. *J Clin Med* 2022;11:4174; 17. Wiegele M, et al. *Crit Care* 2019;23:62.

Thrombosis prophylaxis in trauma

Critically ill patients are at increased risk of thrombotic events[1]

Incidence of thrombotic events

Sepsis[2,3]	Severe trauma[4,*]	COVID-19[5,6]
10.8–16.9%	0.9–28.0%	11.4–35.3%

The link between coagulation and the immune system[7]

In certain contexts, thrombosis plays an important physiological role in early immune defense against pathogens:

This process is termed **immunothrombosis**

However, **uncontrolled immunothrombosis could result in DIC**, which causes widespread microvascular thrombosis and is associated with poor outcomes

Low-molecular-weight heparin

Among critically ill adults, **prophylaxis with LMWH reduces the incidence of DVT** compared with control treatment (no prophylaxis, placebo, or only compression stockings), and is probably more effective than UFH[1]

Anti-Xa levels

Anti-Xa can be used to assess LMWH activity[8]

Studies have shown that **standard prophylactic dosing of enoxaparin, a LMWH, leads to inadequate anti-Xa levels** in critically ill patients[8,9]

Low anti-Xa levels have been associated with **increased thrombotic events**[8,9]

Adjusting the dosage of enoxaparin based on anti-Xa levels has been shown to **reduce the incidence of thrombotic events**[10]

FXII deficiency

- **It is common for critically ill patients to have a deficiency in FXII**[11]
- Reduced FXII activity (<42.5%) has been demonstrated to cause an apparent prolongation of aPTT, potentially resulting in the omission of thrombosis prophylaxis[11]

ACT, activated clotting time; anti-Xa, anti-activated factor X; aPTT, activated partial thromboplastin time; COVID-19, coronavirus disease 2019; DIC, disseminated intravascular coagulation; DVT, deep vein thrombosis; FXII, factor XII; ICU, intensive care unit; ISTH SSC, International Society on Thrombosis and Haemostasis Scientific Subcommittee; LMWH, low-molecular-weight heparin; LY30, % clot lysis at 30 minutes after maximum strength was achieved; POC, point-of-care; TT, thrombin time; UFH, unfractionated heparin; U, unit.

*Range for severe trauma excluded highest and lowest rates from the included studies. †Unreferenced claims based on the personal interpretation and expert experience of Dr. Fries.

Heparin resistance – an underestimated problem![†]

What is heparin resistance?

- Heparin resistance is the need for unusually high doses of UFH to achieve therapeutic aPTT or ACT levels, or failure to reach these targets despite dose escalation[12]
- The ISTH SSC survey respondents most commonly defined it as requiring **>35,000 U/day** or **>30 U/kg/h** of **UFH**[13]

How do you manage heparin resistance?[†]

1. Increase the heparin dose
2. LMWH instead of UFH
3. Antithrombin substitution
4. Direct thrombin inhibitor (bivalirudin or argatroban)

Antithrombin

- **Reduced antithrombin levels** are common after trauma and may contribute to **enoxaparin resistance** and **increased thrombotic risk**[14]
- In heparin-resistant patients undergoing cardiac surgery, administration of antithrombin **increased the mean ACT and heparin dose response**[15]
- However, **antithrombin did not improve anticoagulant response** in heparin-resistant ICU patients who were receiving prolonged UFH therapy[16]

Direct thrombin inhibitors

- In critically ill heparin-resistant patients, **argatroban has demonstrated improved anticoagulant efficacy** when compared with high doses of UFH[17,18]
- **Diluted TT** and **POC viscoelastic ecarin clotting time** have demonstrated increased accuracy over aPTT for monitoring argatroban in critically ill patients[19]

Impaired fibrinolysis

- **Fibrinolysis shutdown (LY30 ≤0.08%)** is common after severe injury and is linked to increased mortality, often from organ failure[20]
- In **sepsis, impaired fibrinolysis** is associated with **worse outcomes**, including organ failure and death[21–24]

→ **Direct thrombin inhibitors** can bind to already fibrin-bound thrombin and thereby reduce the size of a formed clot, influence clot structure, and increase fibrin network porosity thus **facilitating fibrinolysis†**

Key points to remember[†]

- ✔ **Hypercoagulopathy** is one of the **key problems in critically ill patients**
- ✔ **Heparin resistance** seems to be an **underestimated** problem
- ✔ **Close drug monitoring** and **individualized targeted therapy**, including **alternative strategies**, should be considered
- ✔ **Coagulation parameters** can give further **clinically relevant information**

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