Acute traumatic coagulopathy

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NOTHING TO DECLARE

Key points

Severe trauma (ISS >16) can lead to acute traumatic coagulopathy (ATC) by activation of protein C, endothelial glycocalyx disruption, consumption of fibrinogen, and platelet dysfunction.

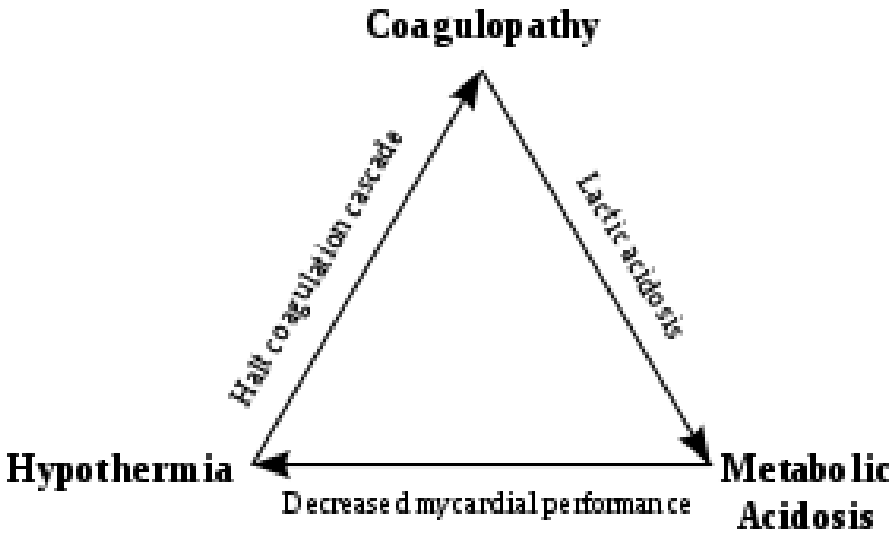
ATC increases mortality and morbidity, and requires coordinated treatment based on damage control resuscitation

Main cause of death before age 40

Par I. Johansson et al. Resuscitation and Emergency Medicine. Current management of massive hemorrhage in trauma. 2012; 20:2-10

Trauma triad of death

Combination of hypothermia, acidosis, and coagulopathy, which is commonly seen in patients who have sustained severe traumatic injuries and results in a significant rise in the mortality rate.



Mikhail, J. (Feb 1999), "The trauma triad of death: hypothermia, acidosis, and coagulopathy", AACN Clin Issues, 10 (1): 85–94.

Key terms

Acute Traumatic Coagulopathy – coagulopathy induced by trauma – results in:

- more severe bleeding
- multi-organ failure
- high mortality

Brohi, Karim et al (June 2003).
"Acute Traumatic Coagulopathy".
The Journal of Trauma: Injury, Infection, and Critical Care.
54 (6): 1127–1130

Major factors

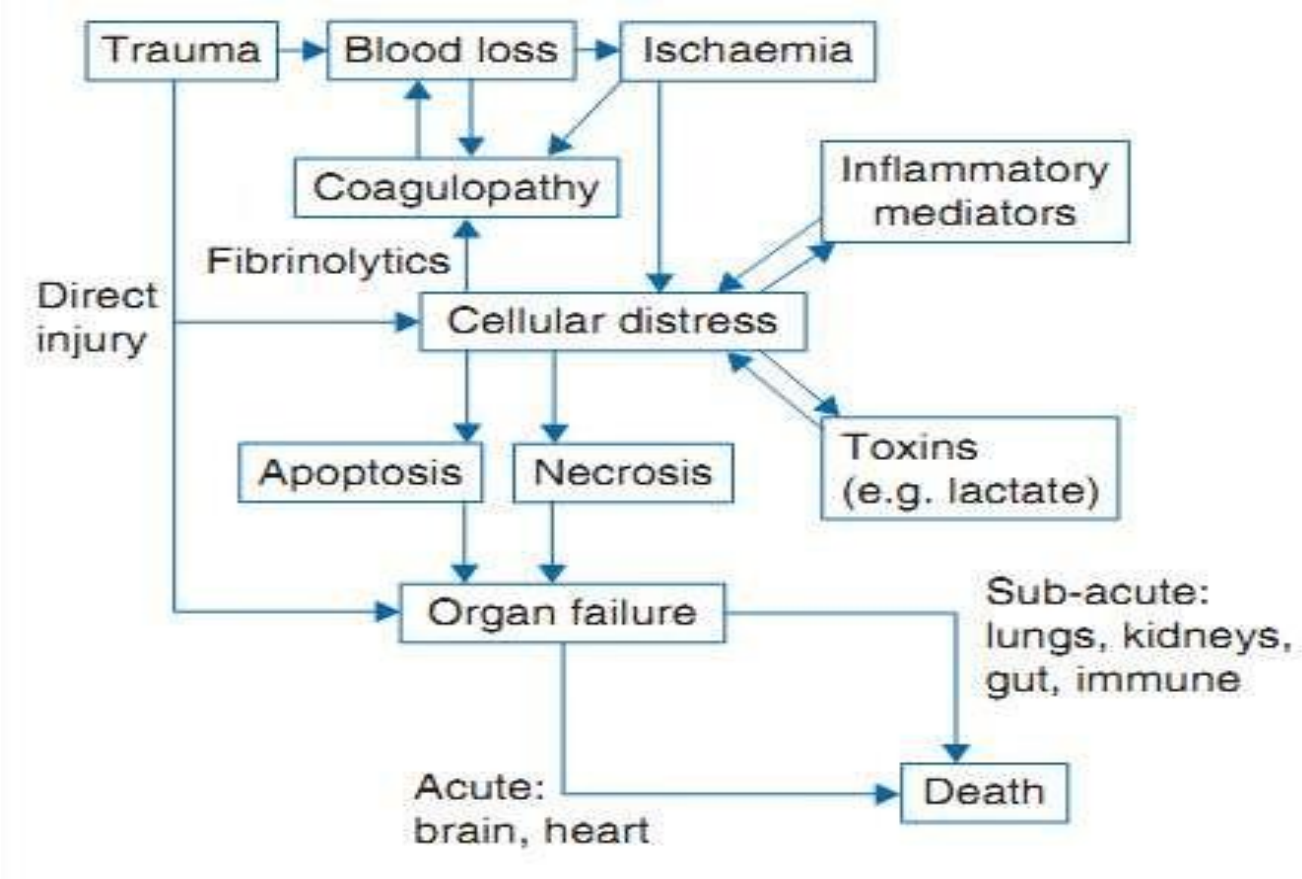
- Coagulopathy worsens outcomes in casualties with uncontrolled hemorrhage
- Causes of coagulopathy in casualties:

  - Hypothermia (especially in shock)
  - Large volume crystalloid resuscitation
  - Platelet-inhibiting drugs (aspirin and other NSAIDs such as ibuprofen)
  - Acidosis (associated with shock)
  - Intrinsic
  - Protracted scene times (>2 hours)
  - Protracted pre-hospital time (>2 hours)

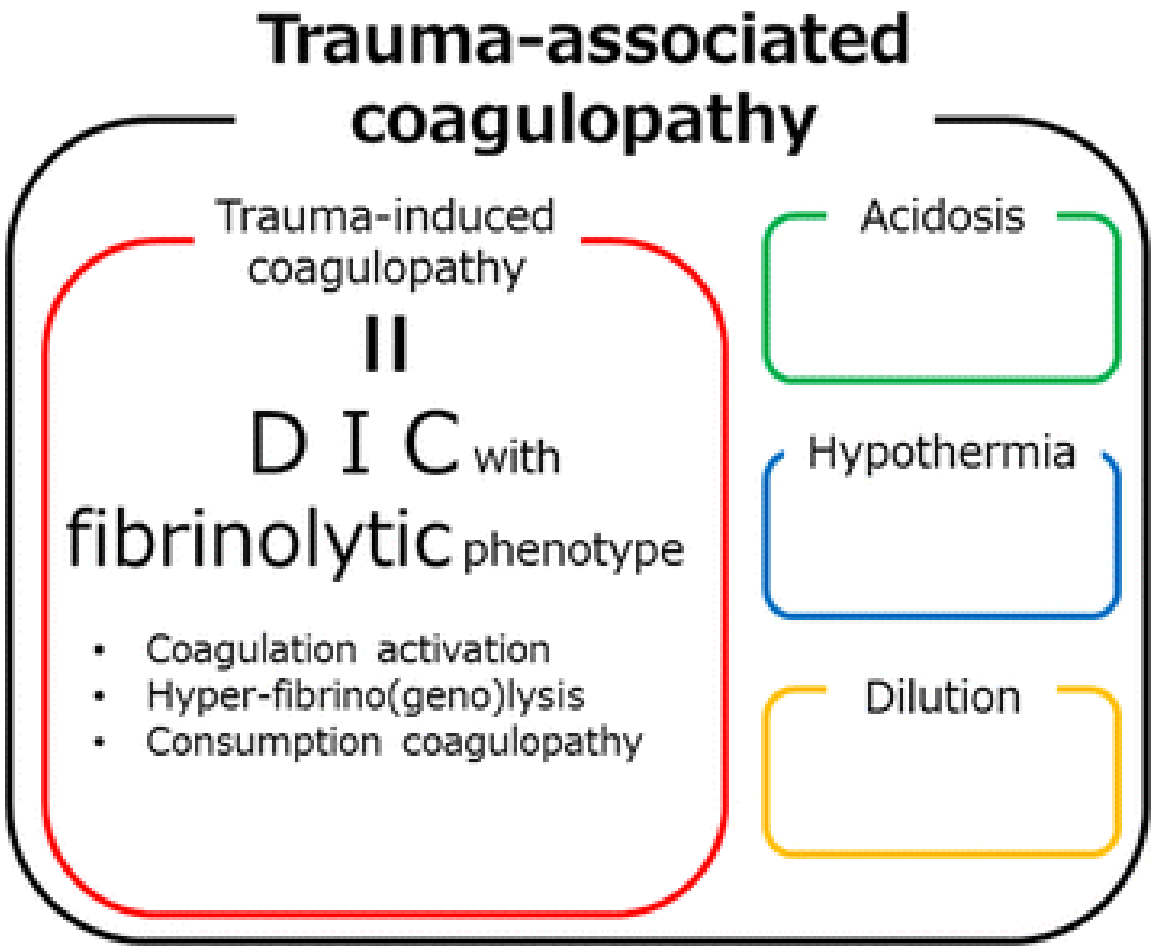
Pathogenesis of Traumatic Coagulopathy

- Multi-factorial global failure of the coagulation system to sustain adequate hemostasis after major trauma
- Combination of tissue trauma and systemic hypoperfusion cause global anticoagulation and hyperfibrinolysis
- Endothelial activation of Protein C is a central mechanism

Pathophysiology of the hemorrhagic shock



Dutton RP. Haemostatic resuscitation. Br J of Anest. 2012; 109 (Suppl. 1): 39 - 46



Mineji Hayakawa. Pathophysiology of trauma-induced coagulopathy: disseminated intravascular coagulation with the fibrinolytic phenotype.

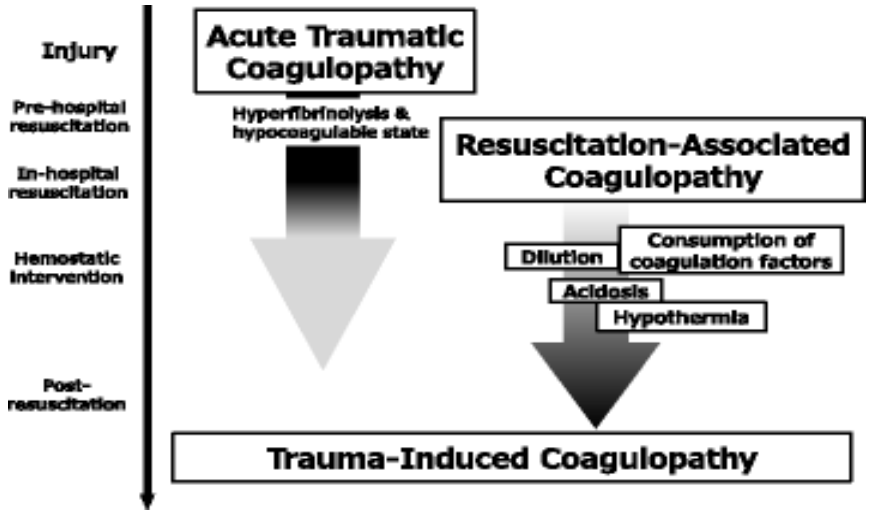
Journal of Intensive Care 2017; 5:14

Coagulopathy

- ✓ presents in 25 - 35% of patients with severe concomitant injury
- ✓ almost always accompanies severe and extremely severe acute blood loss upon admission and is associated with poor outcomes (up to 40% of all deaths)
- ✓ increases mortality by 4 - 5 times
- ✓ great need for transfusion
- ✓ long duration of ICU stay and total hospitalization time
- ✓ long duration of respiratory support
- ✓ high probability of multiple organ failure

Brohi, Karim et al (June 2003).
"Acute Traumatic Coagulopathy".
The Journal of Trauma: Injury, Infection, and Critical Care.
54 (6): 1127–1130

Coagulopathy in multiple trauma



Internal factors (acute traumatic coagulopathy)

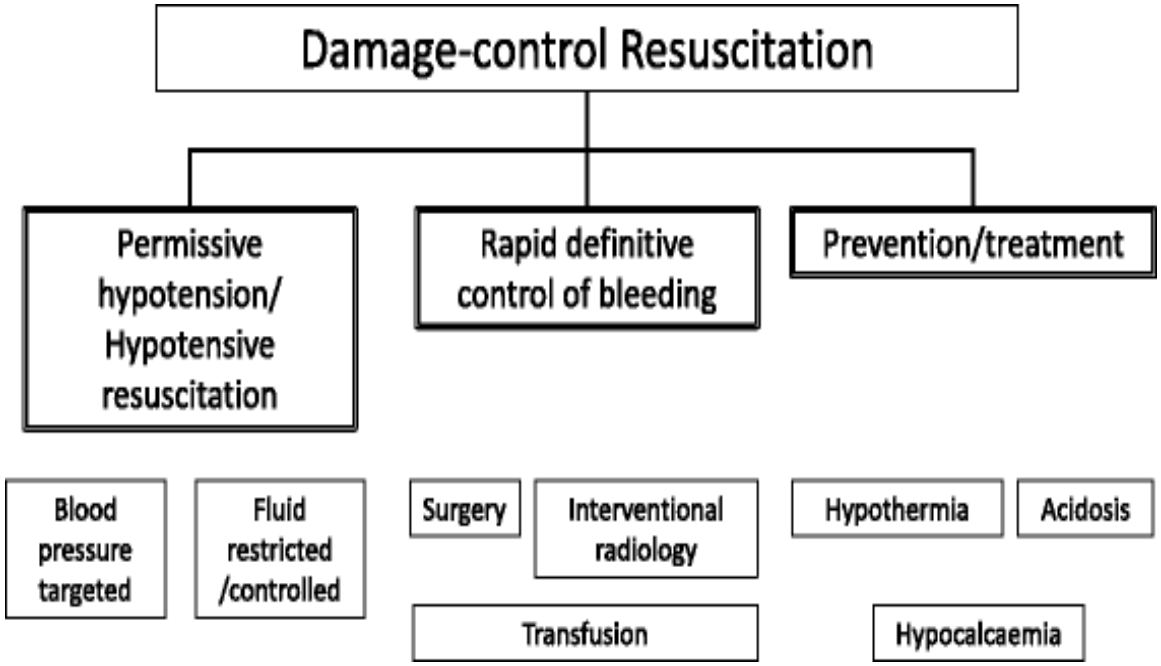
- ✓ hypoperfusion
- ✓ direct tissue damage

External factors (less significant in the first hours)

- ✓ hemodilution
- ✓ hypothermia
- ✓ acidosis
- ✓ anemia
- ✓ electrolyte imbalance

Br J Anaesth. 2013;111(suppl_1):i71-i82

Damage control resuscitation



- ✓ Damage control surgery
- ✓ Balanced resuscitation (controlled hypotension)

  Restrictive tactics of fluids administration
- ✓ Hemostatic resuscitation
- ✓ Management of acidosis, hypothermia and hypo Ca++

Balanced resuscitation

Type of resuscitation strategy	Interventions to patients	Major clinical trials focusing on the concepts
Permissive hypotension, Hypotensive resuscitation	To titrate and control the blood pressure less than normal range	Dutton et al. 2002, Morrison et al. 2011
Restricted resuscitation, Controlled resuscitation	To limit the volume of fluid to be administered	Brown et al. 2013, Schreiber et al. 2015
Delayed resuscitation	To restrict the fluid resuscitation until admission to the hospital (Early resuscitation is opposite term that means to initiate fluid	Bickel et al. 1994, Sampalis et al. 1997, Turner et al. 2000

Balanced resuscitation

Aggressive fluid therapy can lead to

- ✓ increase of cardiac output and blood pressure
- ✓ correlation with metabolic acidosis
- ✓ crystalloids damage the endothelial glycocalyx (increase extravasation)
- ✓ crystalloids and colloids dilute clotting factors and platelets
- ✓ hypothermia
- ✓ abdominal compartment syndrome
- ✓ ARDS
- ✓ acute kidney damage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The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition

Recommendations

- ✓ Systolic blood pressure at 80 - 90 mm Hg. (until ongoing bleeding stops)
- ✓ Mean arterial pressure a not lower than 80 mm Hg in severe traumatic brain injury
- ✓ The volume of infusion support until the possibility of blood transfusion appears - up to 1 liter, starting from the pre-hospital stage

Hemostatic resuscitation
Massive blood transfusion

- Replacement of one entire blood volume within 24 h
- Transfusion of >10 units of packed red blood cells (PRBCs) in 24 h
- Transfusion of >20 units of PRBCs in 24 h
- Transfusion of >4 units of PRBCs in 1 h when on-going need is foreseeable
- Replacement of 50% of total blood volume (TBV) within 3 h.

Indications:

Massive transfusion and massive transfusion protocol
Indian J Anaesth. 2014 Sep-Oct; 58(5): 590–595

✓Severe trauma
✓FAST positive
✓Mental disorders
✓HBR> 120 / min
✓Acidosis - base deficiency more than -6 mmol / l
✓Coagulopathy - INR more than 1.5
✓Anemia - hemoglobin less than 110 g / l
✓Hypothermia - less than 35 ° C

Hemostatic resuscitation
Massive blood transfusion

Protocol initiation:

Package 1: 4 doses of blood from one-group or universal donor and one-group + 4 doses of FFP

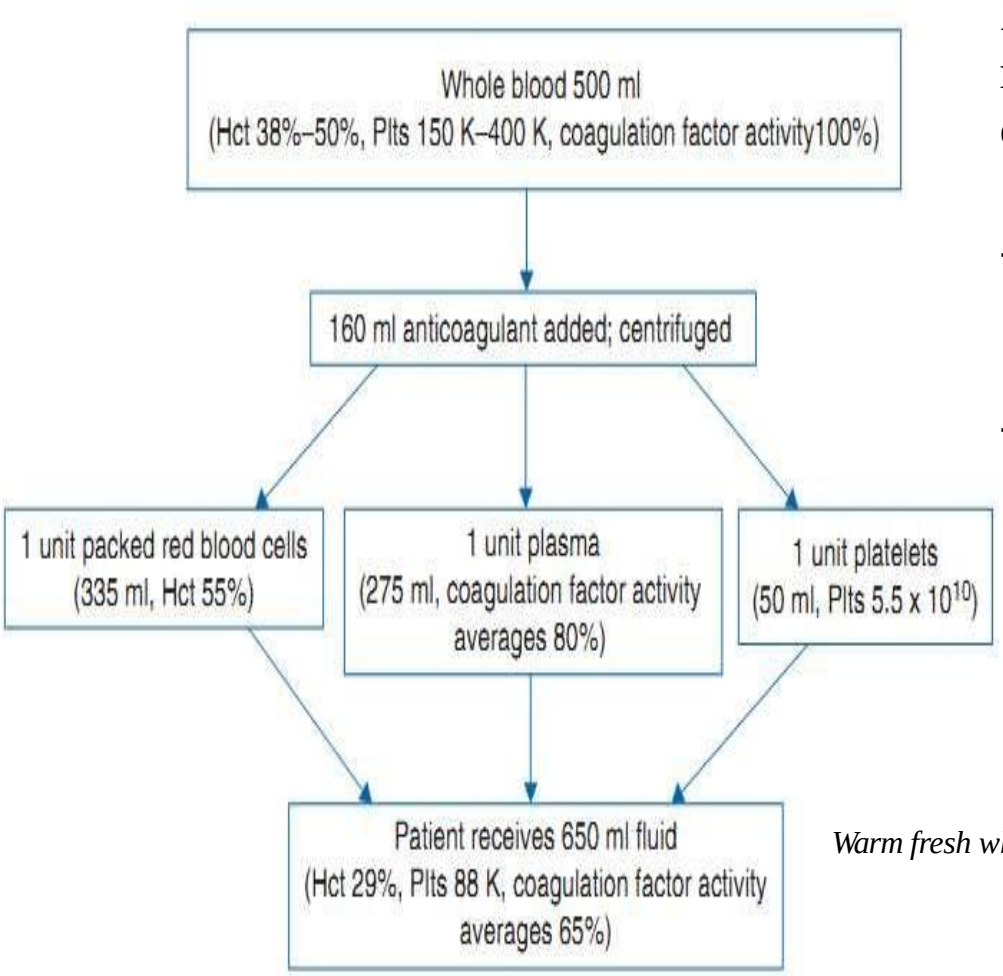
With continued bleeding:

Package 2: 4 doses of single-group blood + 4 doses of FFP + platelates suspension

- RBC - maintenance of hemoglobin level 70 - 90 g/L
- FFP - initial dose 10-15 ml / kg
- Platelets - maintaining levels above 50×10^9 /L (double in case of severe traumatic brain injury)

Stansbury LG, Hess AS, Thompson K, Kramer B, Scalea TM, Hess JR. The clinical significance of platelet counts in the first 24 hours after severe injury. Transfusion. 2013;53(4):783–9

Whole blood transfusion



Prospective study, 354 patients (100 received warm blood, 254 received component therapy)

- 24-hour survival rate: 96% in fresh blood group, 88% in component therapy ($p = 0.018$)
- 30-day survival rates 95% and 82%, respectively ($p = 0.002$)

Spinella PC et al.
Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries.
J Trauma, 2009 Apr, 66(4 Suppl): S69-76

Hemostatic resuscitation

Tranexamic acid

Health Technol Assess. 2013 Mar;17(10):1-79. doi: 10.3310/hta17100.

The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients.

Roberts I[1], Shakur H, Coats T, Hunt B, Balogun E, Barnetson L, Cook L, Kawahara T, Perel P, Prieto-Merino D, Ramos M, Cairns J, Guerriero C.

Author information

Abstract

BACKGROUND: Among trauma patients who survive to reach hospital, exsanguination is a common cause of death. A widely practicable treatment that reduces blood loss after trauma could prevent thousands of premature deaths each year. The CRASH-2 trial aimed to determine the effect of the early administration of tranexamic acid on death and transfusion requirement in bleeding trauma patients. In addition, the effort of tranexamic acid on the risk of vascular occlusive events was assessed.

OBJECTIVE: Tranexamic acid (TXA) reduces bleeding in patients undergoing elective surgery. We assessed the effects and cost-effectiveness of the early administration of a short course of TXA on death, vascular occlusive events and the receipt of blood transfusion in trauma patients.

DESIGN: Randomised placebo-controlled trial and economic evaluation. Randomisation was balanced by centre, with an allocation sequence based on a block size of eight, generated with a computer random number generator. Both participants and study staff (s investigators and trial co-ordinating centre staff) were masked to treatment allocation. All analyses were by intention to treat. A Mar model was used to assess cost-effectiveness. The health outcome was the number of life-years (LYs) gained. Cost data were obtai from hospitals, the World Health Organization database and UK reference costs. Cost-effectiveness was measured in international dollars ($) per LY. Deterministic and probabilistic sensitivity analyses were performed to test the robustness of the results to model assumptions.

Rossaint et al. Critical Care (2016) 20:100
DOI 10.1186/s13054-016-1265-x

Critical Care

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The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Timothy J. Coats[7], Jacques Duranteau[8], Enrique Fernández-Mondéjar[9], Daniela Filipescu[10], Beverley J. Hunt[11], Radko Komadina[12], Giuseppe Nardi[13], Edmund A. M. Neugebauer[14], Yves Ozier[15], Louis Riddez[16], Arthur Schultz[17], Jean-Louis Vincent[18] and Donat R. Spahn[19]*

We recommend that tranexamic acid be administered as early as possible to the trauma patient who is bleeding or at risk of significant hemorrhage at a loading dose of 1 g infused over 10 min, followed by an i.v. infusion of 1 g over 8 h. (Grade 1A) We recommend that tranexamic acid be administered to the bleeding trauma patient within 3 h after injury. (Grade 1B) We suggest that protocols for the management of bleeding patients consider administration of the first dose of tranexamic acid en route to the hospital. (Grade 2C)

Hemostatic resuscitation

Fibrinogen concentrate, cryoprecipitate

If a concentrate-based strategy is used, we recommend treatment with fibrinogen concentrate or cryoprecipitate if significant bleeding is accompanied by viscoelastic signs of a functional fibrinogen deficit or a plasma fibrinogen level of less than 1.5–2.0 g/l. (Grade 1C) We suggest an initial fibrinogen supplementation of 3–4 g. This is equivalent to 15–20 single donor units of cryoprecipitate or 3–4 g fibrinogen concentrate. Repeat doses must be guided by viscoelastic monitoring and laboratory assessment of fibrinogen levels. (Grade 2C)

FIBRINOGEN CONTENT IN VARIOUS BLOOD PRODUCTS	
1 unit of FFP	400 mg/250 ml
1 unit of PRBC	<100 mg
1 unit of apheresis platelets	300 mg
1 unit of whole blood	1000 mg
1 unit cryoprecipitate	2500 mg/150 ml

The main indication for the use of r FVIIa in traumatic bleeding


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Recombinant activated coagulation factor VII

We suggest that the off-label use of rFVIIa be considered only if major bleeding and traumatic coagulopathy persist despite all other attempts to control bleeding and best-practice use of conventional haemostatic measures. (Grade 2C)

The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition
Rossaint et al. Critical Care (2016) 20:100

- ✓ Does not improve outcome in severe trauma
- ✓ Reduces the number of transfusions
- ✓ Does not increase the number of venous thrombosis
- ✓ Reduces the development of ARDS

Hypothermia

- ✓ *accompanies 2/3 of severe trauma*
- ✓ *link in the pathogenesis of hemorrhagic shock in trauma*
- ✓ *consequence of resuscitation (infusion therapy)*
- ✓ *worsens coagulation*
- ✓ *worsens the forecast*

Active external warming

- Ambient temperature - active heating
- Heating mattresses, blankets

Internal warming

- Temperature of infusion media - "warm" solutions (up to 40 - 42 ° C)
- Washing with warm solutions of the stomach, bladder
- Extracorporeal warming

Reduce time spent in the operating room!

Acidosis

- Decreased myocardial contractility
- Vasodilation
- Decreased hepatic and renal blood flow Ventricular premature beats
- Reduces the effectiveness of coagulation factors
- Reduces platelet adhesion and aggregation

Fight against acidosis - fight against hypoperfusion!

Buffer correction at pH < 7.2

Wildenthal K., Mierzwaiak D.S., Myers R.W., et al. Effects of acute lactic acidosis on left ventricular performance. Am J Physiol 1968; 214:1352-1359.

Hypocalcemia

Ca++

- Coagulation
- Platelet adhesion
- Stabilization of fibrinogen and platelets in thrombus formation
- Myocardial contractility
- Contractility of smooth muscles

Elmer J, Wilcox SR, Raja AS. Massive transfusion in traumatic shock. J Emerg Med. 2013 Apr; 44(4):829-838

Severe hypocalcemia <0.9 mmol / L

The admission of 2 g $CaCl_2$ after fixation of hypocalcemia does not lead to the normalization of its level on the background of massive blood transfusion

Giancarelli A, Birrer KL, Alban RF, Hobbs BP, Liu-DeRyke X. Hypocalcemia in trauma patients receiving massive transfusion. J Surg Res. 2016 May; 202(1):182-187.

Aggressive correction - 2 g of $CaCl_2$ for each infused dose of erythro-suspension!

Further prospective of the research

- The place of clotting factors in the protocol of massive blood transfusion
- Effect of the depth of anesthesia on outcome
- Duration and depth of permissible hypotension
- Assessment of endothelial function in shock
- The effectiveness of the use of antioxidants in the first hours after injury
- The use of REBOA at the pre-hospital stage

Thanks for joining!