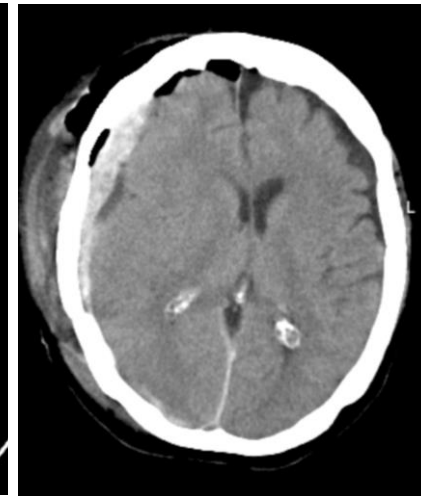
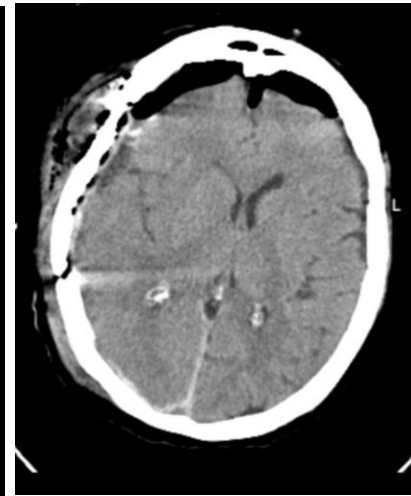




The management of hemostasis and thrombosis in traumatic brain injury

Current evidence and future directions

Marius Rimaitis, MD, PhD

Hospital of Lithuanian University of Health Sciences

Kauno klinikos

Clinic of Anesthesiology

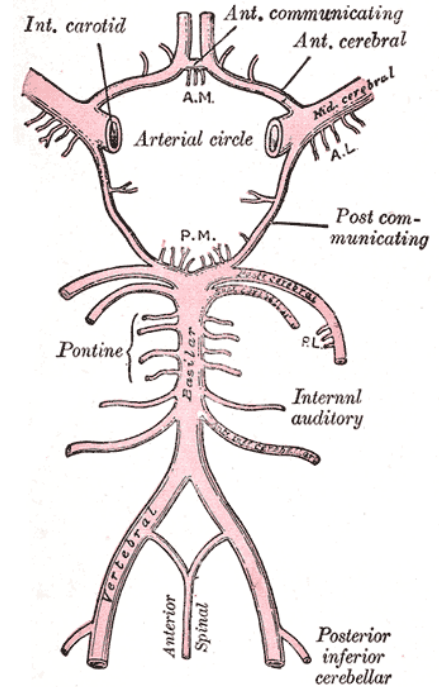
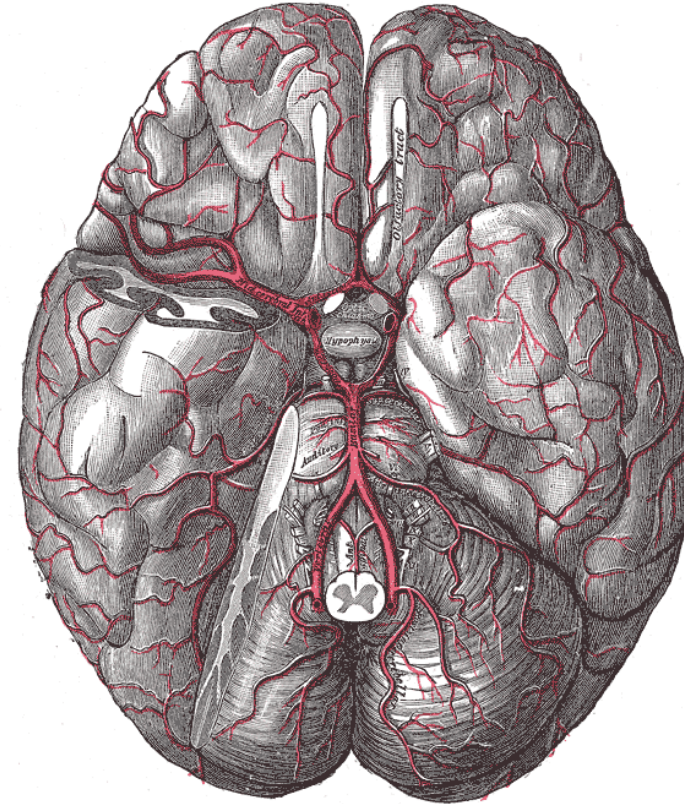
Department of Neurosurgical Anesthesia

werfen

VILNIUS
2025

The brain

- Highest metabolism rate of all organs
- Entirely dependant on constant supply of metabolic substrates
- Weight approx. 1400 g, i.e. 2% TBW
- Receive 12–15% of CO (500–700 ml/min)
- Extremely intense circulation:
 - Cerebral blood volume
3,5–4,5 ml/100g
 - Cerebral blood flow
45–55 ml/100g/min



Traumatic brain injury

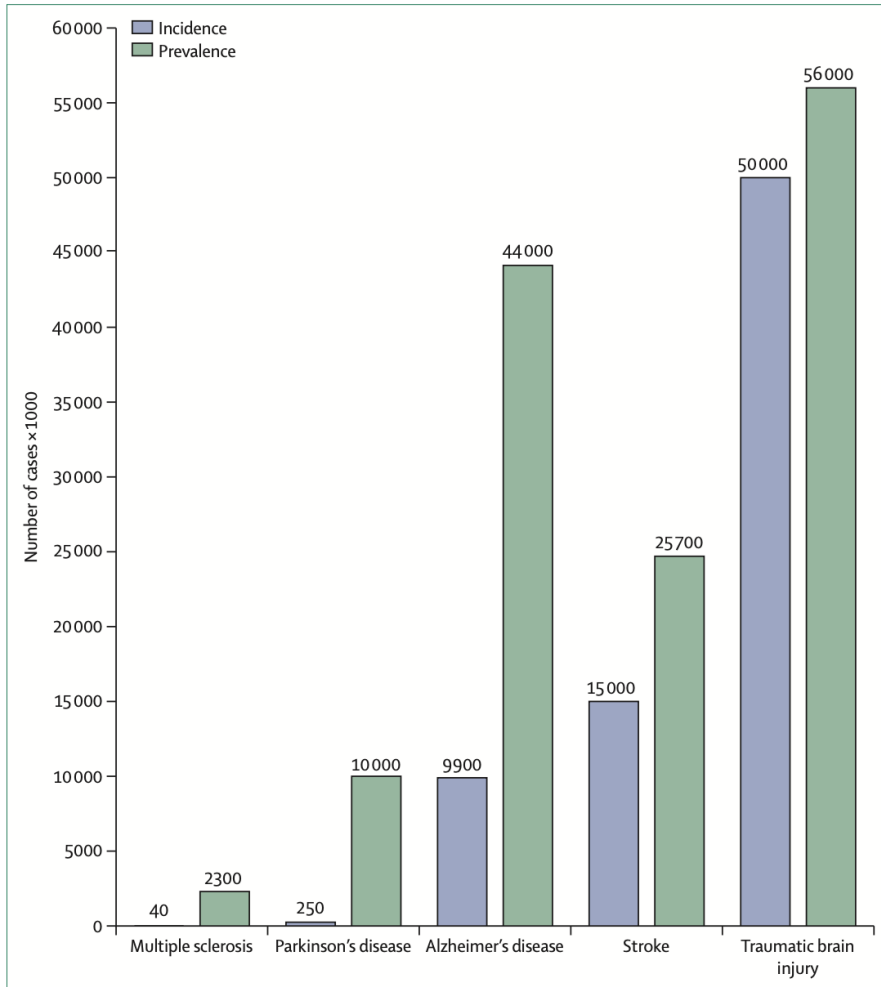


Figure 1: Global incidence and prevalence of traumatic brain injury compared with other common neurological diseases

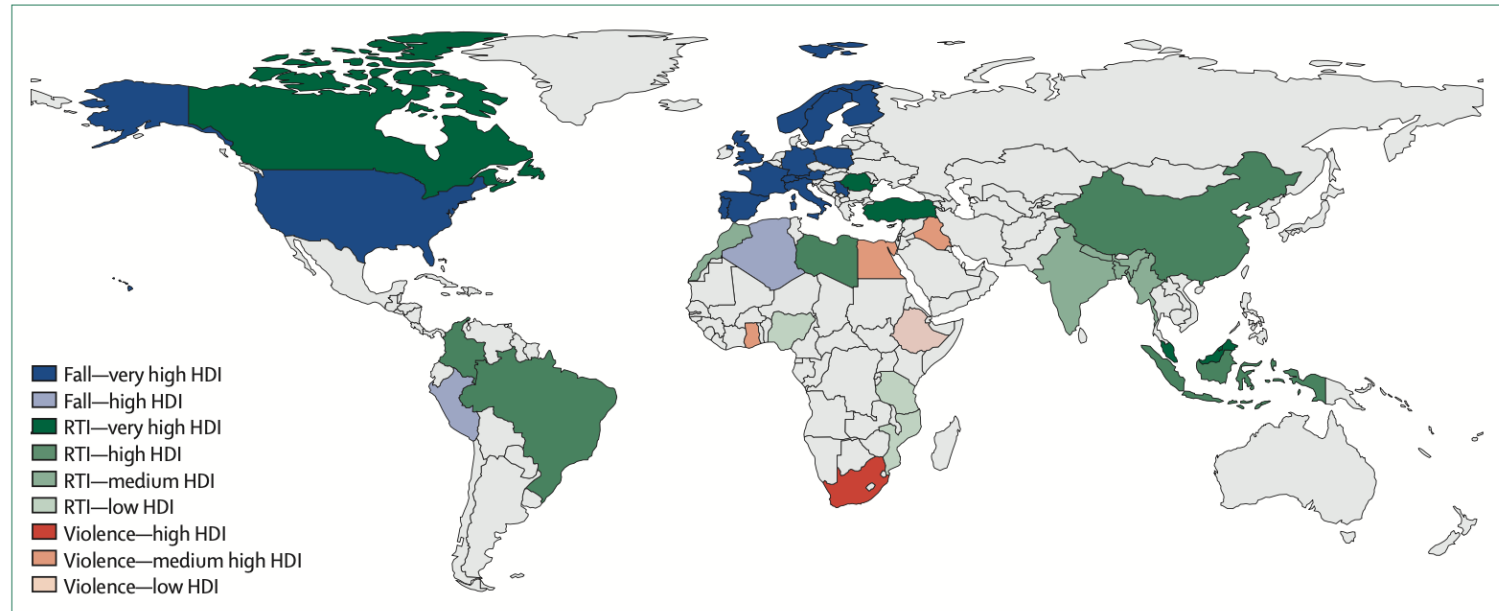


Figure 2: Between-country variations in mechanism of traumatic brain injury according to the Human Development Index

Figure modified from Clark et al with permission.¹⁸ HDI=Human Development Index. RTI=road traffic incident.

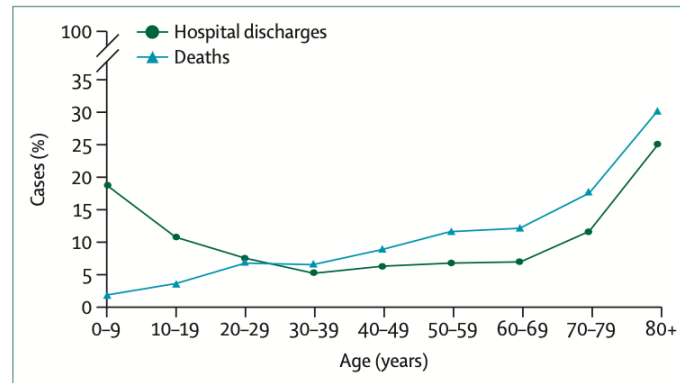


Figure 3: Estimated frequency of hospital discharges and deaths in cases of traumatic brain injury by age group in Europe

- ✓ Approx. 10% of TBI are severe
- ✓ Mortality rate in severe TBI 40% (in acute SDH: 27% to 70%)
- ✓ Unfavourable outcome on the Glasgow Outcome Scale is 60%

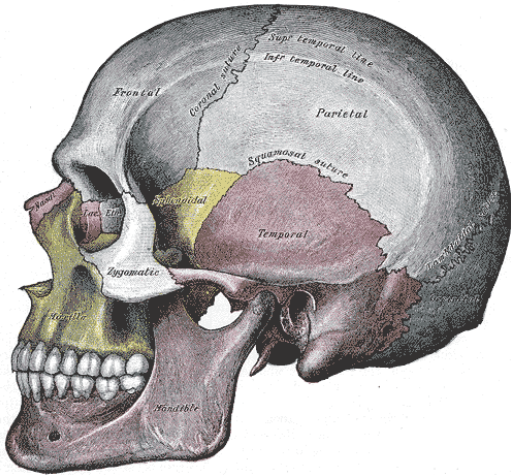
Maas AIR et al. Traumatic brain injury: progress and challenges in prevention, clinical care, and research. *Lancet Neurol* 2022; 21: 1004–60.

Evans LR et al. Prognosis of acute subdural hematoma in the elderly: a systematic review. *J Neurotrauma*. 2019;36:517-522.

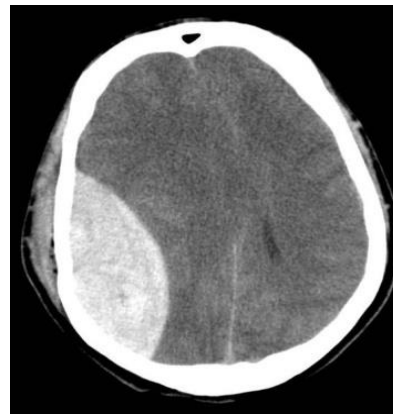
Rosenfeld JV, Maas AI, Bragge P, Morganti-Kossmann MC, Manley GT, Gruen RL. Early management of severe traumatic brain injury. *Lancet* (2012) 380:1088–98.

Significance of the mass effect

"The cranium and its constituents create a state of volume equilibrium, such that any increase in volume of one of the cranial constituents must be compensated by a decrease in volume of another." *The Monro-Kellie hypothesis*



- **Brain tissue 85%**
- **Cerebrospinal fluid 10%**
(approx. 150 ml)
- **Blood 5%**
(50–75 ml)

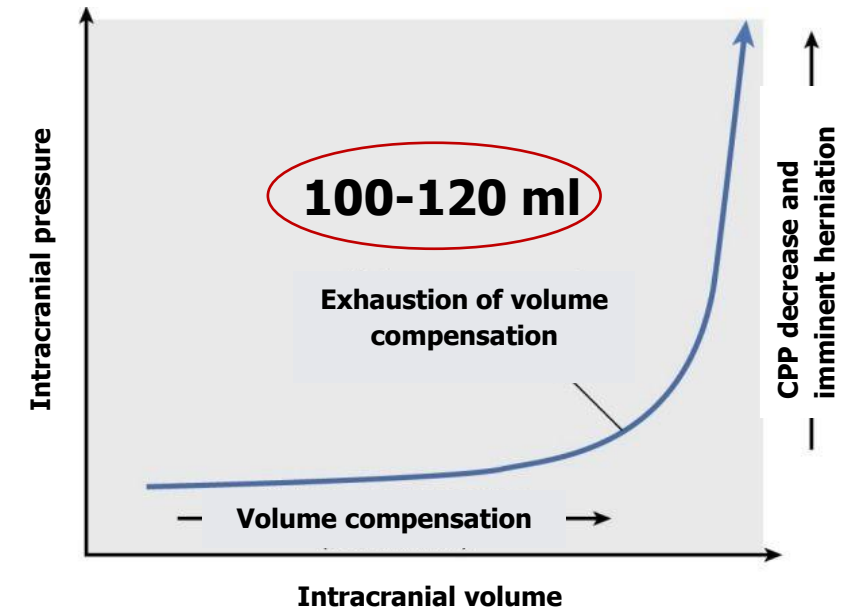


Epidural
hematoma



Subdural
hematoma

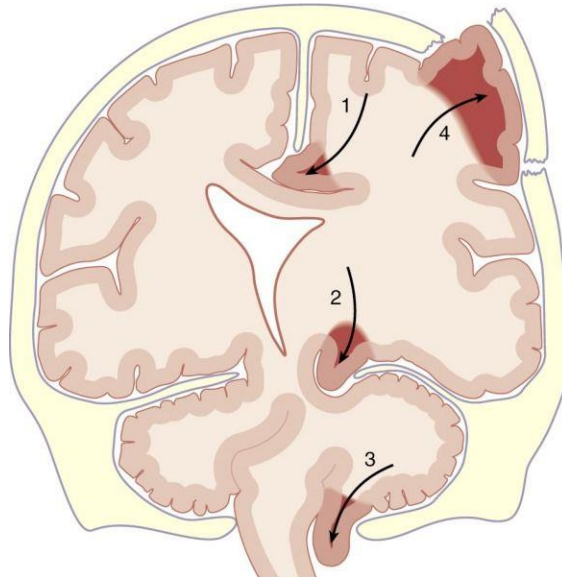
Volume-pressure curve in the intracranial compartment



Bleeding in neurosurgical patients

- **May be massive**
 - Massive bleeding management protocols apply
- Often **does not meet criteria** for massive bleeding, **but is life threatening**
- Relatively **low volumes** of blood in critical areas may lead to **devastating** outcomes

- **To prevent further damage in case of intracranial mass:**
 - Maintain adequate CPP (MAP–ICP)
 - Avoid cerebral herniation



- **Initial compensation:**
 - Translocation of venous blood to extracranial veins
 - Translocation of cerebrospinal fluid to the spinal canal



Hemostatic options in neurosurgery

LIMITED

- Mechanical (unavailable when dealing with microvasculature)
- **Thermal (limited as damage to the adjacent brain tissue and vasculature is undesirable)**
- **Bioactive topical hemostatic agents**
 - Oxidized cellulose polymers, gelatin sponges, fibrin glue, etc.
- **Physiological clot formation**
 - Hemostatic success is highly dependant on the physiological blood clotting capability in the area of lesion

GUIDELINES

Open Access



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

I. Initial resuscitation and prevention of further bleeding

Minimal elapsed time

Recommendation 1 We recommend that severely injured patients be transported directly to an appropriate trauma facility (Grade 1B).

We recommend that the time elapsed between injury and bleeding control be minimised (Grade 1B).

Immediate intervention

Recommendation 6 We recommend that patients with an obvious bleeding source and those presenting with haemorrhagic shock in extremis and a suspected source of bleeding undergo an immediate bleeding control procedure (Grade 1B).

Recommendation 7 We recommend that patients with an unidentified source of bleeding, but without a need for immediate bleeding control, undergo immediate further investigation to determine the bleeding source (Grade 1C).

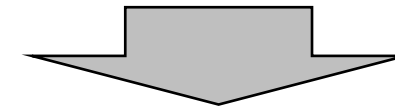
Damage control surgery

Recommendation 19 We recommend damage control surgery in the severely injured patient presenting with haemorrhagic shock, signs of ongoing bleeding, coagulopathy and/or combined abdominal vascular and pancreatic injuries (Grade 1B).

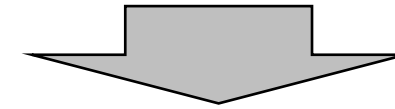
Bleeding source control



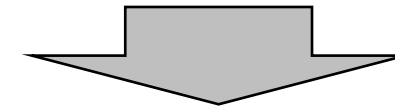
Homeostasis



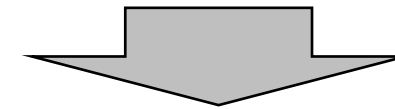
Hyperfibrinolysis



Hypofibrinogenemia



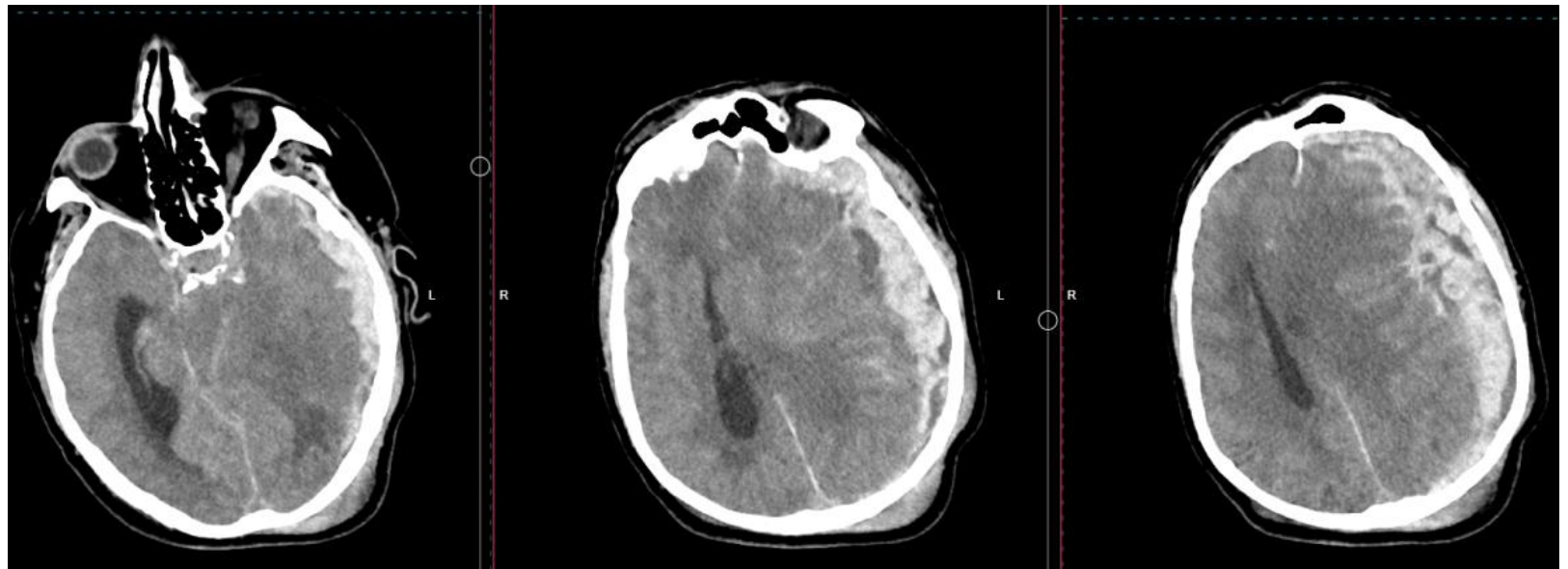
Platelet deficit/dysfunction

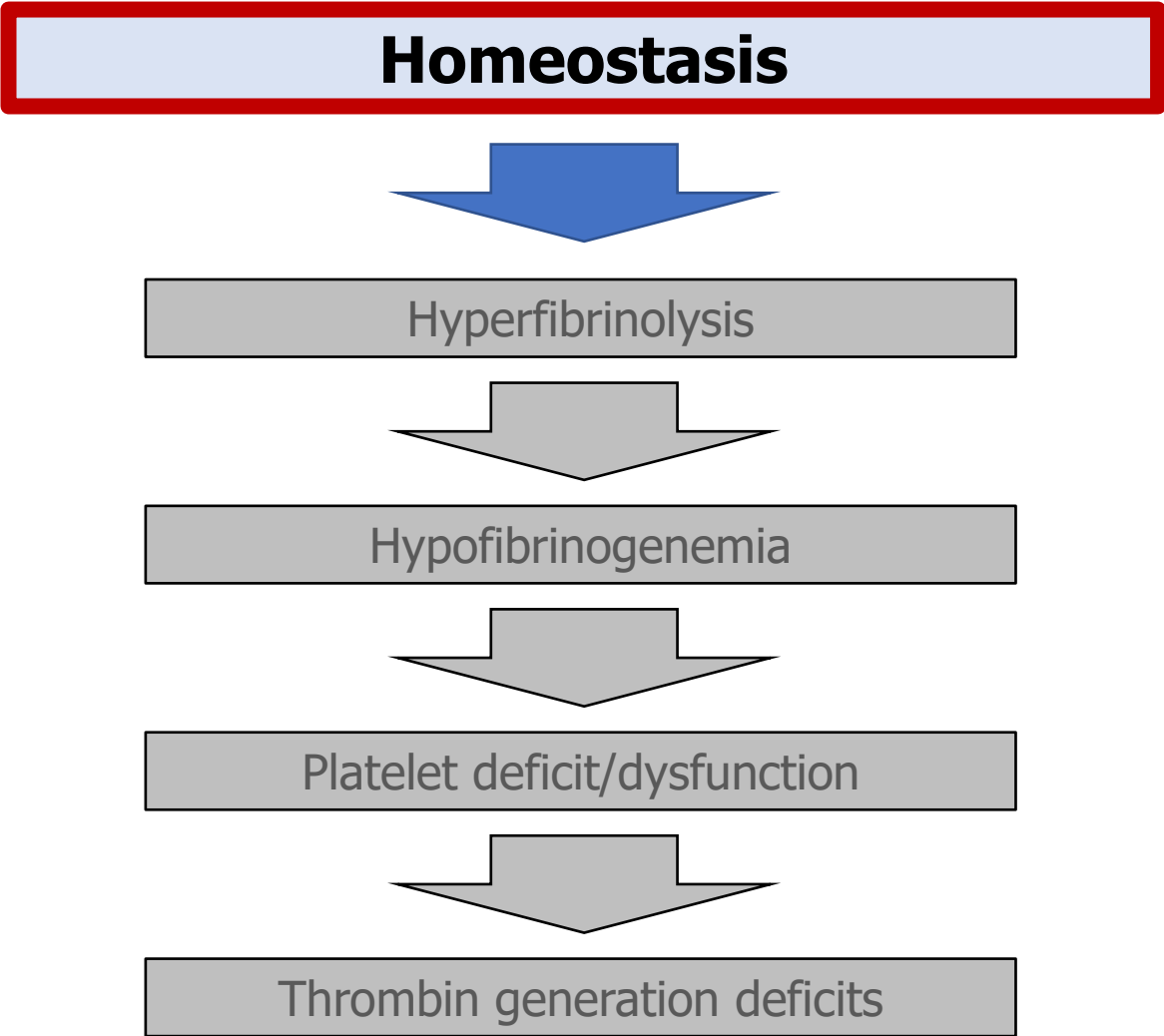
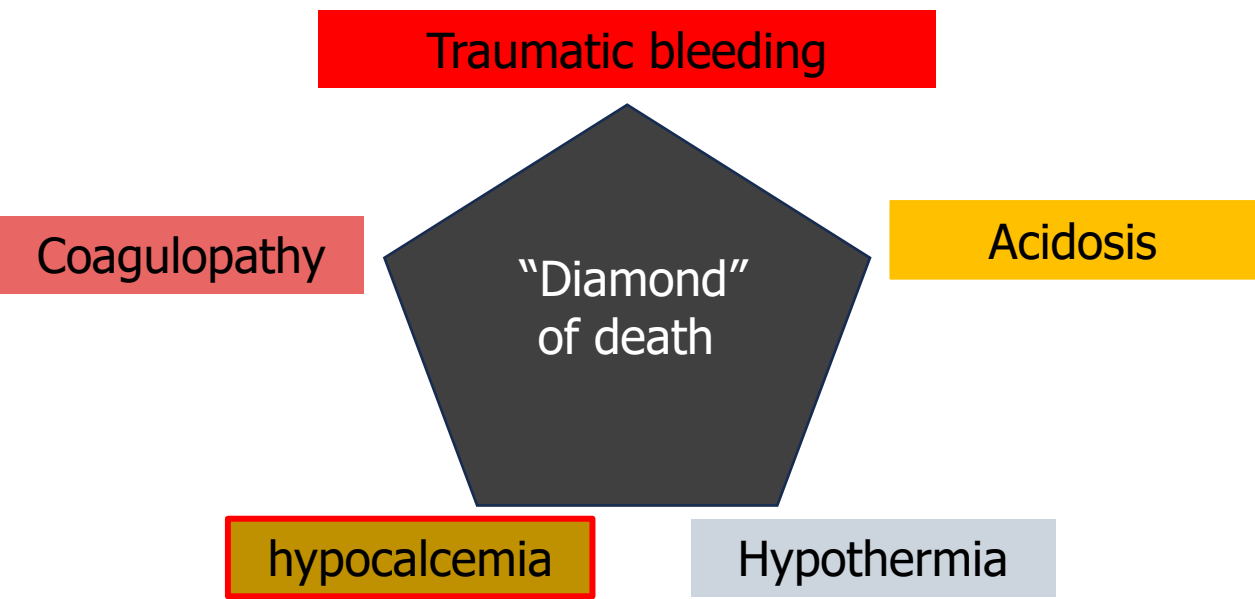


thrombin generation deficits



"Just open the skull before it is too late"





Impaired coagulation is a risk factor for clinical and radiologic deterioration in patients with traumatic brain injury and isolated traumatic subarachnoid hemorrhage

Christian von der Brelie, MD, Insa Schneegans, Leander van den Boom, MD, Ullrich Meier, MD, PhD, Juergen Hedderich, RNDr, and Johannes Lemcke, MD, Berlin, Germany

Research Article Biomed Res Int. 2015;2015:261825.

Coagulation Parameters and Risk of Progressive Hemorrhagic Injury after Traumatic Brain Injury: A Systematic Review and Meta-Analysis

Danfeng Zhang, Shun Gong, Hai Jin, Junyu Wang, Ping Sheng, Wei Zou, Yan Dong, and Lijun Hou

Surgery 2015 Sep;158(3):655-661.

Predicting progressive hemorrhagic injury from isolated traumatic brain injury and coagulation

Lindley E. Folkerson, MD,^{a,b} Duncan Sloan, BS,^{a,b} Bryan A. Cotton, MD, MPH,^{a,b} John B. Holcomb, MD,^{a,b} Jeffrey S. Tomasek, MD,^{a,b} and Charles E. Wade, PhD,^{a,b} Houston, TX



Acute Coagulopathy in Isolated Blunt Traumatic Brain Injury

Arasch Wafaisade · Rolf Lefering · Thorsten Tjardes · Sebastian Wutzler · Christian Simanski · Thomas Paffrath · Philipp Fischer · Bertil Bouillon · Marc Maegele · Trauma Registry of DGU

J Neurotrauma 2016; 33 (14) 1279-1291

Coagulopathy in Traumatic Brain Injury and Its Correlation with Progressive Hemorrhagic Injury: A Systematic Review and Meta-Analysis

Qiang Yuan, Yi-rui Sun, Xing Wu, Jian Yu, Zhi-q Li, Zhuo-ying Du, Xue-hai Wu, Liang-fu Zhou, and Jin Hu ✉

Published Online: 29 Jun 2016 | <https://doi.org/10.1089/neu.2015.4205>

Journal of Clinical Neuroscience 29 (2016) 64–69

Clinical Study

Normalization of coagulopathy is associated with improved outcome after isolated traumatic brain injury

Daniel S. Epstein^{a,b}, Biswadev Mitra^{a,b,c,*}, Peter A. Cameron^{a,b,d}, Mark Fitzgerald^{c,e,f}, Jeffrey V. Rosenfeld^{f,g,h}

TBI, coagulopathy, PHI and mortality

- Prevalence of coagulopathy **approx. 30%**
- Mortality in presence of coagulopathy **approx. 50%**
- Odds of mortality in presence of coagulopathy increases **up to 10-fold**

	Number of patients	Definition of TBI	Definition of coagulopathy	Prevalence of coagulopathy in patients with TBI	Mortality in patients with coagulopathy after TBI	Odds ratio for mortality [unfavourable outcome] in patients with coagulopathy after TBI (95% CI)
Harhangi et al (2008) ^{4*}	5357	Heterogeneous	Heterogeneous	32.7% (10.0–97.5)	51% (25–93)	9.0 (7.3–11.6) [36.3 (18.7–70.5)]
Epstein et al (2014) ^{9†}	7037	Heterogeneous	Heterogeneous	35.2% (7–86.1)	17–86%	Between 3.0 (2.3–3.8) and 9.6 (4.1–25.0)
Zehtabchi et al (2008) ⁹	224	AIS _{head} ≥2 or any intracranial haematoma on CT	aPTT >34 s or INR >1.3	17% (8–30)	..	..
Talving et al (2009) ¹⁰	387	AIS _{head} ≥3 and extracranial AIS <3	aPTT >36 s or INR >1.1 or <100 × 10 ⁹ platelets per L	34%	34.7%	9.6 (4.1–25.0)
Lustenberger et al (2010) ¹¹	278	AIS _{head} ≥3 and extracranial AIS <3	aPTT >36 s or INR >1.4 or <100 × 10 ⁹ platelets per L	45.7%	40.9%	5.0 (1.5–17.0) [12.0 (4.0–29.4)]
Lustenberger et al (2010) ¹²	132	AIS _{head} ≥3 and extracranial AIS <3	aPTT >36 s or INR >1.2 or <100 × 10 ⁹ platelets per L	36.4%	32.5%	3.8 (1.1–13.5)
Wafaisade et al (2010) ¹³	3114	AIS _{head} ≥3 and extracranial AIS <3	PT _R <70% or <100 × 10 ⁹ platelets per L	22.7%	50.4%	3.0 (2.3–3.9)
Chhabra et al (2010) ¹⁴	100	GCS <13	Fibrinogen <2.0 g/L	7%	..	..
Greuters et al (2011) ¹⁵	107	Brain tissue injury on CT and extracranial AIS <3	aPTT >40 s or INR >1.2 or <120 × 10 ⁹ platelets per L	24% (54%‡)	41%	3.8 (1.1–13.5)
Shehata et al (2011) ¹⁶	101	Isolated TBI on admission CT	PT >13 s or INR ≥1.2 or D-dimer-positive or <100 × 10 ⁹ platelets per L	63%	36%	..
Schöchl et al (2011) ¹⁷	88	AIS _{head} ≥3 and extracranial AIS <3	aPTT >35 s or PT _R <70% or fibrinogen <1.5 g/L or <100 × 10 ⁹ platelets per L	15.8%	50%	9.1 (2.2–37.3)
Franschman et al (2012) ¹⁸	226	Isolated TBI on CT and extracranial AIS <3	aPTT >40 s or PT >1.2 s or <120 × 10 ⁹ platelets per L	25% (44%‡)	33%	9.7 (3.1–30.8)
Genet et al (2013) ¹⁹	23	AIS _{head} ≥3 and extracranial AIS <3	aPTT >35 s or INR >1.2	13%	22%	..
Alexiou et al (2013) ²⁰	149	Isolated TBI on CT with exclusion of multisystem trauma	aPTT >40 s or INR >1.2 or <120 × 10 ⁹ platelets per L	14.8% (22.8%‡)	..	..
Joseph et al (2014) ²¹	591	AIS _{head} ≥3 and extracranial AIS <3	aPTT ≥35 s or INR ≥1.5 or ≤100 × 10 ⁹ platelets per L	13.3%	23%	2.6 (1.1–4.8) [4.0 (1.7–10.0)]
Epstein et al (2014) ²²	1718	AIS _{head} ≥3 and extracranial AIS <3	INR ≥1.3	7.7%	45.1%	..
De Oliveira Manoel et al (2015) ²³	48	AIS _{head} ≥3 and extracranial AIS <3	aPTT ≥60 s or INR ≥1.5 or <100 × 10 ⁹ platelets per L§	12.5%	66%	11.5 (3.9–34.2)
Dekker et al (2016) ²⁴	52	AIS _{head} ≥3	aPTT >40 s or INR >1.2 or <120 × 10 ⁹ platelets per L	42%	45.5%	..

Studies reporting the prevalence of coagulopathy in patients with clinical moderate-to-severe and/or CT-confirmed TBI, including mortality rates (and unfavourable outcome if available) for TBI in the presence of coagulopathy. ..=Data not available. TBI=traumatic brain injury. AIS=Abbreviated Injury Scale. GCS=Glasgow Coma Scale. aPTT=activated partial thromboplastin time. INR=international normalised ratio. PT=prothrombin time. PT_R=prothrombin ratio. *Meta-analysis (1966–2007); n=34 studies included. †Meta-analysis (1990–2013); n=22 studies included. ‡After 24 h. §Additional coagulation tests: fibrinogen ≤1.0 g/L, any clotting factor <0.5 (<50% activity), and abnormal viscoelastic test results. ||Based on viscoelastic test results.

Table 1: Studies of the prevalence of coagulopathy after traumatic brain injury

General guidelines in severe TBI

Rossaint et al. *Critical Care* (2023) 27:80
<https://doi.org/10.1186/s13054-023-04327-7>

GUIDELINES

Open Access



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

- Intubate if GCS ≤ 8 to **prevent hypoventilation** and **hypoxemia** (Grade 1B)
- In severe TBI, **maintain MAP ≥ 80 mmHg**, do not tolerate hypotension (Grade 1C)
- **Avoid hypotonic** resuscitation fluids (e.g. Ringer's lactate) (Grade 1C)
- Target **Hb of 70–90 g/L** in bleeding patients (Grade 1C)
 - Data is inconclusive, may be individualized according to multimodal neuromonitoring
- Detect and **treat coagulopathy** using goal-directed strategy (Grade 1B)



Management of acute moderate and severe traumatic brain injury

Author: Venkatakrishna Rajajee, MBBS

Section Editors: Michael J Aminoff, MD, DSc, Maria E Moreira, MD, Alejandro A Rabinstein, MD

Deputy Editor: Janet L Wilterdink, MD

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

Literature review current through: Feb 2020. | This topic last updated: Dec 23, 2019.

Management of coagulopathy –

Coagulation parameters should be measured in the emergency department (ED) in all patients with severe TBI, and *efforts to correct any identified coagulopathy should begin immediately.*

TBI, coagulopathy and mortality

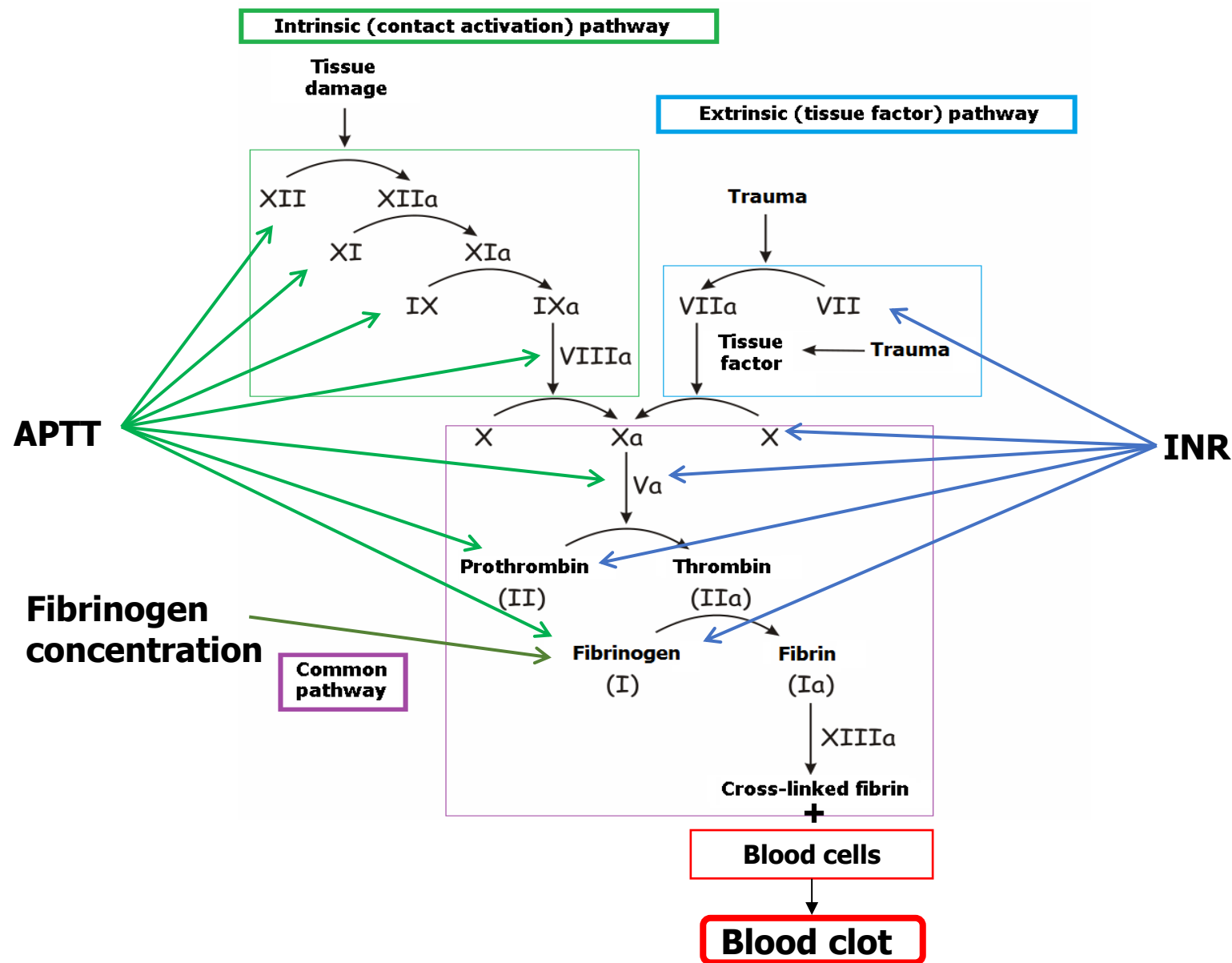
	Number of patients	Definition of TBI	Definition of coagulopathy	Prevalence of coagulopathy in patients with TBI	Mortality in patients with coagulopathy after TBI	Odds ratio for mortality [unfavourable outcome] in patients with coagulopathy after TBI (95% CI)
Harhangi et al (2008) ^{4*}	5357	Heterogeneous	Heterogeneous	32.7% (10.0–97.5)	51% (25–93)	9.0 (7.3–11.6) [36.3 (18.7–70.5)]
Epstein et al (2014) ^{8†}	Definitions of coagulopathy across studies... INR > 1.1, > 1.2, > 1.3, > 1.4, > 1.5...? PT < 70...? APTT > 34, > 35, > 36, > 38, > 40, > 60, 1.5x ...? PLT < 120, < 100, < 80, < 50...? Fibr. < 2, < 1.5...? Definitions of TBI across studies... Heterogeneous... <u><i>A call for consensus among researchers!</i></u>					Between 3.0 (2.3–3.8) and 9.6 (4.1–25.0)
Zehtabchi et al (2008) ⁹						..
Talving et al (2009) ¹⁰						9.6 (4.1–25.0)
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Genet et al (2013) ¹⁹						..
Alexiou et al (2013) ²⁰						..
Joseph et al (2014) ²¹						2.6 (1.1–4.8) [4.0 (1.7–10.0)]
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De Oliveira Manoel et al (2015) ²³	48	AIS _{head} ≥3 and extracra	Association IS NOT Causation			11.5 (3.9–34.2)
Dekker et al (2016) ²⁴	52	AIS _{head} ≥3				..

Studies reporting the prevalence of coagulopathy in patients with cl
of coagulopathy. ..=Data not available. TBI=traumatic brain injury. A
PT=prothrombin time. PT_s=prothrombin ratio. * Meta-analysis (196
≤1.0 g/L, any clotting factor <0.5 (<50% activity), and abnormal viscoelastic test results. ||Based on viscoelastic test results.

es (and unfavourable outcome if available) for TBI in the presence
artial thromboplastin time. INR=international normalised ratio.
s included. ‡After 24 h. §Additional coagulation tests: fibrinogen

Table 1: Studies of the prevalence of coagulopathy after traumatic brain injury

Classic coagulation cascade and coagulation tests



Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence?

T. Haas^{1*}, D. Fries², K. A. Tanaka³, L. Asmis⁴, N. S. Curry⁵ and H. Schöchl^{6,7}

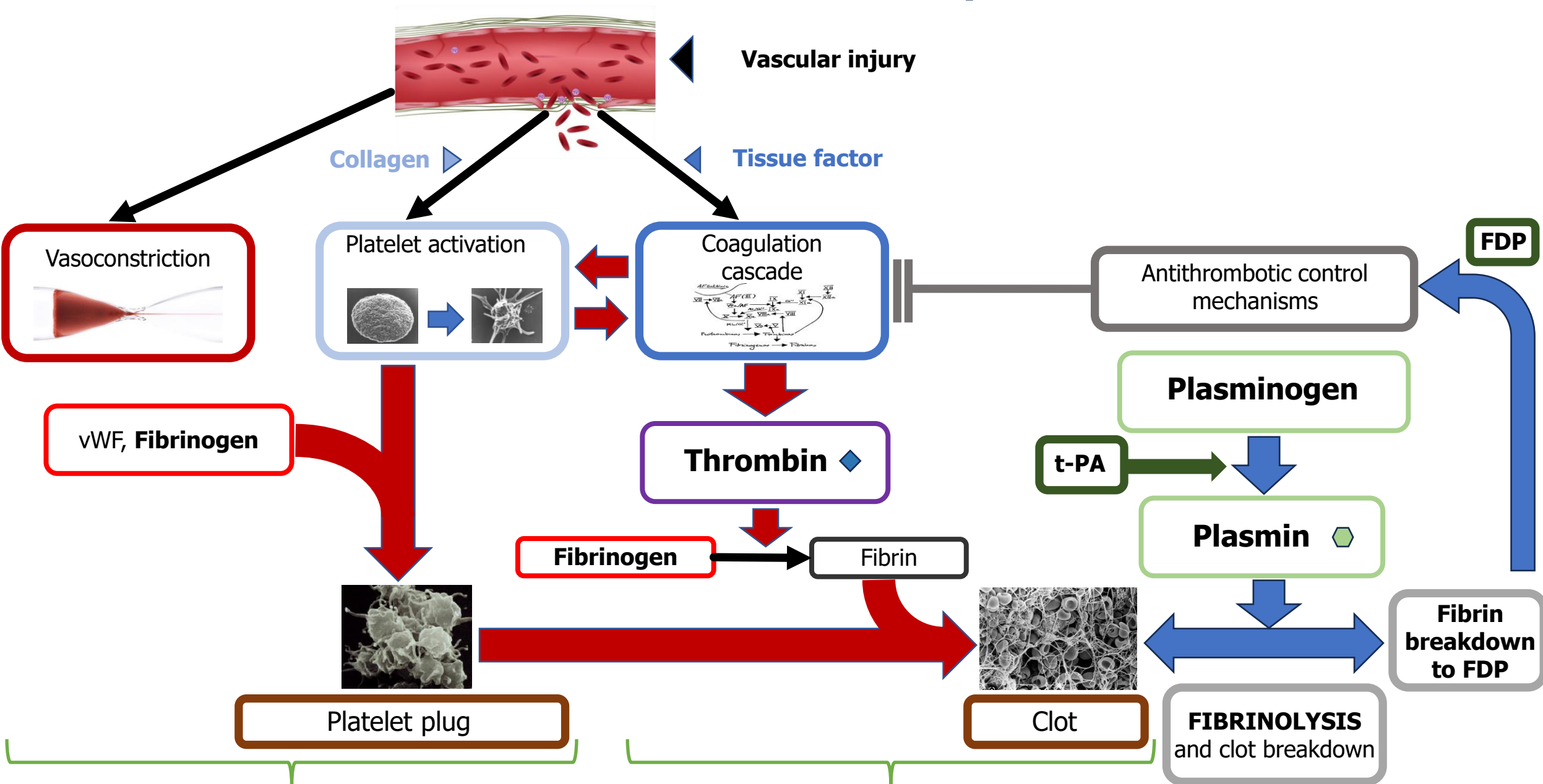
Editor's key points

- The authors review the evidence for the continued use of standard laboratory tests of coagulation.
- They conclude that there is minimal evidence for the use of standard laboratory tests in guiding the management of perioperative bleeding.

Summary. Standard laboratory coagulation tests (SLTs) such as prothrombin time/international normalized ratio or partial thromboplastin time are frequently used to assess coagulopathy and to guide haemostatic interventions. However, this has been challenged by numerous reports, including the current European guidelines for perioperative bleeding management, which question the utility and reliability of SLTs in this setting. Furthermore, the arbitrary definition of coagulopathy (i.e. SLTs are prolonged by more than 1.5-fold) has been questioned. The present study aims to review the evidence for the usefulness of SLTs to assess coagulopathy and to guide bleeding management in the perioperative and massive bleeding setting. Medline was searched for investigations using results of SLTs as a means to determine coagulopathy or to guide bleeding management, and the outcomes (i.e. blood loss, transfusion requirements, mortality) were reported. A total of 11 guidelines for management of massive bleeding or perioperative bleeding and 64 studies investigating the usefulness of SLTs in this setting were identified and were included for final data synthesis. Referenced evidence for the usefulness of SLTs was found in only three prospective trials, investigating a total of 108 patients (whereby microvascular bleeding was a rare finding). Furthermore, no data from randomized controlled trials support the use of SLTs. In contrast, numerous investigations have challenged the reliability of SLTs to assess coagulopathy or guide bleeding management. There is actually no sound evidence from well-designed studies that confirm the usefulness of SLTs for diagnosis of coagulopathy or to guide haemostatic therapy.

Keywords: bleeding; blood; coagulation; coagulopathy; transfusion

Hemostasis and fibrinolysis

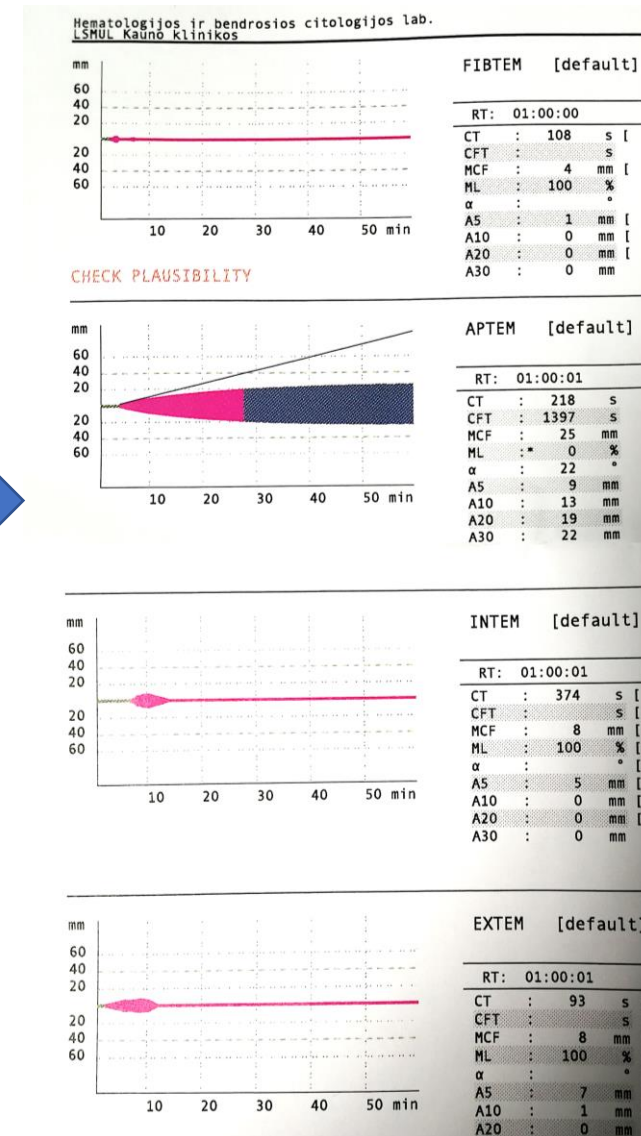
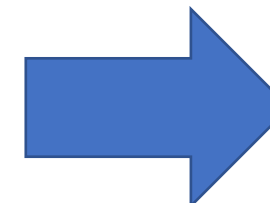
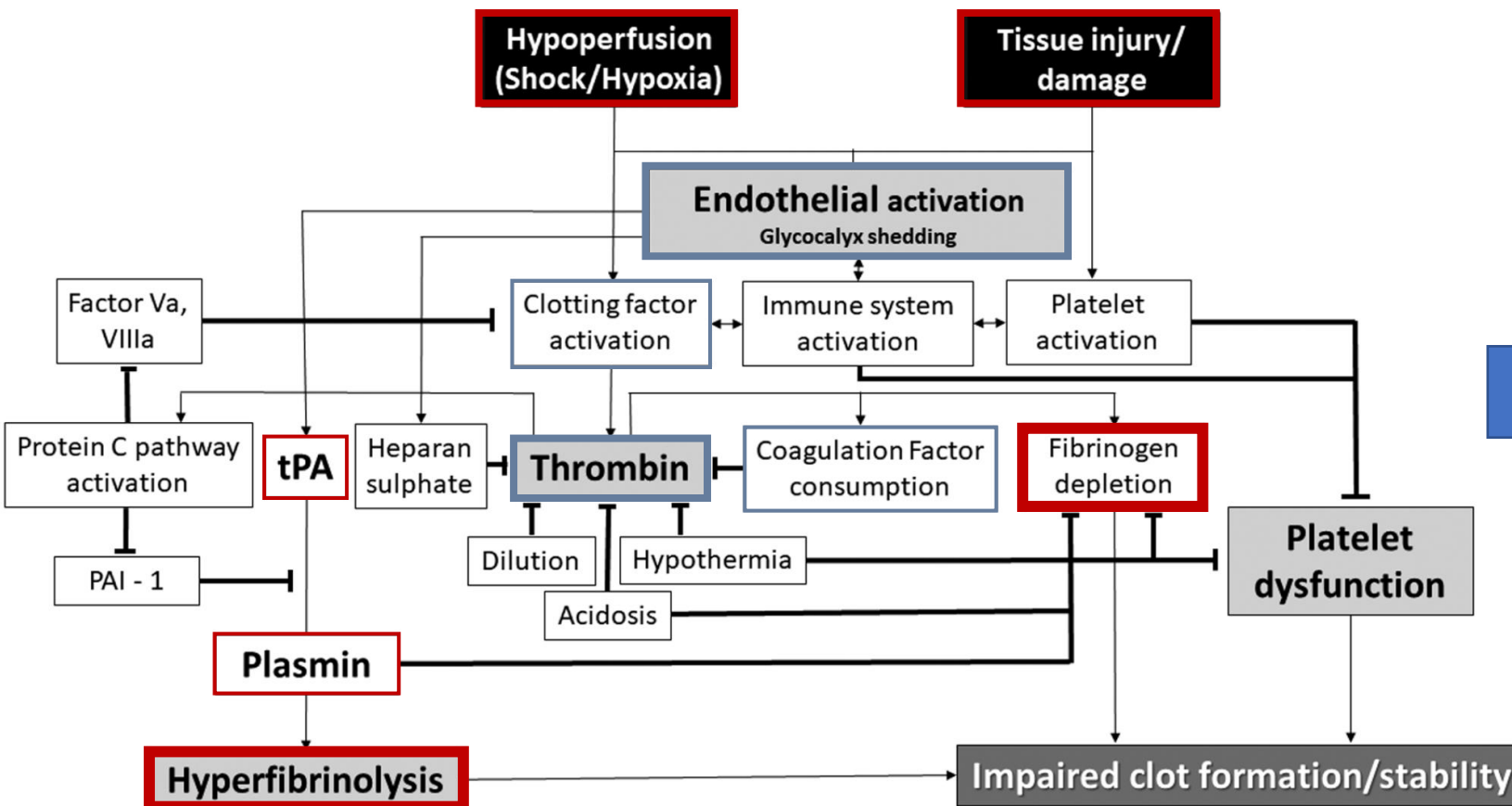


PRIMARY HEMOSTASIS

SECONDARY HEMOSTASIS

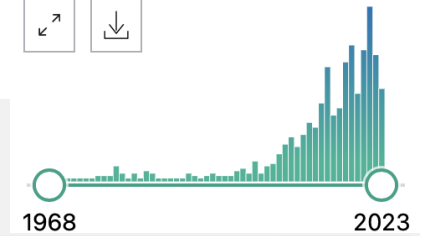
adapted according to: <https://healthjade.net/hemostasis/>

Trauma induced coagulopathy – pathophysiology



Traumatic brain injury induced coagulopathy

RESULTS BY YEAR



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Coagulopathy traumatic brain injury

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Page 1 of 59

Coagulopathy induced by traumatic brain injury: systemic manifestation of a localized injury.

Cite Zhang J, Zhang F, Dong JF. Blood. 2018 May 3;131(18):2001-2006. doi: 10.1182/blood-2017-11-784108. Epub 2018 Mar 5. PMID: 29507078 [Free PMC article](#). [Review](#).

Share **Traumatic brain injury (TBI)-induced coagulopathy** is a common and well-recognized risk for poor clinical outcomes, but its pathogenesis remains poorly understood, and treatment options are limited and ineffective. We discuss the recent progress and know...

Traumatic brain injury-associated coagulopathy.

Cite Zhang J, Jiang R, Liu L, Watkins T, Zhang F, Dong JF. J Neurotrauma. 2012 Nov 20;29(17):2597-605. doi: 10.1089/neu.2012.2348. Epub 2012 Oct 31. PMID: 23020190 [Free PMC article](#). [Review](#).

Share **Traumatic injury** is a common cause of **coagulopathy**, primarily due to **blood loss** and **hemodilution** secondary to fluid resuscitation. ...The incidence of **coagulopathy** is significantly higher in patients with **traumatic brain injury** ...

Viscoelastic Testing and Coagulopathy of Traumatic Brain Injury.

Cite Bradbury JL, Thomas SG, Sorg NR, Mjaess N, Berquist MR, Brenner TJ, Langford JH, Marsee MK, Moody AN, Bunch CM, Sing SR, Al-Fadhli MD, Salamah Q, Saleh T, Patel NB, Shaikh KA, Smith SM, ...

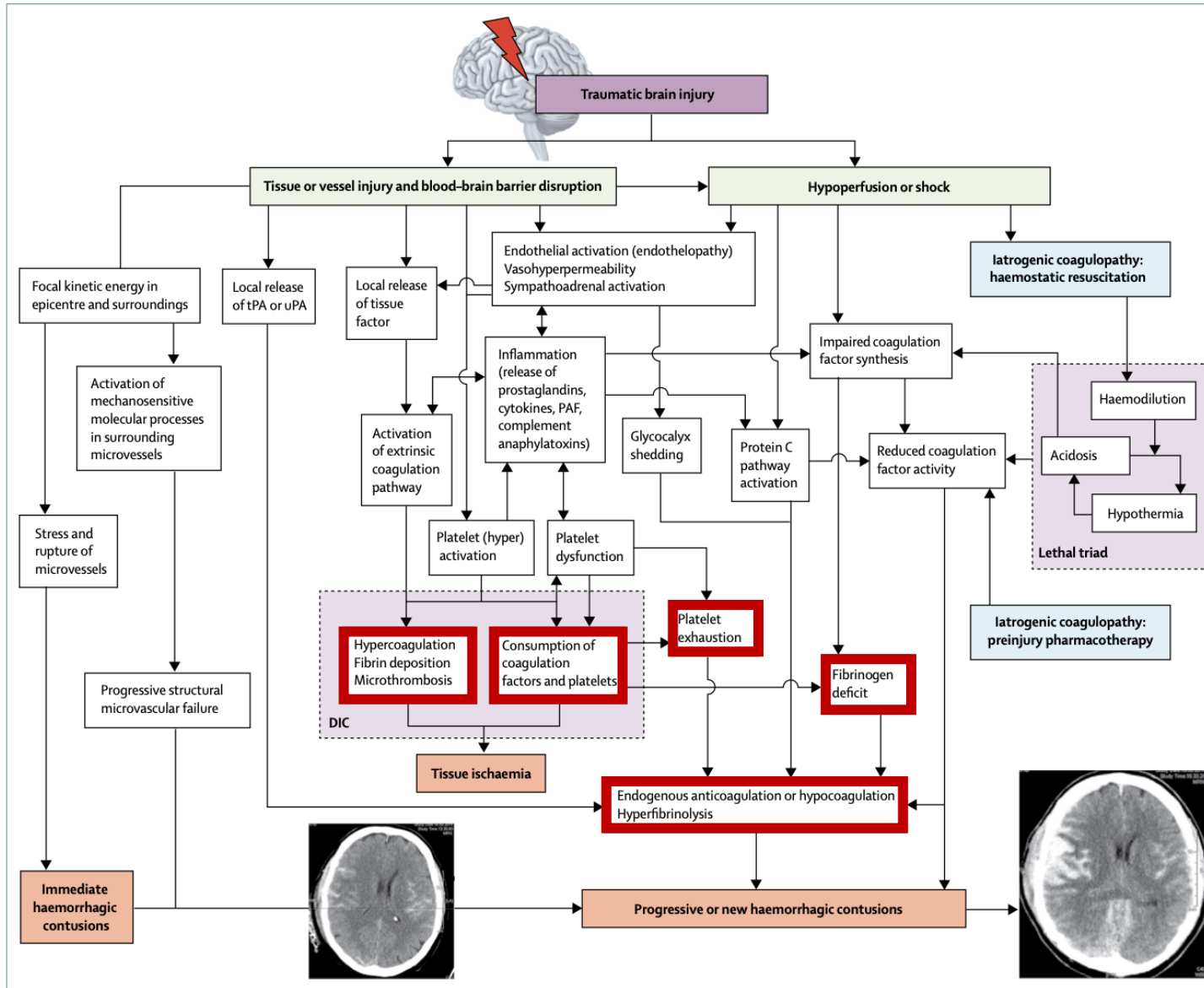


Figure 1: Current understanding of the mechanisms underlying coagulopathy and haemorrhagic contusions after traumatic brain injury

Coagulopathy in TBI – are we sure it is unique?

Neurocrit Care (2023) 38:429–438
<https://doi.org/10.1007/s12028-022-01647-4>

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EXTRACRANIAL COMPLICATIONS AFTER TRAUMATIC BRAIN INJURY

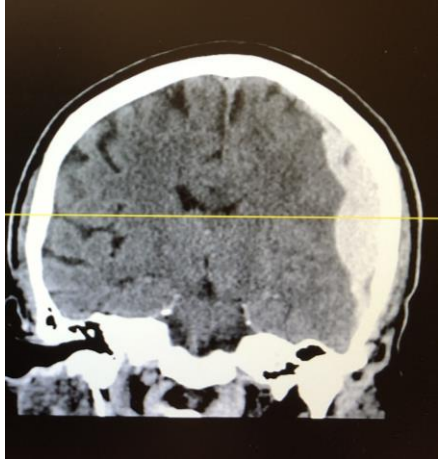
Coagulopathy in Isolated Traumatic Brain Injury: Myth or Reality



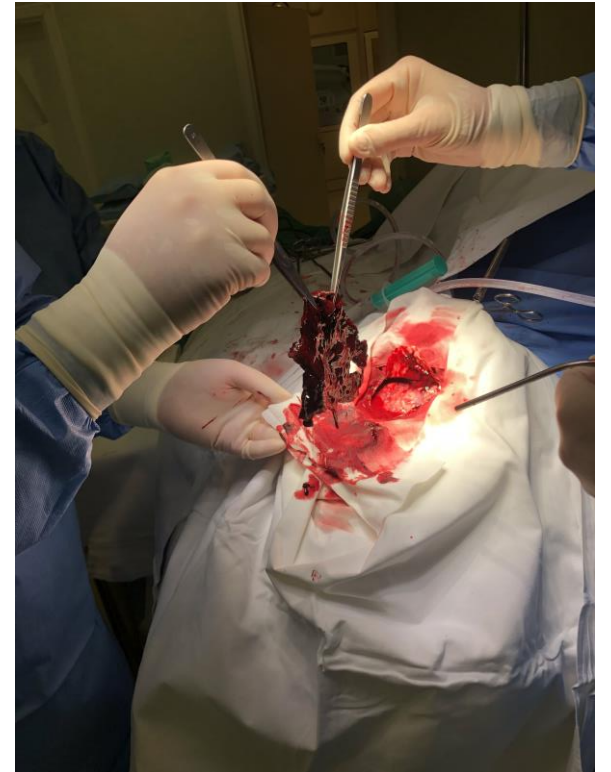
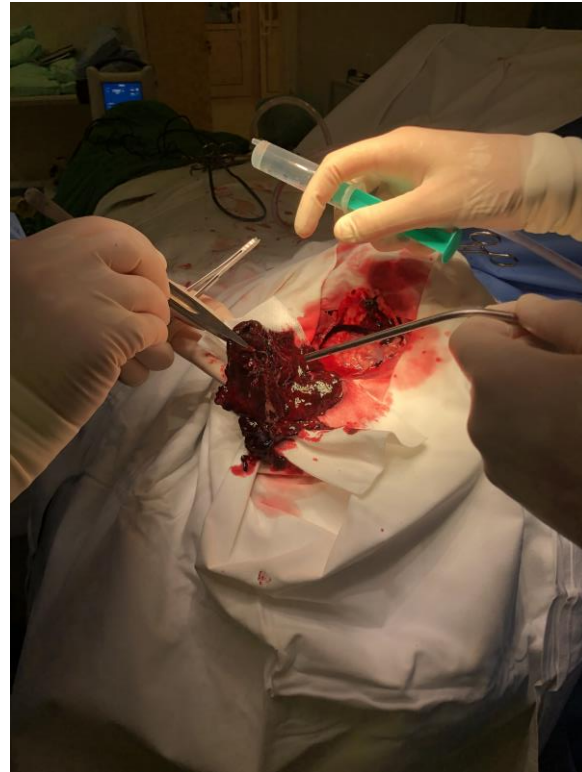
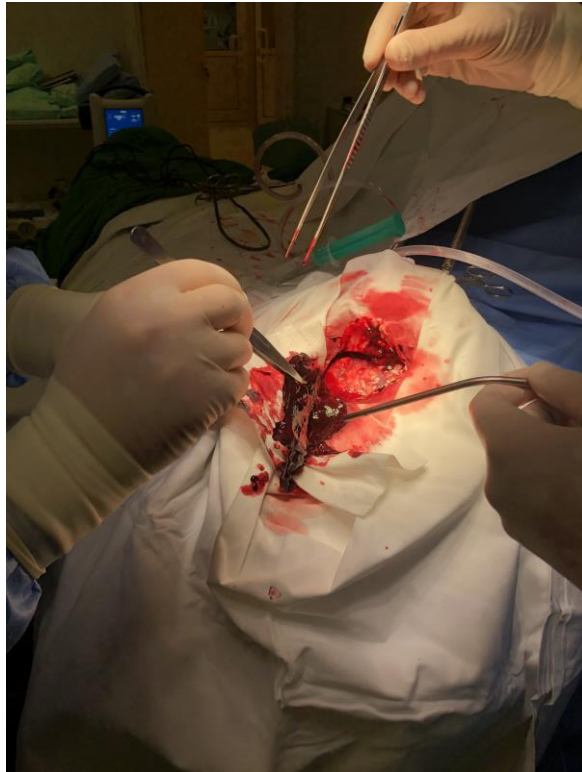
Rohan Mathur*  and Jose I. Suarez

“Most likely, it is not high prevalence of abnormal coagulation, but the *approach to laboratory testing* and test results *accompanied by the fear* of failed intraoperative surgical hemostasis, postoperative bleeding, and high reliance on physiological clot formation, lead to many challenges and difficult decision-making in coagulation management of a neurosurgical patient for the anesthesiologist.”

Rimaitis M, 9th International Baltic Congress of Anaesthesiology, Intensive care and Pain Management, 2018



Consumptive nature of the coagulopathy?...



How do we assess coagulation status and the risk of bleeding?

Eur J Anaesthesiol 2017; **34**:332–395

GUIDELINES

Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology

Kozek-Langenecker *et al.*

1.1. Evaluation of coagulation status

Before surgery or invasive procedures, we recommend the use of a structured patient interview or standardised questionnaire which considers clinical and family bleeding history and detailed information on the patient's medication. **1C**

We recommend the use of standardised questionnaires on bleeding and drug history as preferable to the routine use of conventional coagulation screening tests such as activated partial thromboplastin time (aPTT), international normalised ratio (INR) and platelet count in elective surgery. **1C**

Preoperative use of SLTs is not recommended by current ESA guidelines. Furthermore, in patients without a previous history of bleeding or bleeding disorders, SLTs are not generally recommended.²⁰ In the neurosurgical setting, the value of preoperative PT testing is limited in patients awaiting elective procedures in whom a normal bleeding history can be established.²¹

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Bleeding and Coagulopathies in Critical Care

Beverley J. Hunt, M.D.

THE DEFINITION OF COAGULOPATHY IS “A CONDITION IN WHICH THE blood’s ability to clot is impaired.” However, for some clinicians, the term also covers thrombotic states, and because of the complexity of the hemostatic pathways, the two conditions can exist simultaneously. Some practitioners would consider that mildly abnormal results on coagulation screening without bleeding can also indicate a coagulopathy. This review is confined to the original definition of coagulopathy as given above. Such states are common in patients in the intensive care unit (ICU) and require a clinicopathological approach to ensure that the correct diagnosis is made and the appropriate treatment administered. The lack of evidence for managing coagulopathies in critical care is striking. This review will highlight selected areas in which there is high-quality evidence and at the same time point out areas for which there is poor evidence. In the latter case, there is little consensus on management.

From King’s College London and Guy’s and St. Thomas’ Trust — both in London. Address reprint requests to Dr. Hunt at the Thrombosis and Haemophilia Centre, St Thomas’ Hospital, Westminster Bridge Rd., London SE1 7EH, United Kingdom, or at beverley.hunt@gstt.nhs.uk.

N Engl J Med 2014;370:847-59.

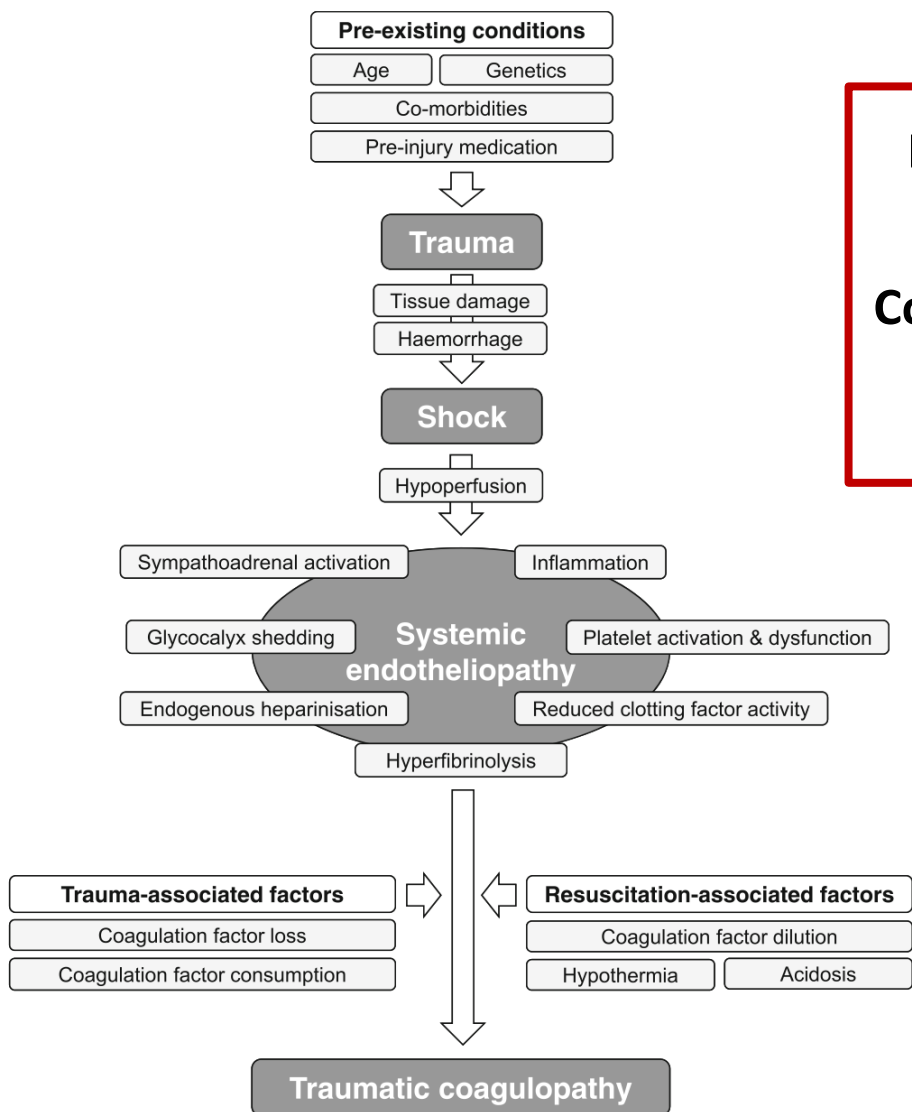
DOI: 10.1056/NEJMra1208626

Copyright © 2014 Massachusetts Medical Society.

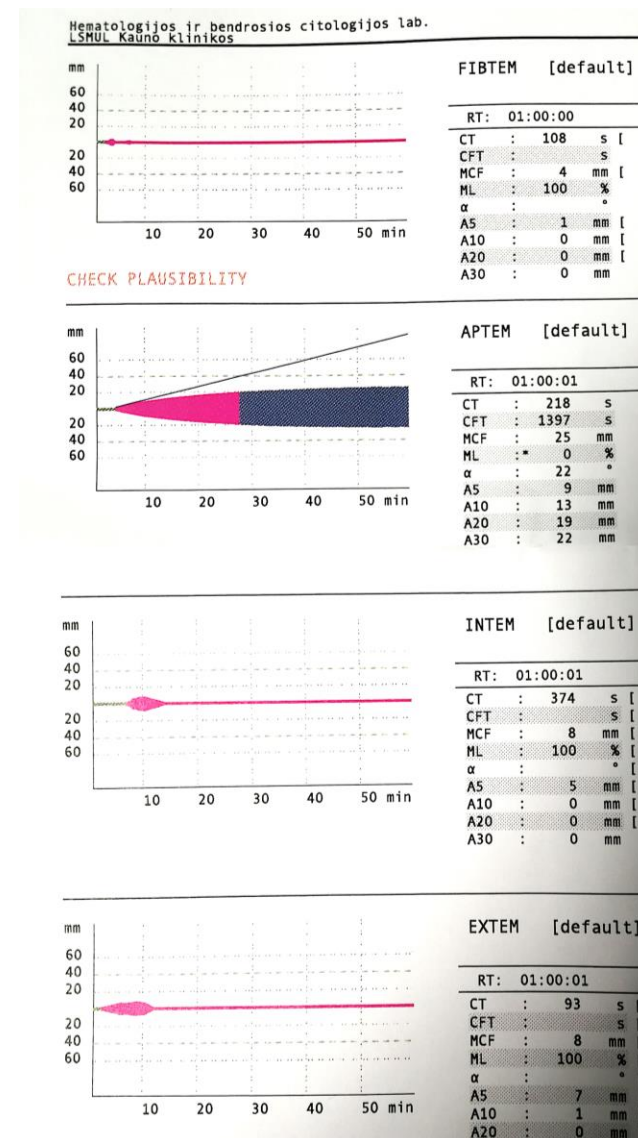
“Treating laboratory numbers without correlation with the clinical status is fundamentally contrary to good medical practice and transfusion medicine is no exception”

Miller RD, editor. Miller's Anesthesia. 8th ed. Philadelphia: Churchill Livingstone; 2015.

Severe traumatic coagulopathy



Loss of substrates and factors
Dilution
Consumption + hyperfibrinolysis
Dysfunction (acidosis, hypothermia)



Do we still need laboratory testing?

- Most of patients with severe TBI are **unconscious**
 - No reliable history
- **Lack of time** for detailed physical examination and instrumental investigations
- Ongoing changes in **patient population**:

Young and high energy trauma



Elderly and low energy trauma

- Poor functional reserves and rehabilitation capabilities
- Comorbidities (hepatic, renal, hematologic, oncology, etc.)
- Polypharmacy (anticoagulants, antiplatelets, etc.)
- Alcohol, drug abuse
- Alimentary deficits



What are the recommendations?

Rossaint et al. *Critical Care* (2023) 27:80
<https://doi.org/10.1186/s13054-023-04327-7>

GUIDELINES

Open Access

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



Lancet 2019; 394: 1713–23

Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial

The CRASH-3 trial collaborators*

Give:

TXA < 3 h from impact **(1A)**

Treat:

PLT < 100 **(2C)**

FIB < 1,5 (2?) **(1C)**

APTT > x 1,5 **(1C)**

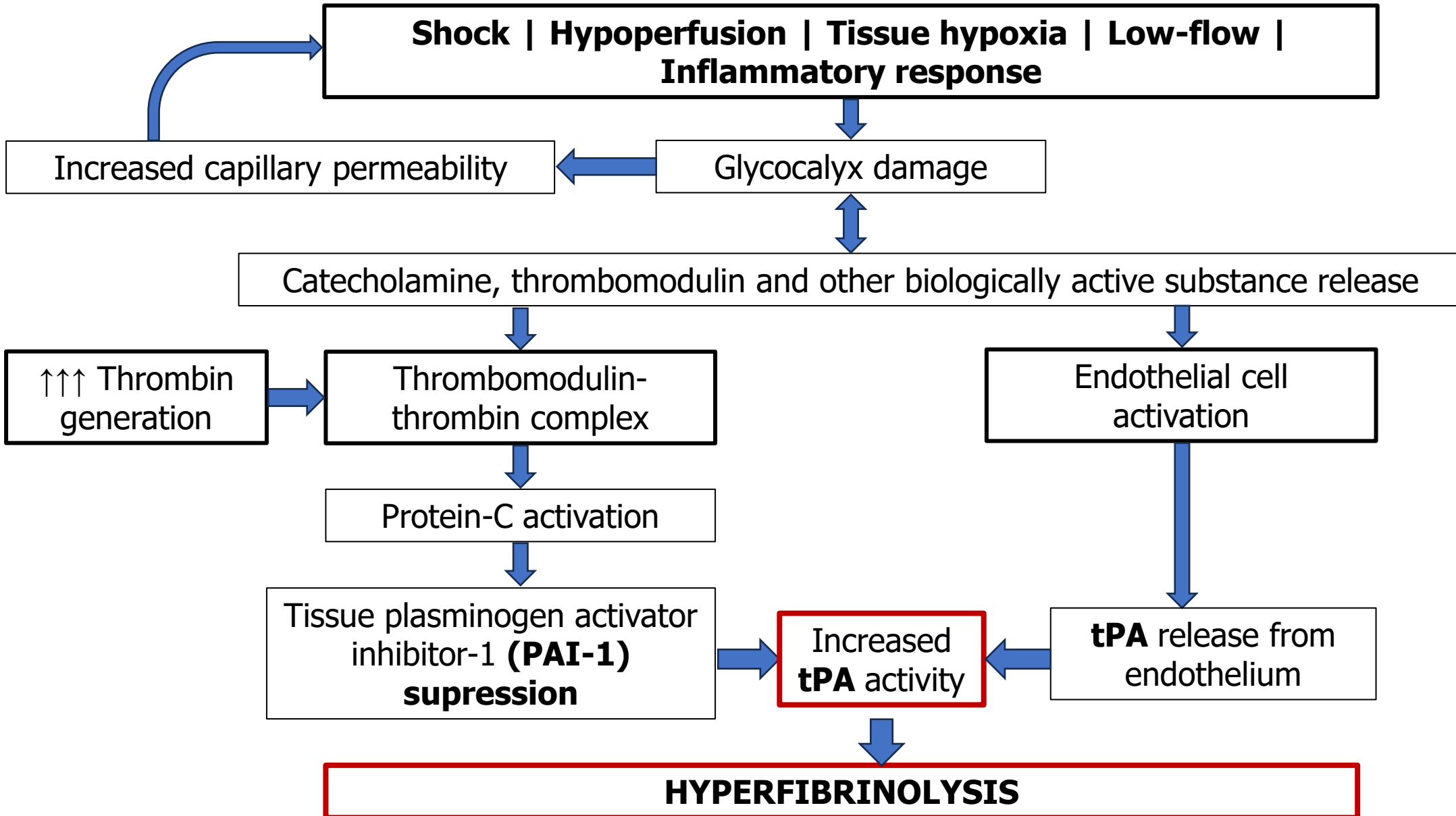
INR > 1,5 **(1C)**

Reverse:

Anticoagulants

Antiplatelets

Trauma induced endotheliopathy and hyperfibrinolysis



“From an evolutionary point of view,
hyperfibrinolysis counteracts shock-related

microvascular stasis,
microthrombosis,
tissue hypoperfusion,
and hypoxemia

to maintain blood flow,

even **at the cost of an increased bleeding rate** due
to the dissolution of already established clots”

Hiperfibrinolysis

GUIDELINES

Open Access



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

Rolf Rossaint^{1*}, Arash Afshari², Bertil Bouillon³, Vladimir Cerny^{4,5}, Diana Cimpoesu⁶, Nicola Curry^{7,8}, Jacques Duranteau⁹, Daniela Filipescu¹⁰, Oliver Grottke¹, Lars Grønlykke¹¹, Anatole Harrois⁹, Beverley J. Hunt¹², Alexander Kaserer¹³, Radko Komadina¹⁴, Mikkel Herold Madsen², Marc Maegele¹⁵, Lidia Mora¹⁶, Louis Riddez¹⁷, Carolina S. Romero¹⁸, Charles-Marc Samama¹⁹, Jean-Louis Vincent²⁰, Sebastian Wiberg¹¹ and Donat R. Spahn¹³

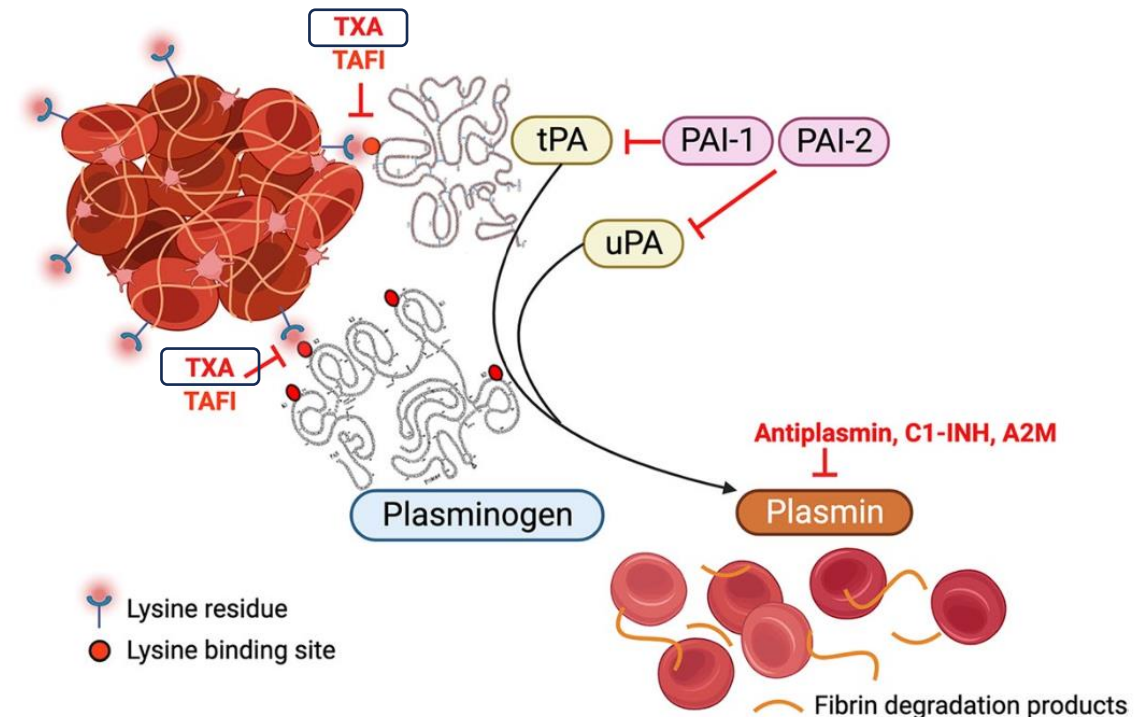
V. Initial management of bleeding and coagulopathy

Antifibrinolytic agents

Recommendation 23 We recommend that tranexamic acid (TXA) be administered to the trauma patient who is bleeding or at risk of significant bleeding as soon as possible, if feasible en route to the hospital, and within 3 h after injury 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 the administration of TXA not await results from a viscoelastic assessment (Grade 1B).

Mechanism of action of tranexamic acid



TXA – tranexamic acid, TAFI – thrombin activated fibrinolysis inhibitor (endogenous), tPA – tissue plasminogen activator, PAI – plasminogen activator inhibitor

Antifibrinolytic ≠ Antihemorrhagic effect

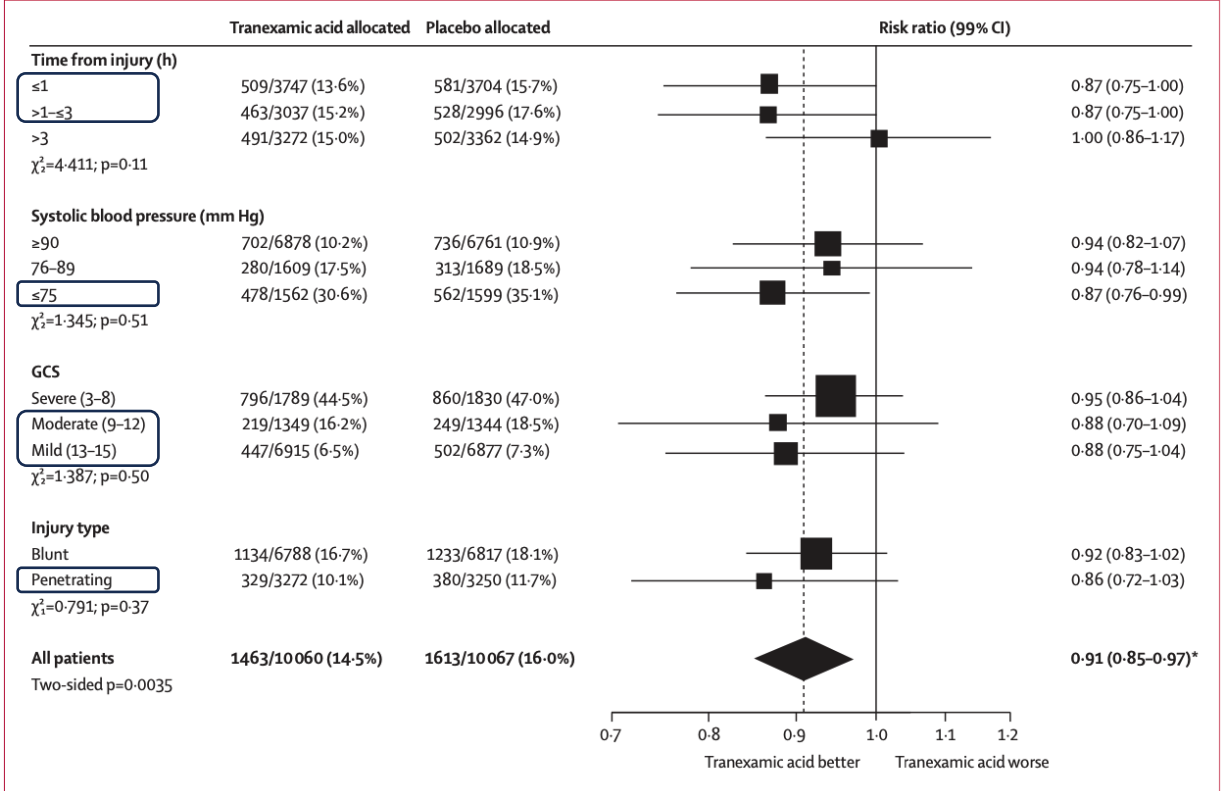
Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

CRASH-2 trial collaborators*



274 hospitals, 40 countries worldwide

- Multicenter, double-blind RCT
- Bleeding (ABP < 90 mmHg and/or HR > 110 bpm) or considered high bleeding risk patient
- Primary endpoint – 4 week post-trauma mortality
- From 2005 to 2010 – 20211 hospitalized patients **within 8 h post-trauma**: TXA vs. placebo (1 g bolus, followed by 1 g in 8 h)



Adult trauma patients with significant haemorrhage (systolic blood pressure <90 mm Hg or heart rate >110 beats per min, or both), or who were considered to be at risk of significant haemorrhage, and who were within 8 h of injury, were eligible for the trial. Patients were included if the responsible doctor was substantially uncertain about whether or not to treat with tranexamic acid (ie, entry was governed by the uncertainty principle).^{*} Patients for whom the responsible doctor considered that there was a clear indication for tranexamic acid were not randomly assigned. Similarly, patients for whom there was considered to be a clear contraindication to tranexamic acid treatment were not randomly assigned. However, when the responsible doctor was substantially uncertain as to whether or not to treat with this agent, these patients were eligible for randomisation.

CRASH-2 collaborators:

Albania (115) Argentina (51) Australia (17) Bangladesh (12) Belgium (51) Cameroon (124) Canada (2) China (51) **Colombia (2940)** **Cuba (575)** Czech Republic (17) **Ecuador (1198)** **Egypt (2234)** El Salvador (84) **Georgia (1783)** Ghana (136) **India (4768)** **Indonesia (706)** Iran (134) **Iraq (392)** Italy (57) Jamaica (11) Japan (9) Kenya (31) **Malaysia (216)** **Mexico (479)** **Nigeria (2053)** **Peru (452)** Saudi Arabia (70) Serbia (1) Singapore (2) Slovakia (38) South Africa (76) Spain (23) Sri Lanka (103) Tanzania (64) **Thailand (903)** Tunisia (36) UK (135) Zambia (62)

	Tranexamic acid (n=10 060)	Placebo (n=10 067)	RR (95% CI)	p value (two-sided)
Any cause of death	1463 (14.5%)	1613 (16.0%)	0.91 (0.85-0.97)	0.0035
Bleeding	489 (4.9%)	574 (5.7%)	0.85 (0.76-0.96)	0.0077
Vascular occlusion*	33 (0.3%)	48 (0.5%)	0.69 (0.44-1.07)	0.096
Multiorgan failure	209 (2.1%)	233 (2.3%)	0.90 (0.75-1.08)	0.25
Head injury	603 (6.0%)	621 (6.2%)	0.97 (0.87-1.08)	0.60
Other causes	129 (1.3%)	137 (1.4%)	0.94 (0.74-1.20)	0.63

Data are number (%), unless otherwise indicated. RR=relative risk. *Includes myocardial infarction, stroke, and pulmonary embolism.

Table 2: Death by cause

Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial

The CRASH-3 trial collaborators*



- 175 hospitals, 29 countries
- Multicenter, double-blind RCT
 - TBI, hospitalized within 3 h, GCS <13 or any intracranial bleed on head CT
 - Primary endpoint – mortality from TBI within 4 weeks post trauma
 - From 2012 to 2019 – 12737 hospitalized patients: TXA vs. placebo (1 g bolus, followed by 1 g in 8 h)

- Final analysis: 9200 patients
- Mortality from TBI: TXA 855 (18,5%) vs. 892 (19,8%) **NS**
- Excluded patients with initial GCS 3 or ono-reactive pupils: Mortality from TBI: TXA 485 (12,5%) vs. 525 (14%) **NS**
 - Only patients with GCS > 8 included: Mortality from TBI: TXA 166 (5,8%) vs. 207 (7,5%) **p<0,05**

In 2016 decision to include only patients who were admitted within 3 h post trauma i.e. 3500 entries excluded

	Tranexamic acid	Placebo	Risk ratio (95% CI)
All	855/4613 (18·5%)	892/4514 (19·8%)	0·94 (0·86–1·02)
Excluding patients with GCS score of 3 or bilateral unreactive pupils*	485/3880 (12·5%)	525/3757 (14·0%)	0·89 (0·80–1·00)

GCS=Glasgow Coma Scale. *Prespecified sensitivity analysis.

Table 2: Effect of tranexamic acid on head injury-related death in patients randomly assigned within 3 h of injury

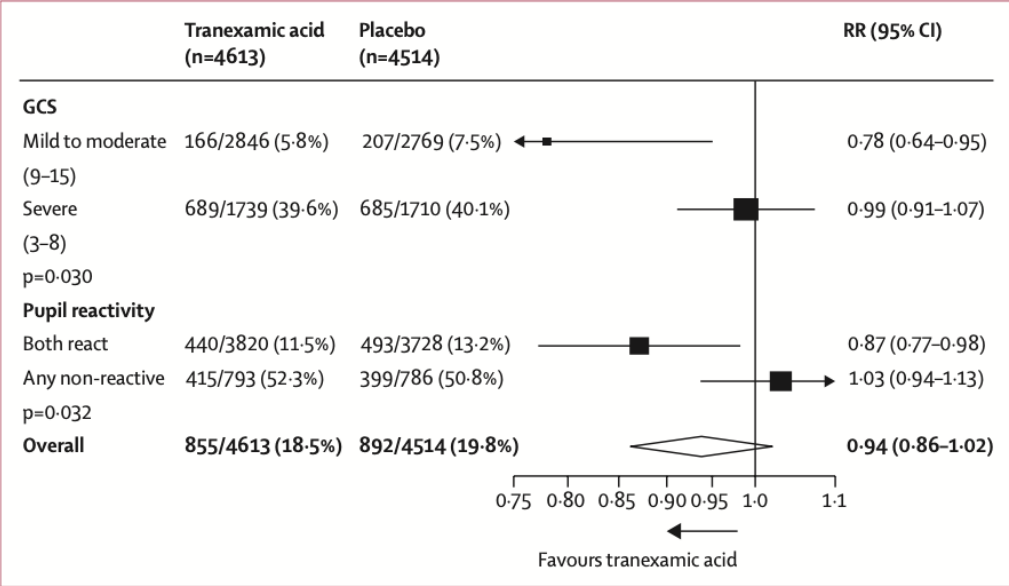


Figure 3: Effect of tranexamic acid on head injury-related death stratified by baseline severity in patients randomised within 3 h of injury

CRASH-3 collaborators: Pakistan (4567) UK (3143) Malaysia (1567) Georgia (771) Spain (425) Nigeria (409) Colombia (335) Nepal (255) Albania (214) Japan (165) UAE (126) Myanmar (121) Cameroon (116) Afghanistan (87) Mexico (79) Italy (72) Iraq (55) Cambodia (45) Zambia (44) Romania (35) El Salvador (28) Egypt (20) Slovenia (15) Ireland (12) Papua New Guinea (10) Canada (7) Jamaica (7) Indonesia (6) Kenya (1)

ORIGINAL ARTICLE

Prehospital Tranexamic Acid for Severe Trauma

RESULTS

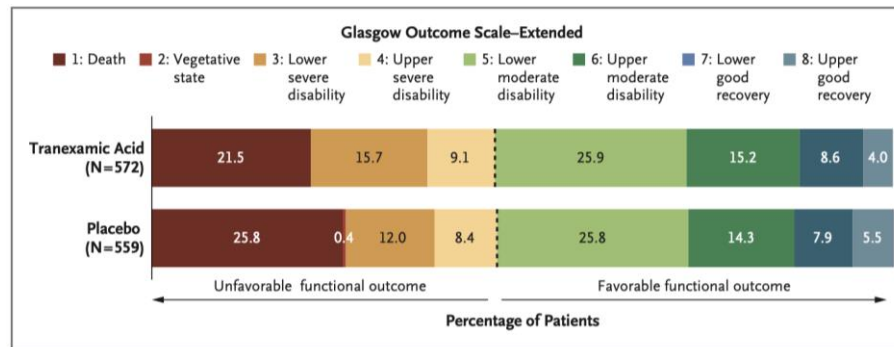
A total of 1310 patients were recruited by 15 emergency medical services in Australia, New Zealand, and Germany. Of these patients, 661 were assigned to receive tranexamic acid, and 646 were assigned to receive placebo; the trial-group assignment was unknown for 3 patients. Survival with a favorable functional outcome at 6 months occurred in 307 of 572 patients (53.7%) in the tranexamic acid group and in 299 of 559 (53.5%) in the placebo group (risk ratio, 1.00; 95% confidence interval [CI], 0.90 to 1.12; $P=0.95$). At 28 days after injury, 113 of 653 patients (17.3%) in the tranexamic acid group and 139 of 637 (21.8%) in the placebo group had died (risk ratio, 0.79; 95% CI, 0.63 to 0.99). By 6 months, 123 of 648 patients (19.0%) in the tranexamic acid group and 144 of 629 (22.9%) in the placebo group had died (risk ratio, 0.83; 95% CI, 0.67 to 1.03). The number of serious adverse events, including vascular occlusive events, did not differ meaningfully between the groups.

CONCLUSIONS

Among adults with major trauma and suspected trauma-induced coagulopathy who were being treated in advanced trauma systems, prehospital administration of tranexamic acid followed by an infusion over 8 hours did not result in a greater number of patients surviving with a favorable functional outcome at 6 months than placebo. (Funded by the Australian National Health and Medical Research Council and others; PATCH-Trauma ClinicalTrials.gov number, NCT02187120.)

Table 2. Primary and Secondary Outcomes.*

Outcome	Tranexamic Acid (N=657)	Placebo (N=643)	Risk Ratio or Hazard Ratio (95% CI) [†]
Primary outcome			
Survival with a favorable functional outcome at 6 months — no./total no. (%)‡	307/572 (53.7)	299/559 (53.5)	1.00 (0.90–1.12)
Secondary outcomes			
Death — no./total no. (%)			
24 hr after injury	64/657 (9.7)	90/640 (14.1)	0.69 (0.51–0.94)
28 days after injury	113/653 (17.3)	139/637 (21.8)	0.79 (0.63–0.99)
6 mo after injury	123/648 (19.0)	144/629 (22.9)	0.83 (0.67–1.03)
Vascular occlusive events — no./total no. (%)			
Deep venous thrombosis	100/657 (15.2)	80/641 (12.5)	1.22 (0.93–1.60)
Pulmonary embolism	43/657 (6.5)	45/641 (7.0)	0.93 (0.62–1.40)
Myocardial infarction	8/657 (1.2)	4/641 (0.6)	1.95 (0.59–6.45)
Ischemic stroke	19/657 (2.9)	14/641 (2.2)	1.32 (0.67–2.62)
Other arterial event	10/657 (1.5)	10/641 (1.6)	0.98 (0.41–2.33)
Any of the above	155/657 (23.6)	126/641 (19.7)	1.20 (0.97–1.48)
Sepsis — no./total no. (%)	226/657 (34.4)	198/641 (30.9)	1.11 (0.95–1.30)

**Figure 2. Levels on the Glasgow Outcome Scale–Extended (GOS-E) at 6 Months.**

The GOS-E ranges from 1 to 8, with higher levels indicating better outcomes. The percentages represent the percentage of patients with each level. No patients in the tranexamic acid group had a GOS-E level of 2. The dotted line indicates the demarcation between death or survival with an unfavorable functional outcome (GOS-E levels of 1 to 4) and survival with a favorable functional outcome (GOS-E levels of 5 to 8). Results are shown without imputation; the results of an analysis that used imputation are provided in Figure S3 in the Supplementary Appendix. Percentages may not total 100 because of rounding.

Tranexamic Acid for Traumatic Injury in the Emergency Setting: A Systematic Review and Bias-Adjusted Meta-Analysis of Randomized Controlled Trials

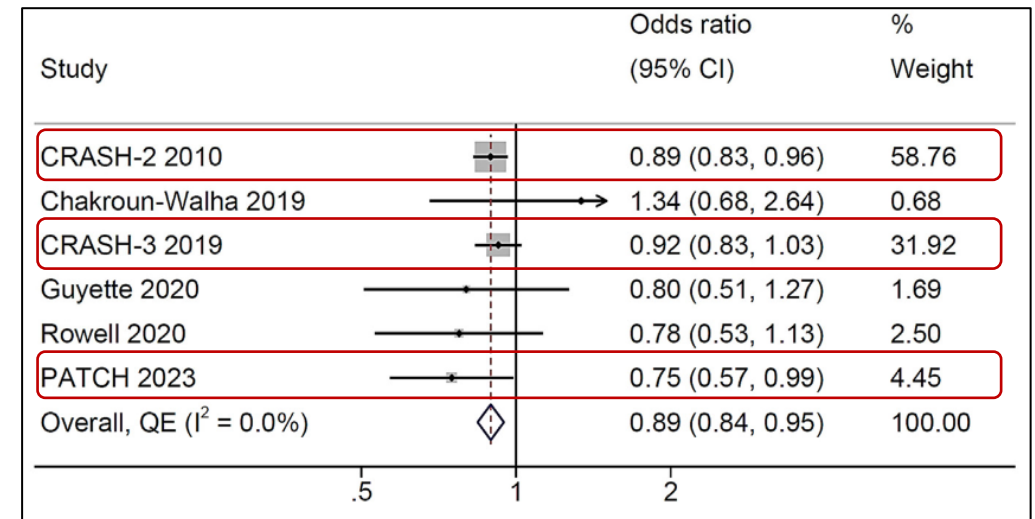
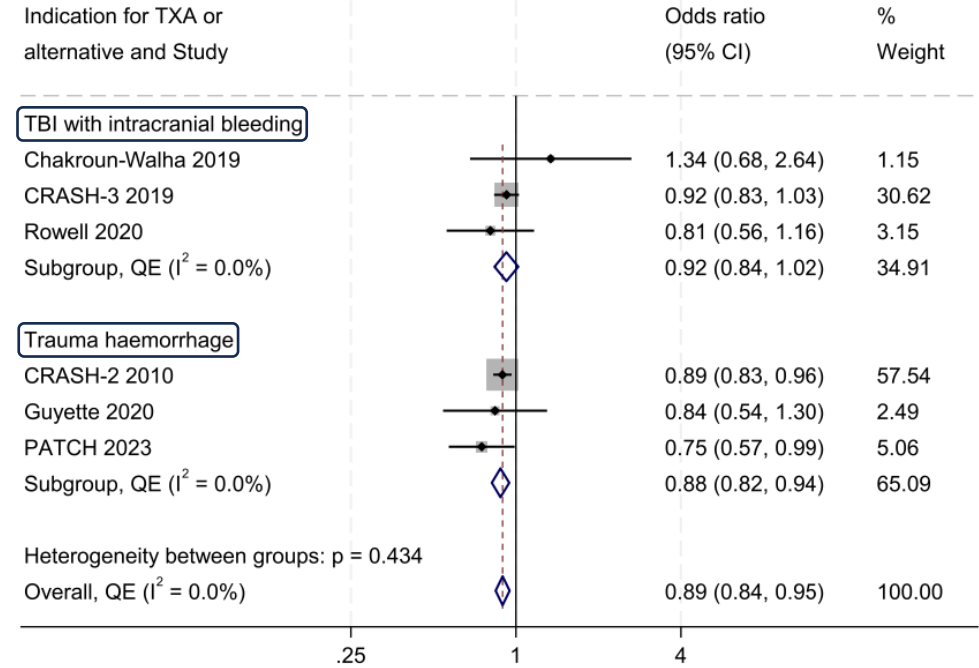
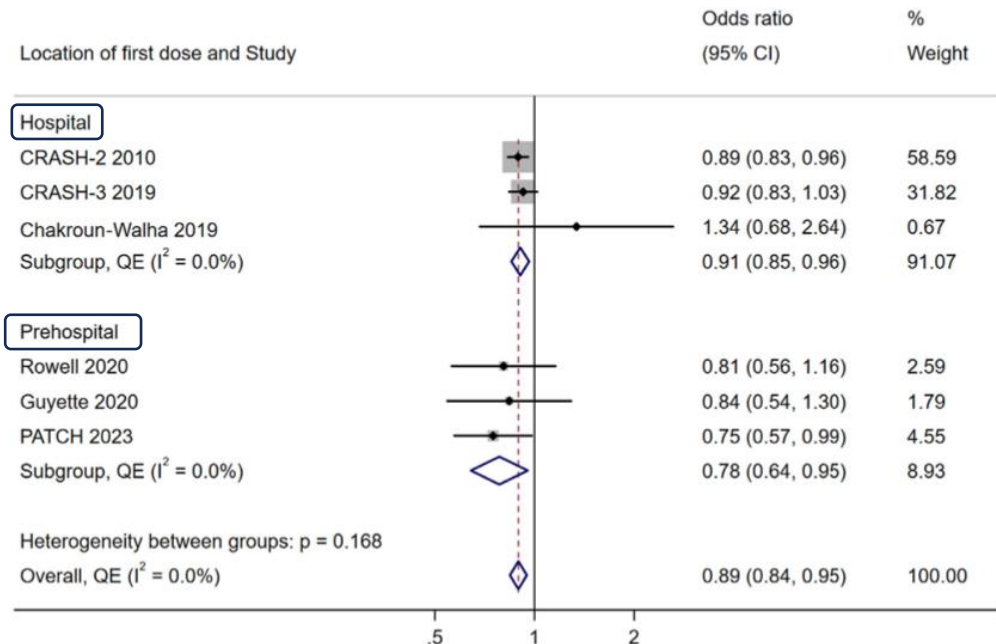
Pieter Francois Fouche, MScMed (ClinEpi), PhD*; Christopher Stein, PhD; Martin Nichols, MHLthSc, MBA; Benjamin Meadley, PhD; Jason C. Bendall, MBBS, MM (ClinEpi), PhD; Karen Smith, BSc (Hons), Grad Dip Epi&Biostats, Grad Cert Exec BA, PhD; David Anderson, MBChB; Suhail A. Doi, MBBS, MCLinEpid, PhD



> 33000 trauma patients: TXA vs. placebo

Results: Seven randomized controlled trials met the set criteria. This meta-analysis indicated an 11% decrease in the death risk at 1 month after TXA use (odds ratio [OR] 0.89, 95% confidence interval [CI] 0.84 to 0.95) with a [number needed to treat of 61 to avoid 1 additional death](#). The meta-analysis also revealed reduced 24-hour mortality (OR 0.76, 95% CI 0.65 to 0.88) for TXA. No compelling evidence of increased vascular occlusive events emerged (OR 0.96, 95% CI 0.73 to 1.27). Subgroup analyses highlighted TXA's effectiveness in general trauma versus traumatic brain injury and survival advantages when administered out-of-hospital versus in-hospital.

Conclusions: This synthesis demonstrates that [TXA use for trauma in emergencies leads to a reduction in 1-month mortality](#), with no significant evidence of problematic vascular occlusive events. Administering TXA in the [out-of-hospital setting](#) is associated with reduced mortality compared to in-hospital administration, and less mortality with TXA [in systemic trauma is noted compared with traumatic brain injury specifically](#). [Ann Emerg Med. 2024;83:435-445.]



Tranexamic Acid for Acute Hemorrhage: A Narrative Review of Landmark Studies and a Critical Reappraisal of Its Use Over the Last Decade

Heiko Lier, MD,* Marc Maegele, MD,† and Aryeh Shander, MD‡

Ubiquitous, generous, liberal, and indiscriminate application following outdated “one-size/dose-fits- all” concepts is not reasonable and not supported by the data currently available.”

“TXA should not replace another effective intervention” and “results do not support the prophylactic use of tranexamic acid.”⁹⁸ Potential adverse effects also need to be considered for the prophylactic use of TXA in settings of elective and emergency surgeries

What are the other recommendations?

Rossaint et al. *Critical Care* (2023) 27:80
<https://doi.org/10.1186/s13054-023-04327-7>

GUIDELINES

Open Access



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

Lancet 2019; 394: 1713–23

Give:

TXA < 3 h from impact **(1A)**

Treat:

PLT < 100 **(2C)**

FIB < 1,5 (2?) **(1C)**

APTT > x 1,5 **(1C)**

INR > 1,5 **(1C)**

Reverse:

Anticoagulants

Antiplatelets

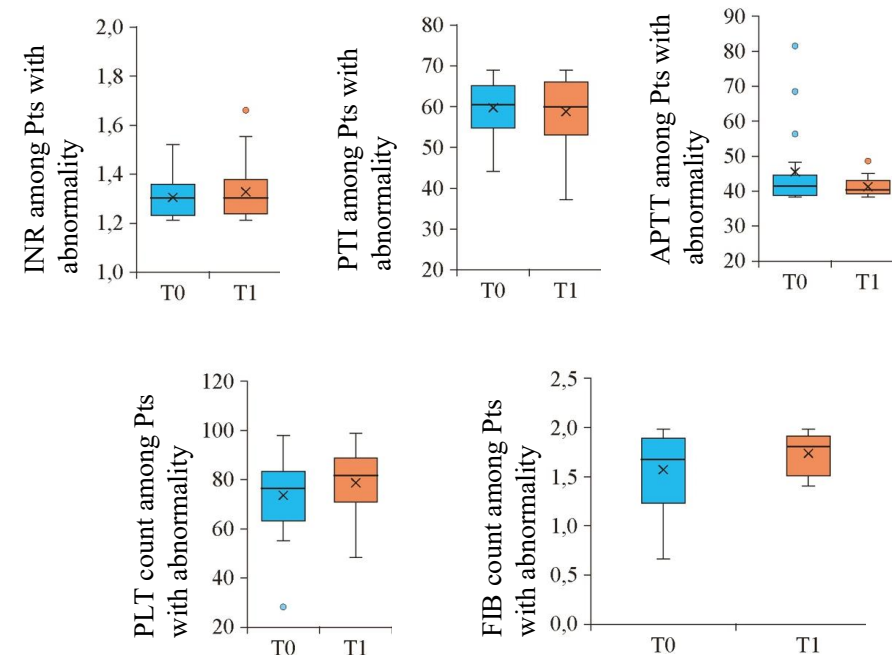
The "grey" zone...

Implementation of Thromboelastometry for Coagulation Management in Isolated Traumatic Brain Injury Patients Undergoing Craniotomy

Table 2. Patients with abnormal preoperative SCT and the extent of test abnormalities.

Variable	Controls	Cases	p	Controls	Cases	p	Total	
	Abnormal (n,%)	Abnormal (n,%)		Value within abnormal (median, IQR)	Value within abnormal (median, IQR)		Abnormal (n,%)	Value within abnormal (median, IQR)
PLT	10 (15.4)	8 (11.6)	0.520	78.5 (64.5–87.25)	72.5 (62–83)	0.762	18 (13.4)	76.5 (62–83.5)
PTI	13 (20)	10 (14.5)	0.398	60 (55–64)	63.5 (57.25–66)	0.446	23 (17.2)	61 (55–65)
INR	11 (16.9)	9 (13)	0.529	1.30 (1.24–1.33)	1.23 (1.22–1.34)	0.175	20 (14.9)	1.28 (1.23–1.33)
APTT	8 (12.3)	8 (11.6)	0.899	40.75 (38.55–52.63)	42.75 (38.7–48.95)	0.505	16 (11.9)	41.55 (38.93–47.1)
FIB	6 (10.2)	9 (13.2)	0.112	1.64 (1.32–1.92)	1.82 (1.54–1.89)	0.776	15 (11.8)	1.7 (1.49–1.89)
Any SCT abnormality	26 (40)	25 (36.2)	0.653				51 (38.1)	

Continuous variables are reported as median (interquartile range). Categorical variables are reported in terms of frequency (percentage). SCT – standard coagulation tests; PLT – platelet count (10⁹/L); PTI – prothrombin time index (%); INR – international normalized ratio (value); APTT – partial thromboplastin time (s); FIB – fibrinogen (g/L).



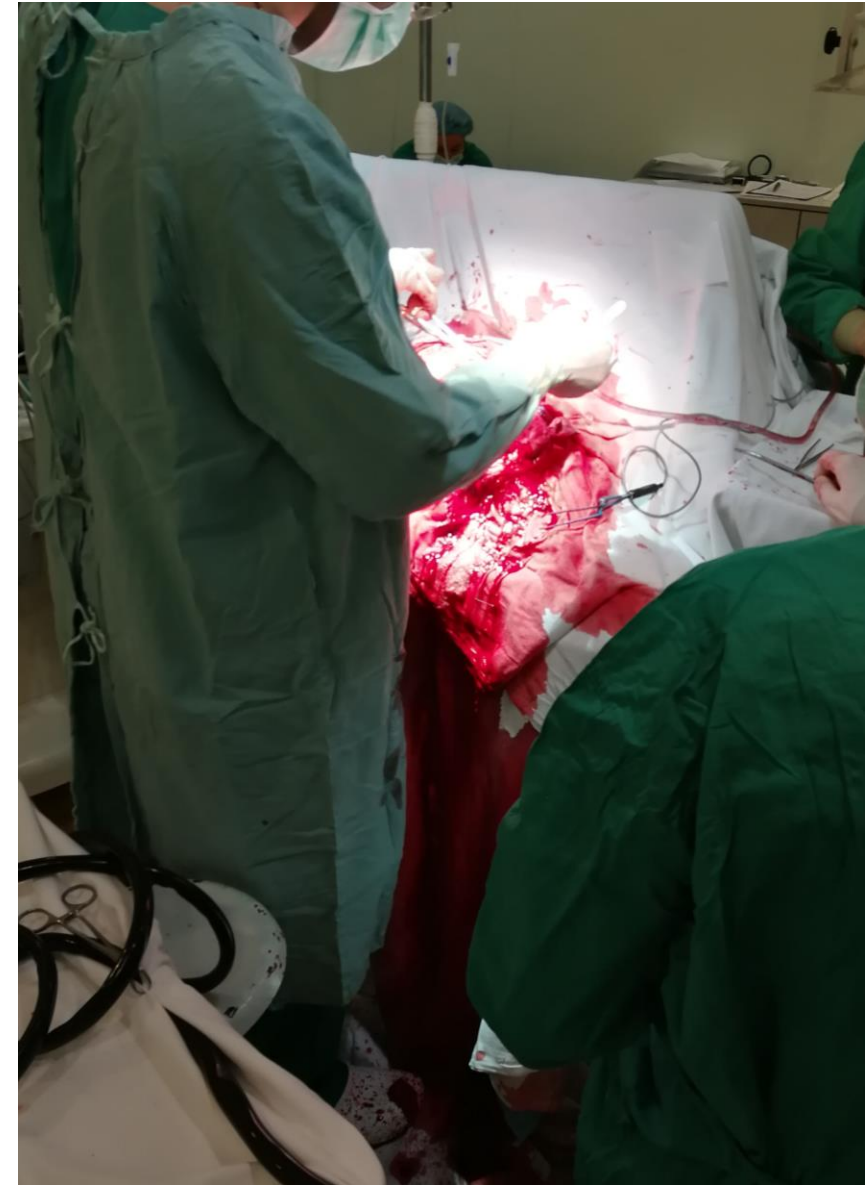
Coagulopathy management

Out of 26 patients in the control-CP subgroup, 17 patients (65.4%) received procoagulant intervention either with tranexamic acid (TXA), blood products, or coagulation factor concentrates. Nine patients (34.6%) in the control-CP subgroup did not receive any procoagulant intervention despite observed abnormalities in standard coagulation tests as the treating anesthesiologist considered them clinically insignificant.

The importance of clinical awareness...



VS.



The potential of goal-directed hemostatic management in patients with TBI



VHA and goal-directed coagulation management

GUIDELINES

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

Second update 2022

Sibylle Kietaihl, Aamer Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Giedrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Anne Godier, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V. Llau, Jens Meier, Zsolt Molnar, Lidia Mora, Niels Rahe-Meyer, Charles M. Samama, Ecaterina Scarlatescu, Christoph Schlimp, Anne J. Wikkelsø and Kai Zacharowski

Recommendations

We recommend the application of intervention algorithms incorporating pre-defined triggers and targets based on VHA coagulation monitoring to guide individualised haemostatic intervention in the case of perioperative bleeding. 1C

If VHA is not available we recommend the application of intervention algorithms incorporating pre-defined triggers based on conventional coagulation tests. 1C

Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding (Review)

Wikkelsø A, Wetterslev J, Møller AM, Afshari A

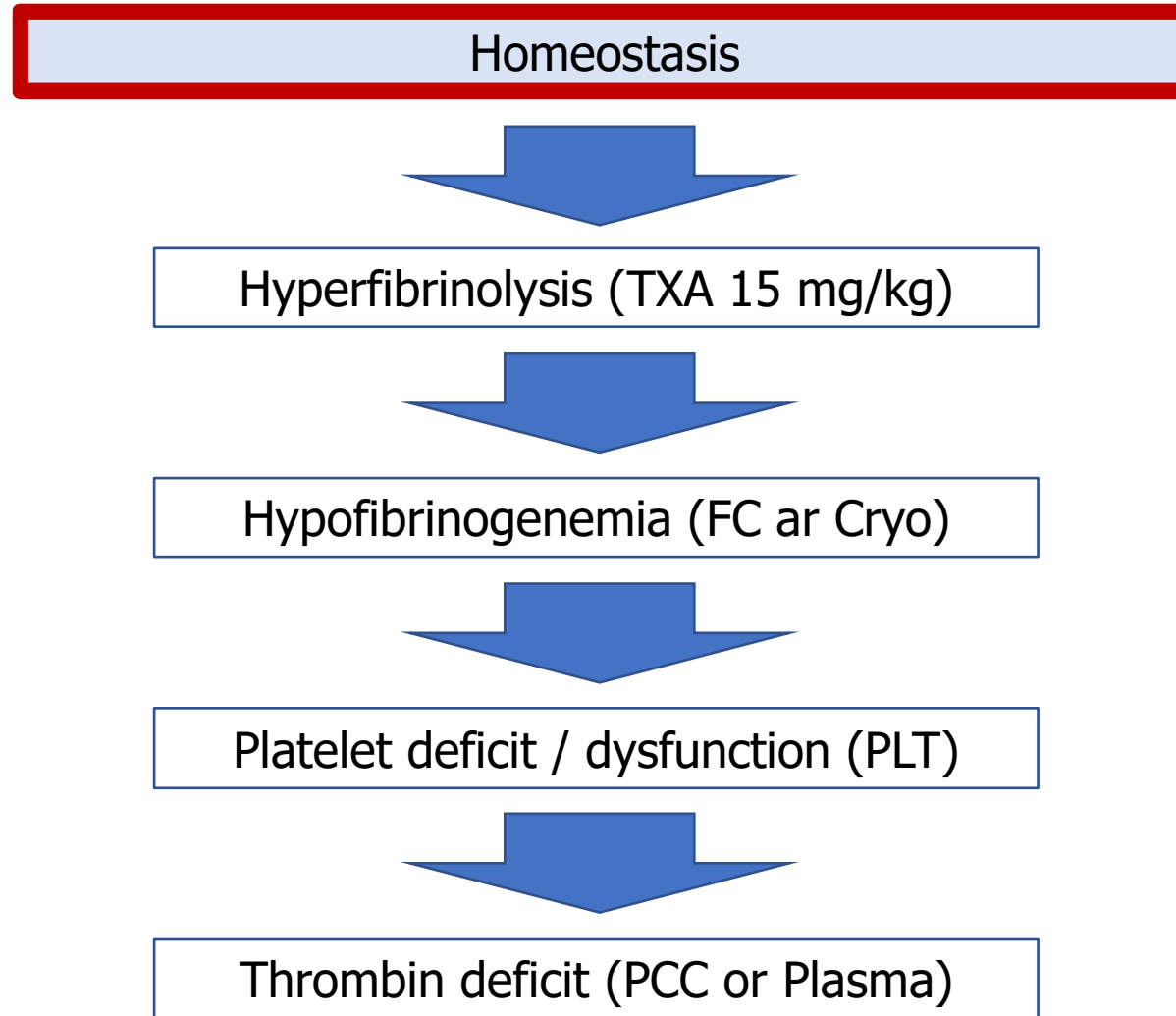


Metaanalysis:

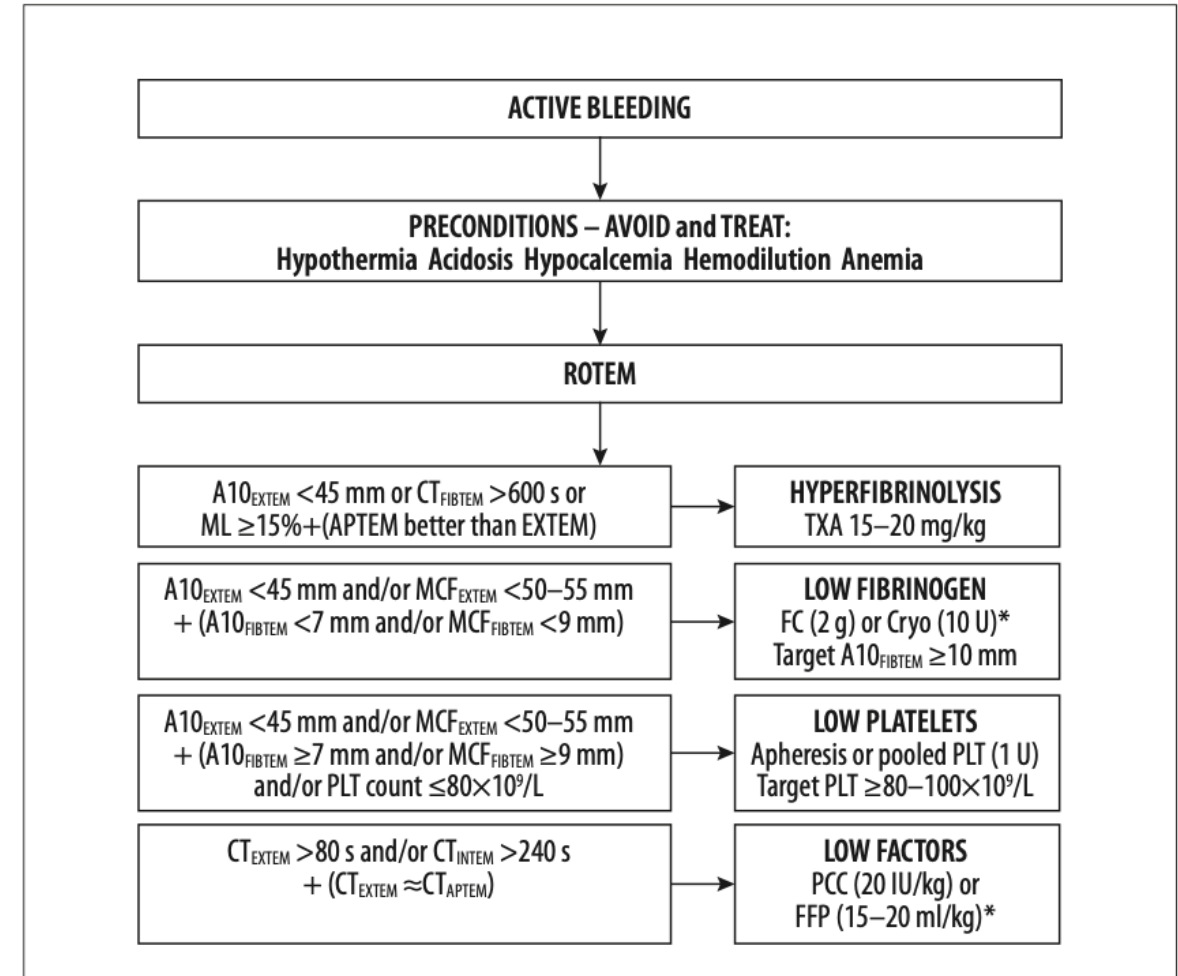
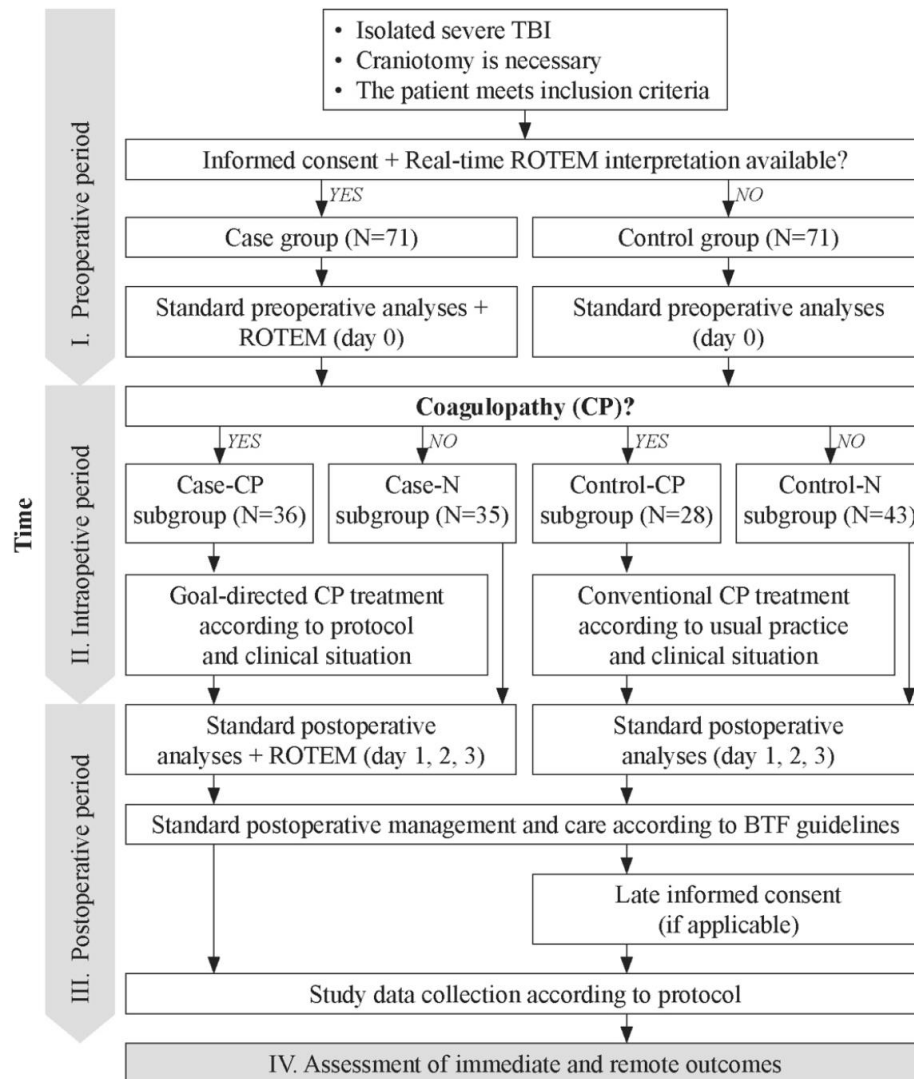
- 17 studies
- 1500 patient data

Conclusion: There is growing evidence that application of TEG- or ROTEM-guided transfusion strategies may reduce the need for blood products and improve morbidity in patients with bleeding. <<...>>

General principles of goal-directed hemostatic management algorithms



Goal-directed hemostatic management in TBI patients during craniotomy



Görlinger K, Pérez-Ferrer A, Dirkmann D, Saner F, Maegele M, Calatayud ÁAP, Kim TY. The role of evidence-based algorithms for rotational thromboelastometry-guided bleeding management.

Korean J Anesthesiol. 2019; 72(4):297-322.

Rimaitis M et al. Implementation of thromboelastometry for coagulation management in isolated traumatic brain injury patients undergoing craniotomy. Medical Science Monitor 2020;26:e922879.

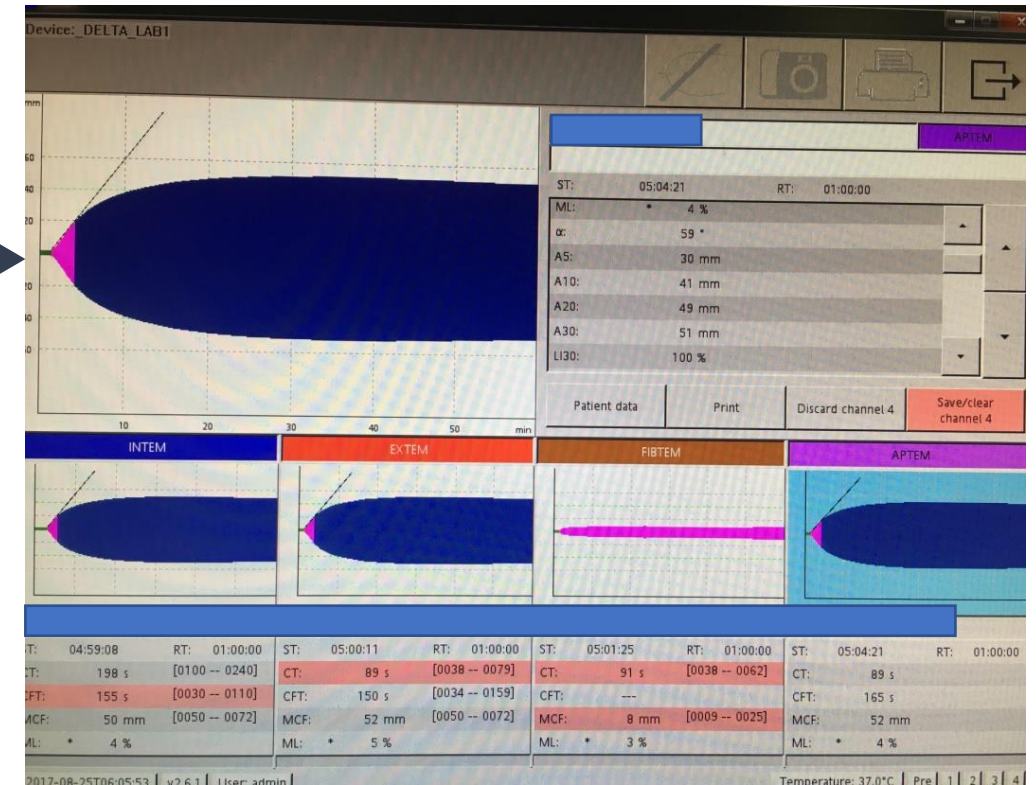
Goal-directed hemostatic management in practice

- 65 yo Male
- 175 cm / 78 kg
- Severe isolated TBI – SDH
- GCS 4

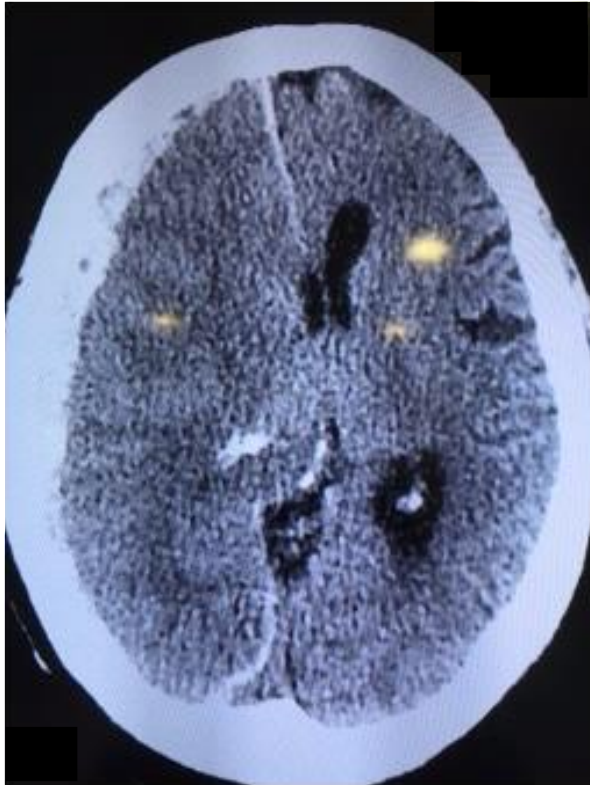
Laboratory analyses:

Hb 115 g/L INR 1.20
Plt 149*10⁹/L APTT 34.3 s
PTI 68 % Fib. 1.86 g/L

- Surgeons note diffuse bleeding
- Prolonged clotting time (CT) on EXTEM
- FFP was administered
- Hematoma was removed and adequate hemostasis was achieved

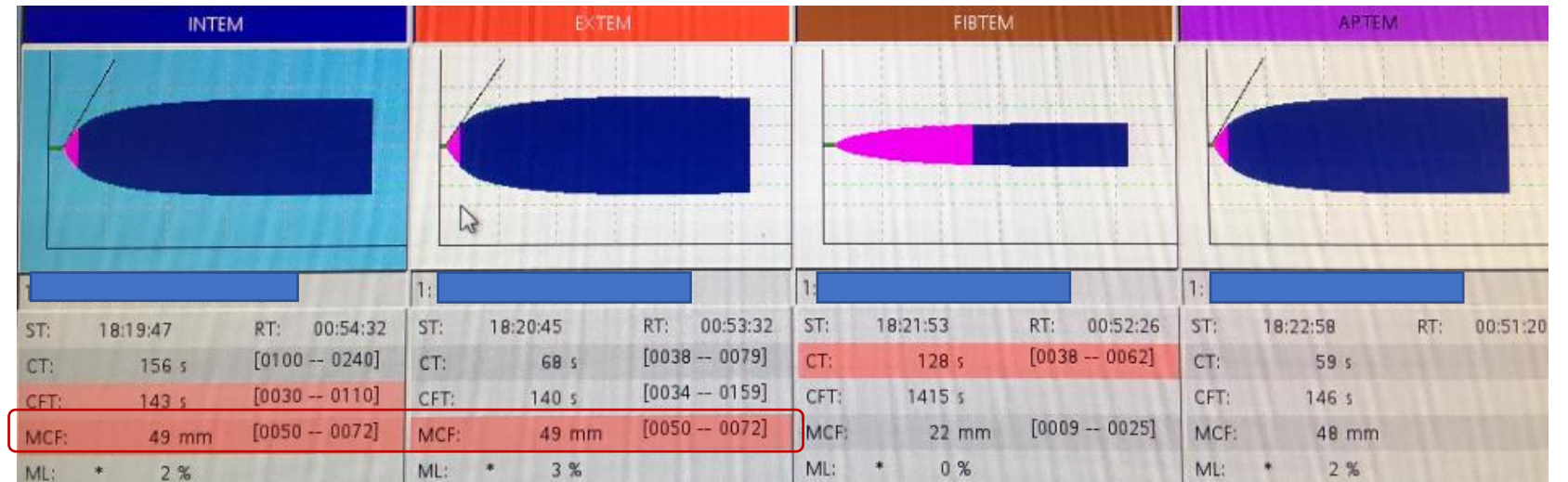


Clinically significant thrombocytopenia

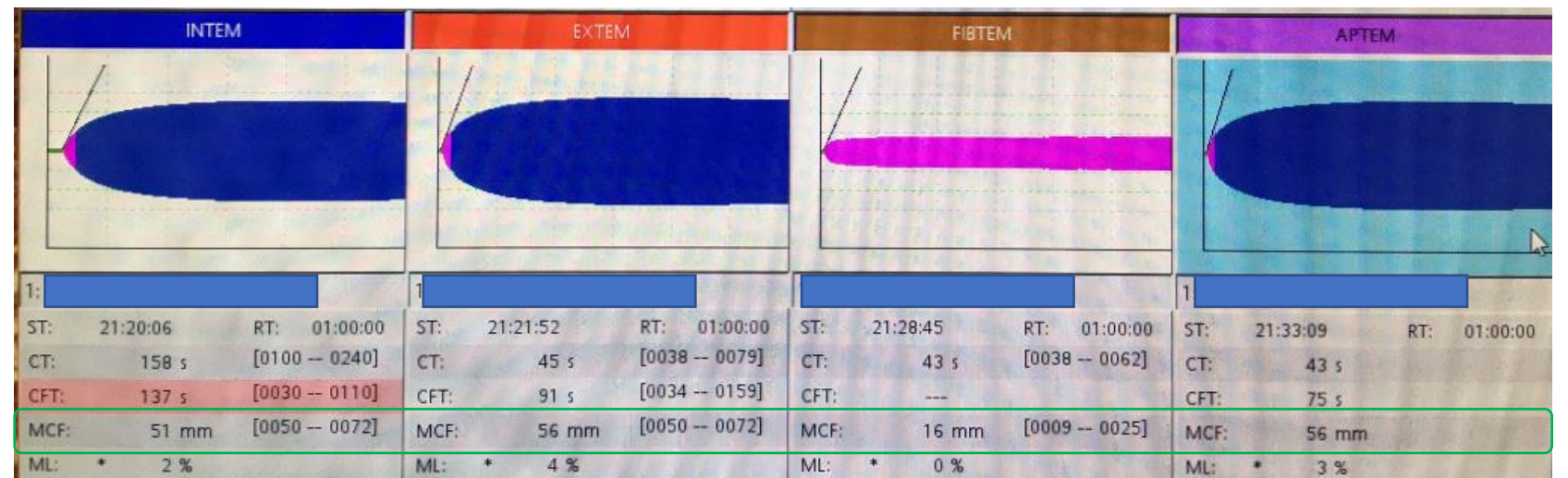


- 46 YO Male
- Acute SDH, GCS 12
- Laboratory analyses:
 - Hb 147 g/l
 - Plt $62 \times 10^9/l$
 - PTI 150 %
 - INR 0.86
 - APTT 30.9 s

Initial ROTEM



Following 1U of pooled platelets



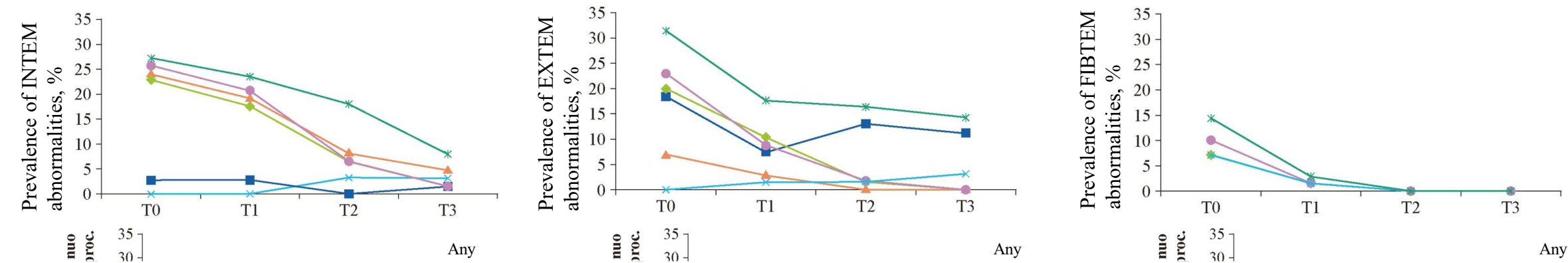
Implementation of Thromboelastometry for Coagulation Management in Isolated Traumatic Brain Injury Patients Undergoing Craniotomy

- Prospective case-control study, N=134
- Management of coagulopathic pts: ROTEM-based vs. CCT
- Protocol adherence rate 85%
- ↑Clot quality
- ↓PHI and re-intervention
- ↔ GOS and mortality

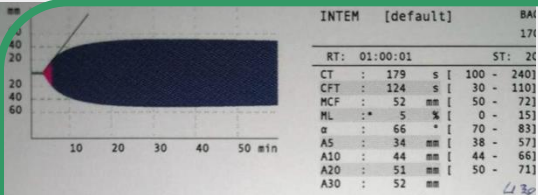
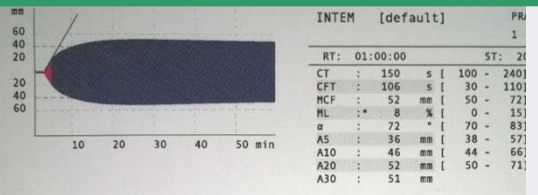
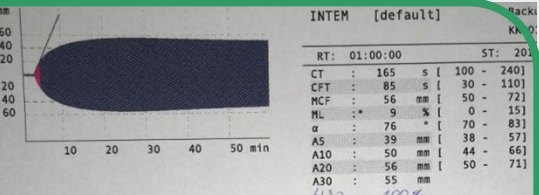
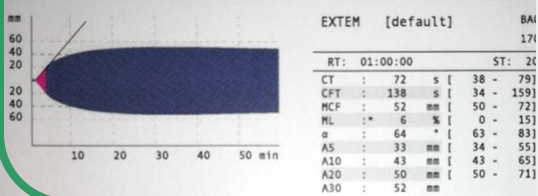
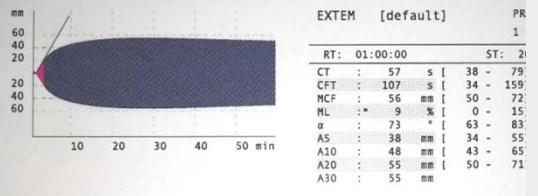
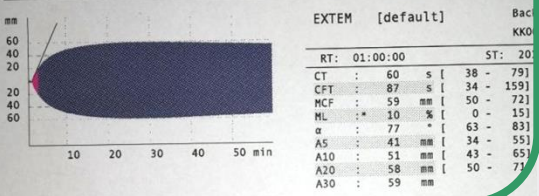
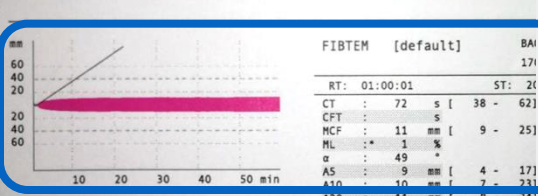
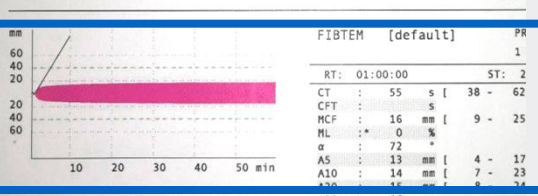
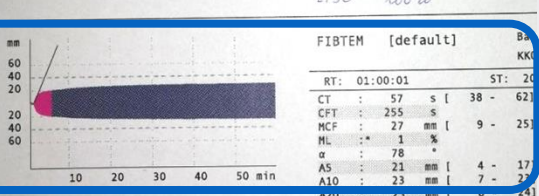
Conclusions: ROTEM led to consistent coagulation management, improved clot quality, and decreased incidence of PHI and neurosurgical re-intervention. Further studies are needed to confirm benefits of ROTEM in cases of TBI.

		Controls			Cases			P		
		¹ Normal (n=39)	² CP (n=26)	³ All (N=65)	⁴ Normal (n=35)	⁵ CP (n=34)	⁶ All (N=69)	1 vs. 4	2 vs. 5	3 vs. 6
Progressive injury	Hemorrhagic	18 (46.2)	13 (50)	31 (47.7)*	10 (28.6)	11 (32.4)	21 (30.4)*	0.119	0.167	0.040*
	Ischemic	6 (15.4)	14 (53.8)	20 (30.8)	5 (14.3)	13 (38.2)	18 (26.1)	0.894	0.228	0.548
	Edematous	2 (5.1)	3 (11.5)	5 (7.7)	4 (11.4)	6 (17.6)	10 (14.5)	0.322	0.511	0.212
Re-intervention		6 (15.8)	10 (40)*	16 (25.4)	5 (14.3)	4 (12.9)*	9 (13.6)	0.858	0.020*	0.091
Length of hospital stay (survivors)		17 (10–27)	25 (14–32)	22 (10.75–27.25)	17 (9.75–25.75)	19 (11–24.5)	17 (11–24)	0.683	0.101	0.277
GCS	Day 3	12 (7–15)	9 (5–14)	11 (5–14)	13 (6–15)	11.5 (5–15)	12.5 (5–15)	0.483	0.292	0.289
	Day 7	13 (8.5–15)	10.5 (5–14.75)	12 (5–15)	15 (6–15)	13 (5.5–15)	13 (6–15)	0.294	0.271	0.205
	At discharge	15 (12–15)	14 (8–15)	15 (10.75–15)	15 (13.5–15)	15 (13–15)	15 (13–15)	0.386	0.190	0.158
Clinical outcome	Favorable (GOS 4–5)	19 (48.7)	4 (15.4)	23 (35.4)	19 (54.3)	13 (38.2)	32 (46.4)	0.632	0.052	0.196
	Poor (GOS 1–3)	20 (51.3)	22 (84.6)	42 (64.6)	16 (45.7)	21 (61.8)	37 (53.6)			
Death		4 (10.3)	11 (42.3)	15 (23.1)	5 (14.3)	13 (38.2)	18 (26.1)	0.596	0.750	0.686

Continuous variables are reported as median (interquartile range); categorical variables are reported in terms of frequency (percentage). Superscript numbers (1 to 6) mark columns to clarify comparisons. * Statistically significant differences. CP – coagulopathy; GCS – Glasgow coma score; GOS – Glasgow outcome score.



Dynamic coagulation changes in patients with TBI

	Postoperative day 1	Day 2	Day 3
Lab	Hb 88 g/l Plt 122*10 ⁹ /L	Hb 86 g/l Plt 103*10 ⁹ /L	Hb 99 g/l Plt 96*10 ⁹ /L
	PTI 64 % INR 1.21 APTT 38 s	PTI 44 % INR 1.48 APTT 42.1 s	PTI 66 % INR 1.20 APTT 46.4 s
	Fibrinogen 2.05 g/L	Fibrinogen 3.29 g/L	Fibrinogen 5.83 g/L
I/V	Crystalloid: 3000 mL Colloid: 1000 mL Other: RBC 2 units	Crystalloid: 1000 mL Colloid: - Other: RBC 2 units, enteral fluids	Crystalloid: - Colloid: - Other: enteral fluids
ROTEM	 INTEM [default] BAI 17i RT: 01:00:01 ST: 2i CT : 179 s [100 - 240] CFT : 124 s [30 - 110] MCF : 52 mm [50 - 72] ML : * 5 % [0 - 15] α : 66 * [70 - 83] A5 : 34 mm [38 - 57] A10 : 44 mm [44 - 66] A20 : 51 mm [50 - 71] A30 : 52 mm	 INTEM [default] PR 1 RT: 01:00:00 ST: 2i CT : 150 s [100 - 240] CFT : 106 s [30 - 110] MCF : 52 mm [50 - 72] ML : * 8 % [0 - 15] α : 72 * [70 - 83] A5 : 36 mm [38 - 57] A10 : 46 mm [44 - 66] A20 : 52 mm [50 - 71] A30 : 51 mm	 INTEM [default] Back KN 0 RT: 01:00:00 ST: 2i CT : 165 s [100 - 240] CFT : 85 s [30 - 110] MCF : 56 mm [50 - 72] ML : * 9 % [0 - 15] α : 76 * [70 - 83] A5 : 39 mm [38 - 57] A10 : 50 mm [44 - 66] A20 : 56 mm [50 - 71] A30 : 55 mm
	 EXTEM [default] BAI 17i RT: 01:00:00 ST: 2i CT : 72 s [38 - 79] CFT : 138 s [34 - 159] MCF : 52 mm [50 - 72] ML : * 6 % [0 - 15] α : 64 * [63 - 83] A5 : 33 mm [34 - 55] A10 : 43 mm [43 - 65] A20 : 50 mm [50 - 71] A30 : 52 mm	 EXTEM [default] PR 1 RT: 01:00:00 ST: 2i CT : 57 s [38 - 79] CFT : 107 s [34 - 159] MCF : 56 mm [50 - 72] ML : * 9 % [0 - 15] α : 73 * [63 - 83] A5 : 38 mm [34 - 55] A10 : 48 mm [43 - 65] A20 : 55 mm [50 - 71] A30 : 55 mm	 EXTEM [default] Back KN 0 RT: 01:00:00 ST: 2i CT : 60 s [38 - 79] CFT : 87 s [34 - 159] MCF : 59 mm [50 - 72] ML : * 10 % [0 - 15] α : 77 * [63 - 83] A5 : 41 mm [34 - 55] A10 : 51 mm [43 - 65] A20 : 58 mm [50 - 71] A30 : 59 mm
	 FIBTEM [default] BAI 17i RT: 01:00:01 ST: 2i CT : 72 s [38 - 62] CFT : 11 s [9 - 25] MCF : 11 mm [9 - 25] ML : * 1 % [0 - 15] α : 49 * [4 - 17] A5 : 9 mm [7 - 23] A10 : 10 mm [8 - 24] A20 : 11 mm A30 : 11 mm	 FIBTEM [default] PR 1 RT: 01:00:00 ST: 2i CT : 55 s [38 - 62] CFT : 16 mm [9 - 25] MCF : 16 mm [9 - 25] ML : * 0 % [0 - 15] α : 72 * [4 - 17] A5 : 13 mm [7 - 23] A10 : 14 mm [8 - 24] A20 : 14 mm A30 : 16 mm	 FIBTEM [default] Back KN 0 RT: 01:00:01 ST: 2i CT : 57 s [38 - 62] CFT : 255 s [9 - 25] MCF : 27 mm [9 - 25] ML : * 1 % [0 - 15] α : 78 * [4 - 17] A5 : 21 mm [7 - 23] A10 : 23 mm [8 - 24] A20 : 23 mm A30 : 26 mm

Time course of coagulation in patients with TBI

Neurocrit Care
https://doi.org/10.1007/s12028-022-01639-4

NEUROCRITICAL
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ORIGINAL WORK

Dynamic Changes of Hemostasis in Patients with Traumatic Brain Injury Undergoing Craniotomy: Association with in-Hospital Mortality

Marius Rimaitis^{1,2*}, Vaiva Cechanovičiūtė¹, Diana Bilskienė^{1,2}, Neringa Balčiūnienė^{1,3}, Rimantas Vilcinis^{1,3}, Kęstutis Rimaitis^{1,2} and Andrius Macas^{1,2}



Early fibrinogen-related coagulation disorders were associated with mortality of patients with TBI undergoing major neurosurgical procedures.

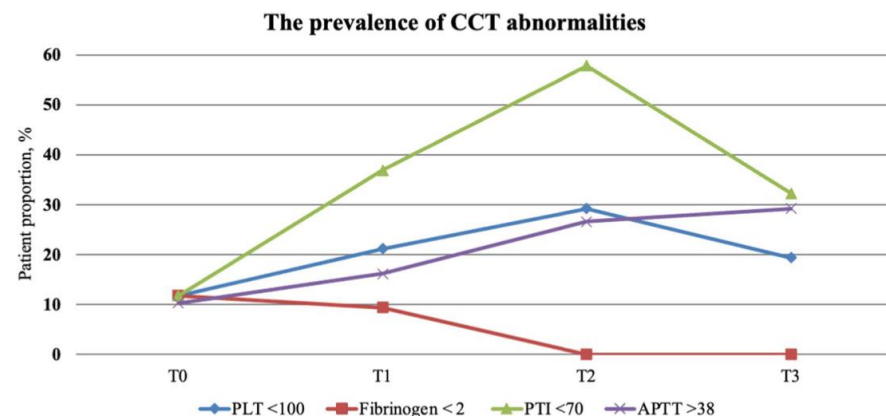


Fig. 2 The prevalence of CCT abnormalities in the perioperative period. Fibrinogen is expressed in g/L. APTT activated partial thromboplastin time (s), CCT conventional coagulation tests, PLT platelets ($10^9/L$), PTI prothrombin time index (%)

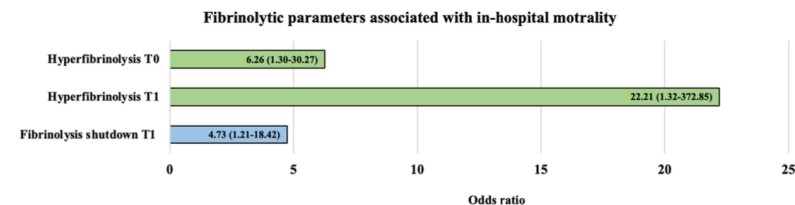


Fig. 7 Fibrinolytic parameters associated with in-hospital mortality. Data are expressed as odds ratio (95% CI). All $p < 0.05$. CI confidence interval

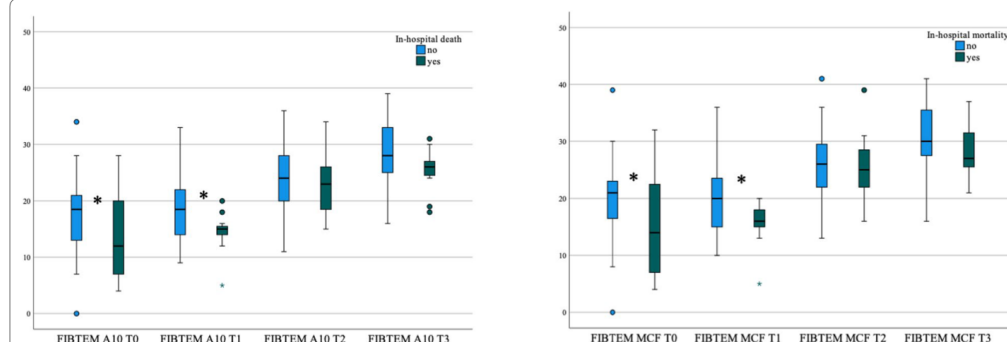


Fig. 6 Dynamic changes of fibrin polymerization thromboelastometry (FIBTEM) among survivors and nonsurvivors. *Statistically significant differences, $p < 0.05$. Boxplots represent medians, interquartile ranges, and minimum and maximum values. A10 clot amplitude at 10 min after CT (mm), CT clotting time (s), MCF maximum clot firmness (mm)

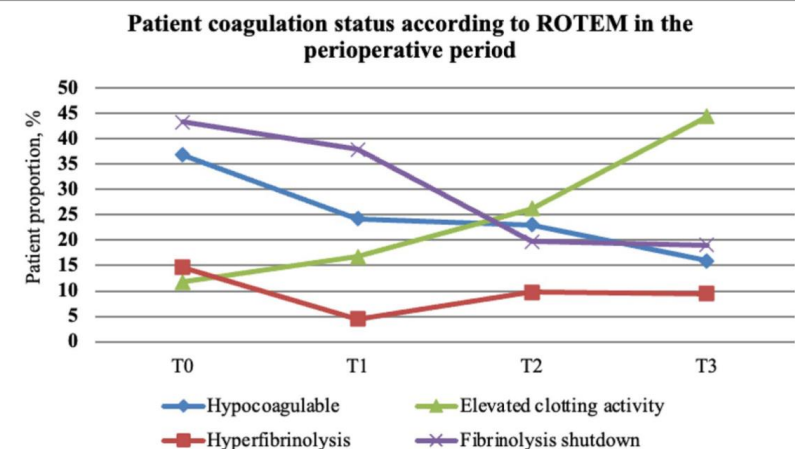


Fig. 4 Patient coagulation status according to rotational thromboelastometry in the perioperative period. ROTEM rotational thromboelastometry

Coagulation markers of poor prognosis in patients with TBI

Analysis of the coagulation parameters associated with in-hospital mortality

		OR (95% CI)	p	AUC (95% CI)	p	Optimal cutoff	Sensitivity of cutoff	Specificity of cutoff
Preoperative testing (T0)	INTEM ML	0.74 (0.55–0.99)	0.041	0.72 (0.56–0.88)	0.008	1.5%	0.53	0.91
	EXTEM TPI	0.44 (0.21–0.92)	0.029	0.70 (0.56–0.85)	0.018	2.0	0.47	0.93
	FIBTEM A10	0.90 (0.82–0.99)	0.038	0.68 (0.51–0.85)	0.033	13 mm	0.60	0.79
	FIBTEM MCF	0.91 (0.83–0.99)	0.033	0.69 (0.52–0.86)	0.025	14.5 mm	0.53	0.85
	FIBTEM ML	1.17 (1.02–1.33)	0.021	0.67 (0.50–0.85)	0.042	8.5%	0.40	0.94
Postoperative day 1 (T1)	Fibrinogen	0.33 (0.12–0.93)	0.035	0.71 (0.57–0.85)	0.019	3.0 g/L	0.77	0.61
	INTEM ML	0.71 (0.54–0.94)	0.015	0.77 (0.64–0.91)	0.002	4.5%	0.67	0.72
	EXTEM ML	0.68 (0.51–0.91)	0.01	0.80 (0.68–0.91)	0.001	6.5%	0.93	0.45
	FIBTEM A10	0.82 (0.70–0.96)	0.015	0.74 (0.62–0.86)	0.006	16.5 mm	0.80	0.66
	FIBTEM MCF	0.83 (0.71–0.97)	0.02	0.72 (0.60–0.85)	0.010	18.5 mm	0.80	0.59

A10 clot amplitude at 10 min after CT, AUC area under the curve, CI confidence interval, EXTEM extrinsic coagulation pathway thromboelastometry, FIBTEM fibrin polymerization thromboelastometry, INTEM intrinsic coagulation pathway thromboelastometry, MCF maximum clot firmness, ML maximum lysis, OR odds ratio, TPI thrombodynamic potential index

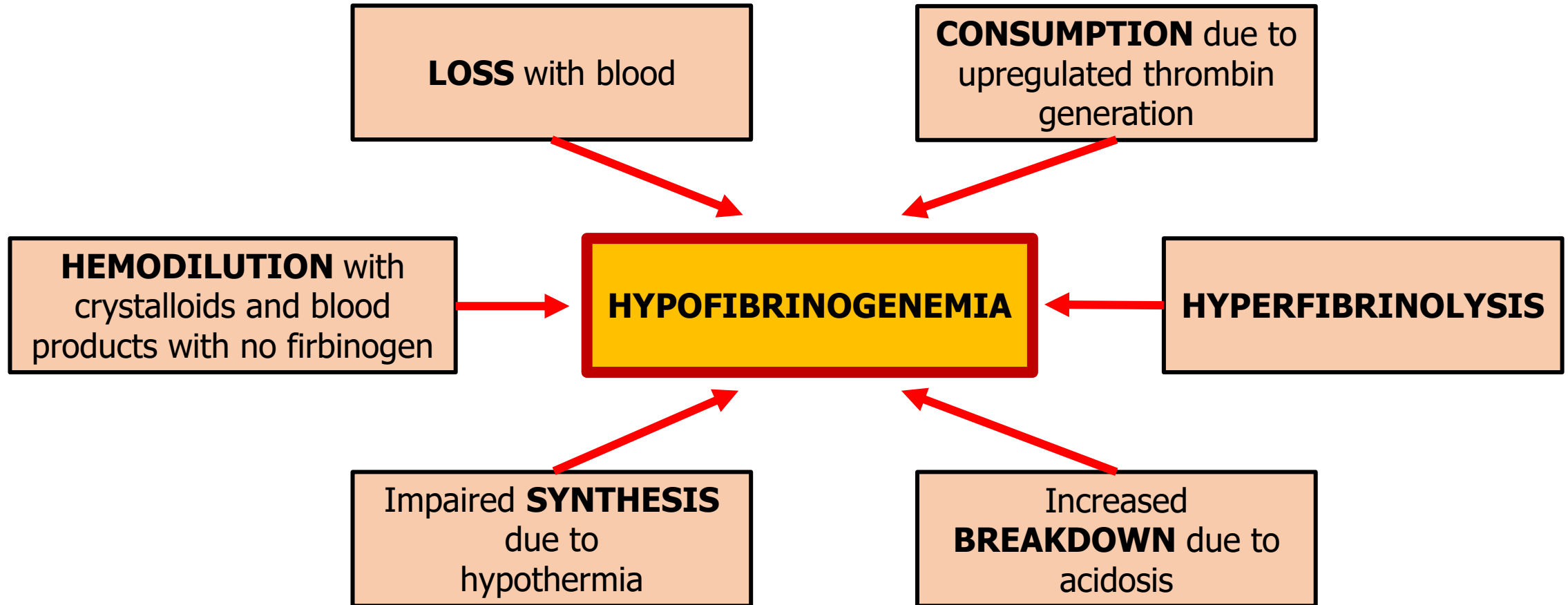
Fibrinogen concentrations necessary to achieve cut-off FIBTEM values

FIBTEM, mm	A10 > 13 (T0)	MCF > 14.5 (T0)	A10 > 16.5 (T1)	MCF > 18.5 (T1)
Fibrinogen, g/L	2.91	2.91	3.0	3.12

A10 clot amplitude at 10 min after CT, FIBTEM fibrin polymerization thromboelastometry, MCF maximum clot firmness

Optimal triggers for early coagulation support in patients with severe TBI require further investigation

Hypofibrinogenemia in trauma





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

Rolf Rossaint^{1*}, Arash Afshari², Bertil Bouillon³, Vladimir Cerny^{4,5}, Diana Cimpoesu⁶, Nicola Curry^{7,8}, Jacques Duranteau⁹, Daniela Filipescu¹⁰, Oliver Grottkel¹, Lars Grønlykke¹¹, Anatole Harrois⁹, Beverley J. Hunt¹², Alexander Kaserer¹³, Radko Komadina¹⁴, Mikkel Herold Madsen¹, Marc Maegele¹⁵, Lidia Mora¹⁶, Louis Riddez¹⁷, Carolina S. Romero¹⁸, Charles-Marc Samama¹⁹, Jean-Louis Vincent²⁰, Sebastian Wiberg¹¹ and Donat R. Spahn¹³

Two currently co-existing strategies for initial management

Initial coagulation resuscitation

Recommendation 25 In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies:

- Fibrinogen concentrate or cryoprecipitate and pRBC (Grade 1C)
- FFP or pathogen-inactivated FFP in a FFP/pRBC ratio of at least 1:2 as needed (Grade 1C)

In addition, we suggest a high platelet/pRBC ratio (Grade 2B).

Coagulation factor concentrate-based management

Recommendation 27 If a CFC-based strategy is used, we recommend treatment with factor concentrates based on standard laboratory coagulation parameters and/or viscoelastic evidence of a functional coagulation factor deficiency. (Grade 1C)

Provided that fibrinogen levels are normal, we suggest that PCC is administered to the bleeding patient based on evidence of delayed coagulation initiation using VEM. (Grade 2C)

We suggest that monitoring of FXIII be included in coagulation support algorithms and that FXIII be supplemented in bleeding patients with a functional FXIII deficiency. (Grade 2C)

Fresh frozen plasma-based management

Recommendation 27 If a FFP-based coagulation resuscitation strategy is used, we recommend that further use of FFP be guided by standard laboratory coagulation screening parameters (PT and/or APTT > 1.5 times normal and/or viscoelastic evidence of a coagulation factor deficiency) (Grade 1C).

We recommend that the use of FFP be avoided for the correction of hypofibrinogenemia if fibrinogen concentrate and/or cryoprecipitate are available (Grade 1C).

VI. Further goal-directed coagulation management

Goal-directed therapy

Recommendation 26 We recommend that resuscitation measures be continued using a goal-directed strategy, guided by standard laboratory coagulation values and/or VEM (Grade 1B).

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

Petra Innerhofer, Dietmar Fries, Markus Mittermayr, Nicole Innerhofer, Daniel von Langen, Tobias Hell, Gottfried Gruber, Stefan Schmid, Barbara Friesenecker, Ingo H Lorenz, Mathias Ströhle, Verena Rastner, Susanne Trübsbach, Helmut Raab, Benedikt Tremel, Dieter Wally, Benjamin Treichl, Agnes Mayr, Christof Kranewitter, Elgar Oswald

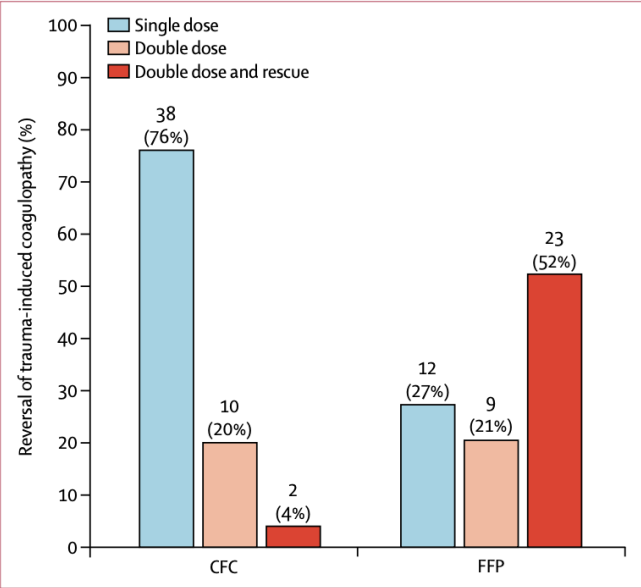


Figure 3: Percentage of patients with reversal of coagulopathy after either single-dose or double-dose study drug administration during the first therapy loop, and percentage of patients needing double-dose and rescue medication during the first 24 h in the intention-to-treat population CFC=coagulation factor concentrates. FFP=fresh frozen plasma.

- RCT, **ROTEM based goal-directed therapy**
- CFC (n=44) and FFP (n=50) groups
- > 50% need for rescue therapy in FFP group
- 3x more need for massive transfusion in FFP group
- Study was terminated at interim result analysis

P.S. No differences in primary outcome

	CFC (n=50)	FFP (n=44)	Estimated difference or odds ratio* (95% CI)	p value
Multiple organ failure†	25 (50%)	29 (66%)	1.92 (0.78 to 4.86)	0.15
Days of multiple organ failure	4 (2 to 7)	3 (2 to 9)	0 (-2 to 2)	0.68
ISS-adjusted mean SOFA score	0.16 (0.13 to 0.21)	0.20 (0.15 to 0.27)	-0.03 (-0.07 to -0.01)	0.019
Haemofiltration†	5 (10%)	7 (16%)	1.69 (0.42 to 7.36)	0.54
Days of haemofiltration	11.0 (5.8 to 21.5)	27.0 (21.5 to 28.5)	-13.0 (-23.0 to -1.0)	0.038
Ventilator-free days	23 (13 to 27)	21 (13 to 27)	0 (-2 to 3)	0.99
Sepsis†	9 (18%)	7 (16%)	0.86 (0.25 to 2.91)	1
Infection†	32 (64%)	32 (73%)	1.49 (0.57 to 4.01)	0.39
Venous thrombosis†	4 (8%)	8 (18%)	2.53 (0.62 to 12.42)	0.22
Peripheral pulmonary embolism†	3 (6%)	1 (2.3%)	0.37 (0.01 to 4.78)	0.62
Days in the ICU	9.0 (4.0 to 22.0)	10.0 (4.8 to 23.3)	0 (-4.0 to 3.0)	0.65
Length of hospital stay (days)	28 (18 to 28)	27 (16 to 28)	0 (0 to 1)	0.61
In-hospital mortality†	5 (10%)	2 (5%)	0.43 (0.04 to 2.82)	0.44

Data are n (%) or median (IQR). CFC=coagulation factor concentrates. FFP=fresh frozen plasma. ISS=Injury Severity Score. SOFA=Sequential Organ Failure Assessment. ICU=intensive care unit. *CF group minus FFP group. †Binary variables presented with odds ratios.

Table 2: Primary outcome in the modified intention-to-treat population

Interpretation Our results underline the importance of early and effective fibrinogen supplementation for severe clotting failure in multiple trauma. The available sample size in our study appears sufficient to make some conclusions that first-line CFC is superior to FFP.

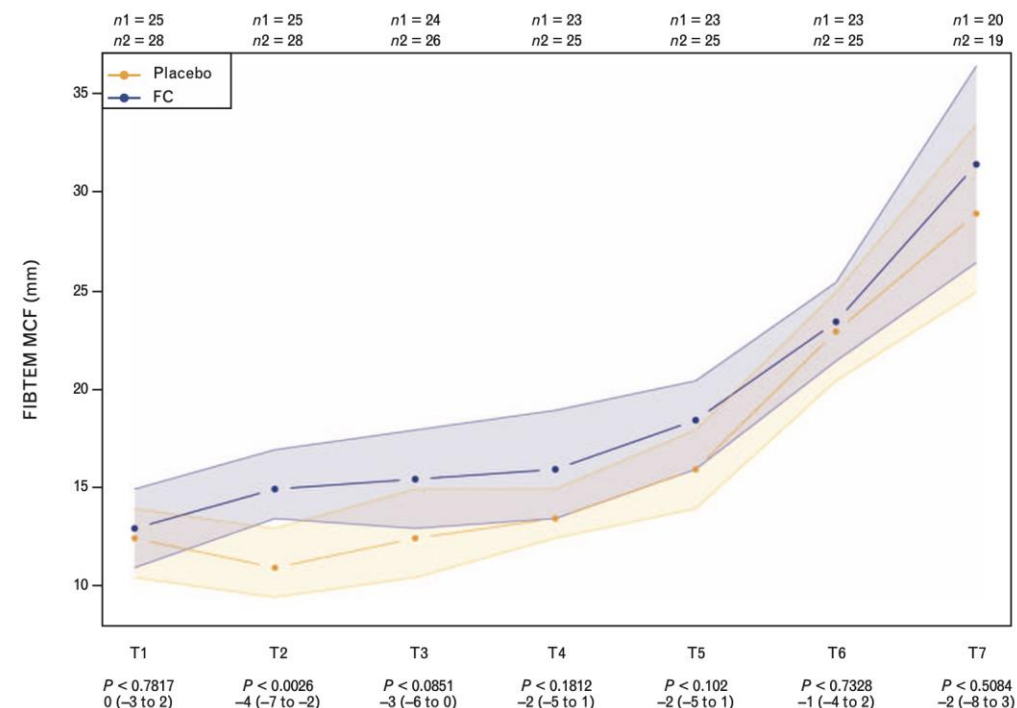
ORIGINAL ARTICLE

Efficacy of prehospital administration of fibrinogen concentrate in trauma patients bleeding or presumed to bleed (FlinTIC)

A multicentre, double-blind, placebo-controlled, randomised pilot study

- RCT, FC 50 mg/kg (n=28) vs Placebo (n=25)
- Early fibrinogen concentrate administration improved fibrinogen levels
- No increase in thromboembolic complications at day 7
- Clinical outcome data not yet reported.

Fig. 3 Changes in FIBTEM maximum clot firmness (FIBTEM MCF) between baseline (T1) and 7 days posttrauma (T7)



Conclusion

The FlinTIC study indicates that timely fibrinogen concentrate administration is feasible in the complex, dynamic and time-sensitive environment of acute prehospital trauma care. Early fibrinogen concentrate supplementation prevented fibrinogen plasma concentrations from decreasing to critical levels and improved blood clot stability between on-scene and ED arrival.

Early and Empirical High-Dose Cryoprecipitate for Hemorrhage After Traumatic Injury

The CRYOSTAT-2 Randomized Clinical Trial

Ross Davenport, PhD; Nicola Curry, MD; Erin E. Fox, PhD; Helen Thomas, MSc; Joanne Lucas, MSc; Amy Evans, MMedSci; Shamini Shanmugaranjan, BSc; Rupa Sharma, BSc; Alison Deary, MSc; Antoinette Edwards, MA; Laura Green, MD; Charles E. Wade, MD; Jonathan R. Bengner, MD; Bryan A. Cotton, MD; Simon J. Stanworth, MD, DPhil; Karim Brohi, MD; for the CRYOSTAT-2 Principal Investigators

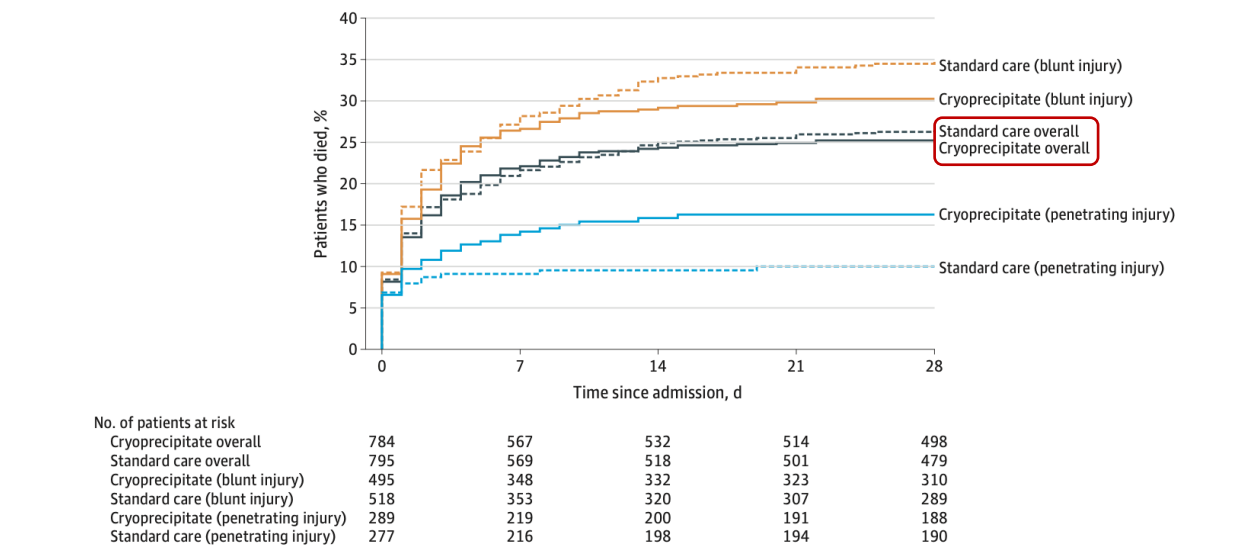
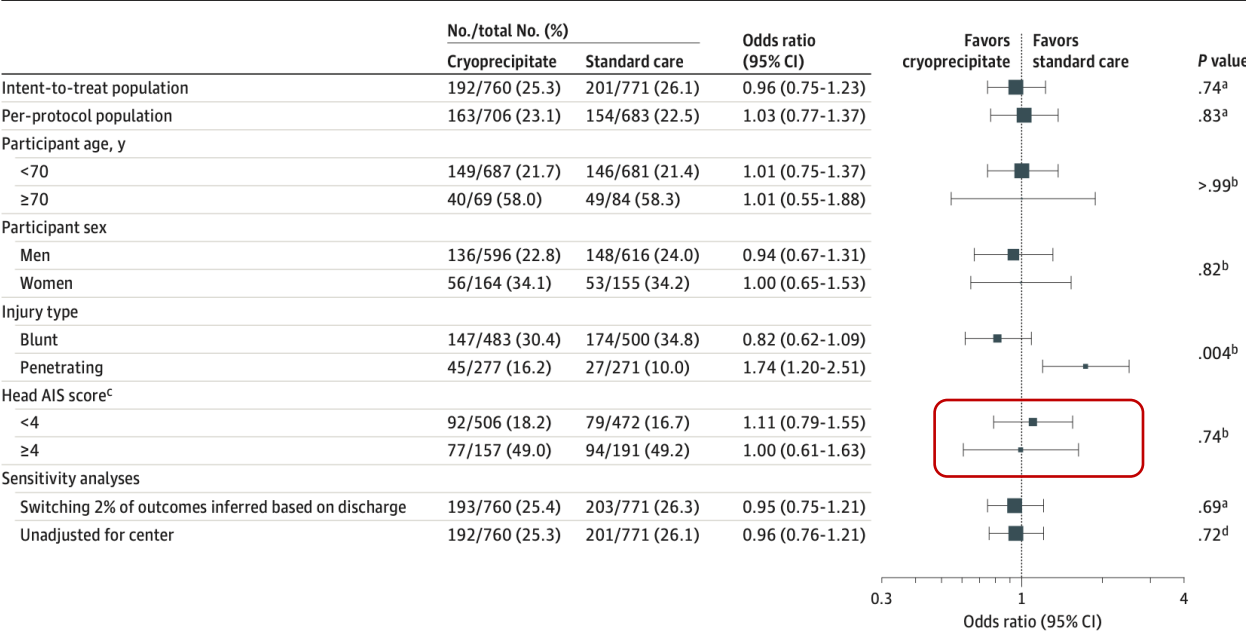
DESIGN, SETTING, AND PARTICIPANTS CRYOSTAT-2 was an interventional, randomized, open-label, parallel-group controlled, international, multicenter study. Patients were enrolled at 26 UK and US major trauma centers from August 2017 to November 2021. Eligible patients were injured adults requiring activation of the hospital's major hemorrhage protocol with evidence of active hemorrhage, systolic blood pressure less than 90 mm Hg at any time, and receiving at least 1 U of a blood component transfusion.

INTERVENTION Patients were randomly assigned (in a 1:1 ratio) to receive standard care, which was the local major hemorrhage protocol (reviewed for guideline adherence), or cryoprecipitate, in which 3 pools of cryoprecipitate (6-g fibrinogen equivalent) were to be administered in addition to standard care within 90 minutes of randomization and 3 hours of injury.

RESULTS Among 1604 eligible patients, 799 were randomized to the cryoprecipitate group and 805 to the standard care group. Missing primary outcome data occurred in 73 patients (principally due to withdrawal of consent) and 1531 (95%) were included in the primary analysis population. The median (IQR) age of participants was 39 (26-55) years, 1251 (79%) were men, median (IQR) Injury Severity Score was 29 (18-43), 36% had penetrating injury, and 33% had systolic blood pressure less than 90 mm Hg at hospital arrival. All-cause 28-day mortality in the intention-to-treat population was 26.1% in the standard care group vs 25.3% in the cryoprecipitate group (odds ratio, 0.96 [95% CI, 0.75-1.23]; $P = .74$). There was no difference in safety outcomes or incidence of thrombotic events in the standard care vs cryoprecipitate group (12.9% vs 12.7%).

CONCLUSIONS AND RELEVANCE Among patients with trauma and bleeding who required activation of a major hemorrhage protocol, the addition of early and empirical high-dose cryoprecipitate to standard care did not improve all cause 28-day mortality.

Figure 3. Primary Outcome Analyses of All-Cause Mortality by 28 Days



The median number of days observed was 28 days for all groups. Mortality at day 28 was analyzed as a binary outcome with odds ratios, 95% CIs, and P values reported in the results and in Figure 3.

Efficacy and Safety of Early Administration of 4-Factor Prothrombin Complex Concentrate in Patients With Trauma at Risk of Massive Transfusion

The PROCOAG Randomized Clinical Trial

RESULTS Of 4313 patients with the highest trauma level activation, 350 were eligible for emergency inclusion, 327 were randomized, and 324 were analyzed (164 in the 4F-PCC group and 160 in the placebo group). The median (IQR) age of participants was 39 (27-56) years, Injury Severity Score was 36 (26-50 [major trauma]), and admission blood lactate level was 4.6 (2.8-7.4) mmol/L; prehospital arterial systolic blood pressure was less than 90 mm Hg in 179 of 324 patients (59%), 233 patients (73%) were men, and 226 (69%) required expedient hemorrhage control. There was no statistically or clinically significant between-group difference in median (IQR) total 24-hour blood product consumption (12 [5-19] U in the 4F-PCC group vs 11 [6-19] U in the placebo group; absolute difference, 0.2 U [95% CI, -2.99 to 3.33]; $P = .72$). In the 4F-PCC group, 56 patients (35%) presented with at least 1 thromboembolic event vs 37 patients (24%) in the placebo group (absolute difference, 11% [95% CI, 1%-21%]; relative risk, 1.48 [95% CI, 1.04-2.10]; $P = .03$).

CONCLUSIONS AND RELEVANCE Among patients with trauma at risk of massive transfusion, there was no significant reduction of 24-hour blood product consumption after administration of 4F-PCC, but thromboembolic events were more common. These findings do not support systematic use of 4F-PCC in patients at risk of massive transfusion.

Key Points

Question Does 4-factor prothrombin complex concentrate (4F-PCC) reduce 24-hour blood product consumption in patients with trauma at risk of massive transfusion?

Findings In this superiority randomized trial involving 324 patients, there was no difference in total 24-hour blood product consumption among patients treated with 4F-PCC (12 U) vs placebo (11 U). More thromboembolic events occurred in the 4F-PCC group.

Meaning These findings do not support the administration of 4F-PCC in patients with trauma at risk of massive transfusion.

Prothrombin complex concentrate (PCC) for treatment of trauma-induced coagulopathy: systematic review and meta-analyses

Ioannis Hannadjas^{1†}, Arthur James^{1,2†}, Ross Davenport¹, Charlotte Lindsay¹, Karim Brohi¹ and Elaine Cole¹

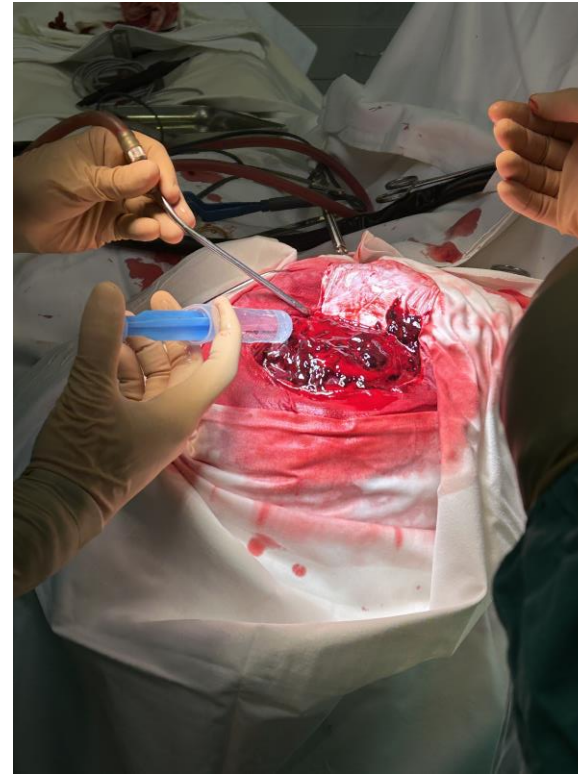
Results After removing duplicates, 1745 reports were screened and nine observational studies and one randomized controlled trial (RCT) were included, with a total of 1150 patients receiving PCC. Most studies used 4-factor-PCC with a dose of 20–30U/Kg. Among observational studies, co-interventions included whole blood ($n = 1$), fibrinogen concentrate ($n = 2$), or fresh frozen plasma ($n = 4$). Outcomes were inconsistently reported across studies with wide variation in both measurements and time points. The eight observational studies included reported mortality with a pooled odds ratio of 0.97 [95% CI 0.56–1.69], and five reported deep venous thrombosis (DVT) with a pooled OR of 0.83 [95% CI 0.44–1.57]. When pooling the observational studies and the RCT, the OR for mortality and DVT was 0.94 [95% CI 0.60–1.45] and 1.00 [95% CI 0.64–1.55] respectively.

Conclusions Among published studies of TIC, PCCs did not significantly reduce mortality, nor did they increase the risk of VTE. However, the potential thrombotic risk remains a concern that should be addressed in future studies. Several RCTs are currently ongoing to further explore the efficacy and safety of PCC.

Patient or population: Adult patients with expected trauma-induced coagulopathy						
Settings: In-hospital care						
Intervention: Patients treated with PCC						
Comparison: Patients treated without PCC						
Outcomes	Odds ratio	Anticipated absolute effects			Certainty of the evidence (GRADE)	Comments
No of participants (studies)		Without PCC	With PCC	Difference		
Mortality (8 studies, $n = 1685$)	0.94 [0.60, 1.45]	27.2%	22.4%	– 4.8%	⊕ ⊕ ⊕ ⊕ Very low ^{a,b}	May decrease in-hospital mortality
DVT (6 studies, $n = 1497$)	1.00 [0.64; 1.55]	5.3%	7.0%	+ 1.3%	⊕ ⊕ ⊕ ⊕ Very Low ^{a,c,d}	May increase DVT

Bouzat P ir bendr. PROCOAG Study Group. Efficacy and Safety of Early Administration of 4-Factor Prothrombin Complex Concentrate in Patients With Trauma at Risk of Massive Transfusion: The PROCOAG Randomized Clinical Trial. **JAMA.** 2023 Apr 25;329(16):1367-1375. Hannadjas I, James A, Davenport R, Lindsay C, Brohi K, Cole E. Prothrombin complex concentrate (PCC) for treatment of trauma-induced coagulopathy: systematic review and meta-analyses. **Crit Care.** 2023 Nov 2;27(1):422.

Not so easy to prove good...



38 YO male (GCS 5)
Isolated severe TBI (SDH)

Initial labs:

- Hb 130 g/L
- PLT $117 \times 10^9/L$
- INR 1,03
- APTT 41 s



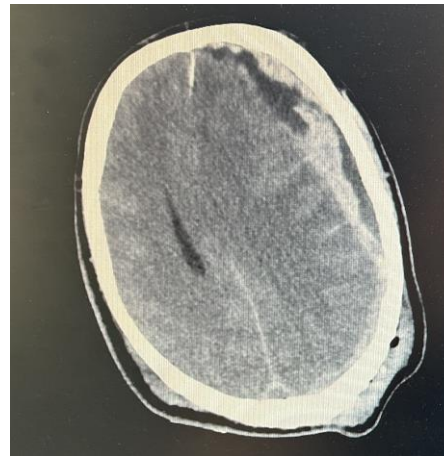
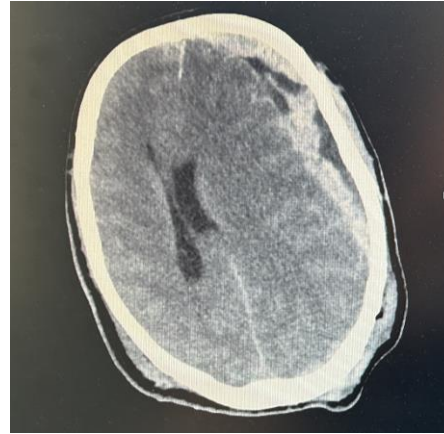
- Blood loss > 1000 ml
- FIB < 2 g/L
- Platelet dysfunction
- ROTEM MCF < 50 mm



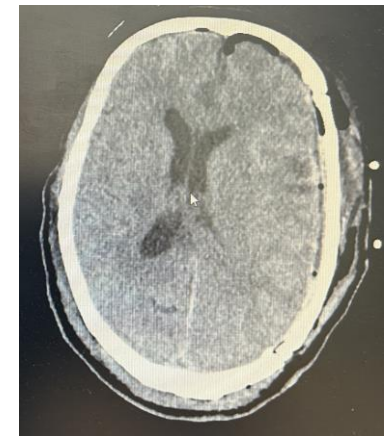
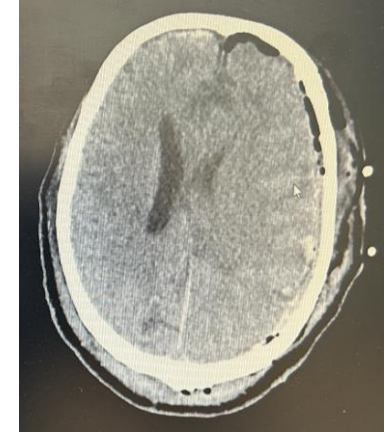
- TXA
- FC
- Pooled platelets



Before



After



Outcome: chronic vegetative state, tracheostomy, gastrostomy, etc.

Persisting headaches for the researcher...

Poor outcome of TBI is often determined by the severity of primary injury

Full extent of injury may not be visible on initial CT scans and may be falsely considered as progressive injury even if it could not have been prevented

Association between coagulopathy and mortality

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Coagulopathy causes mortality

It is still not clear whether coagulopathy is a reversible source of secondary damage,
or a marker of severe irreversible brain damage

Time course of coagulation in patients with TBI

Neurocrit Care
<https://doi.org/10.1007/s12028-022-01639-4>

NEUROCRITICAL
CARE SOCIETY

ORIGINAL WORK

Dynamic Changes of Hemostasis in Patients with Traumatic Brain Injury Undergoing Craniotomy: Association with in-Hospital Mortality

Marius Rimaitis^{1,2*}, Vaiva Cechanovičiūtė¹, Diana Bilskienė^{1,2}, Neringa Balčiūnienė^{1,3}, Rimantas Vilcinis^{1,3}, Kęstutis Rimaitis^{1,2} and Andrius Macas^{1,2}



The prevalence of CCT abnormalities

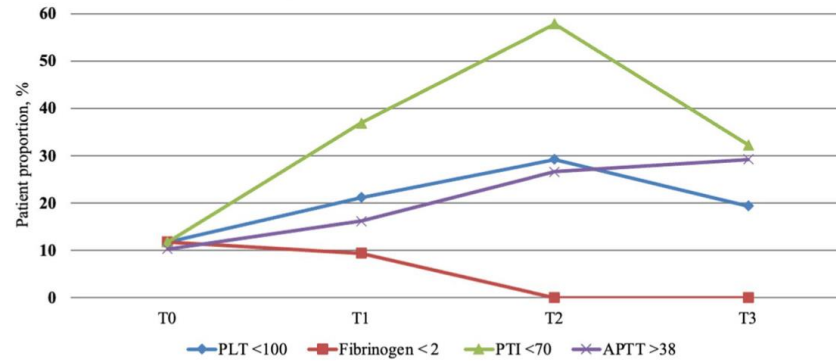


Fig. 2 The prevalence of CCT abnormalities in the perioperative period. Fibrinogen is expressed in g/L. APTT activated partial thromboplastin time (s), CCT conventional coagulation tests, PLT platelets ($10^9/L$), PTI prothrombin time index (%)

Patient coagulation status according to ROTEM in the perioperative period

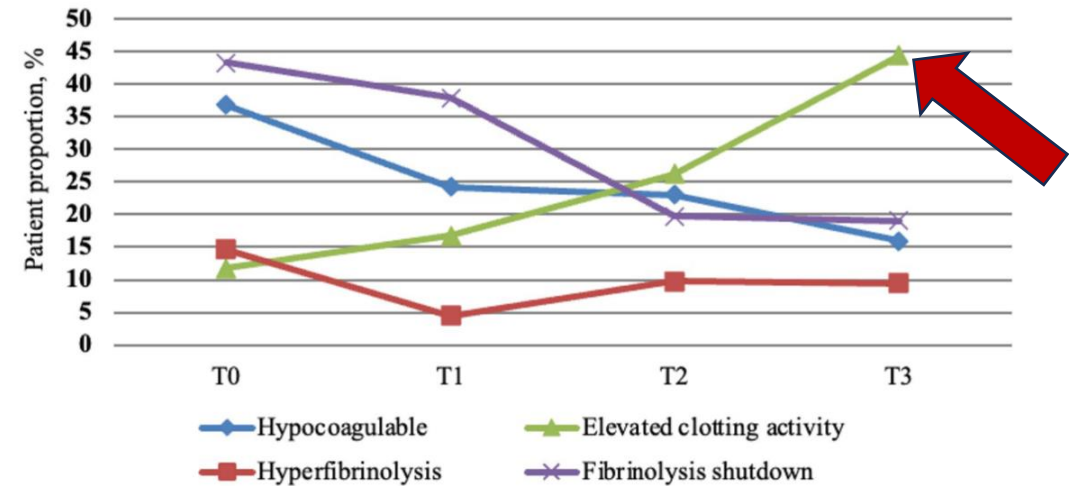


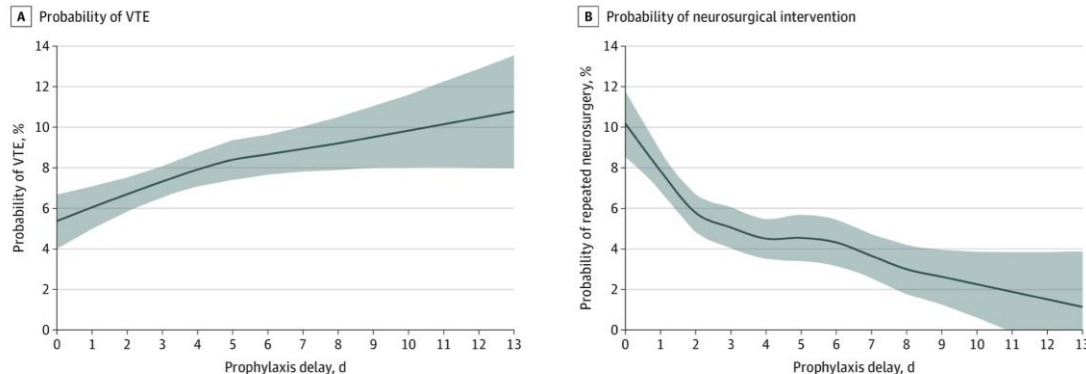
Fig. 4 Patient coagulation status according to rotational thromboelastometry in the perioperative period. ROTEM rotational thromboelastometry

A trend towards a **hypercoagulable state** following initial hypocoagulability was observed.

Prophylaxis of venous thromboembolism

Association of Venous Thromboembolism Prophylaxis After Neurosurgical Intervention for Traumatic Brain Injury With Thromboembolic Complications, Repeated Neurosurgery, and Mortality

- 5000 neurosurgical pts in 300 USA trauma centers
- 74% males, median age 50 YO.
- Craniotomy / craniectomy
- Median prophylaxis delay – 3 days (IQR 1-5)
- VTE rate – 8%, reoperation – 6%
- Earlier prophylaxis decreases VTE rate, but at the cost of increased rebleeding risk



Unadjusted Probabilities of Venous Thromboembolism (VTE) and Repeated Neurosurgery as a Function of Prophylaxis Delay



When is it safe to resume anticoagulation in traumatic brain injury?

Ireana C. Ng^a, Christopher Barnes^a, Subarna Biswas^b, David Wright^a, and Arman Dagal^a

Pharmacological prophylaxis following TBI may be started **during the first 3 days** following trauma, if stable lesion is confirmed by head CT.
***72 hours** after craniotomy, and other high-risk cases

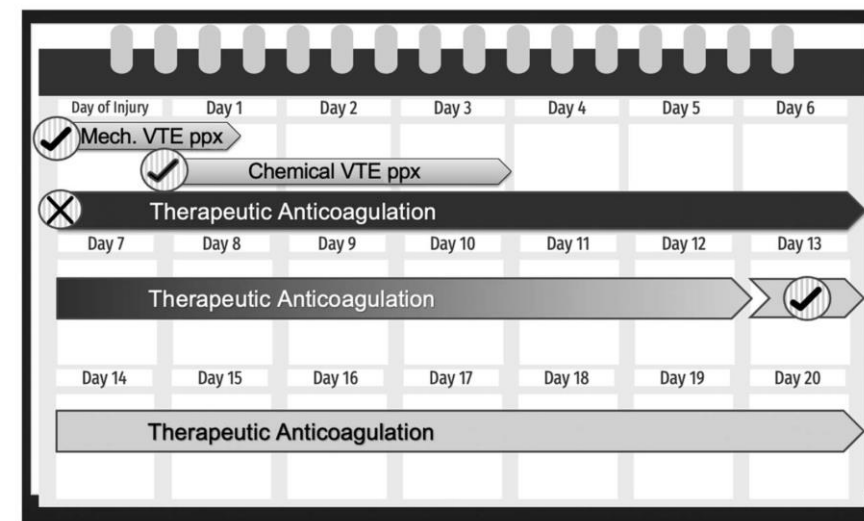
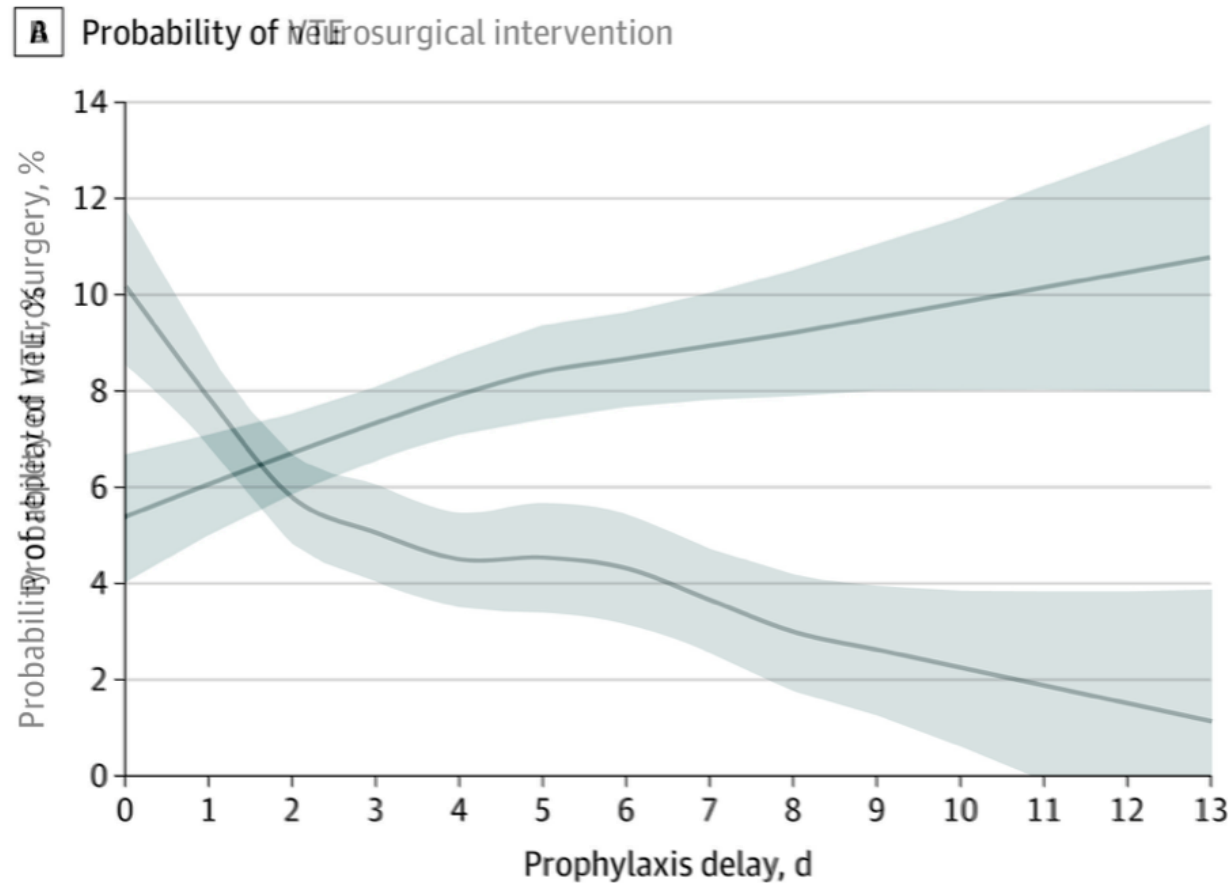


FIGURE 2. Therapeutic anticoagulation timing following TBI (Gray: safe to start VTE; Black: unsafe to start VTE). TBI, traumatic brain injury; VTE, venous thromboembolism.

VTE risk vs. Reintervention



“These findings suggest that although **timely initiation** of prophylaxis should be **prioritized**, caution should be used particularly during the first 3 days after the index procedure, when this risk appears to be highest.”

Coagulation management as a component of multimodal treatment of TBI

Anaesthesia 2022, 77 (Suppl. 1), 102-112

Wiles | Management of traumatic brain injury

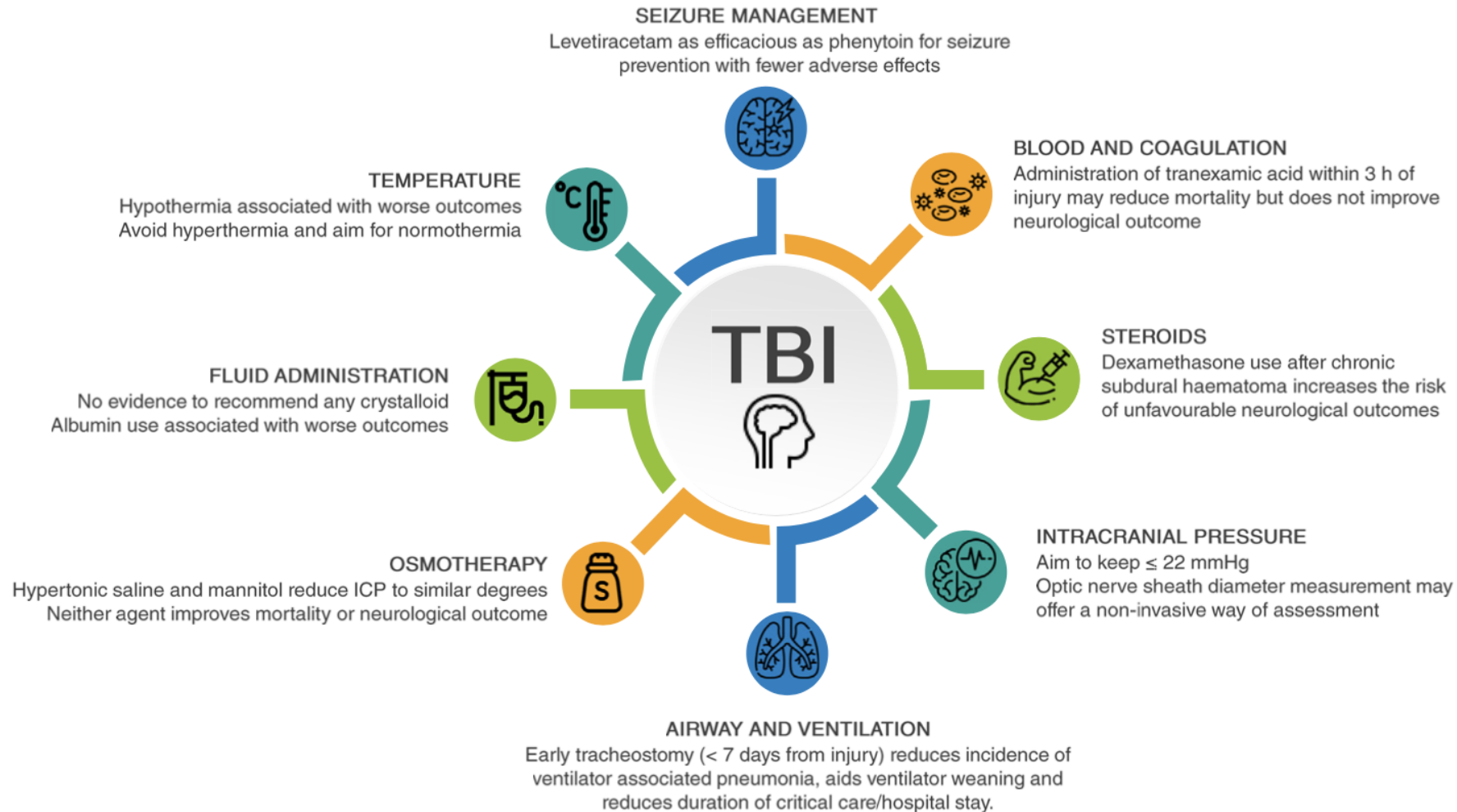


Figure 1 Summary of recent evidence-based recommendations for the management of traumatic brain injury (TBI).

Conclusions

- TBI-associated coagulopathy is prevalent and associated with progressive hemorrhagic injury and mortality
- Coagulopathy could be one of candidates to optimize TBI treatment and affect outcomes
- ROTEM based, goal-directed management of TBI patients is promising but well-organized studies are still needed
- Coagulation management is an integral component of multimodal treatment of patients with TBI

Directions for future research...

- Reach **consensus** on the **definition** of coagulopathy and TBI severity
- **Stratify patients** carefully with regard to intracranial lesion characteristics and clinical presentation
 - *Develop prediction tools to select patients who have the potential to benefit from treatment*
- **Challenge current evidence** as their quality is low
- Investigate the effect of **early coagulation support** on clinical outcomes (proper study design is a must)

Thank you!