Baltanest 2023

11th International Baltic Congress of anaesthesioogy and Intensive care

28–30 September 2023, Tartu, Estonia Estonian National Museum

The management of hemostasis and thrombosis in traumatic brain injury

Current evidence and future directions

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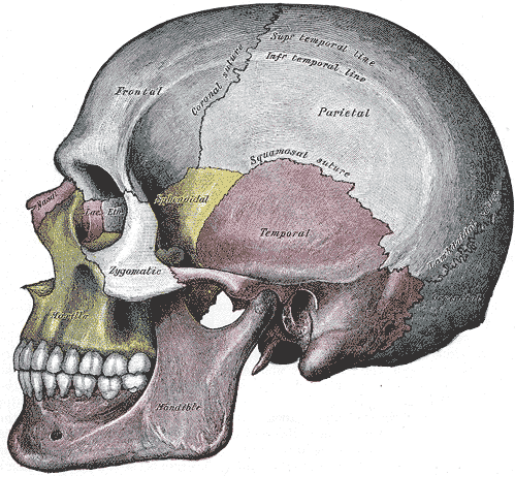
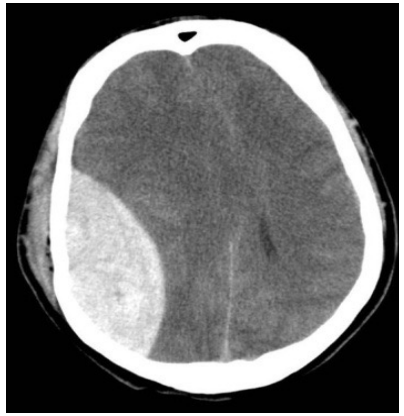
The mass effect

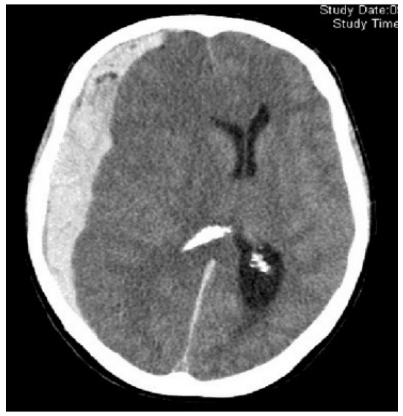
"The cranium and its constituents create a state of volume equilibrium, such that any increase in volume of one of the cranial constituents must be compensated by a decrease in volume of another." *The Monro-Kellie hypothesis*



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

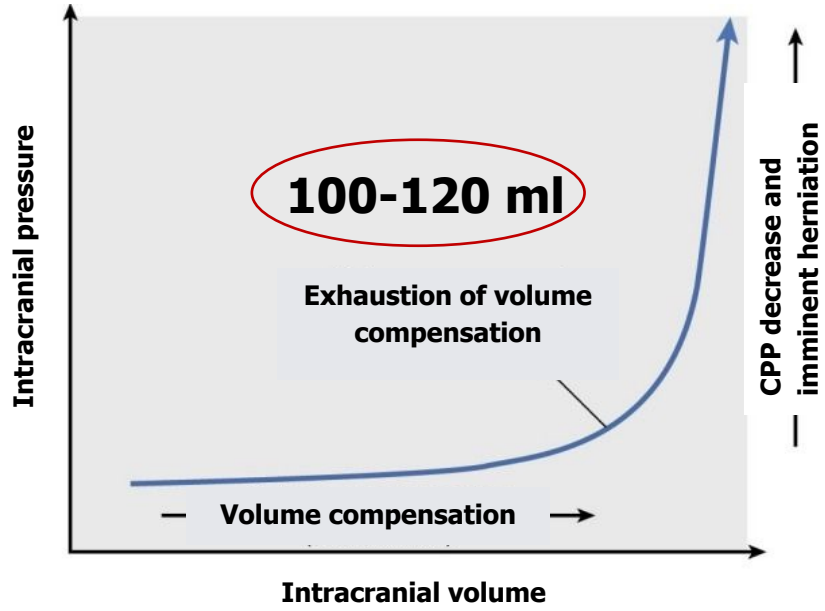


Epidural hematoma



Subdural hematoma

Volume-pressure curve in the intracranial compartment



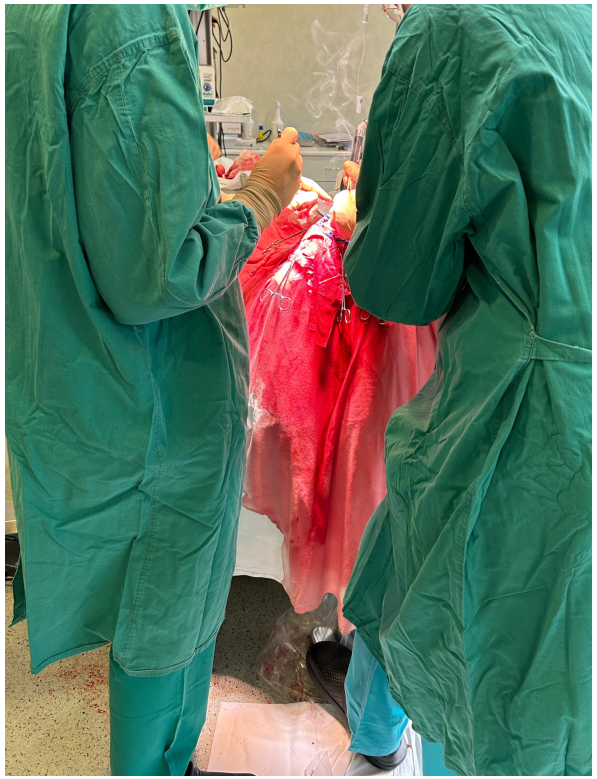
Mokri B. The Monro-Kellie hypothesis: applications in CSF volume depletion. Neurology 2001; 56: 1746–8
Miller RD et al., Miller's Anesthesia, 7th ed. Philadelphia: Churchill Livingstone, 2009.
Tameem A, Krovvidi H. Cerebral physiology. Continuing Education in Anaesthesia, Critical Care & Pain, 2013
Henry Gray (1918) Anatomy of the Human Body

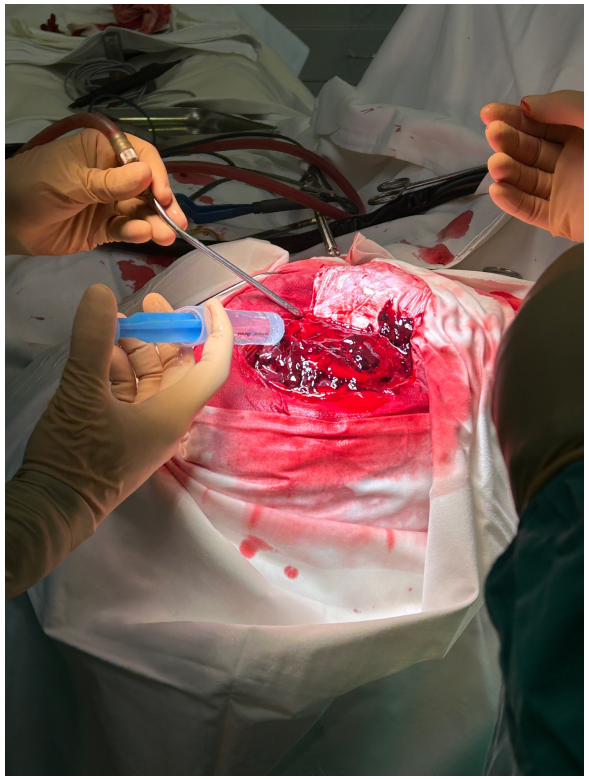
Hemostatic options in neurosurgery

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

Real-life scenario...





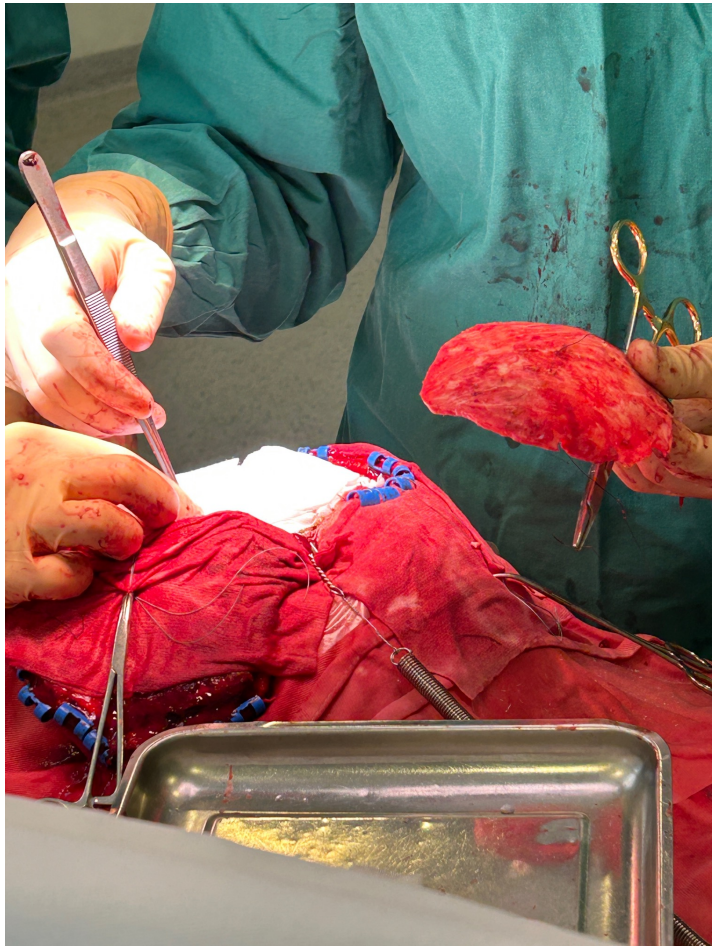
38 YO male (GCS 5)
Isolated severe TBI (SDH)

Initial labs:

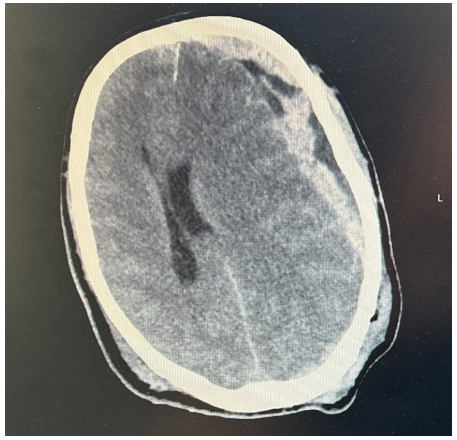
- Hb 130 g/L
- PLT 117 x 10^9/L
- INR 1,03
- APTT 41 s

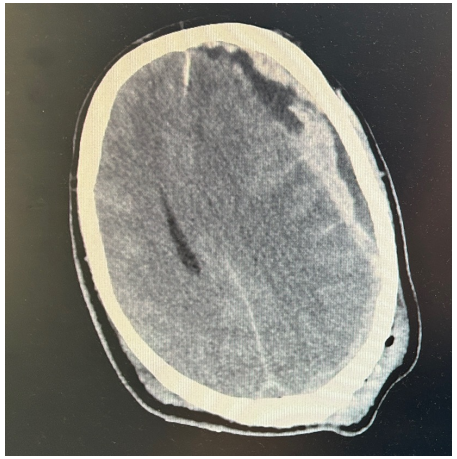
- Blood loss > 1000 ml
- FIB < 2 g/L
- Platelet dysfunction
- ROTEM MCF < 50 mm

- TXA
- FC
- Pooled platelets

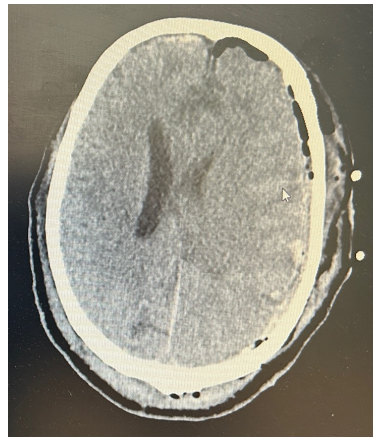


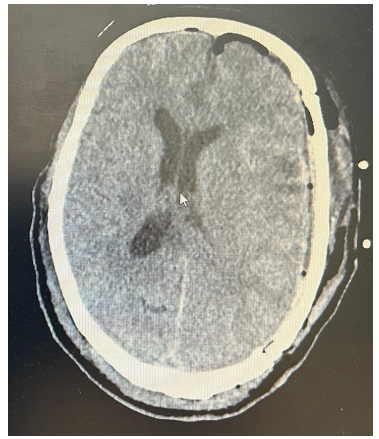
Before





After





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

TBI, coagulopathy 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

Association
IS NOT
Causation

	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]†	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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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 × 10⁹ 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**

Maegele M et al. The Lancet Neurol 2017; 16(8): 630–47.

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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...

A call for consensus among researchers!

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.

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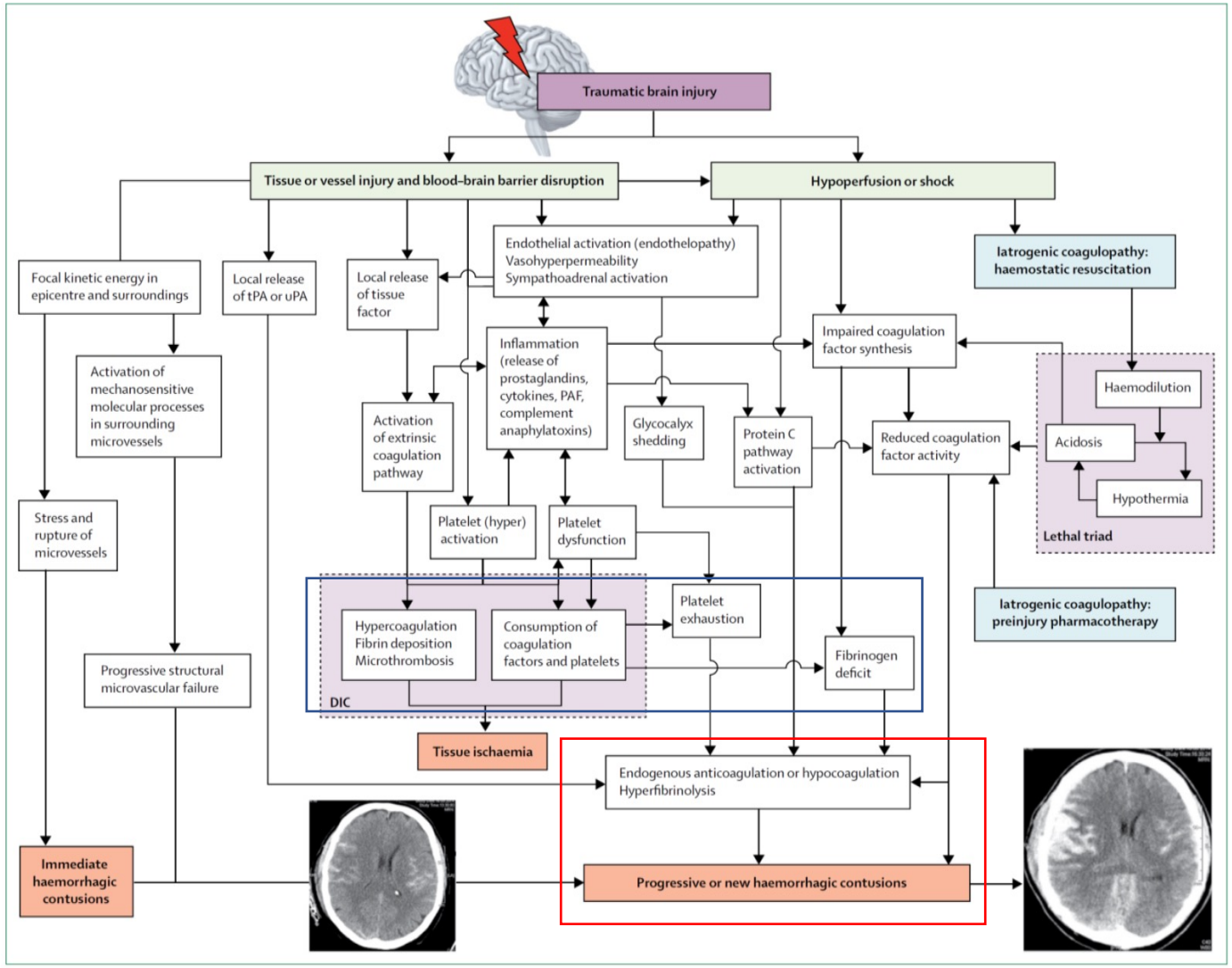
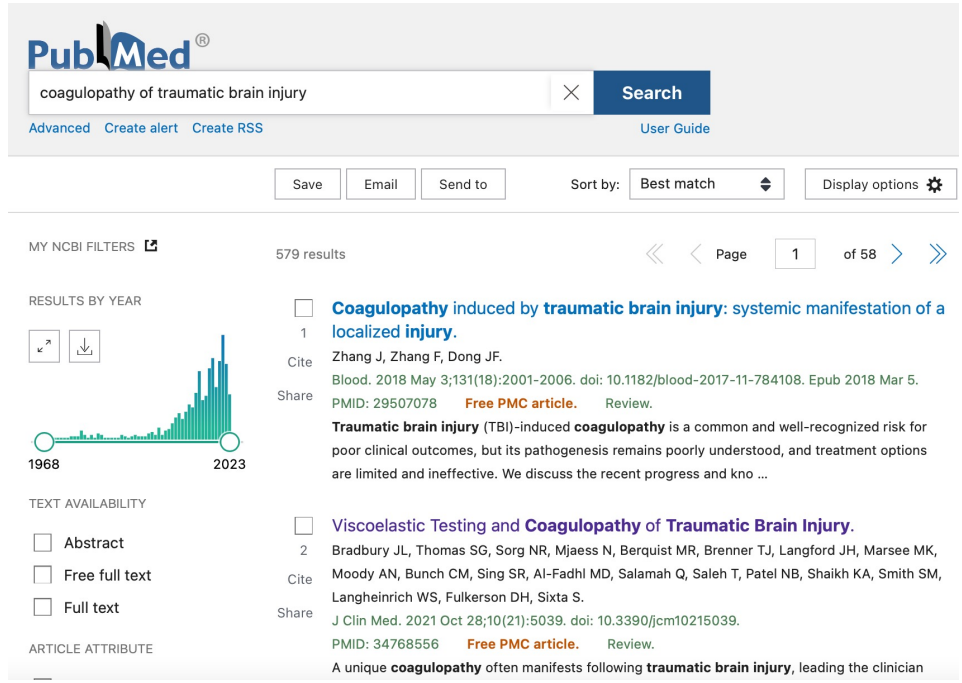
Traumatic brain injury induced cogulopathy

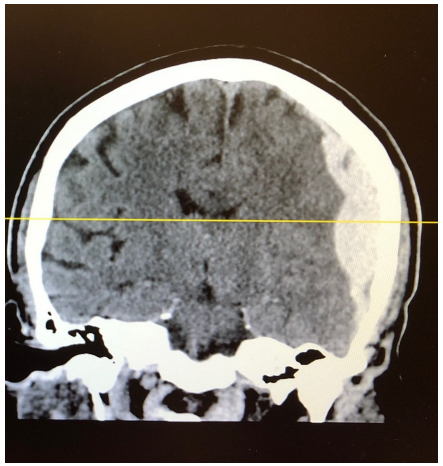


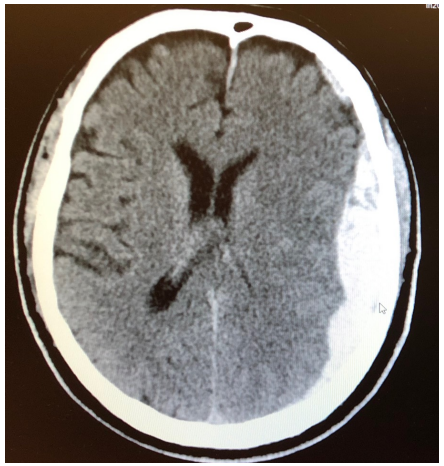
Current understanding of the mechanisms underlying coagulopathy and haemorrhagic contusions after traumatic brain injury

Apart from the mechanical force of the impact on the brain, tissue and vessel injuries including blood–brain barrier disruption trigger multiple, highly complex, interactive pathways that can result in haemostatic failure and haemorrhagic progression. Hypoperfusion and shock aggravate coagulopathy and progressive haemorrhagic contusions via endotheliopathy and activation of the protein C pathway, thereby promoting endogenous anticoagulation and hyperfibrinolysis. Loss, consumption, dilution, and dysfunction of coagulation factors and platelets further aggravate the bleeding. Iatrogenic liberal volume resuscitation might trigger the so-called lethal triad consisting of coagulopathy, hypothermia, and acidosis. Understanding of mechanisms is based on multiple sources DIC=disseminated intravascular coagulation. PAF=platelet-activating factor. tPA=tissue-type plasminogen activator. uPA=urokinase-type plasminogen activator.

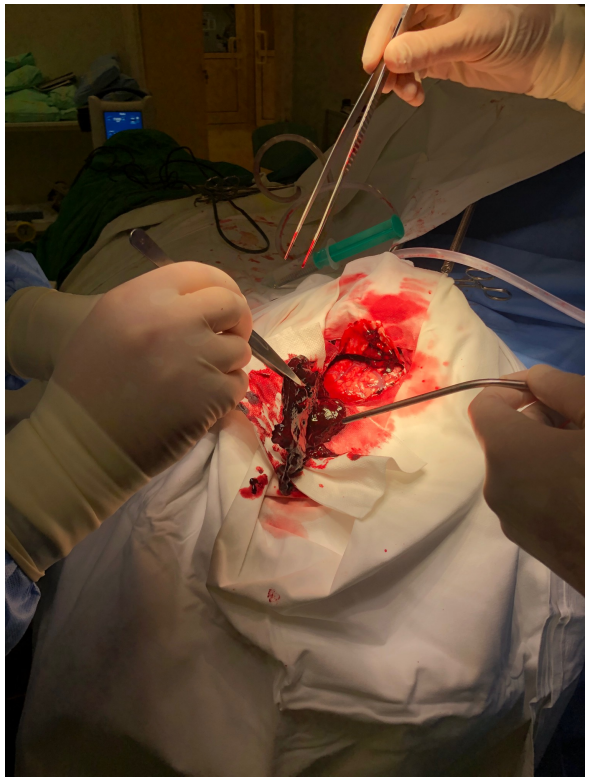


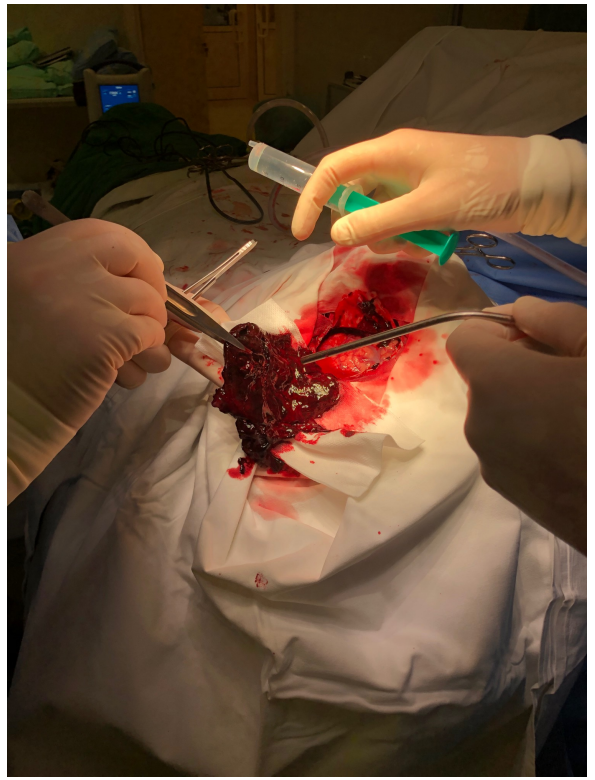
Maegele M et al. Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management. The Lancet Neurol 2017; 16(8): 630–47.





Consumptive nature of the coagulopathy?...





Coagulopathy in TBI – are we sure it is unique?

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

NEUROCRITICAL CARE SOCIETY

EXTRACRANIAL COMPLICATIONS AFTER TRAUMATIC BRAIN INJURY

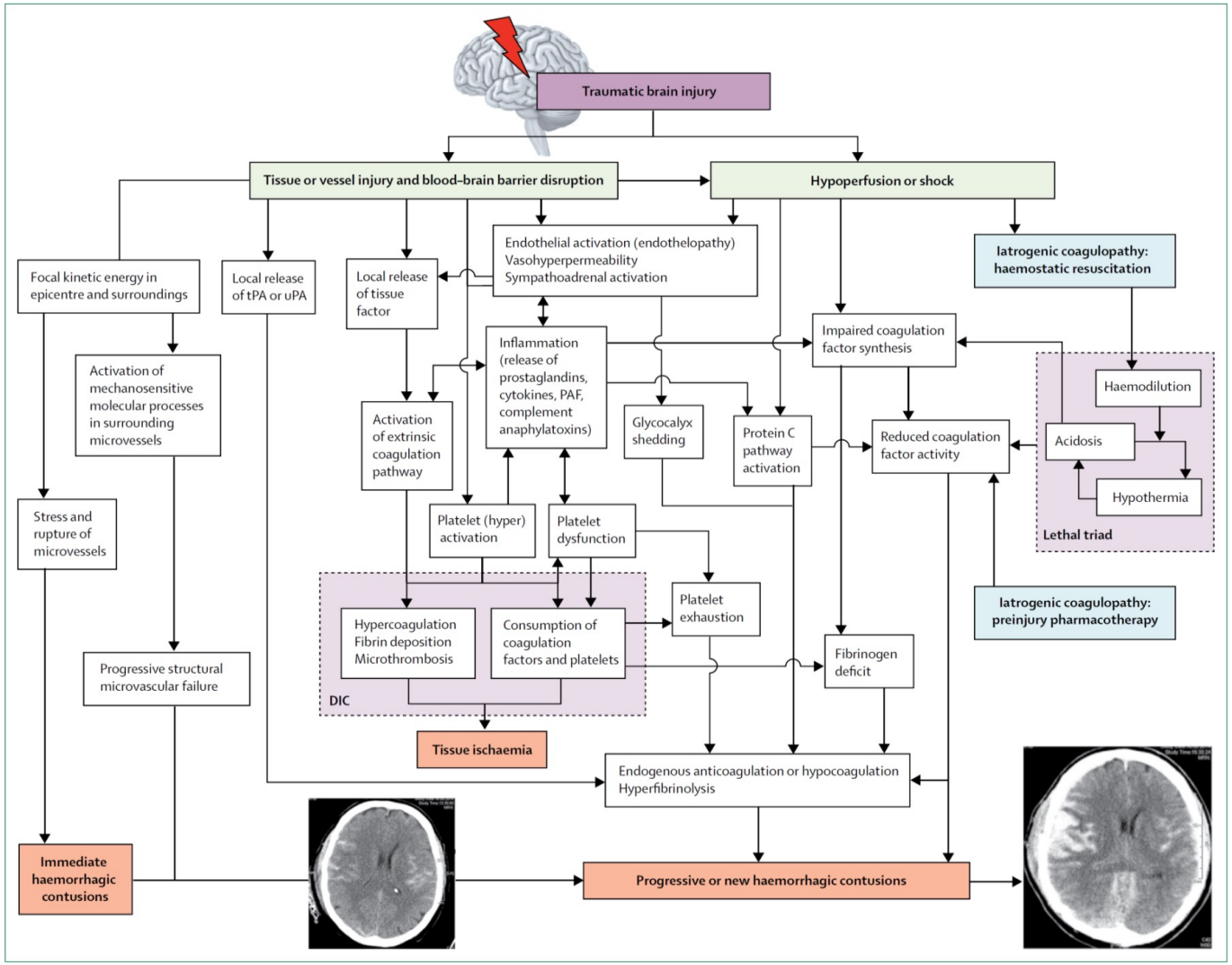
Coagulopathy in Isolated Traumatic Brain Injury: Myth or Reality

Rohan Mathur* and Jose I. Suarez

"Most likely, it is <u>not high prevalence</u> 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

Traumatic brain injury induced coagulopathy



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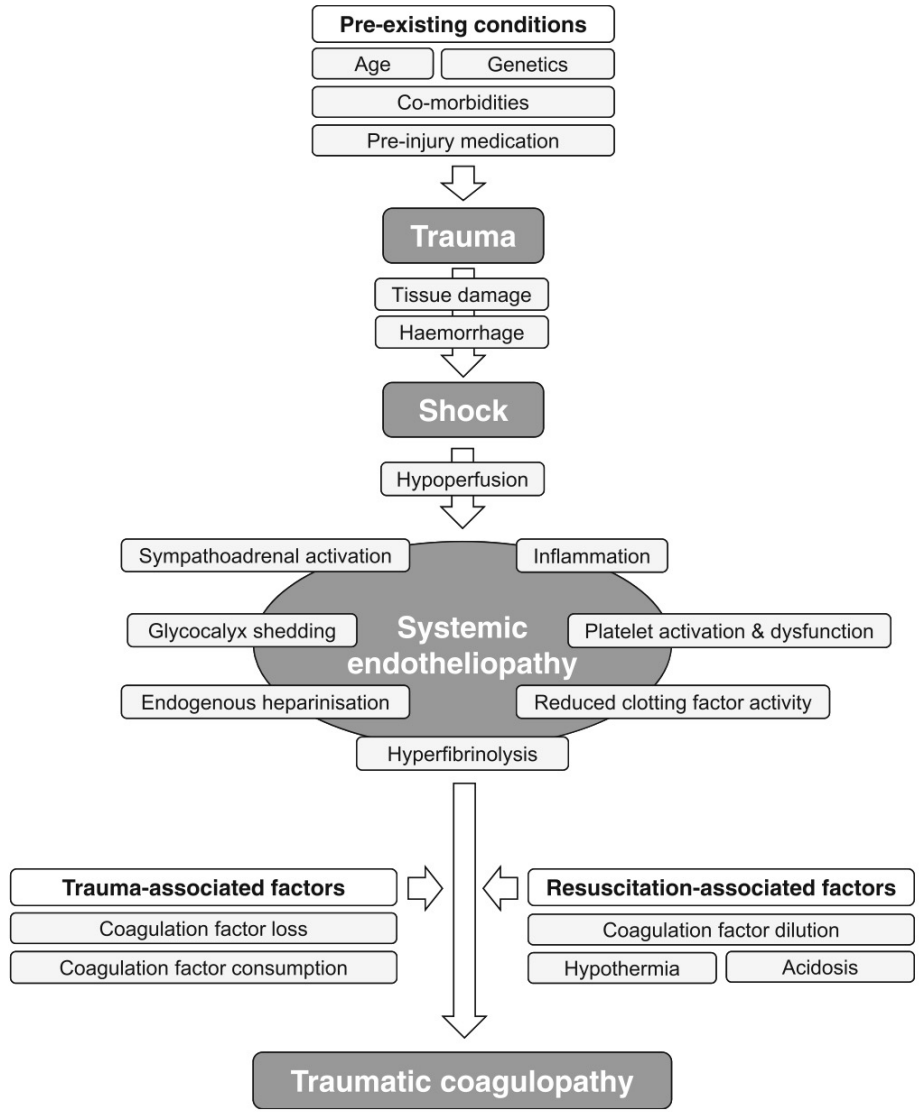
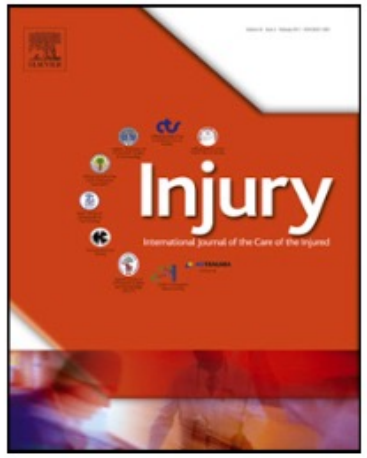


Maegele M et al. Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management. The Lancet Neurol 2017; 16(8): 630–47.
Spahn DR, Bouillon B, Cerny V, Duranteau J, Filipescu D, Hunt BJ, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care 2019 Mar 27;23(1):98-019-2347-3.

Fibrinogen is an independent predictor of mortality in major trauma patients: A five-year statewide cohort study

Zoe K. McQuilten[a,b,*], Erica M. Wood[b], Michael Bailey[a], Peter A. Cameron[c], David J. Cooper[a]

[a] Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), Monash University, Melbourne, Australia
[b] Transfusion Research Unit, Monash University, Melbourne, Australia
[c] Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia



> 4700 trauma patients (ISS > 15, ICU admission, urgent syrgery)

FIB ≤ 2 g/L – 21 %

Significant fibrinogen-associated relationship between hypofibrinogenemia and in-hospital mortality

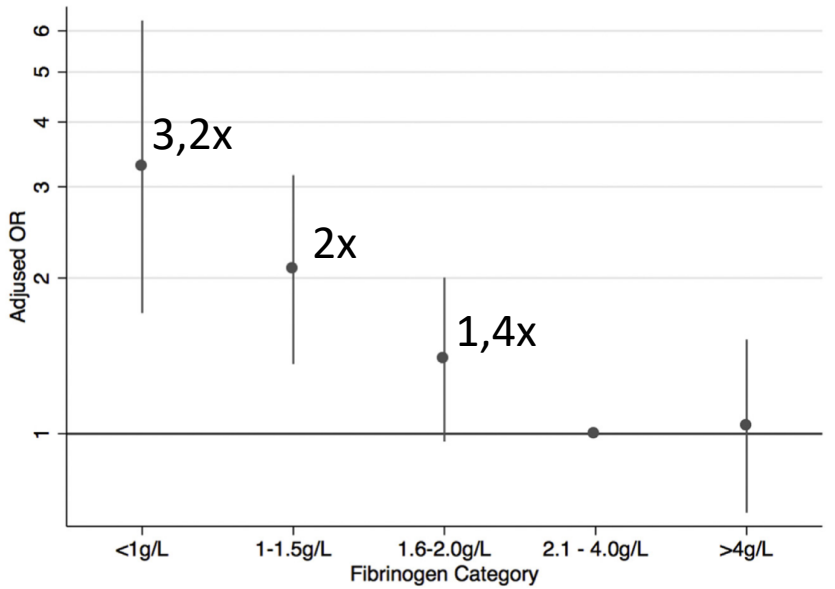
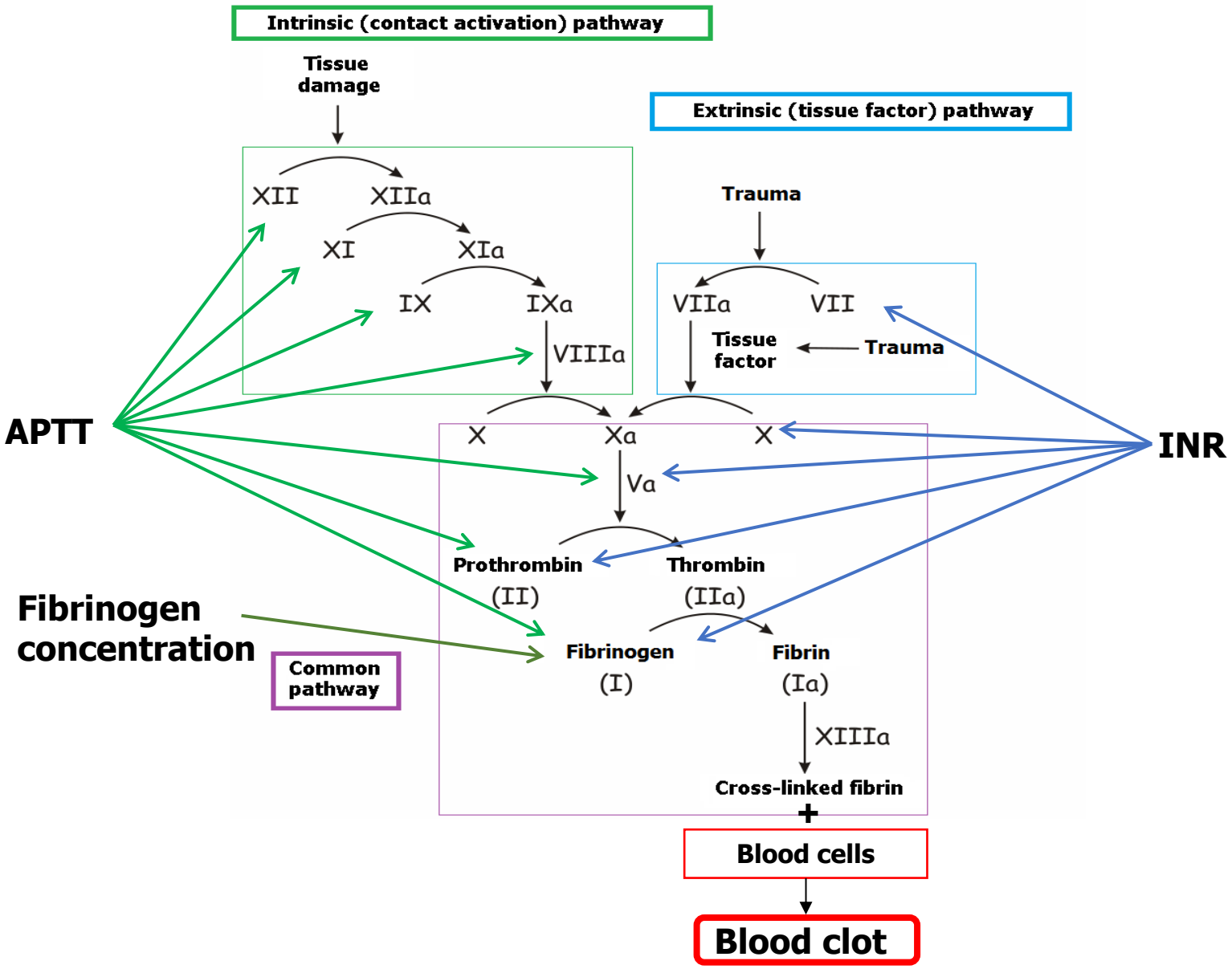


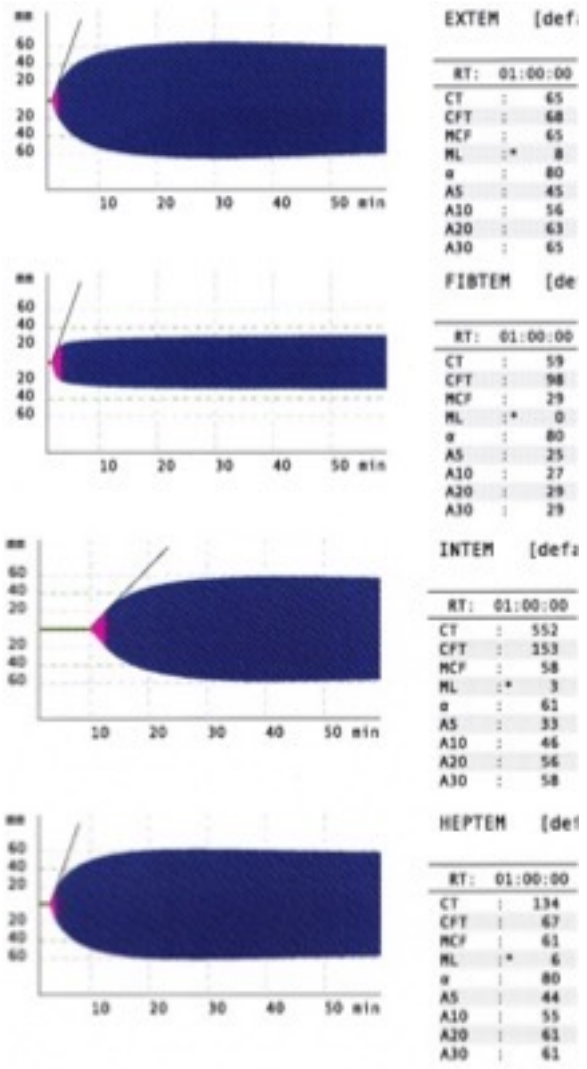
Fig. 3. Predicted adjusted mortality according to fibrinogen level on admission.
Probability of death as a function of fibrinogen level on admission, adjusted for ISS, injury type, age, GCS, pH, temperature, gender and INR. Probability shown at mean values for the other variable.

McQuilten ZK, Wood EM, Bailey M, Cameron PA, Cooper DJ. Fibrinogen is an independent predictor of mortality in major trauma patients: A five-year statewide cohort study. Injury. 2017 May;48(5):1074-1081.

Classic coagulation cascade and coagulation tests

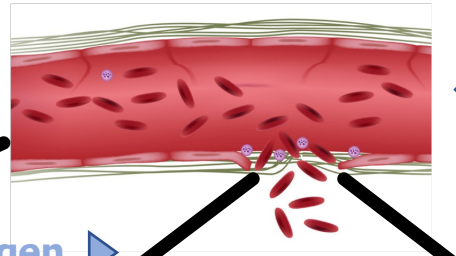


ROTEM



Horsti J. Agreement of Owren and Quick Prothrombin Times: Effects of Citrate and Calcium Concentrations and International Sensitivity Index Correction. Clinical Chemistry 2001;47(5):940–944.

Current understanding of hemostasis



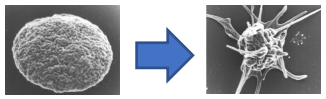
Vascular wall injury

collagen

tissue factor

vasoconstriction

platelet activaion



coagulation cascade

antithrombotic control mechanisms

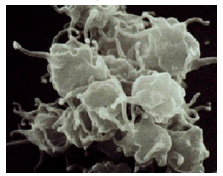
vWF, fibrinogen

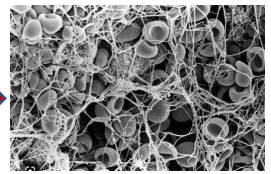
thrombin

fibrinogen

fibrin

plasmin





fibrinolysis and clot dissolution

platelet plug

blood clot

primary hemostasis

secondary hemostasis

https://healthjade.net/hemostasis/

Management of acute moderate and severe traumatic brain injury

Author: Venkatakrishna Rajajee, MBBS
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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.***

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

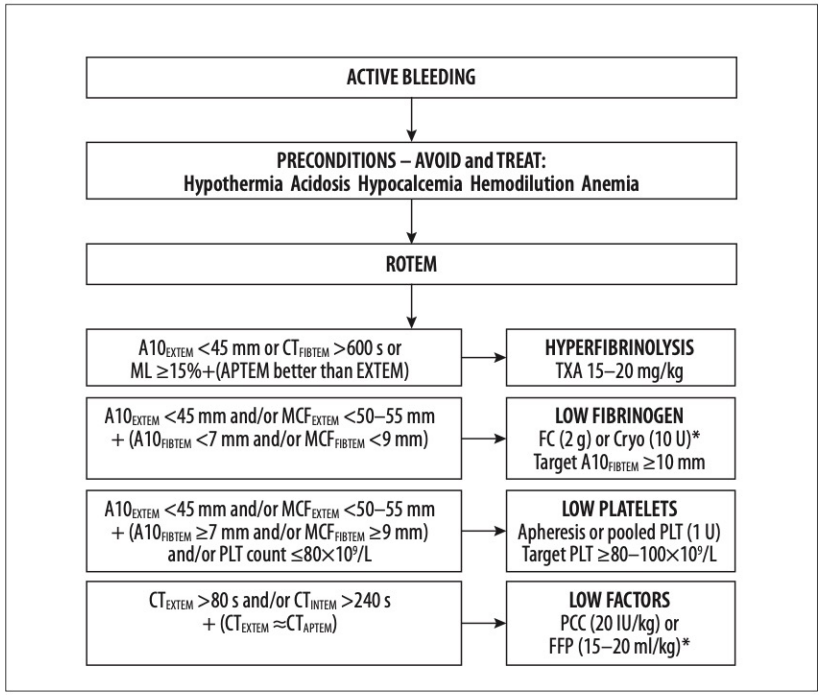
The „grey" zone...

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 (10^9/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.

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

Ongoing changes in demography and pharmacology…

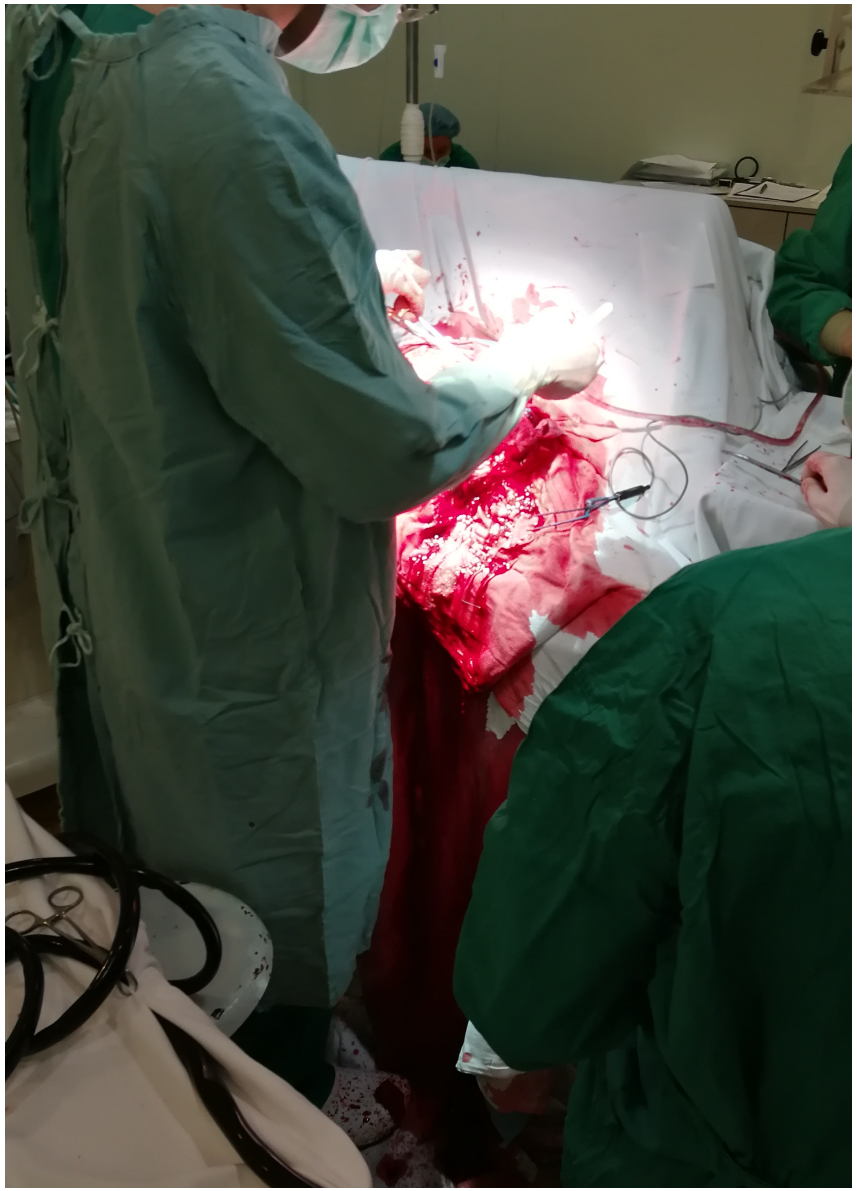
Young and high energy trauma

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

The importance of clinical awareness...

vs.



The NEW ENGLAND JOURNAL of MEDICINE

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

"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.

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 Kietaibl, 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

Cochrane Library

Cochrane Database of Systematic Reviews

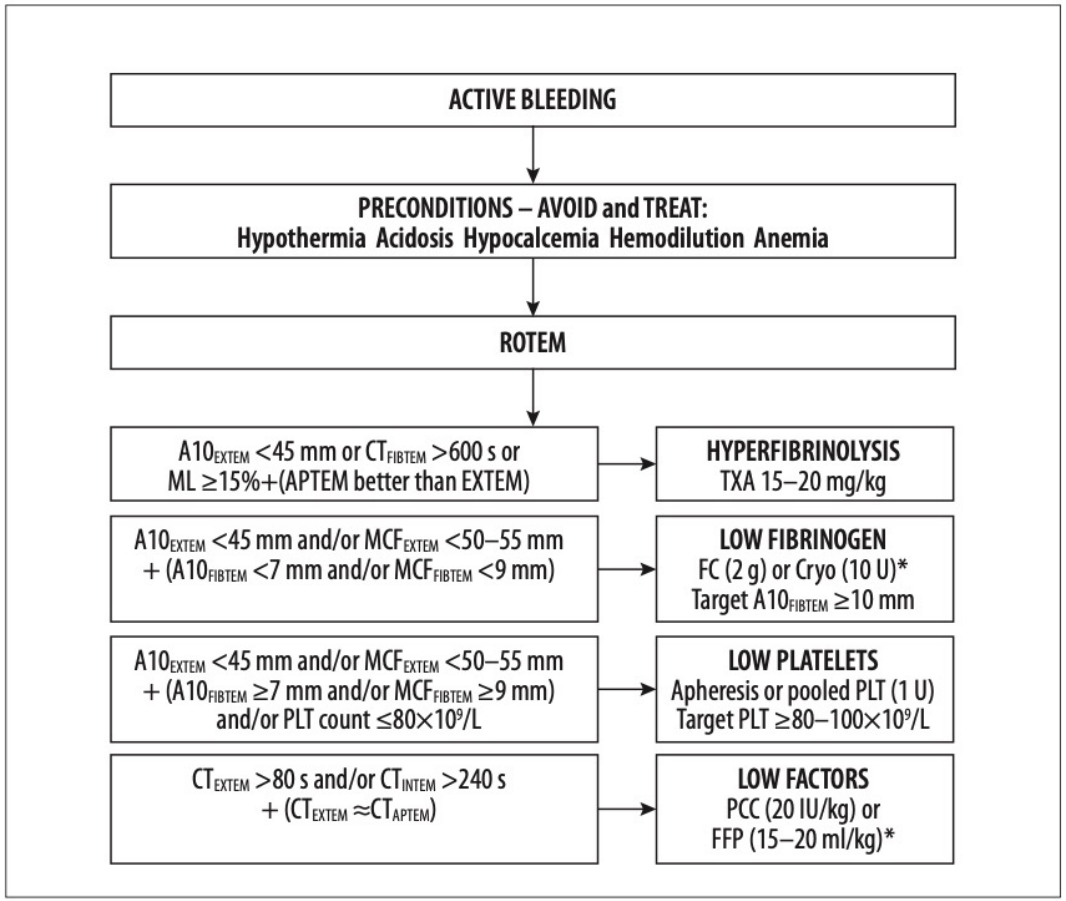
Metaanalysis:

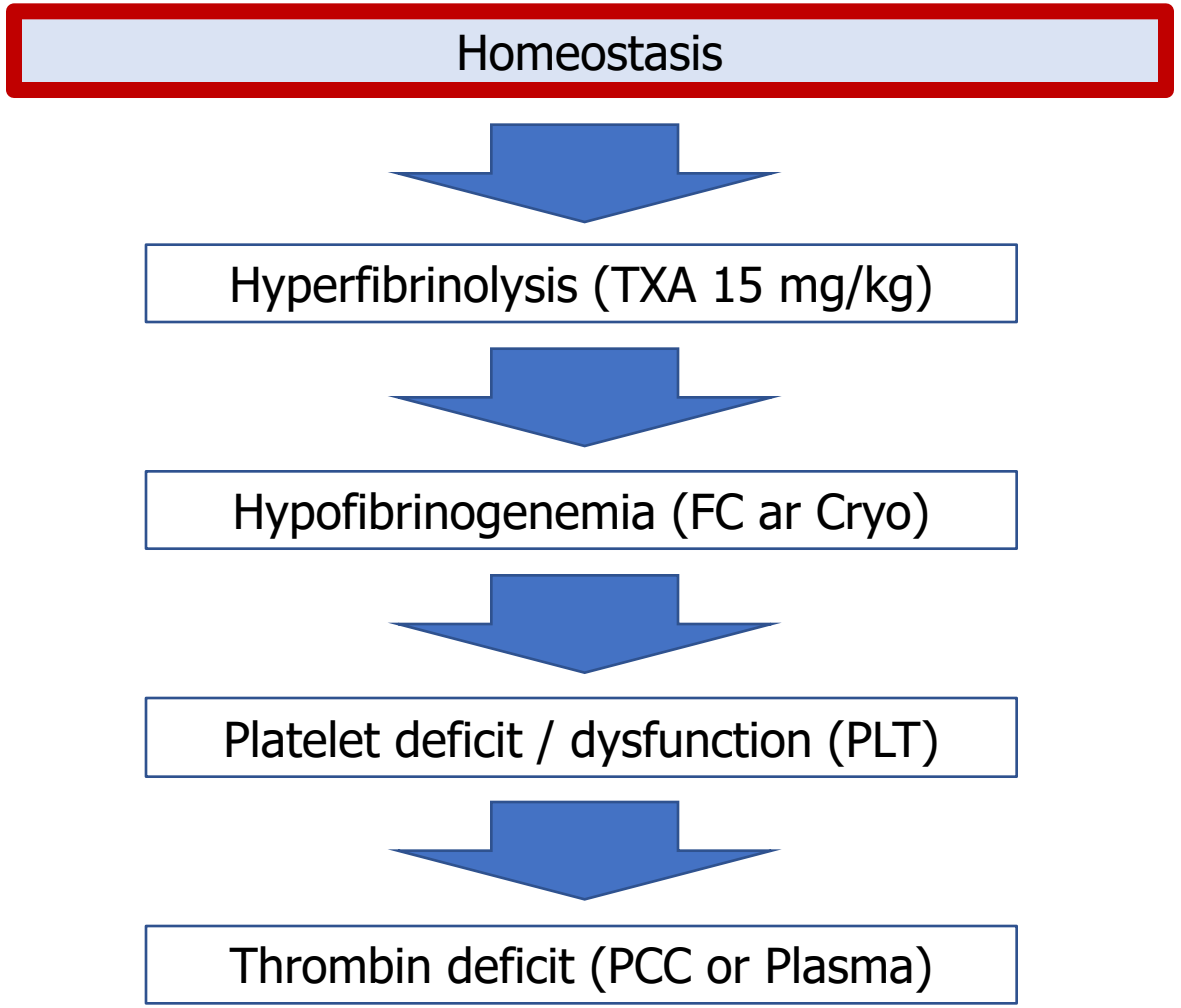
- 17 studies
- 1500 patient data

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. <<…>>

Wikkelsø A. et al. Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding. Cochrane Database Syst Rev 2016 Aug 22;2016(8): CD007871.

Goal-directed hemostatic management





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.

GUIDELINES Open Access

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

Rolf Rossaint[1*], Arash Afshari[2], Bertil Bouillon[3], Vladimir Cerny[4,5], Diana Cimpoesu[6], Nicola Curry[7,8], Jacques Duranteau[9], Daniela Filipescu[10], Oliver Grottke[1], Lars Grønlykke[11], Anatole Harrois[9], Beverley J. Hunt[12], Alexander Kaserer[13], Radko Komadina[14], Mikkel Herold Madsen[2], Marc Maegele[15], Lidia Mora[16], Louis Riddez[17], Carolina S. Romero[18], Charles-Marc Samama[19], Jean-Louis Vincent[20], Sebastian Wiberg[11] and Donat R. Spahn[13]

Two currently coexisting strategies

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).

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

Material/Methods: A prospective, case-control study was performed. Adult patients with isolated TBI requiring craniotomy were included in this study. All patients underwent standard coagulation tests (SCT). Patients were identified as either in control group or in case group. Patients in the case group were additionally tested with ROTEM to specify their coagulation status. Management of the patients in the control group was based on SCT, whereas management of patients in the case group was guided by ROTEM. Outcome measures were as follows: CP rate, protocol adhesion, blood loss, transfusions, progressive hemorrhagic injury (PHI), re-intervention, Glasgow coma score (GCS) and Glasgow outcome score (GOS) at discharge, and in-hospital mortality.

Results: There were 134 patients enrolled (65 patients in the control group and 69 patients in the case group). Twenty-six patients in the control group (40%) were found to be coagulopathic (control-CP subgroup) and 34 patients in the case group (49.3%) were found to be coagulopathic (case-CP subgroup). Twenty-five case-CP patients had ROTEM abnormalities triggering protocolized intervention, and 24 of them were treated. Overall ROTEM-based protocol adhesion rate was 85.3%. Postoperative ROTEM parameters of case-CP patients significantly improved, and the number of coagulopathic patients decreased. The incidence of PHI (control versus case group) and neurosurgical re-intervention (control-CP versus case-CP subgroup) was in favor of ROTEM guidance ($P<0.05$). Mortality and GCS and GOS at discharge did not differ significantly between groups.

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.

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.

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

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 Cechanovičiūtė[1], 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.

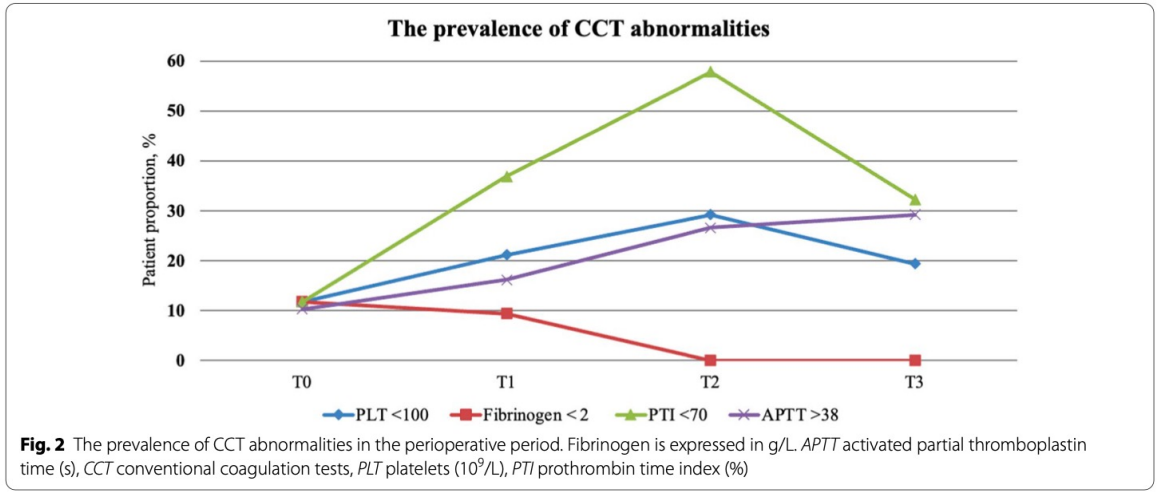


Fig. 2 The prevalence of CCT abnormalities in the perioperative period. Fibrinogen is expressed in g/L. *APTT* activated partial thromboplastin time (s), *CCT* conventional coagulation tests, *PLT* platelets (10^9/L), *PTI* prothrombin time index (%)

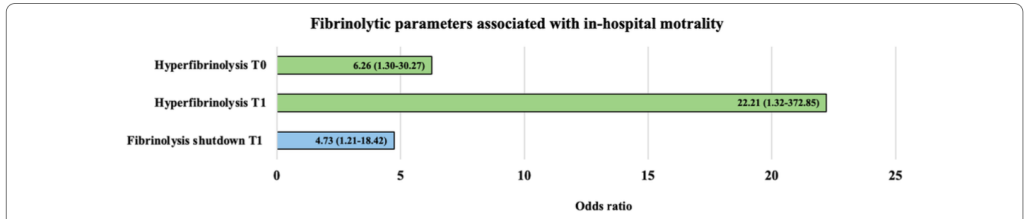


Fig. 7 Fibrinolytic parameters associated with in-hospital mortality. Data are expressed as odds ratio (95% CI). All $p < 0.05$. *CI* confidence interval

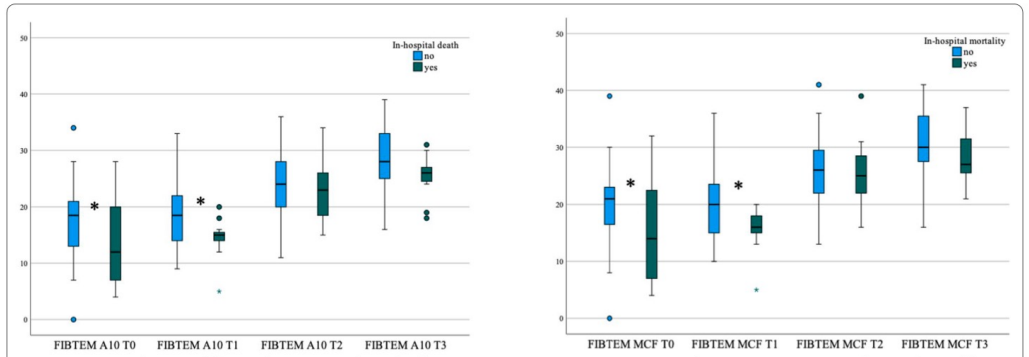


Fig. 6 Dynamic changes of fibrin polymerization thromboelastometry (FIBTEM) among survivors and nonsurvivors. *Statistically significant differences, $p < 0.05$. Boxplots represent medians, interquartile ranges, and minimum and maximum values. *A10* clot amplitude at 10 min after CT (mm), *CT* clotting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

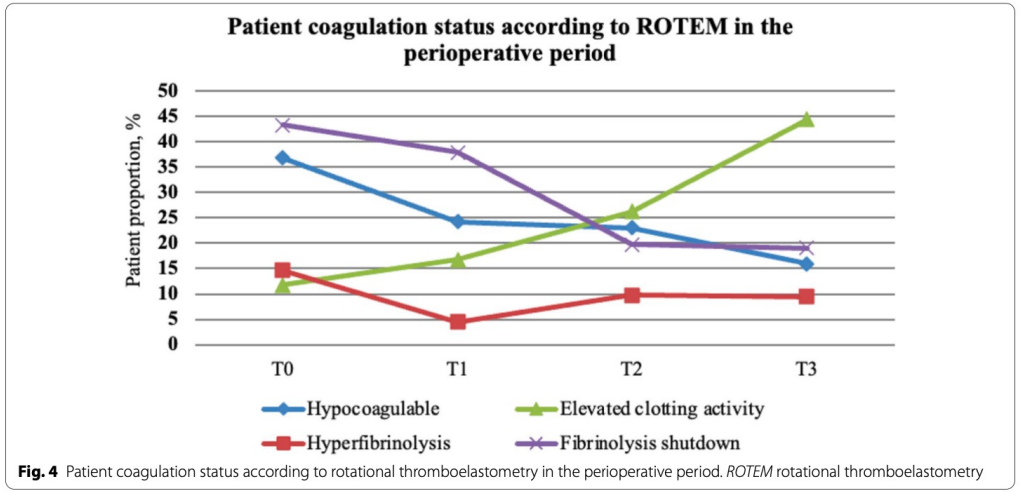


Fig. 4 Patient coagulation status according to rotational thromboelastometry in the perioperative period. *ROTEM* rotational thromboelastometry

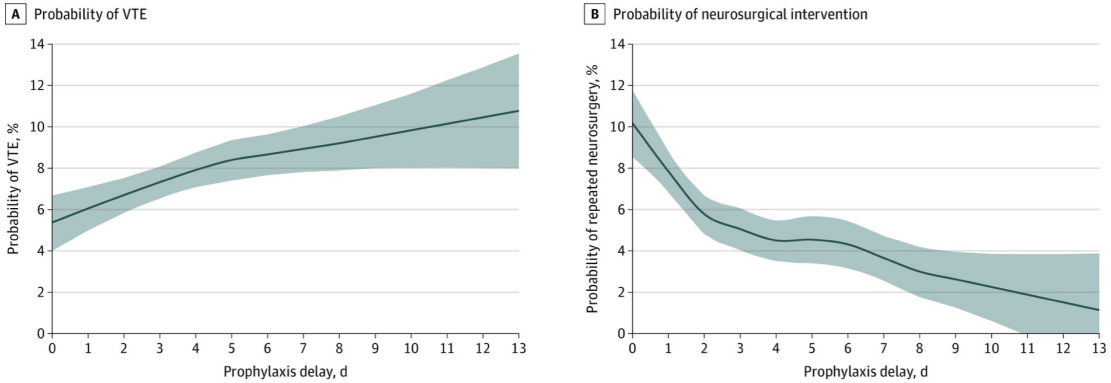
Prophylaxis of venous thromboembolism

JAMA Surg. 2022 Mar; 157(3): e215794. Published online 2021 Dec 15.
doi: 10.1001/jamasurg.2021.5794: 10.1001/jamasurg.2021.5794

PMCID: PMC8674806 | PMID: 34910096

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

- 5000 neurosurgical pts in 300 trauma centers
- Craniotomy / craniectomy
- Median prophylaxis delay 3 days
- VTE rate 8%, reintervention 6%



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]

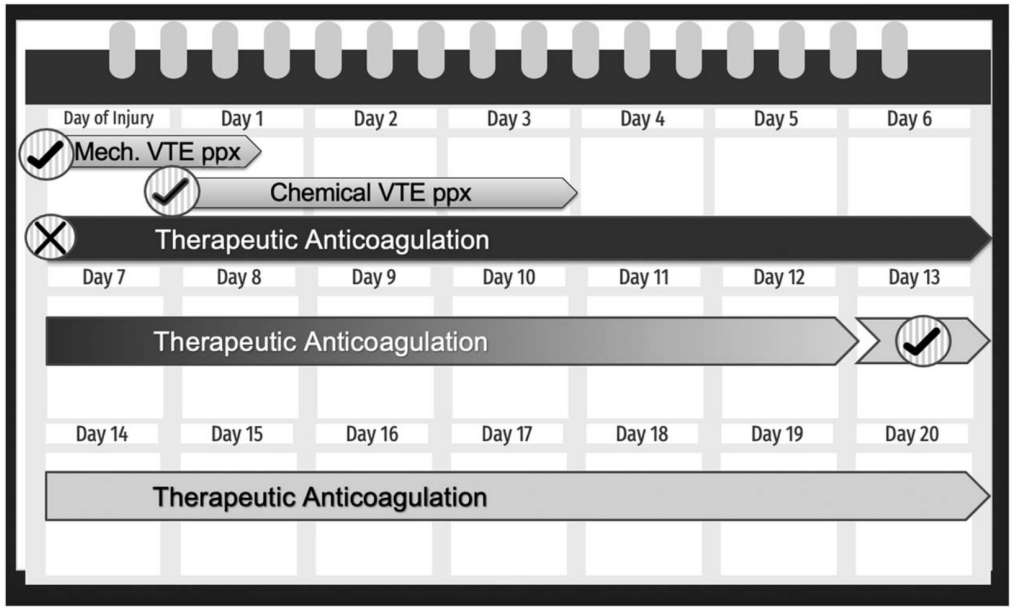


FIGURE 2. Therapeutic anticoagulation timing following TBI (Gray: safe to start VTE; Black: unsafe to start VTE). TBI, traumatic brain injury; VTE, venous thromboembolism.

Summary
Strategies and timing to start prophylactic and TAC differ significantly between institutions and physicians. Each TBI patient should be evaluated on a case-by-case basis on when to start anticoagulation. More investigation is required to guide best practice.

Ng IC, Barnes C, Biswas S, Wright D, Dagal A. When is it safe to resume anticoagulation in traumatic brain injury? Curr Opin Anaesthesiol. 2022;35(2):166-171.
Byrne JP, Witiw CD, Schuster JM et al. Association of Venous Thromboembolism Prophylaxis After Neurosurgical Intervention for Traumatic Brain Injury With Thromboembolic Complications, Repeated Neurosurgery, and Mortality. JAMA Surg. 2022;157(3):e215794.

Coagulation management as a component of multimodal treatment of TBI

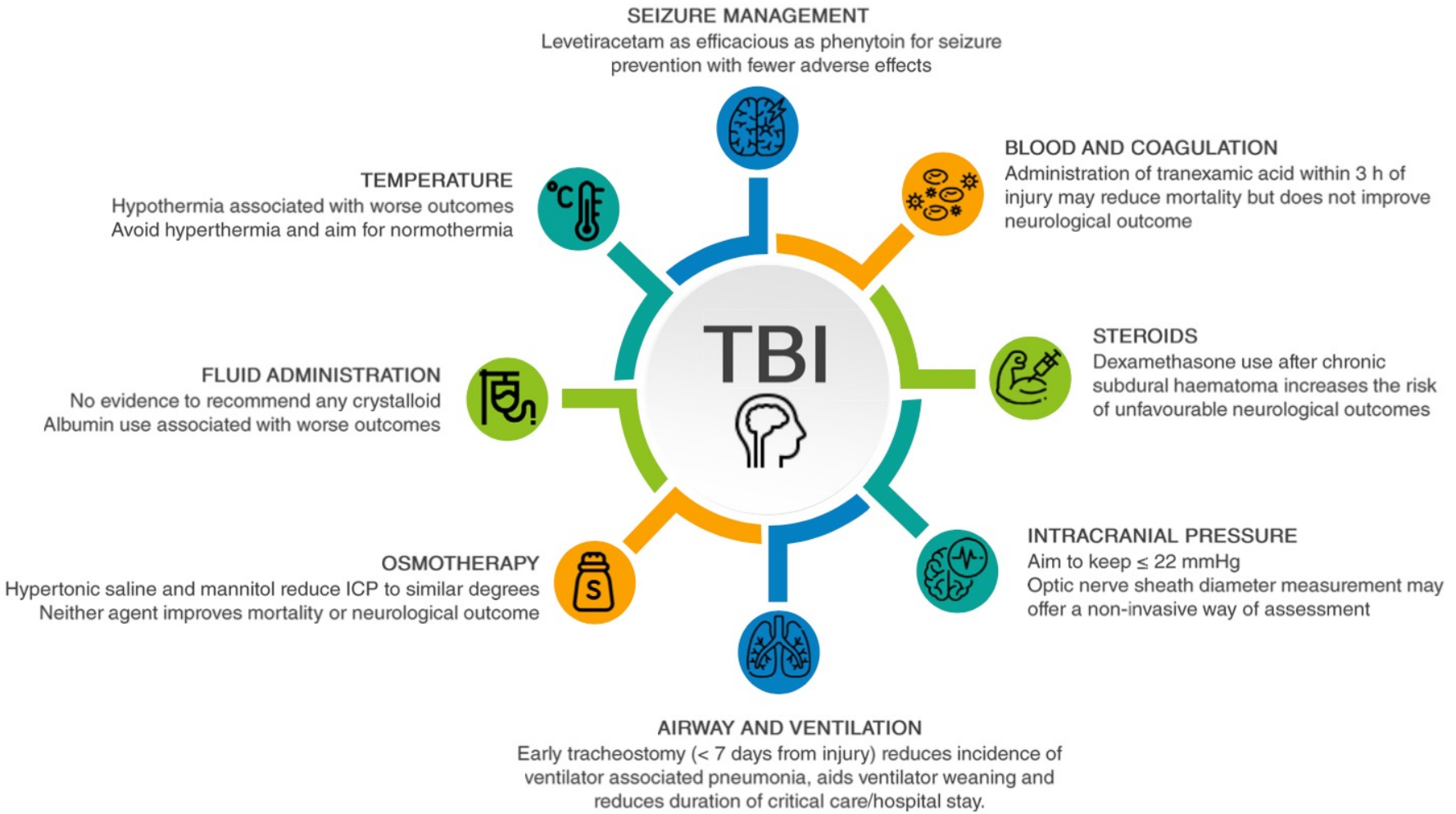


Figure 1 Summary of recent evidence-based recommendations for the management of traumatic brain injury (TBI).

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

≠

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

Conclusions

- The uniqueness of TBI-associated coagulopathy may be overestimated

  (a topic for a pro- con- debate?)

- Initial hemostatic management of patients with traumatic brain injury is based on fundamental knowlegde and contemporary guidelines

- There is no perfect blood coagulation test and clinical awareness remains of major importance in decision-making

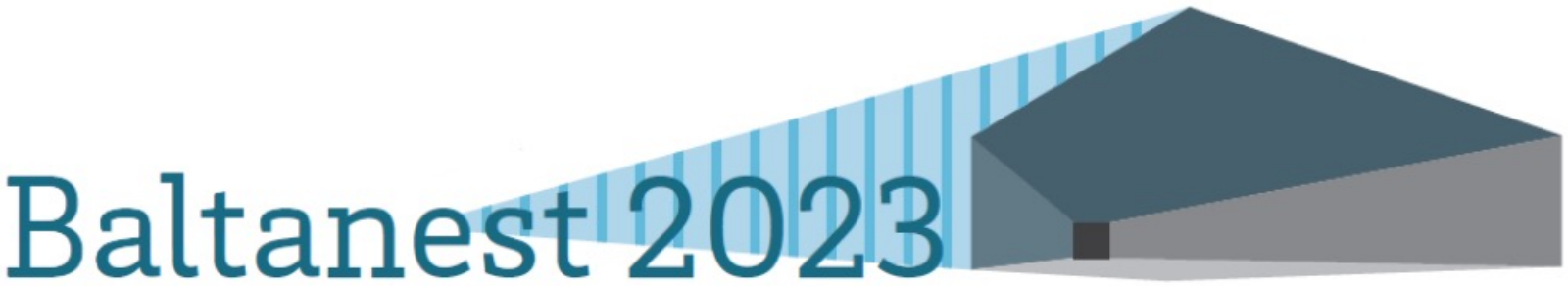
- Goal-directed coagulation management of TBI patients is promising but not yet proven to affect outcomes

- Coagulation management is an integral component of multimodal treatment of patients with TBI and should include not only procoagulant, but also consider antithrombotic measures

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!


Baltanest 2023
11th International Baltic Congress of anaesthesioogy and Intensive care
28–30 September 2023, Tartu, Estonia
Estonian National Museum