KOAGULOPATIE U PACIENTŮ S TĚŽKÝM KRANIOCEREBRÁLNÍM PORANĚNÍM

15/9/2022

XVIII. Kongres ČSARIM

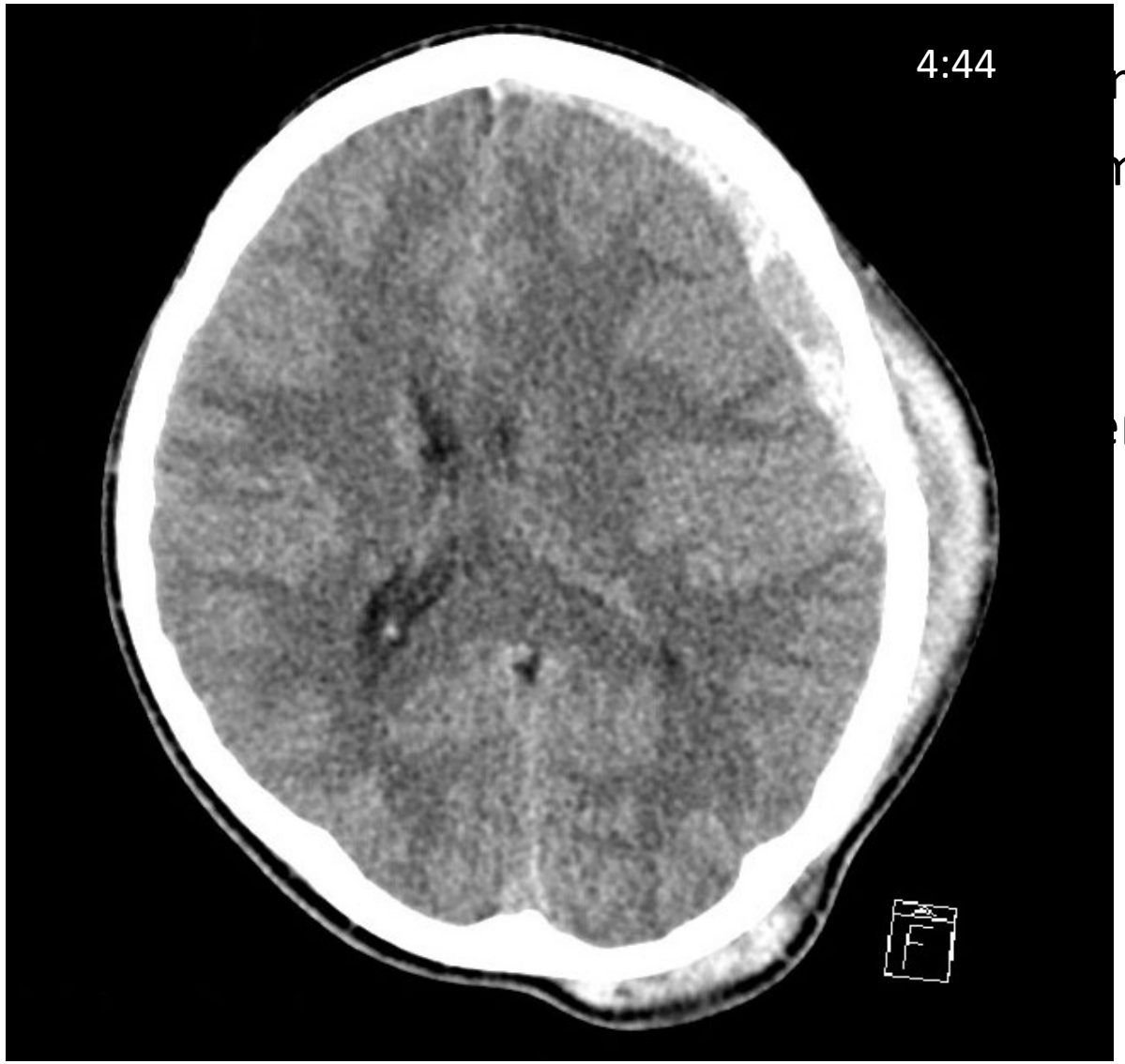
MUDr. Kamil Vrbica

Klinika anesteziologie, resuscitace a intenzivní medicíny

MUNI MED

FAKULTNÍ NEMOCNICE BRNO

Proč toto téma?



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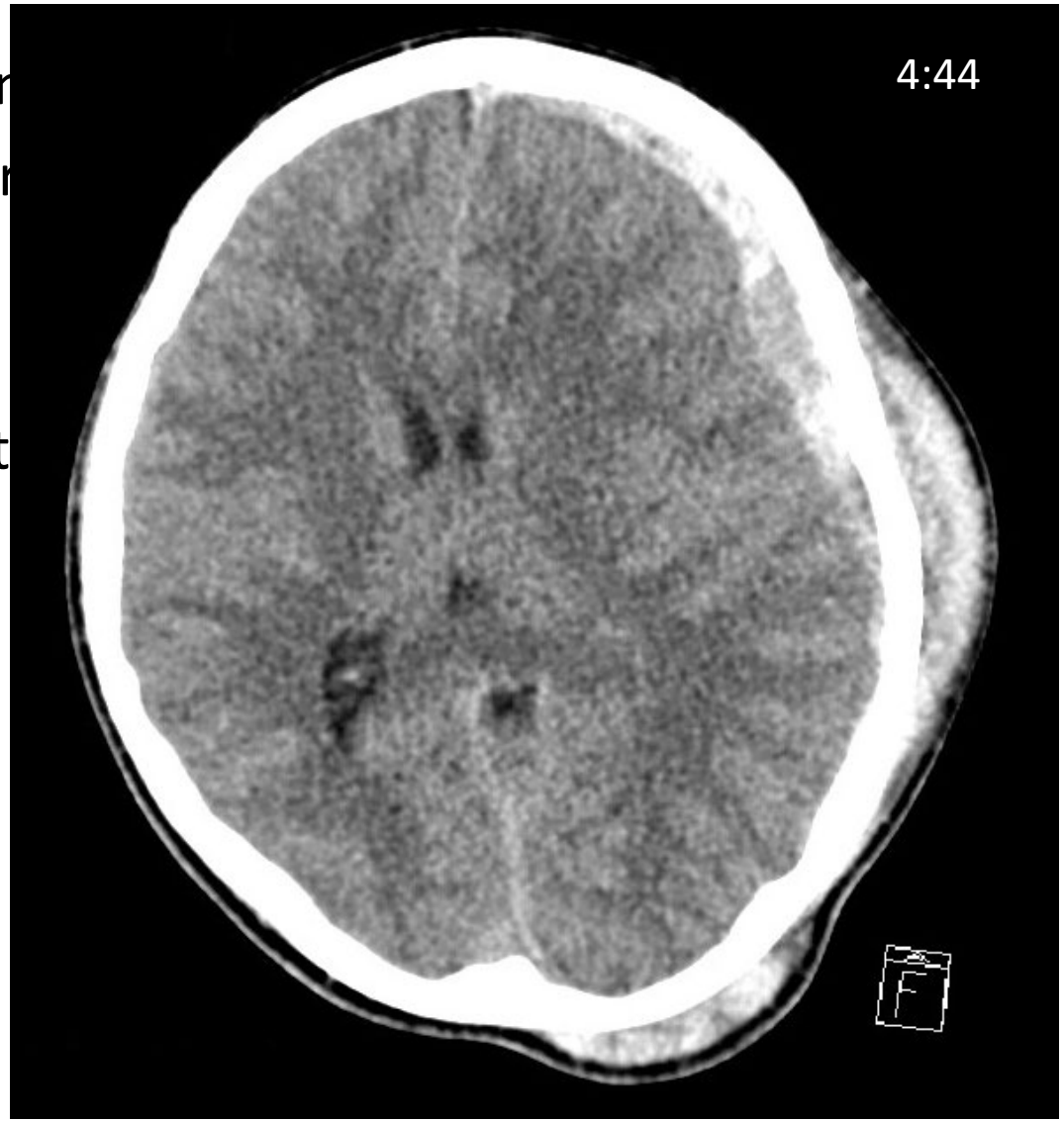
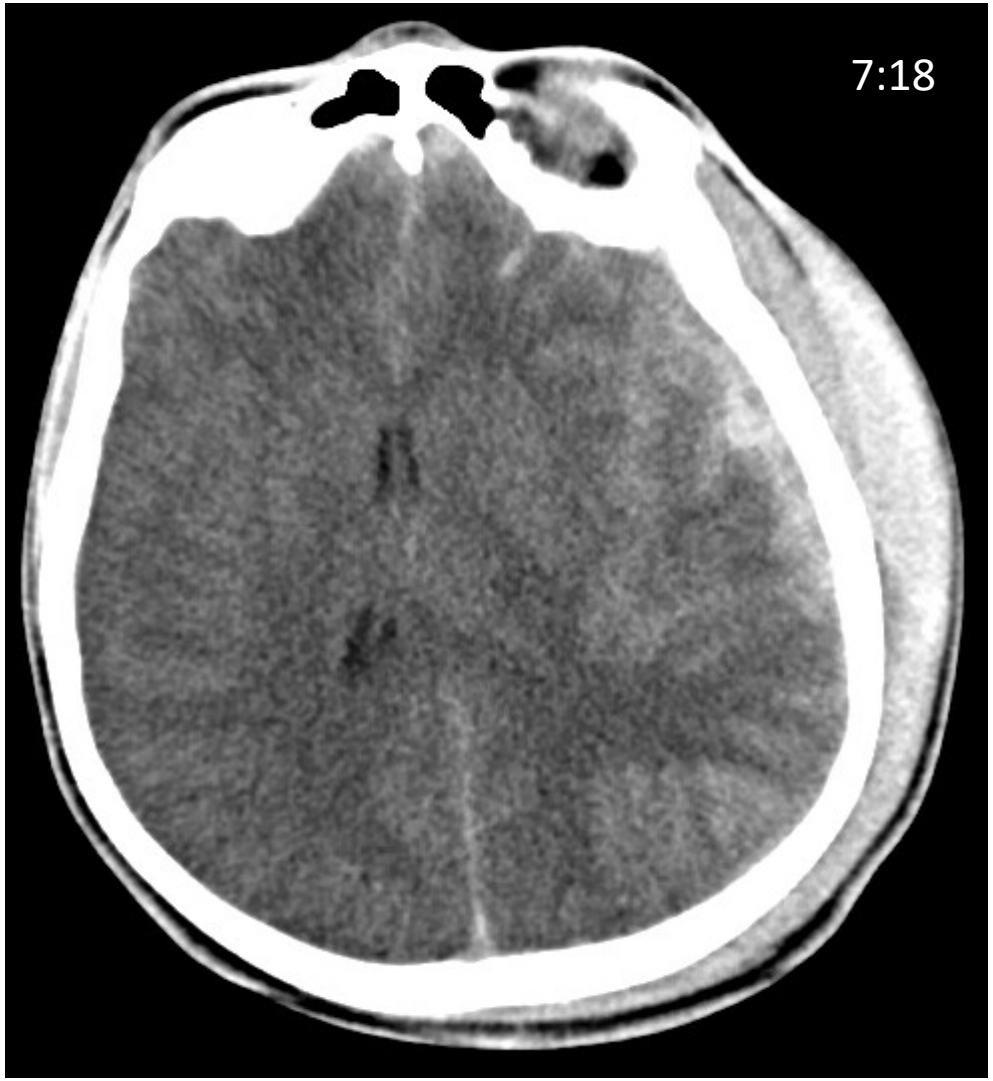
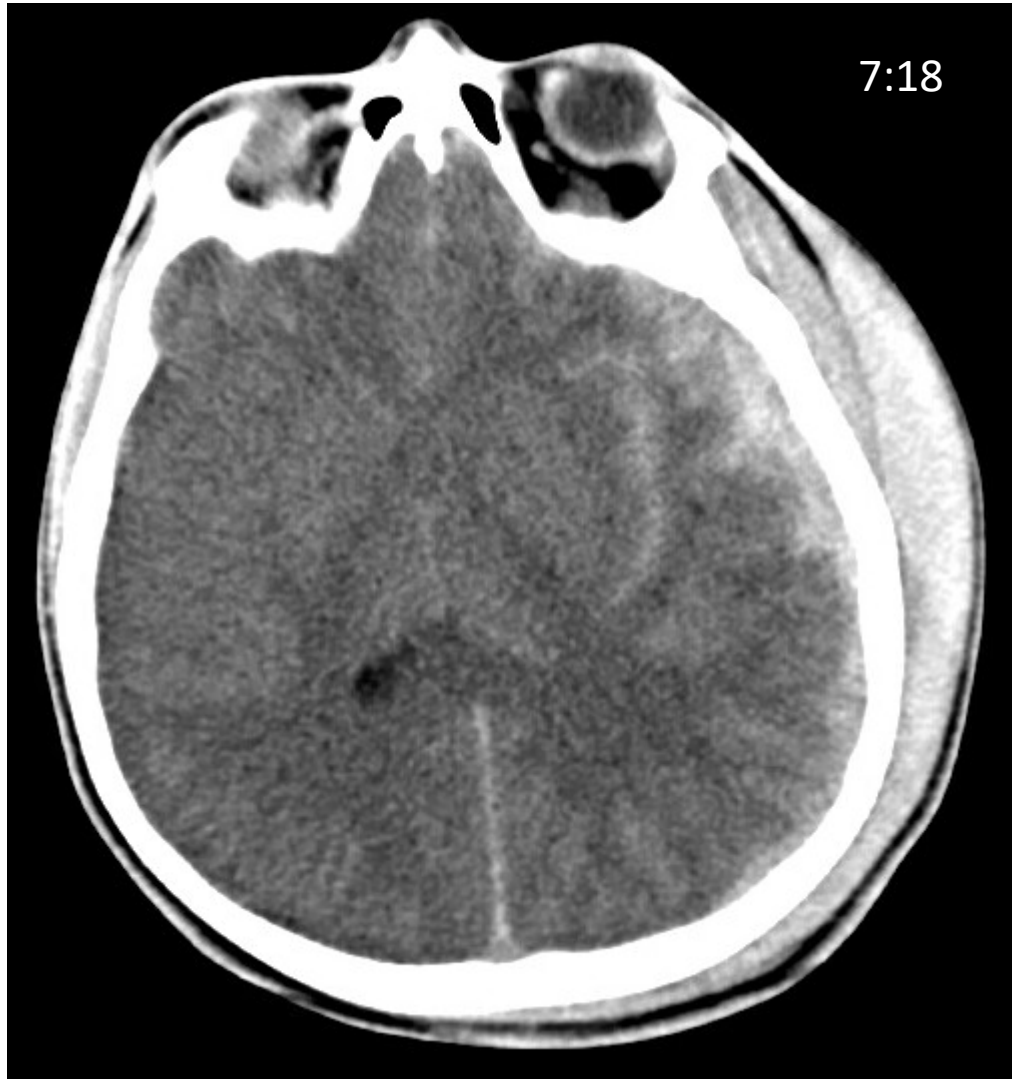


Proč toto téma?

- intubován, přepraven LZS na oddělení urgentní příjmu traumacentra





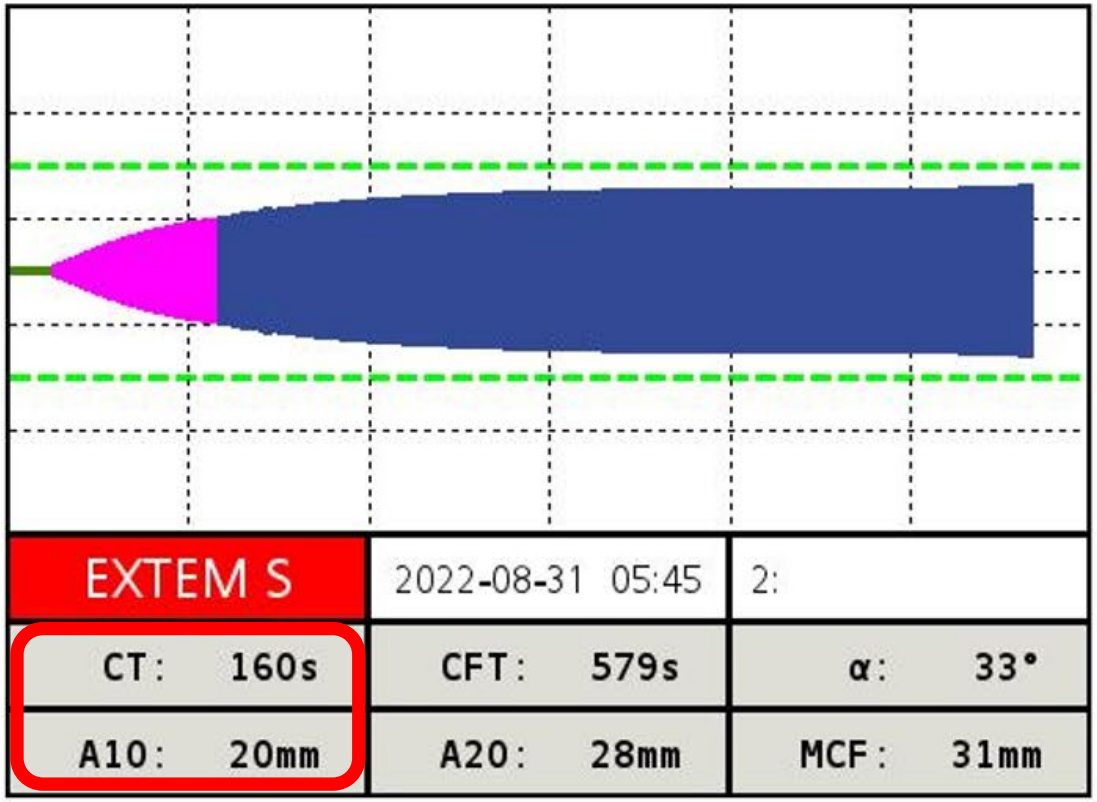
Proč toto téma? Přesně proto!

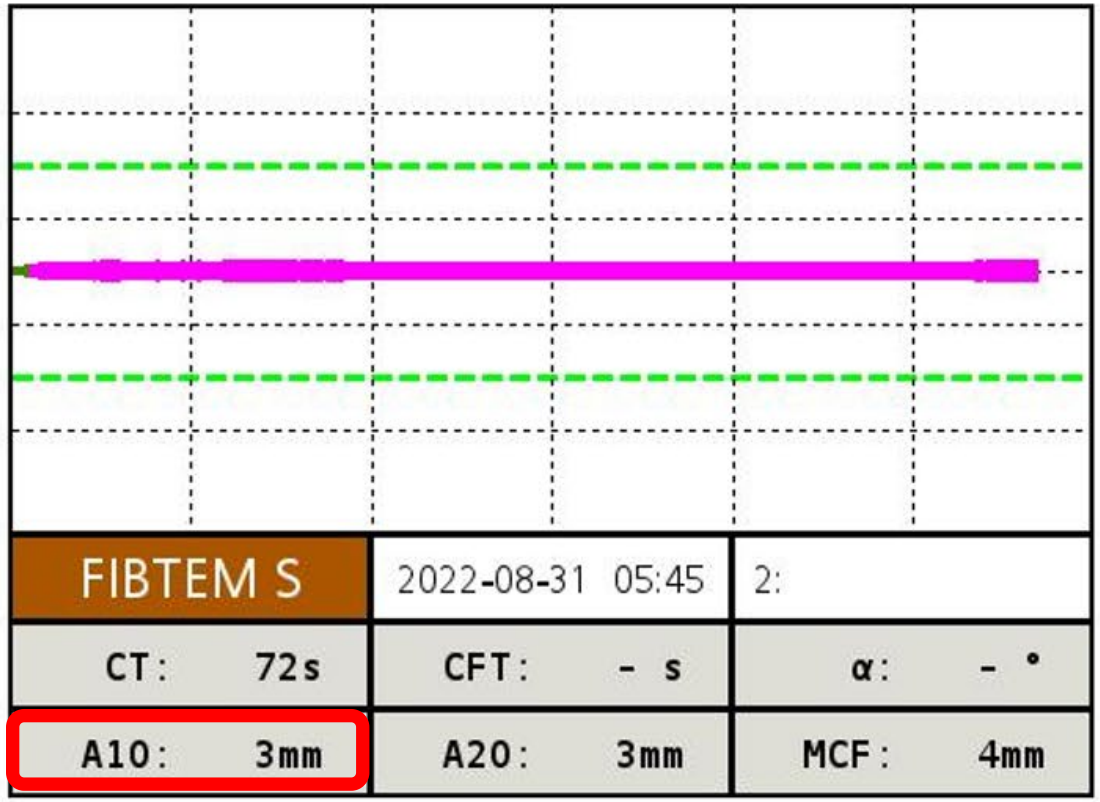
Datum a čas odběru: 31.08.2022 07:02 Te

Vyšetření	Hodn.	Výsl.	Jedn.	Meze/koment.
Leukocyty	<VH>	15.630	10^9/l	(4 - 10)
Erytrocyty	<. >	4.40	10^12/l	(4 - 5.8)
Hemoglobin	<VL>	130.0	g/l	(135 - 175)
Hematokrit	<VL>	0.360	l/l	(0.4 - 0.5)
Střední objem ERY	<VL>	81.6	fL	(84 - 96)
Trombocyty	<. >	184.0	10^9/l	(150 - 400)
Množství HGB v ERY	<. >	29.5	pg	(28 - 34)
Koncentr. HGB v ERY	<VH>	362.0	g/l	(320 - 360)
Střední objem trombo	<. >	10.70	fl	(7.8 - 11)
Šíře distribuce ERY	<. >	12.6	%	(10 - 15.2)

Datum a čas odběru: 31.08.2022 07:08 T

Vyšetření	Hodn.	Výsl.	Jedn.	Meze/koment.
Protrombin.čas	<H >	1.51	INR	(0.8 - 1.2)
Protrombin.čas	<VH>	20.5	s	(11 - 17)
Protrombin.čas	<VH>	1.51	R	(0.8 - 1.2)
Fibrinogen	<VL>	1.42	g/l	(1.8 - 4.2)
aPTT -ratio	<VH>	1.31	R	(0.8 - 1.2)
aPTT s	<VH>	42.00	s	(26 - 40)
Trombinový čas	<VH>	1.13	R	(0.8 - 1.1)
Trombinový čas	<VH>	20.1	s	(14 - 19)





Pro klid duše…

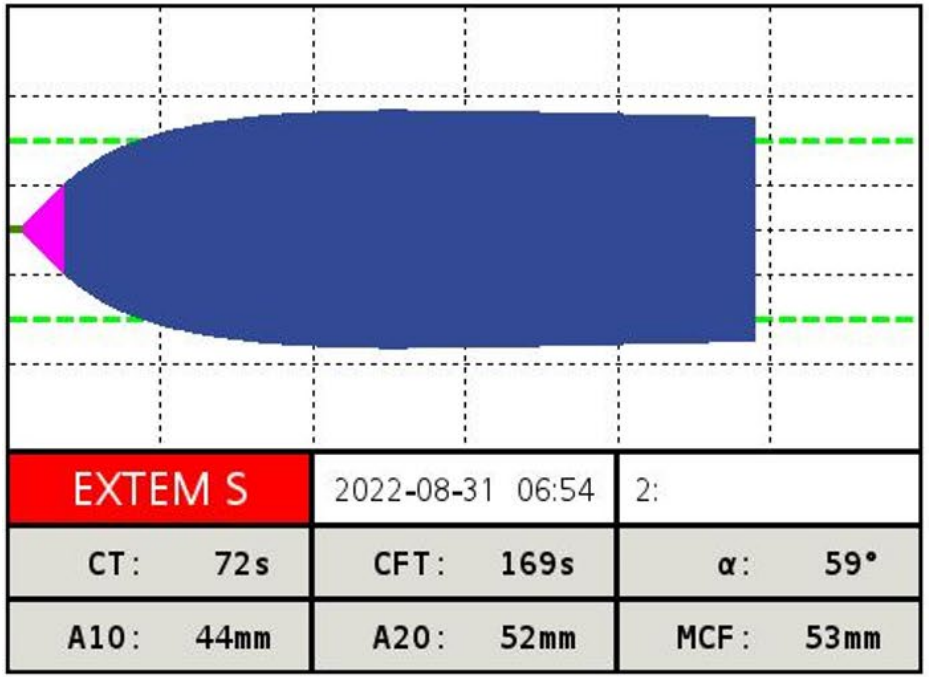
- podán Fibrinogen 6g, PCC 500IU, Exacyl 1g

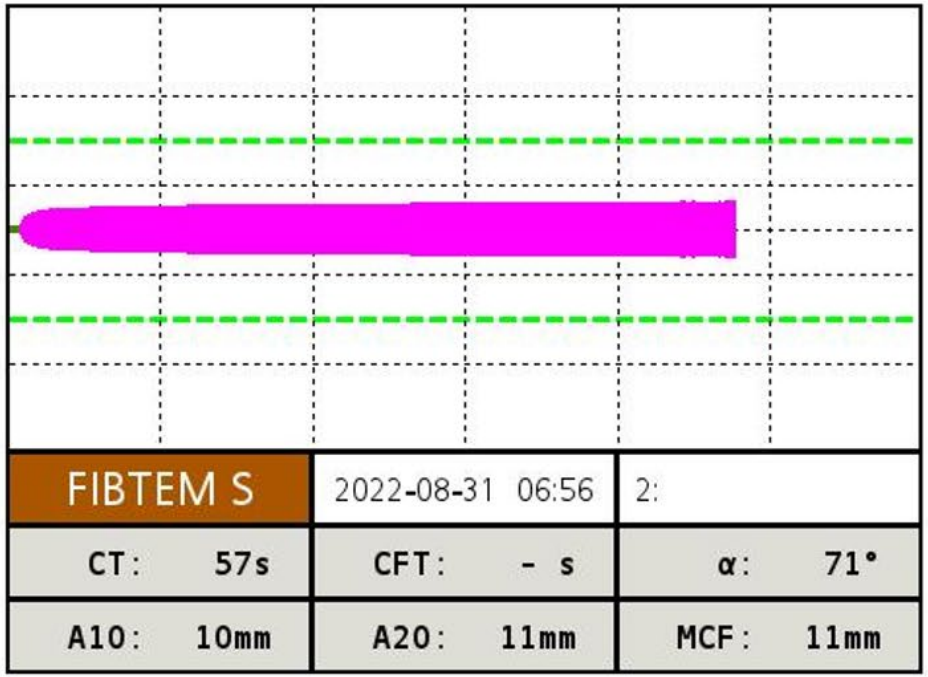
Datum a čas odběru: 31.08.2022 08:18

Vyšetření	Hodn.	Výsl.	Jedn.	Meze/koment.
Leukocyty	<VH>	11.410	10^9/l	(4 - 10)
Erytrocyty	<VL>	3.95	10^12/l	(4 - 5.8)
Hemoglobin	<VL>	115.0	g/l	(135 - 175)
Hematokrit	<VL>	0.320	l/l	(0.4 - 0.5)
Střední objem ERY	<VL>	81.5	fL	(84 - 96)
Trombocyty	<. >	157.0	10^9/l	(150 - 400)
Množství HGB v ERY	<. >	29.1	pg	(28 - 34)
Koncentr. HGB v ERY	<. >	357.0	g/l	(320 - 360)
Střední objem trombo	<. >	11.00	fl	(7.8 - 11)
Šíře distribuce ERY	<. >	12.6	%	(10 - 15.2)

Datum a čas odběru: 31.08.2022 09:24

Vyšetření	Hodn.	Výsl.	Jedn.	Meze/koment.
Protrombin.čas	<H >	1.45	INR	(0.8 - 1.2)
Protrombin.čas	<VH>	19.6	s	(11 - 17)
Protrombin.čas	<VH>	1.44	R	(0.8 - 1.2)
Fibrinogen	<. >	2.53	g/l	(1.8 - 4.2)
aPTT -ratio	<VH>	1.25	R	(0.8 - 1.2)
aPTT s	<H >	40.10	s	(26 - 40)
Trombinový čas	<VH>	1.12	R	(0.8 - 1.1)
Trombinový čas	<VH>	19.9	s	(14 - 19)





Patofyziologie

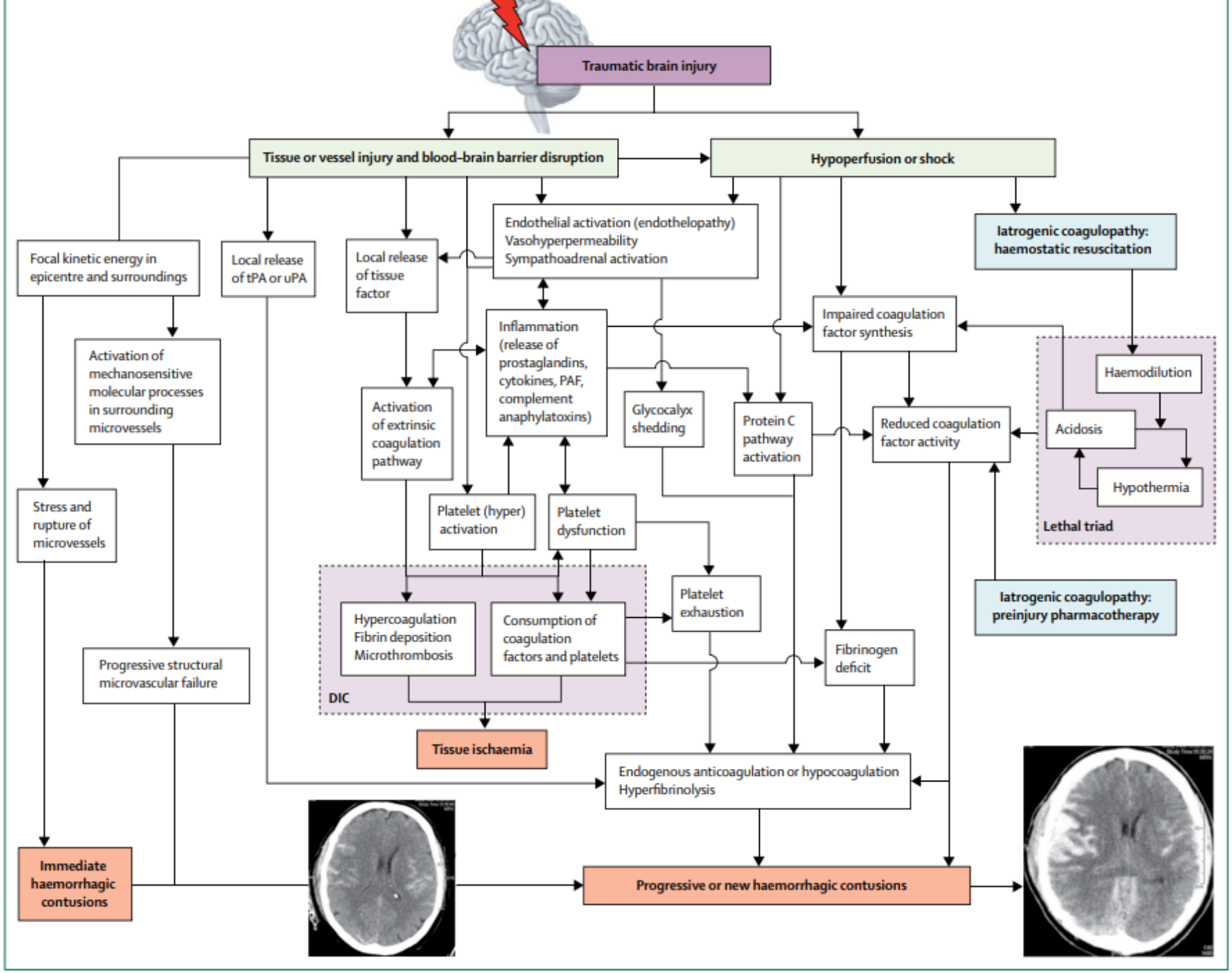


Figure 1: Current understanding of the mechanisms underlying coagulopathy and haemorrhagic contusions after traumatic brain injury

Review > Neurosurgery. 2021 Nov 18;89(6):954-966. doi: 10.1093/neuros/nyab358.

Coagulopathy and Progression of Intracranial Hemorrhage in Traumatic Brain Injury: Mechanisms, Impact, and Therapeutic Considerations

Marc Maegele [1 2 3]

Traumatic brain injury 2

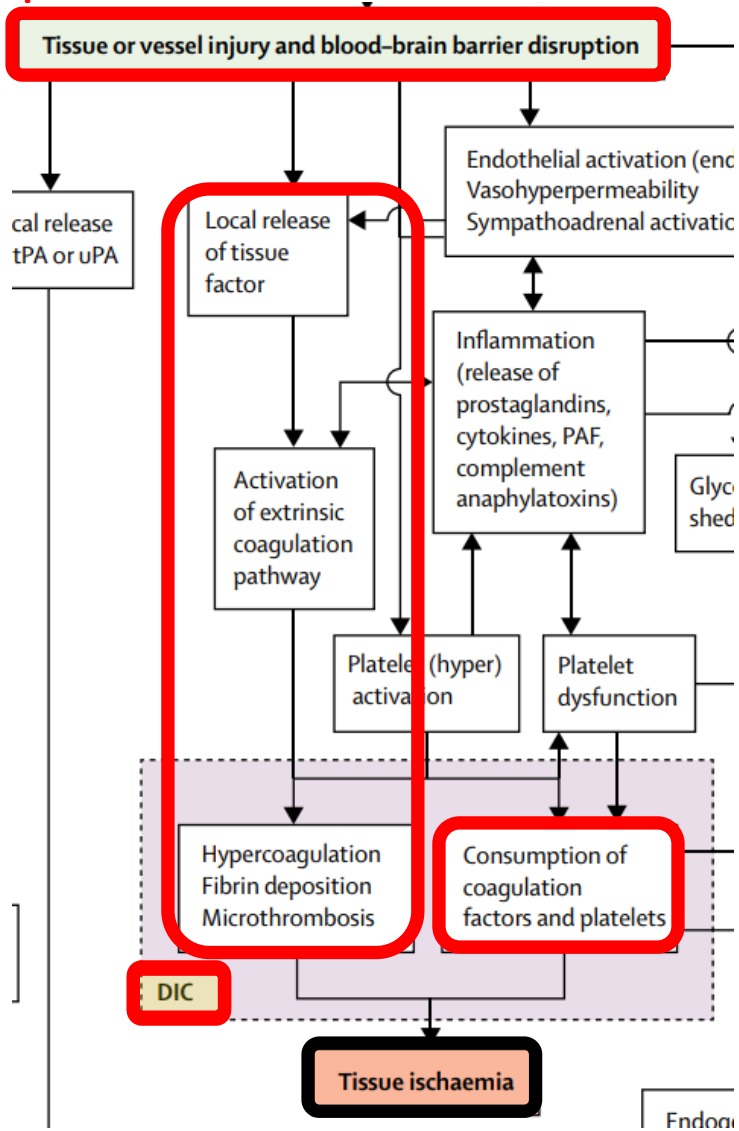
Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management

Marc Maegele, Herbert Schöchl, Tomas Menovsky, Hugues Maréchal, Niklas Marklund, Andras Buki, Simon Stanworth

Klinika anesteziologie, resuscitace a intenzivní medicíny
Fakultní nemocnice Brno
Lékařská fakulta Masarykovy univerzity

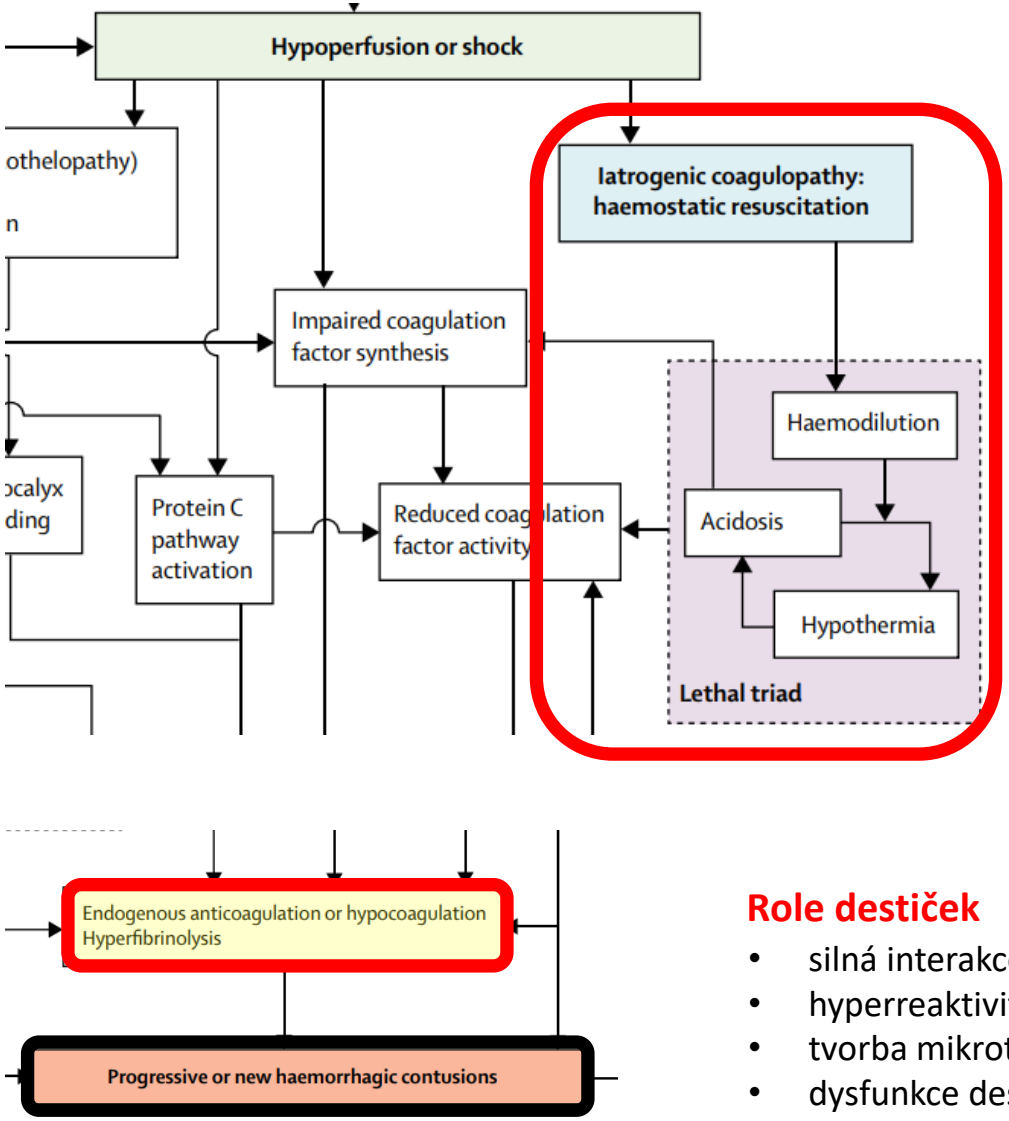
Patofyziologie – rychlé shrnutí

Koagulopatie vázaná na TBI



Koagulopatie vázaná na šok

Endotheliopathy, inflammation, and glycocalyx shedding Protein C pathway activation



Shrnutí

- **progrese z hyperkoagulačního do hypogoagulačního stavu**
- **podílí se**
  - aktivace endotelu
  - tkáňový faktor
  - endogenní antikoagulace
  - zánět
  - dysfunkce destiček
  - přeměna fibrinogenu
  - hyperfibrinolýza

Role destiček

- silná interakce poškozeného endotelu a destiček
- hyperreaktivita destiček (PAF)
- tvorba mikrotrombů a konzumpce destiček
- dysfunkce destiček

Traumatic brain injury 2
Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management
Marc Maegele, Herbert Schöchl, Tomas Menovsky, Hugues Maréchal, Niklas Marklund, Andras Buki, Simon Stanworth

Epidemiologie

TABLE 1. Prevalences of Coagulopathy in iTBI Including Outcome in the Presence of Coagulopathy

Study	No. of patients	Definition of TBI	Definition of coagulopathy	Prevalence of coagulopathy (%)	Mortality with coagulopathy (%)
Harhangi[34]*	5357	Heterogeneous	Heterogeneous	32.7 (10-97.5)	51 (25-93)
Epstein[82]**	7037	Heterogeneous	Heterogeneous	35.2 (7-86.1)	17-86
Zehtabchi[83]	224	$AIS_{head} > 2$ *and/or* any intracranial hematoma on CT	INR > 1.3 *or* PTT > 34 s	17 (8-30)	–
Talving[84]	387	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	Platelets < 100 000 mm^3 *or* INR > 1.1 *or* aPTT > 36 s	34	34.7
Lustenberger[22]	278	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	Platelets < 100 000 mm^3 *and/or* INR > 1.4 *and/or* aPTT > 36 s	45.7	40.9
Lustenberger[85]	132	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	Platelets < 100 000 mm^3 *or* INR > 1.2 *or* aPTT > 36 s	36.4	32.5
Wafaisade[86]	3114	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	Quick (PT_R) < 70% *and/or* platelets < 100 000/ml	22.7	50.4
Chhabra[87]	100	GCS < 13	Fibrinogen < 200 mg/dL	7	–
Greuters[20]	107	Brain tissue injury on CT *and* extracranial AIS < 3	aPTT > 40s *and/or* INR > 1.2 *and/or* platelets < 120 × 10^9/l	24 (54[#])	41
Shehata[88]	101	iTBI on admission brain CT	INR ≥ 1.2, PT > 13s, d-dimer positive, platelets < 100 × 10^3/CC	63	36
Schöchl[58]	88	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	Quick (PT_R) < 70% *and/or* aPTT > 35 s *and/or* fibrinogen < 150 mg/dL *and/or* platelets < 100 × 10^9/l	15,8	50
Franschman[89]	226	iTBI on CT *and* extracranial AIS < 3	aPTT > 40 s *and/or* PT > 1.2 *and/or* platelets < 120 × 10^9/l	25 (44[#])	33
Genet[90]	23	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	aPTT > 35 s *and/or* INR > 1.2	13	22
Alexiou[91]	149	iTBI *with* exclusion of multisystem trauma	aPTT > 40s *and/or* INR > 1.2 *and/or* platelets < 120 × 10^9/l	14.8 (22.8[#])	–
Joseph[7]	591	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	INR ≥ 1.5 *and/or* PTT ≥ 35s *and/or* platelets ≤ 100 × 10^3/ml	13.3	23
Epstein[92]	1718	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	INR ≥ 1.3	7.7	45.1
De Oliveira Manoel[93]	48	$AIS_{head} \geq 3$ *and* extracranial AIS < 3	INR ≥ 1.5 *and/or* aPTT ≥ 60s *and/or* platelets < 100 × $10^3/mm^3$[§]	12.5	66
Dekker[50]	52	$AIS_{head} \geq 3$	INR > 1.2 *and/or* aPTT > 40s *and/or* platelets < 120 × 10^9/l	42	45.5
Yuan[94]	2319	Intracranial injury on CT *and* extracranial AIS < 3	INR > 1.25 *and/or* PT >14 s *and/or* aPTT >36 s and/or platelets < 100 × 10^9/l	18.6	17.6
Albert[47]	561	iTBI on admission brain CT	INR ≥ 1.27 *and/or* PT ≥ 16.7 s *and/or* aPTT > 28.8 s	41.6%	61.1%
Böhm[8]	598	iTBI on CT *and* no extracranial injuries	INR > 1.2 *and/or* aPTT > 35 s *and/or* fibrinogen < 150 mg/dL and/or platelets < 100 × 10^3/nL	19.6	-

Review > Neurosurgery. 2021 Nov 18;89(6):954-966. doi: 10.1093/neuros/nyab358.

Coagulopathy and Progression of Intracranial Hemorrhage in Traumatic Brain Injury: Mechanisms, Impact, and Therapeutic Considerations

Marc Maegele [1 2 3]

Měření koagulopatie

RESEARCH Open Access

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

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Timothy J. Coats[7], Jacques Duranteau[8],

portance of fibrinogen and platelet measurements. It is often assumed that the conventional coagulation screens [international normalised ratio (INR) and APTT] monitor coagulation, however these tests monitor only the initiation phase of blood coagulation, and represent only the first 4 % of thrombin production [178]. It is there-

tion is abnormal [13, 179–183]. In addition, the delay in detection of traumatic coagulopathy can influence outcome, and the turnaround time of thromboelastometry has been shown to be significantly shorter than conventional laboratory testing, with a time saving of 30–60 min [181, 184, 185]. Viscoelastic testing may

Proč vůbec INR a aPTT ????

Měření koagulopatie

J Neurotrauma. 2011 Oct;28(10):2033-41. doi: 10.1089/neu.2010.1744. Epub 2011 Sep 23.

Thromboelastometric (ROTEM) findings in patients suffering from isolated severe traumatic brain injury

Herbert Schöchl [1], Cristina Solomon, Stefan Traintinger, Ulrike Nienaber, Astrid Tacacs-Tolnai, Christian Windhofer, Soheyl Bahrami, Wolfgang Voelckel

results. Thirty-two patients were included in the study. Complete adherence to the algorithm was observed in 20 out of 32 cases. The availability of thromboelastometric results after hospital admission was reported significantly earlier than conventional coagulation tests (median (IQR [range]) 33 (20-40 [14-250]) min vs. 71 (51-101 [32-290]) min; p = 0.037). Although only 5 out of 32 patients had abnormalities of conventional coagulation tests 21 out of 32 patients had a coagulopathic baseline thromboelastometric trace. Implementing a thromboelastometric-guided algorithm for the

Výhody:

- **přesnější popis reálné hemostázy**
- **rychlejší výsledky**

Multicenter Study > Anaesthesia. 2019 Jul;74(7):883-890. doi: 10.1111/anae.14670. Epub 2019 Apr 29.

Protocolised thromboelastometric-guided haemostatic management in patients with traumatic brain injury: a pilot study

J Gratz [1], H Güting [2], S Thorn [3], A Brazinova [4], K Görlinger [5 6], N Schäfer [2], H Schöchl [7 8],

https://www.clot.pro/

https://www.werfen.com/cz/cs/diagnostika-hemostazy/rotem-delta

https://www.medgadget.com/2019/05/haemonetics-teg-6s-hemostasis-analyzer-cleared-for-trauma-testing.html

Komplikace…

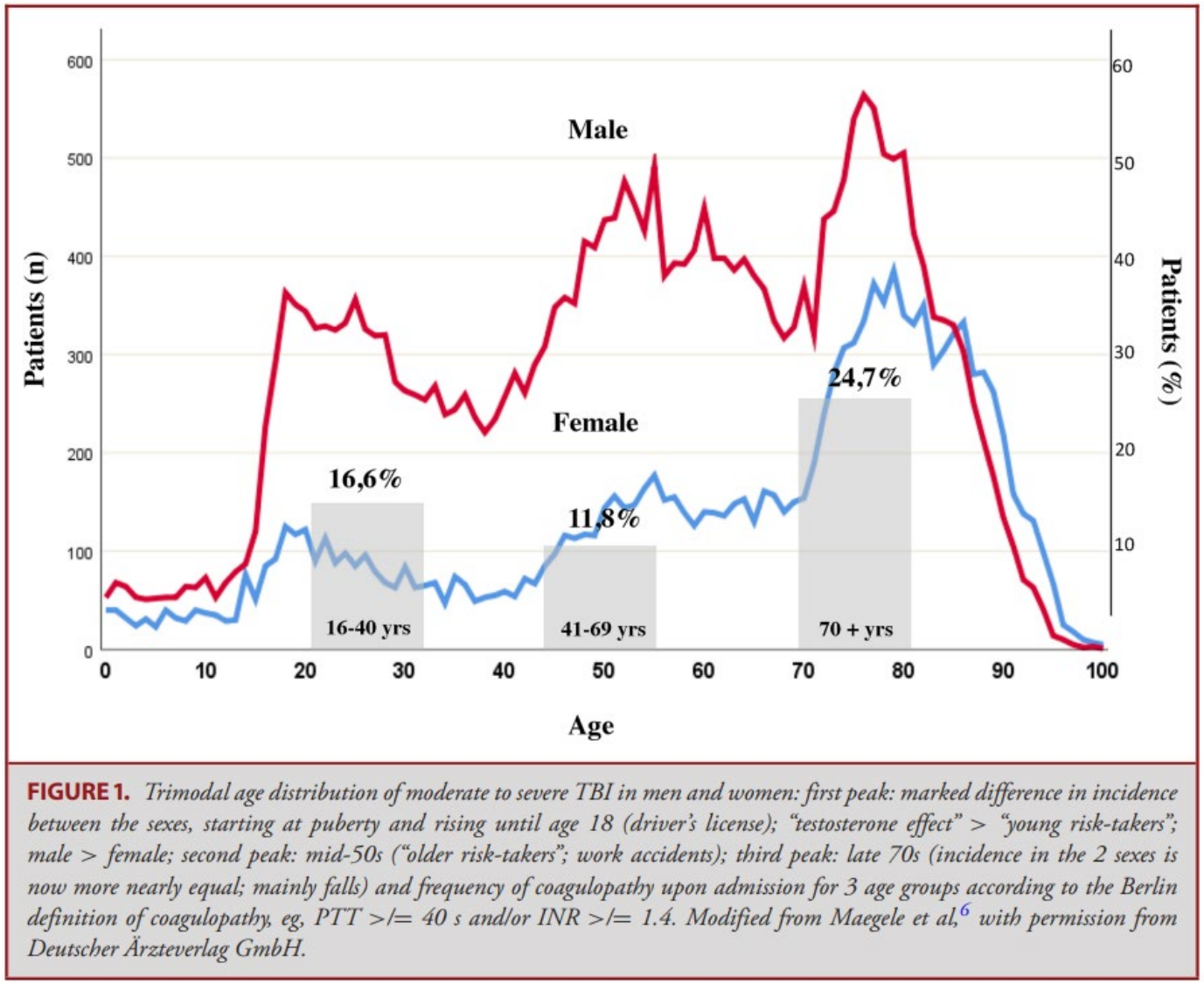


FIGURE 1. *Trimodal age distribution of moderate to severe TBI in men and women: first peak: marked difference in incidence between the sexes, starting at puberty and rising until age 18 (driver's license); "testosterone effect" > "young risk-takers"; male > female; second peak: mid-50s ("older risk-takers"; work accidents); third peak: late 70s (incidence in the 2 sexes is now more nearly equal; mainly falls) and frequency of coagulopathy upon admission for 3 age groups according to the Berlin definition of coagulopathy, eg, PTT >/= 40 s and/or INR >/= 1.4. Modified from Maegele et al,[6] with permission from Deutscher Ärzteverlag GmbH.*

- antikoagulační/antiagregační terapie – 20% pacientů

ORIGINAL WORK

Global Characterisation of Coagulopathy in Isolated Traumatic Brain Injury (iTBI): A CENTER-TBI Analysis

Julia K. Böhm[1], Helge Güting[1], Sophie Thorn[2], Nadine Schäfer[1], Victoria Rambach[1], Herbert Schöchl[4,5], Oliver Grottke[6], Rolf Rossaint[6], Simon Stanworth[7], Nicola Curry[7], Rolf Lefering[1], Marc Maegele[1,8] and CENTER-TBI Participants and Investigators

- zhoršení krvácení a outcome

Acta Neurochir (Wien). 2016 Jan;158(1):117-23. doi: 10.1007/s00701-015-2645-8. Epub 2015 Nov 27.

High prevalence of pharmacologically induced platelet dysfunction in the acute setting of brain injury

Vincent Prinz[1], Tobias Finger[1], Simon Bayerl[1], Christoph Rosenthal[2], Stefan Wolf[1],

- warfarin zdvojnásobuje riziko špatného outcomu

Review. Br J Neurosurg. 2012 Aug;26(4):525-30. doi: 10.3109/02688697.2011.650736. Epub 2012 Feb 10.

A meta-analysis to determine the effect of anticoagulation on mortality in patients with blunt head trauma

John Stephen Batchelor[1], Alan Grayson

- antiagregační léčba zhoršuje riziko tvorby víe druhů krvácení u lehkého TBI

World Neurosurg. 2018 Feb;110:e339-e345. doi: 10.1016/j.wneu.2017.10.173. Epub 2017 Nov 10.

Are Antiplatelet and Anticoagulants Drugs A Risk Factor for Bleeding in Mild Traumatic Brain Injury?

Laura Uccella[1], Cesare Zoia[2], Daniele Bongetta[3], Paolo Gaetani[2], Franz Martig[4], Christian Candrian[4], Raffaele Rosso[4]

- málo dat na DOAC, při ICH horší průběh než s VKA

Eur J Trauma Emerg Surg. 2021 Apr;47(2):565-571. doi: 10.1007/s00068-019-01228-9. Epub 2019 Sep 16.

Intake of NOAC is associated with hematoma expansion of intracerebral hematomas after traumatic brain injury

Markella Markou[1,2], Burkhard Pleger[3], Martin Grözinger[4], Bogdan Pintea[5], Uwe Hamsen[6],

Review. Neurosurgery. 2021 Nov 18;89(6):954-966. doi: 10.1093/neuros/nyab358.

Coagulopathy and Progression of Intracranial Hemorrhage in Traumatic Brain Injury: Mechanisms, Impact, and Therapeutic Considerations

Marc Maegele[1,2,3]

Jak detekovat DOAC?

- laboratorní stanovení hladiny jednotlivých DOAC
- point of care testy
  - DOAC Dipstick®
  - Clotpro®

longed in VKA-treated patients. If time and amount of the most recent dose of dabigatran are unknown, normal values for thrombin time, ecarin clotting time and diluted thrombin time suggest the absence of dabigatran in clinically relevant concentrations [275]. A normal standard anti-Xa test may also exclude intake (or efficacy) of an anti-Xa agent (rivaroxaban, apixaban, edoxaban, betrixaban). If these tests are prolonged, a diluted thrombin time (Hemoclot® for dabigatran) or a specific anti-Xa test (for anti-Xa agents) should be performed [280]. Chromogenic anti-factor-Xa-activity tests can be used to estimate the plasma concentrations of factor Xa-inhibitors (apixaban, edoxaban, rivaroxaban), but require calibration with substance-specific reagents [275, 281, 282].

- laboratorní screening
  - TT – dabigatran
  - antiXa – inibitory f.Xa

Received: 17 February 2019 | Revised: 22 March 2019 | Accepted: 25 March 2019
DOI: 10.1002/ajh.25475

CRITICAL REVIEW

AJH WILEY

Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum

Adam Cuker[1] | Allison Burnett[2] | Darren Triller[3] | Mark Crowther[4] | Jack Ansell[5] | Elizabeth M. Van Cott[6] | Diane Wirth[7] | Scott Kaatz[8]

Léčba koagulopatie u TBI

Brain Trauma FOUNDATION

Guidelines for the Management of Severe Traumatic Brain Injury
4th Edition

RESEARCH Open Access

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

Donat R. Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Jacques Duranteau[7], Daniela Filipescu[8], Beverley J. Hunt[9], Radko Komadina[10], Marc Maegele[11], Giuseppe Nardi[12], Louis Riddez[13], Charles-Marc Samama[14], Jean-Louis Vincent[15] and Rolf Rossaint[16*]

EJA

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

GUIDELINES

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

First update 2016

Sibylle A. Kozek-Langenecker, Aamer B. Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Guidrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V.L. Pitarch, Susan Mallett, Jens Meier, Zsolt L. Molnar, Niels Rahe-Meyer, Charles M. Samama, Jakob Stensballe, Philippe J.F. Van der Linden, Anne J. Wikkelsø, Patrick Wouters, Piet Wyffels and Kai Zacharowski

Intensive Care Med (2022) 48:649–666
https://doi.org/10.1007/s00134-022-06702-4

NARRATIVE REVIEW

Management of moderate to severe traumatic brain injury: an update for the intensivist

Geert Meyfroidt[1*], Pierre Bouzat[2], Michael P. Casaer[1], Randall Chesnut[3], Sophie Rym Hamada[4],

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**

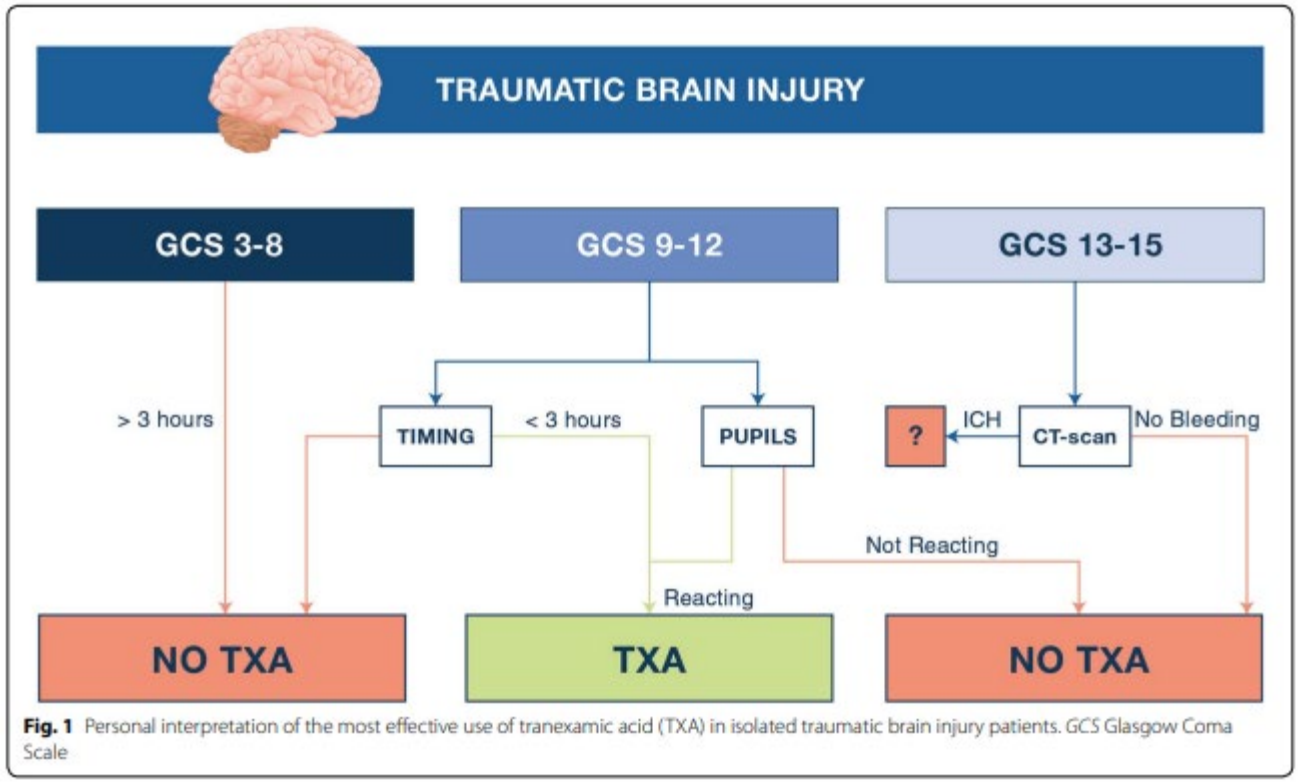


Fig. 1 Personal interpretation of the most effective use of tranexamic acid (TXA) in isolated traumatic brain injury patients. *GCS* Glasgow Coma Scale

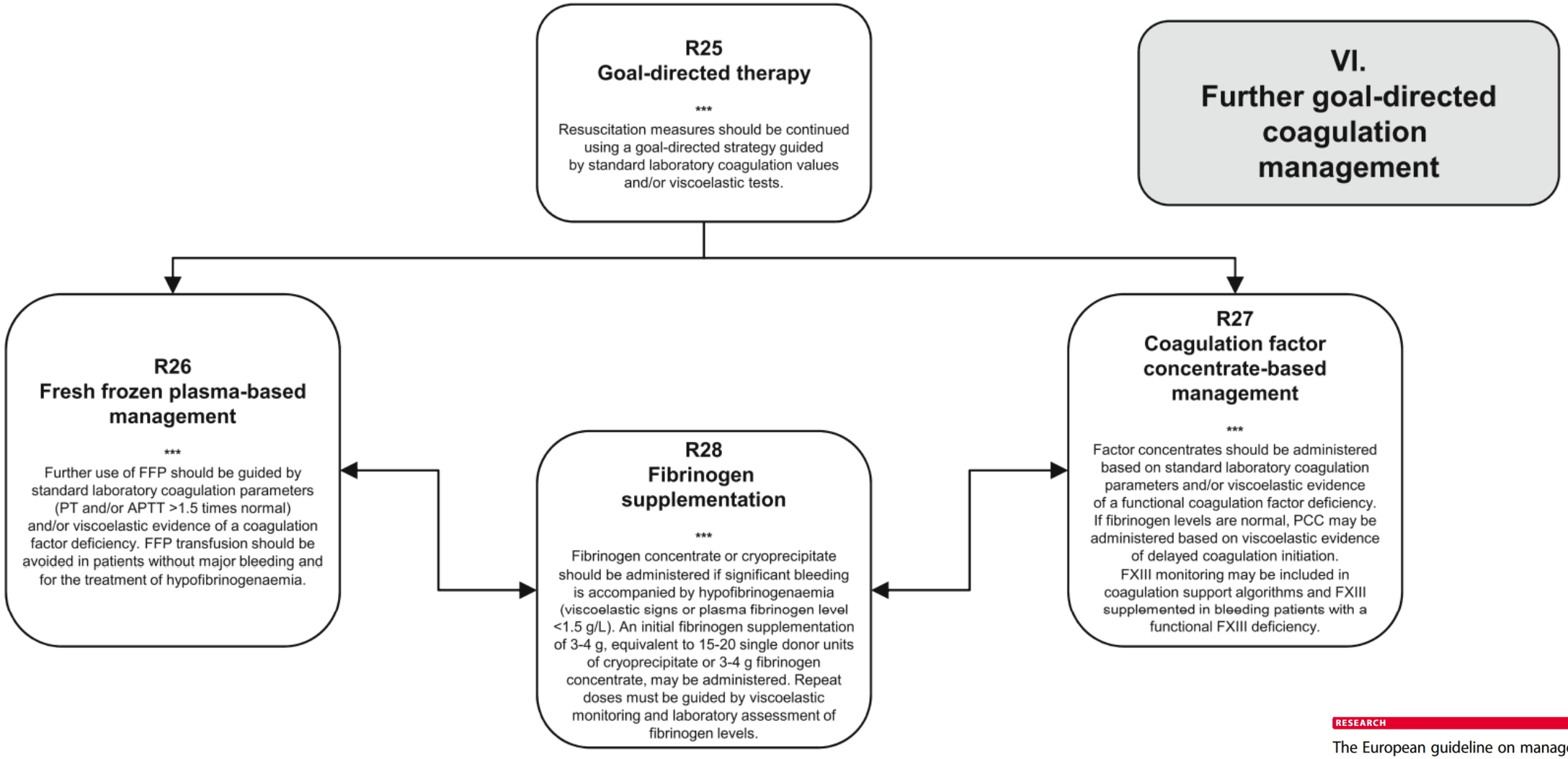
the first 3 h. In isolated TBI, the CRASH3 trial showed a reduction in TBI-related death when tranexamic acid (TXA) was administered in the subgroup of patients with mild-to-moderate TBI (Glasgow Coma Score (GCS) 9–15) within the first 3 h [91], but not in severe TBI. Moreover, a systematic review of 9 RCTs (including CRASH3) in 14,747 isolated TBI patients [92] did not find such mortality benefit of TXA (even while there was a reduction in hematoma expansion), and no increased risk of adverse events. As such, TXA is not indicated in severe isolated TBI, but can be considered in mild-to-moderate TBI, when administered within the first 3 h [93].

EDITORIAL

Is tranexamic acid going to CRASH the management of traumatic brain injury?

Fabio Silvio Taccone[1*], Giuseppe Citerio[2] and Nino Stocchetti[3]

Léčba koagulopatie u TBI



RESEARCH Open Access

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

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Léčba koagulopatie u TBI

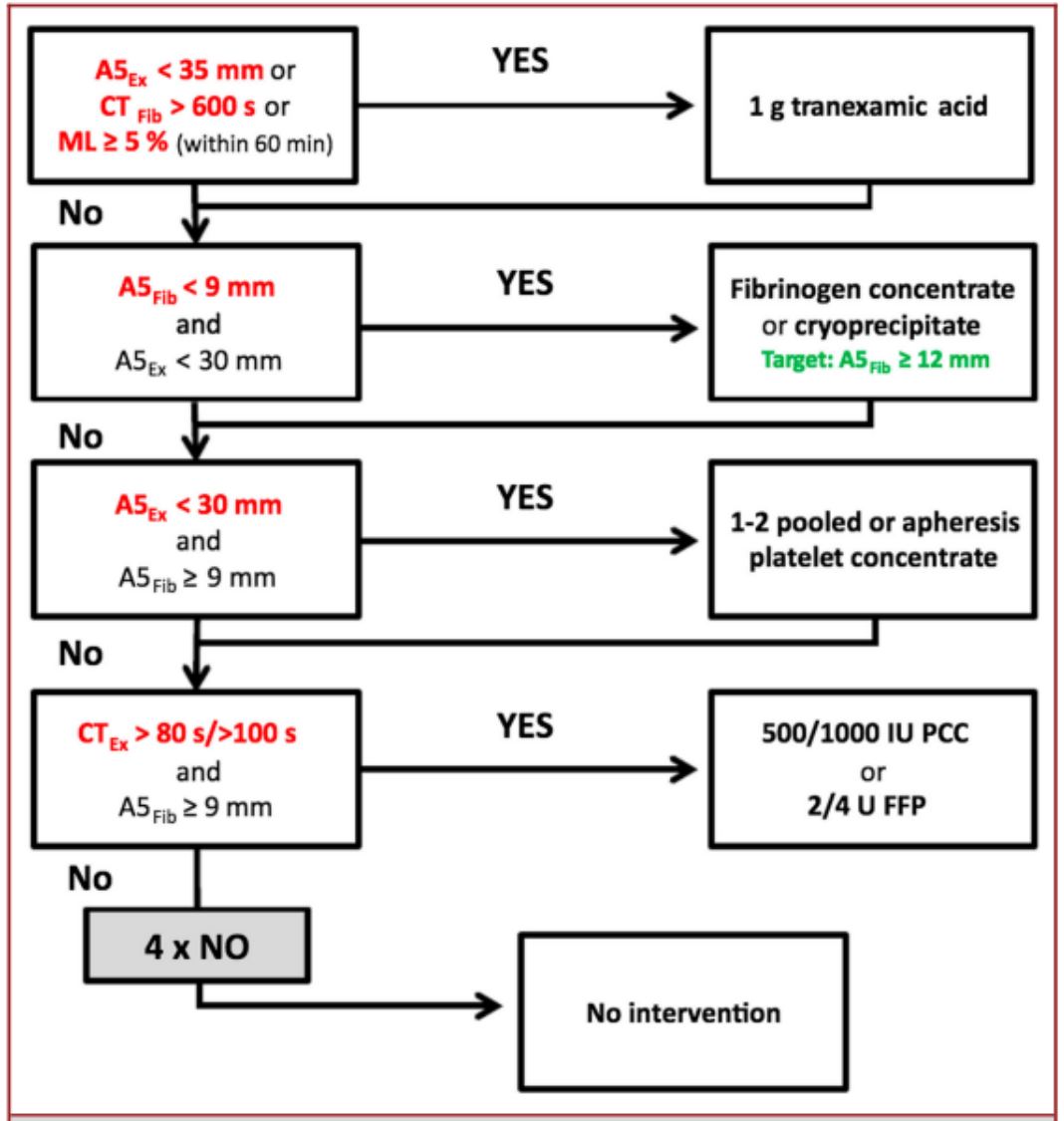

FIGURE 5. *Exemplar algorithm to guide hemostatic therapies by the use of functional viscoelastic testing results (ROTEM®) successfully implemented at centers formerly naïve to this technology. Test results were available for clinical decision-making within median 15 min of blood sampling. When the algorithm recommended specific interventions and was followed, thromboelastometric test results improved significantly by the second blood sampling performed 30 to 60 min after decision-making and at least 10 min after the intervention. Reprinted from Gratz et al,[59] with permission from John Wiley and Sons. A10 = clot amplitude after 5 and 10 min (in mm); CT = clotting time (in seconds); Ex = ROTEM® EXTEM assay; FFP = fresh frozen plasma; Fib = ROTEM® FIBTEM assay; g = gram; IU = international units; ML = maximum lysis (in percent); PCC = prothrombin complex concentrate.*

Review > Neurosurgery. 2021 Nov 18;89(6):954-966. doi: 10.1093/neuros/nyab358.

Coagulopathy and Progression of Intracranial Hemorrhage in Traumatic Brain Injury: Mechanisms, Impact, and Therapeutic Considerations

Marc Maegele [1 2 3]

Multicenter Study > Anaesthesia. 2019 Jul;74(7):883-890. doi: 10.1111/anae.14670. Epub 2019 Apr 29.

Protocolised thromboelastometric-guided haemostatic management in patients with traumatic brain injury: a pilot study

J Gratz [1], H Güting [2], S Thorn [3], A Brazinova [4], K Görlinger [5 6], N Schäfer [2], H Schöchl [7 8],

Take home message

- patofyziologie koagulopatie po těžkém kraniocerebrálním poranění jde pochopit
- používejte viskoelastické metody a point of care testy
- používejte goal directed therapy

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NARRATIVE REVIEW

Management of moderate to severe traumatic brain injury: an update for the intensivist

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Table 1 Initial resuscitation targets

Parameter	Values/targets	Objectives
Blood pressure	MAP > 80 mmHg SBP > 100 or 110 mmHg	Preserving CBF
SpO_2	> 90%	Avoiding brain hypoxia
$EtCO_2$	30–35 mmHg	Preserving CBF
Hb	> 7 g/dl	Avoiding brain hypoxia
Anticoagulant	Reversal	Limiting blood loss and expansion of hemorrhagic contusions