LÉKAŘSKÁ FAKULTA
MASARYKOVY UNIVERZITY
A FAKULTNÍ NEMOCNICE BRNO

KLINIKA DĚTSKÉ
ANESTEZIOLOGIE
A RESUSCITACE

Nová doporučení pro léčbu traumatické koagulopatie– role fibrinogenu v léčbě ŽOK/TIC

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FAKULTNÍ NEMOCNICE BRNO

Cíle

- Monitorace hypofibrinogenémie
- Léčba hyperfibrinolýzy
- Substituce fibrinogenu

Spahn *et al. Critical Care* (2019) 23:98
https://doi.org/10.1186/s13054-019-2347-3

Critical Care

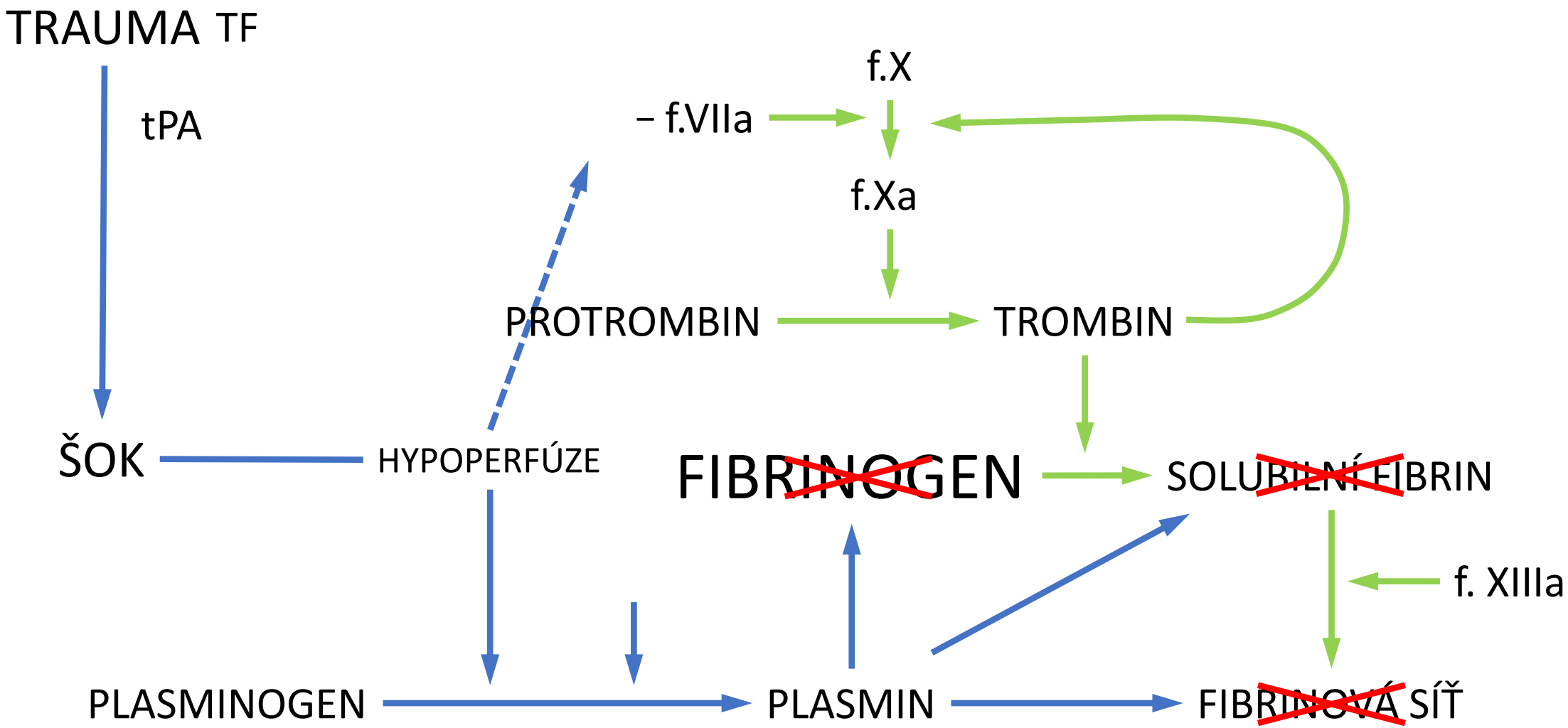
RESEARCH Open Access

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*]

Uncontrolled post-traumatic bleeding is still the leading cause of potentially preventable death among injured patients [7–9] and one third of all bleeding trauma patients show signs of coagulopathy at hospital admission [10–17]. These patients develop multiple organ failure

Spahn et al. Critical Care (2019) 23:98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f.X
– f.VIIa
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PROTROMBIN
TROMBIN
ŠOK
HYPOPERFÚZE
FIBRINOGEN
SOLUBILNÍ FIBRIN
f. XIIIa
PLASMINOGEN
PLASMIN
FIBRINOVÁ SÍŤ

Monitoring

Goal-directed therapy

Recommendation 25 We recommend that resuscitation measures be continued using a goal-directed strategy, guided by standard laboratory coagulation values and/or VEM. (Grade 1B)

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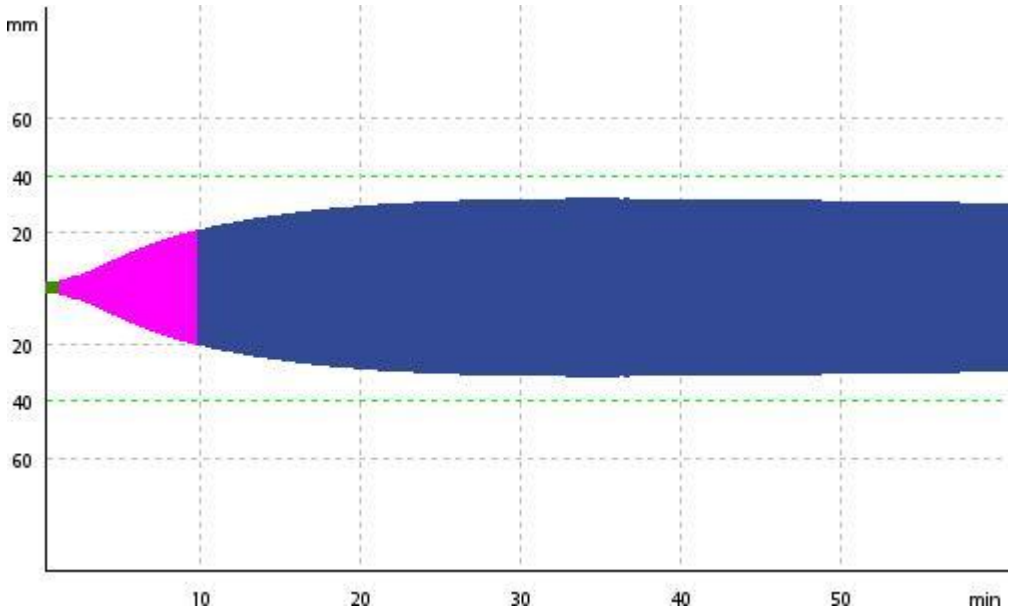
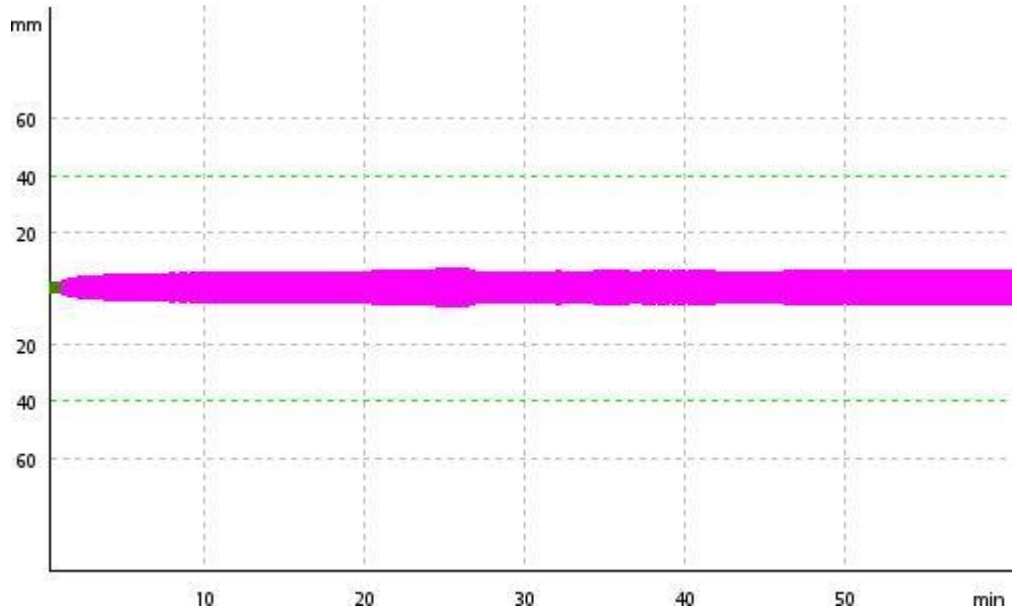
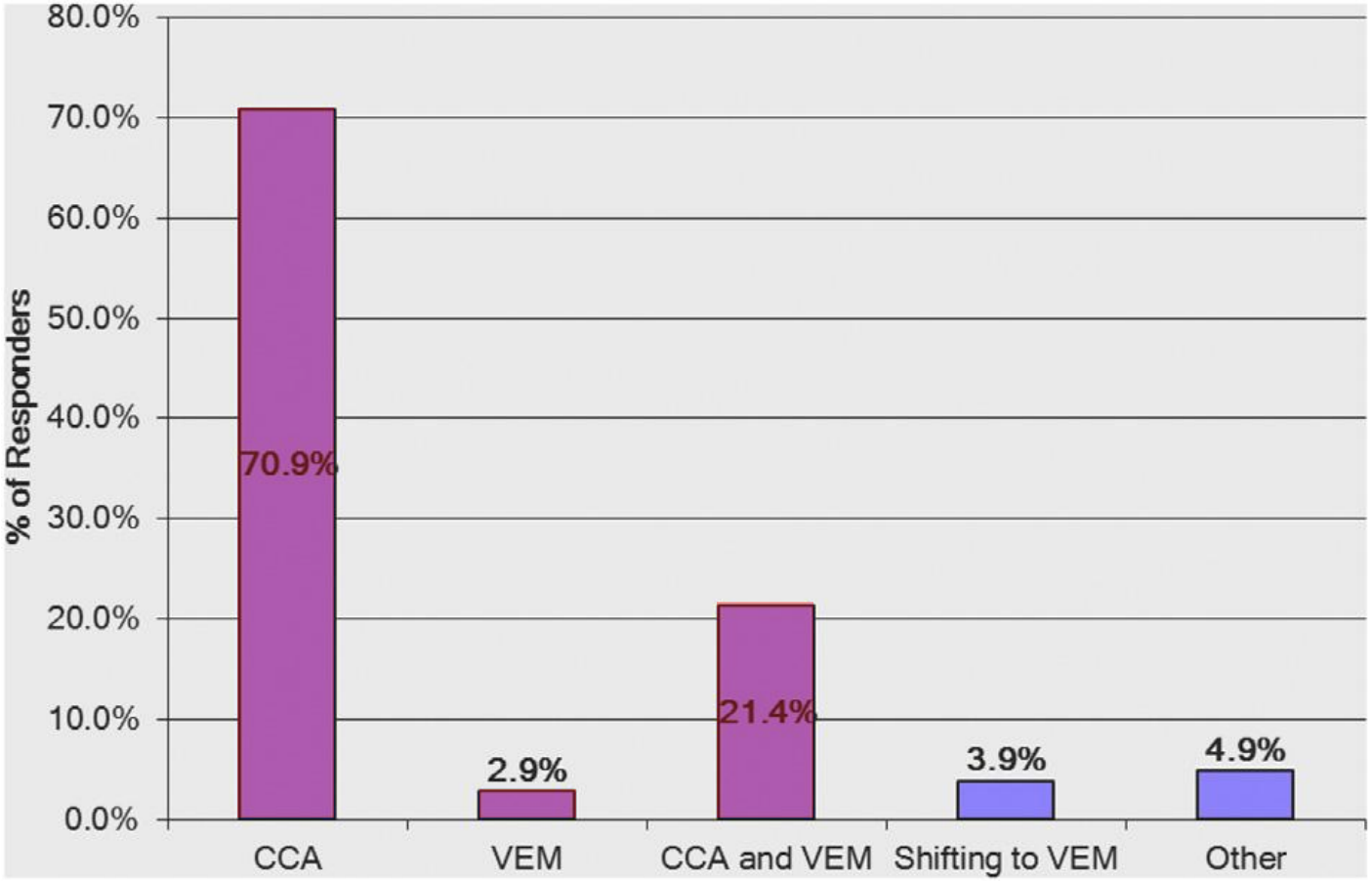
Protrombin.čas	INR	1.19	1.13	1.15	1.04
Protrombin.čas	R	1.19	1.13	1.15	1.03
Fibrinogen	g/L	3.91	2.94	1.6	1.75
aPTT -ratio	R	1.19	1.08	0.89	0.77
Trombinový čas	R	1.05	1.19	1.24	0.99
Trombinový čas	s	17.7	20	20.9	16.6
AT III	%	83	81	75	94
D-Dimery(LIA)	mg/L >	1.18	1.4	2.8	3.11

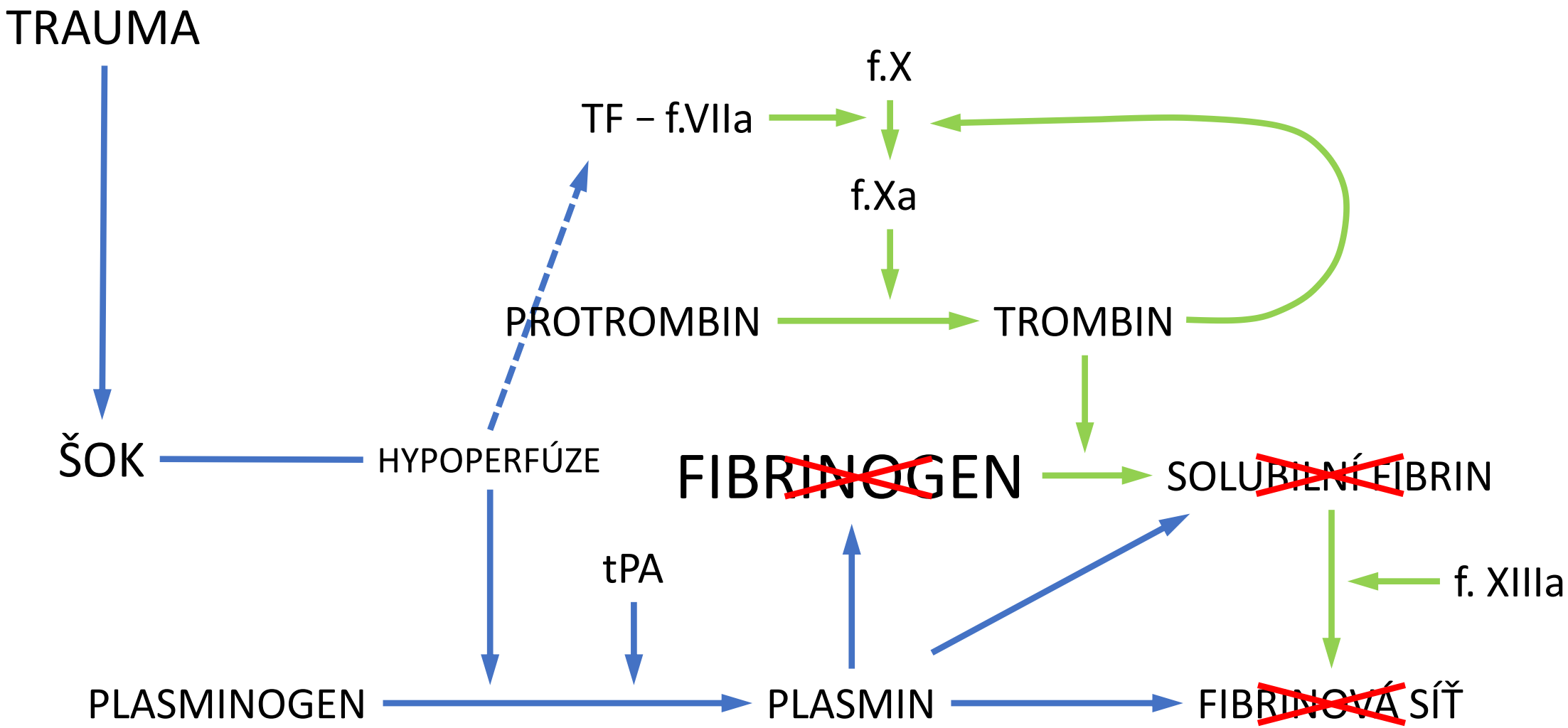






Russel, J Surg Res 2017; 216-220

Hyperfibrinolýza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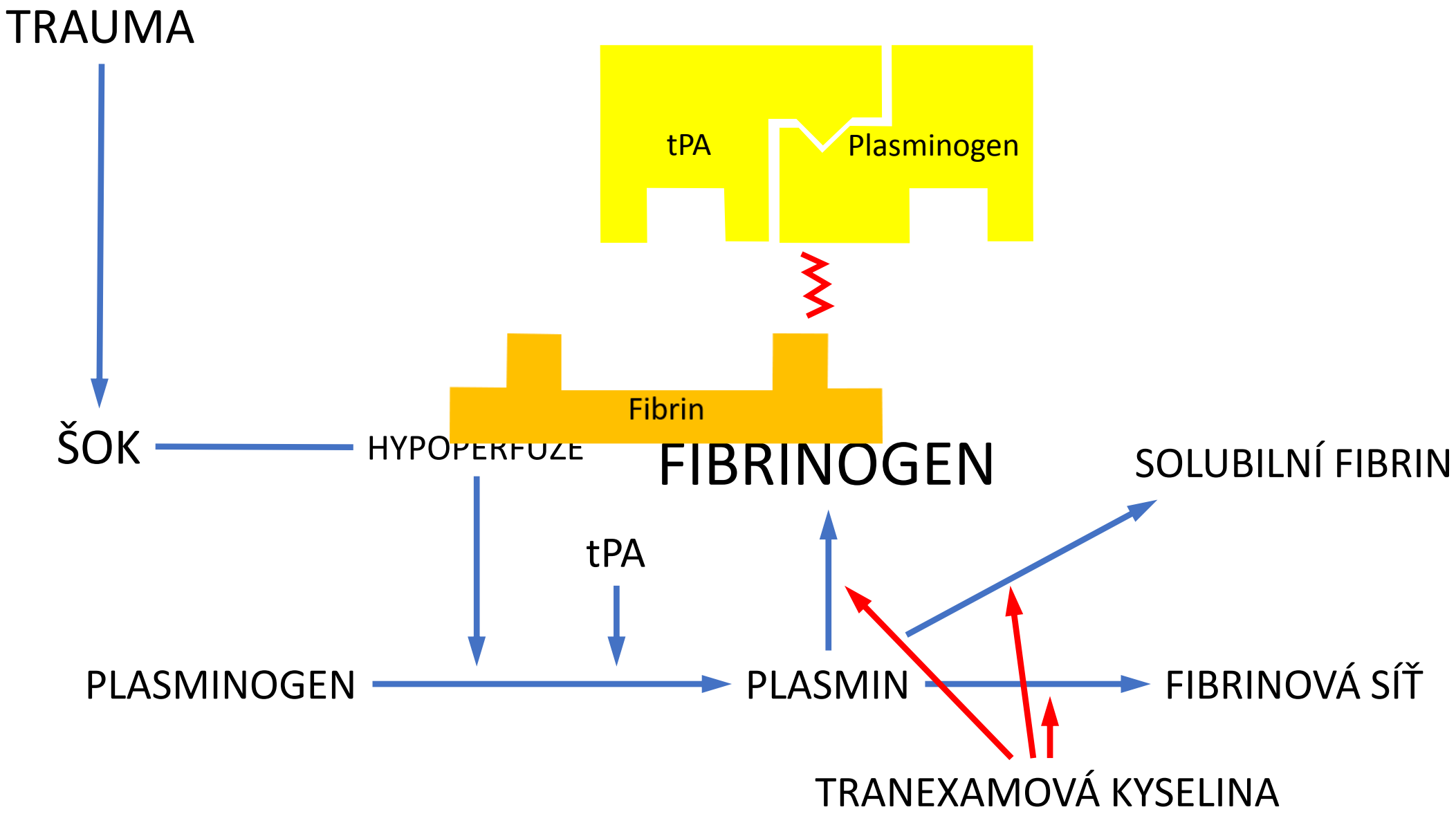
SOLUBILNÍ FIBRIN
tPA
f. XIIIa
PLASMINOGEN
PLASMIN
FIBRINOVÁ SÍŤ

V. Initial management of bleeding and coagulopathy

Antifibrinolytic agents

Recommendation 22 We recommend that TXA be administered to the trauma patient who is bleeding or at risk of significant haemorrhage as soon as possible 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)

Spahn et al. Critical Care (2019) 23:98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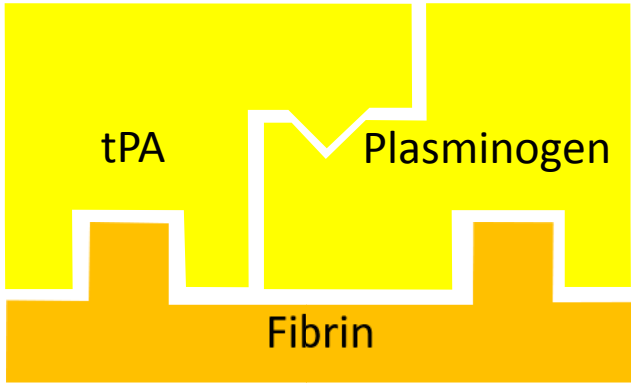
PLASMIN
FIBRINOVÁ SÍŤ
TRANEXAMOVÁ KYSELINA

TRAUMA



ŠOK — HYPOPERFÚZE

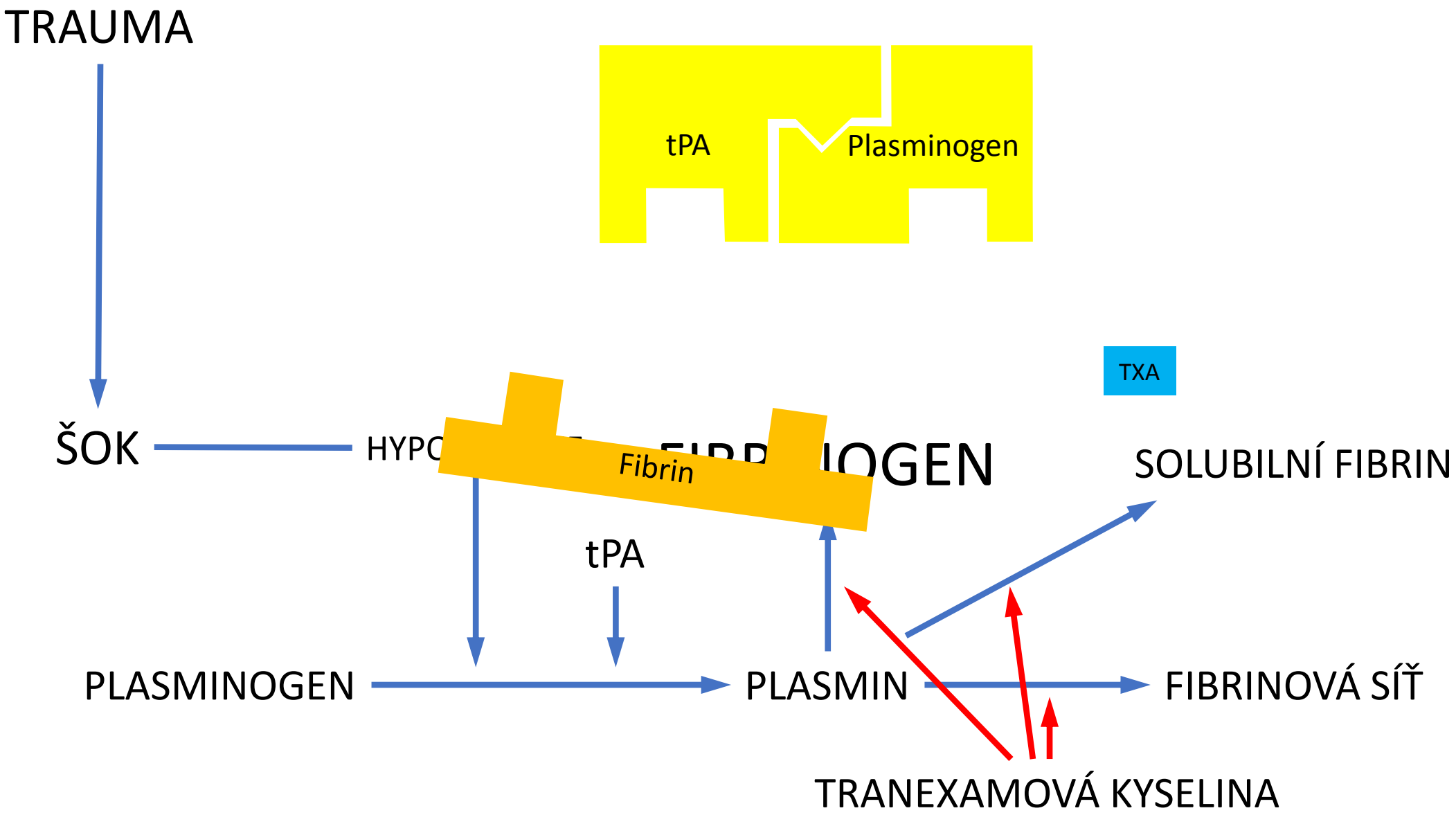
FIBRINOGEN

SOLUBILNÍ FIBRIN

tPA

PLASMINOGEN → PLASMIN → FIBRINOVÁ SÍŤ

TRANEXAMOVÁ KYSELINA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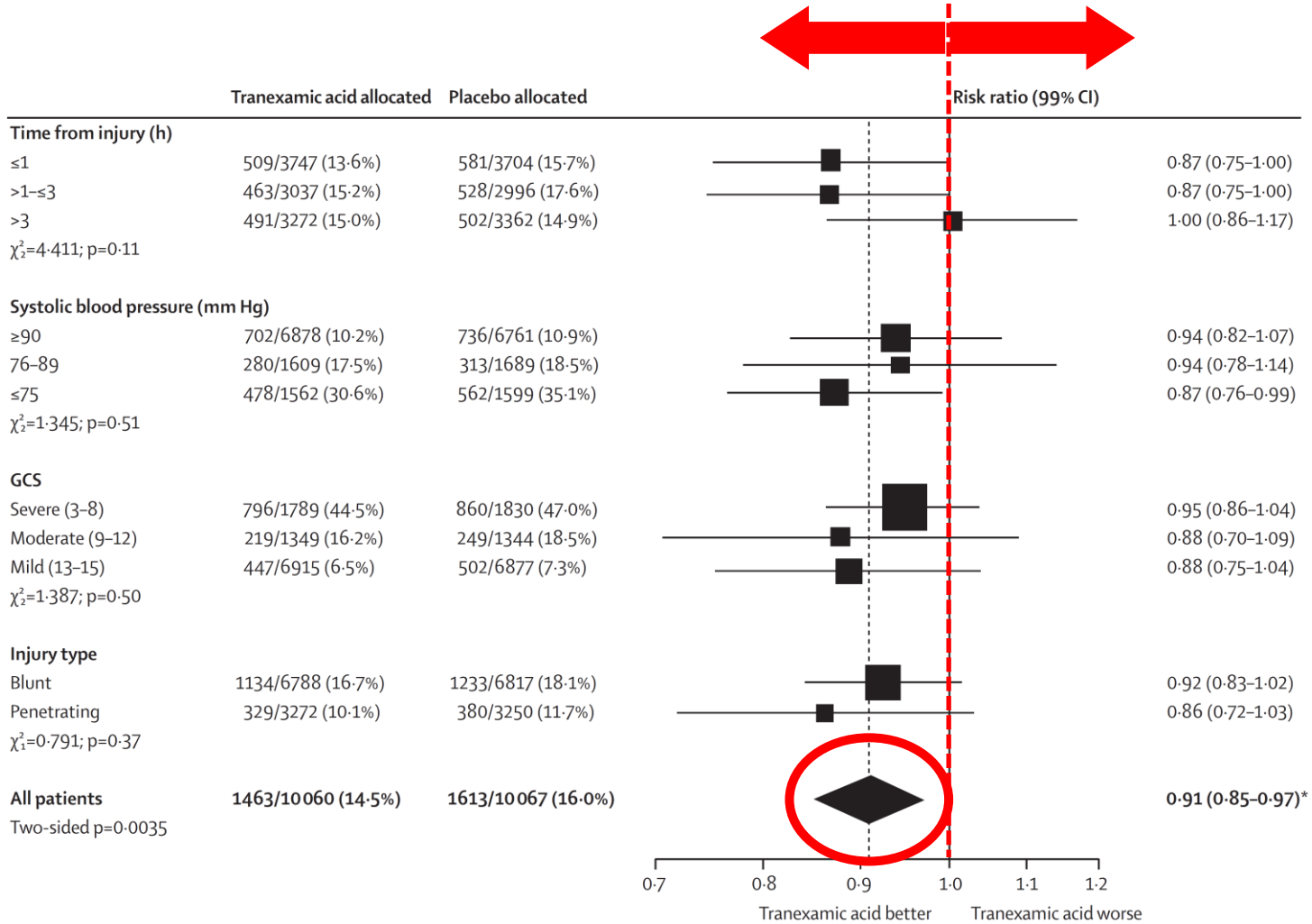
PLASMIN
FIBRINOVÁ SÍŤ
TRANEXAMOVÁ KYSELINA

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**



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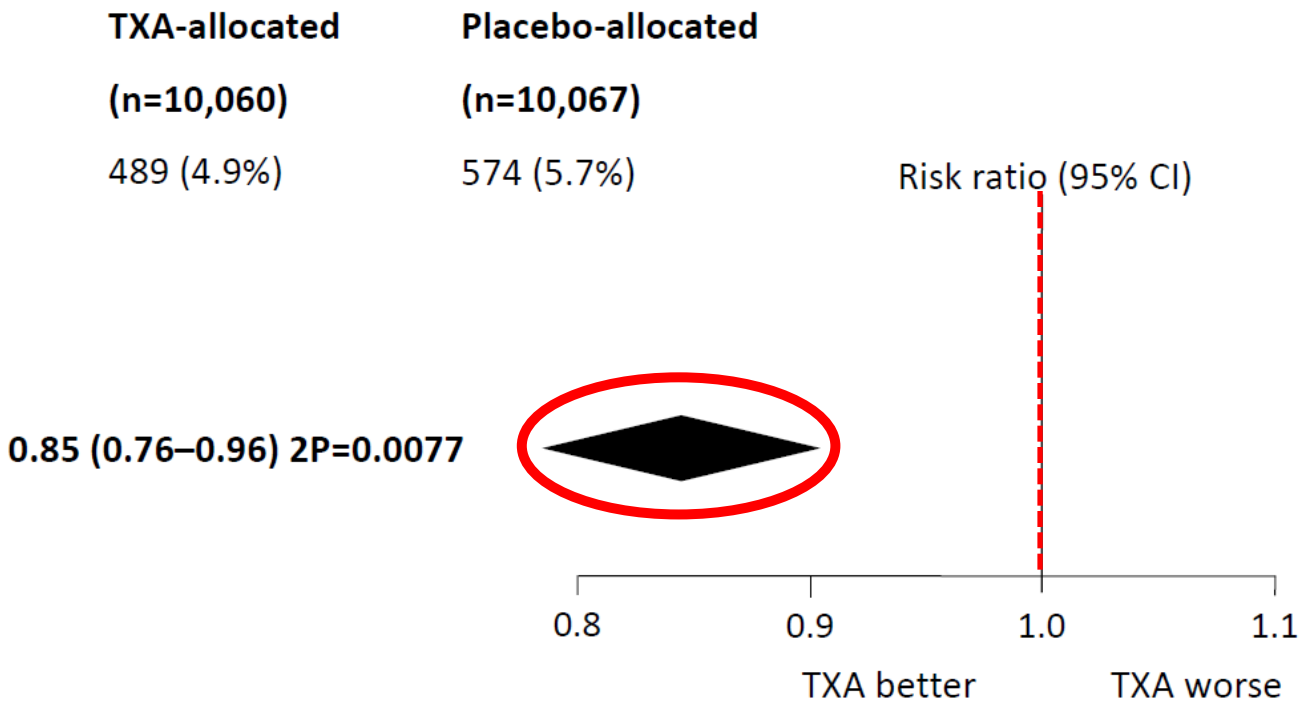
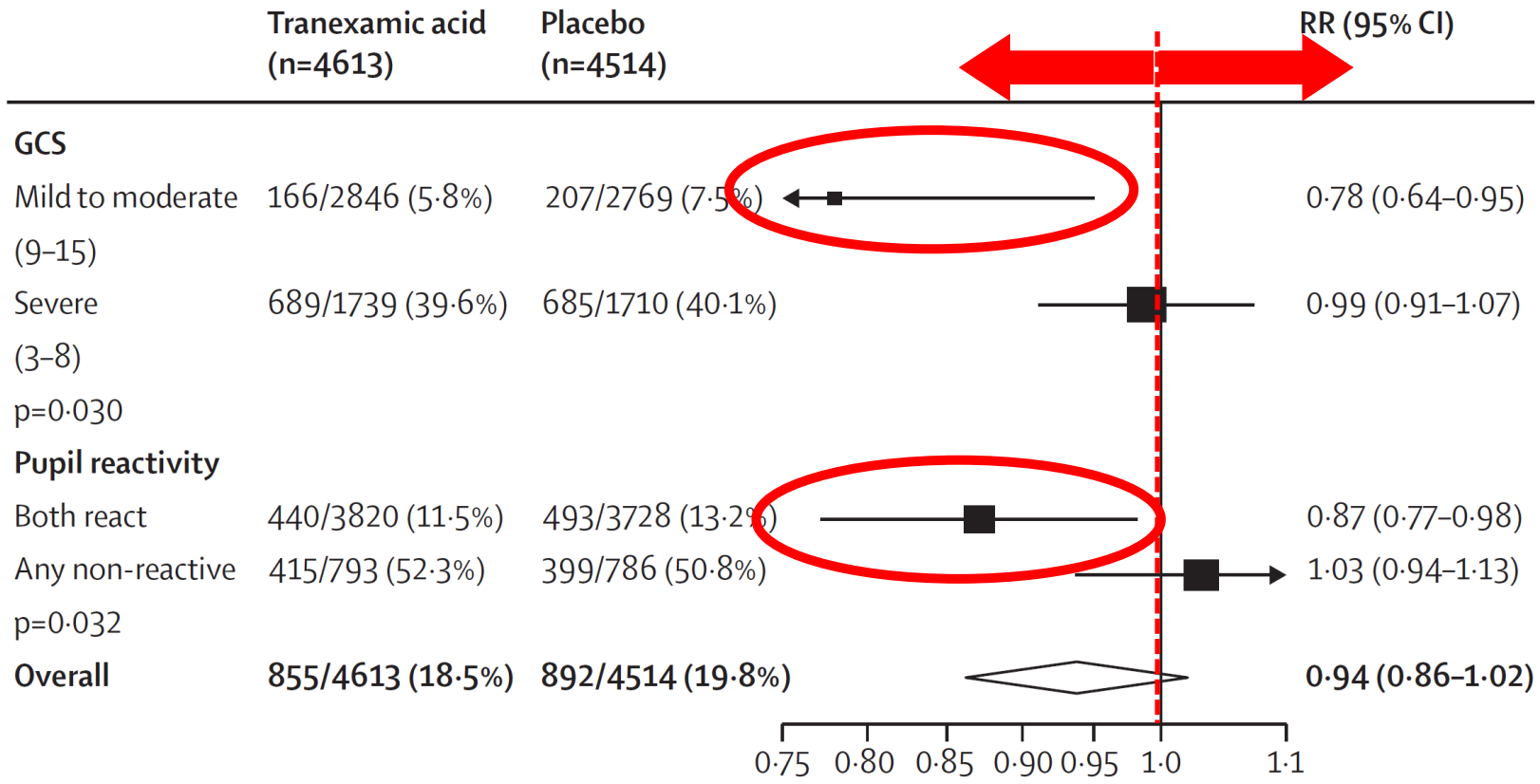


Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial

*The CRASH-3 trial collaborators**

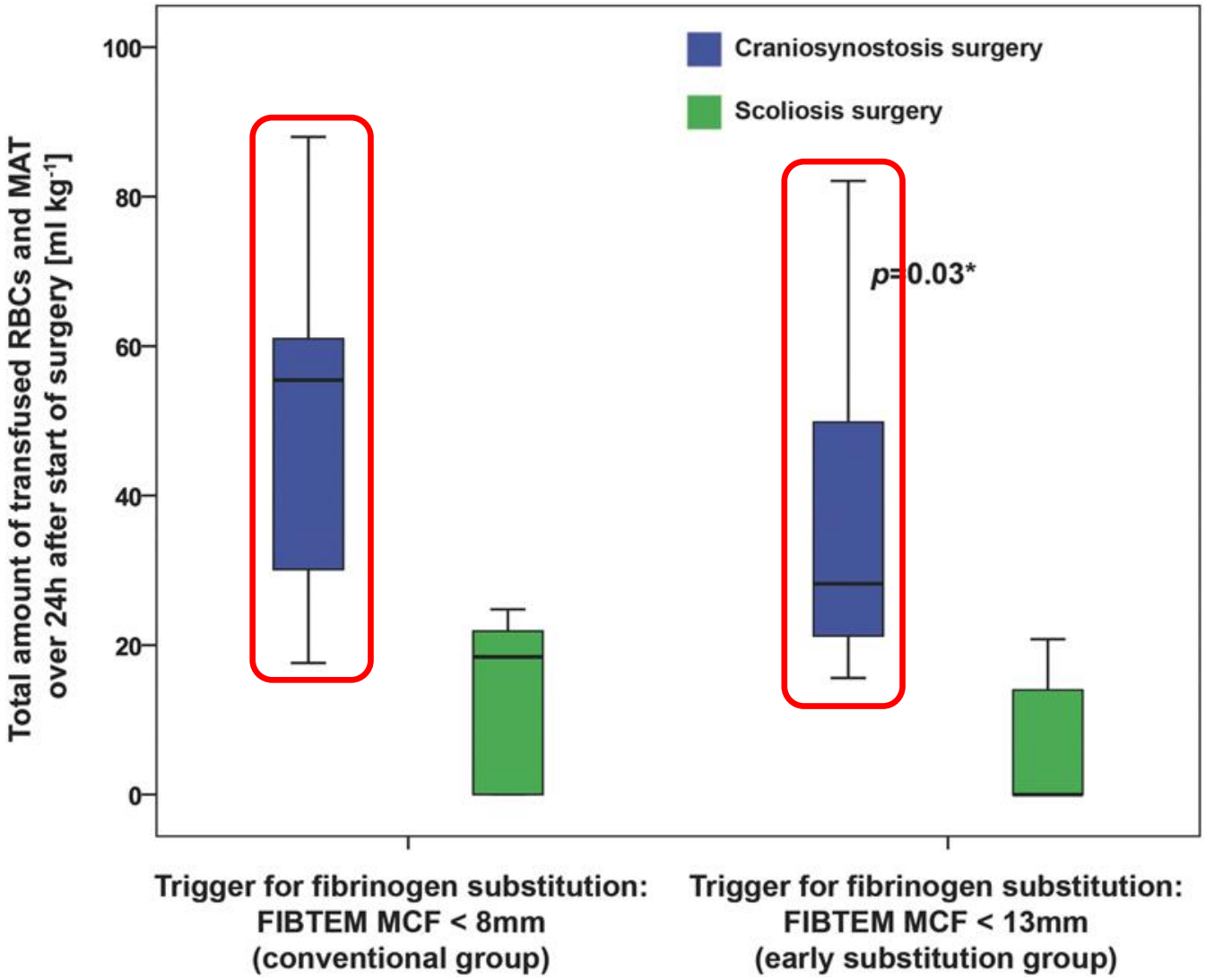


Lancet 2019; 394: 1713–23

TXA u dětského polytraumatu

Outcomes	Reference, *n* = 1,914, *n* (%)	Tranexamic Acid Administration, *n* = 1,914, *n* (%)	Risk Difference in % (95% CIs)	*p*
Primary outcomes				
Seizure	0 (0)	7 (0.37)	0.37 (0.10–0.64)	0.008
Thromboembolism	2 (0.1)	1 (0.05)	−0.05 (−0.23 to −0.12)	0.56
Renal dysfunction	0 (0)	3 (0.16)	0.16 (−0.02 to −0.33)	0.08
Secondary outcomes				
In-hospital mortality	18 (0.94)	13 (0.68)	−0.26 (−0.83 to −0.31)	0.37

Pediatr Crit Care Med 2018; 19:e637–e642



Haas Br J Anaesth 2015;115(2):234–243

STUDY PROTOCOL Open Access

Traumatic injury clinical trial evaluating tranexamic acid in children (TIC-TOC): study protocol for a pilot randomized controlled trial

Daniel K. Nishijima[1*], John VanBuren[2], Hilary A. Hewes[3], Sage R. Myers[4], Rachel M. Stanley[5], P. David Adelson[6], Sarah E. Barnhard[7], Matthew Bobinski[8], Simona Ghetti[9], James F. Holmes[1], Ian Roberts[10], Walton O. Schalick III[11], Nam K. Tran[12], Leah S. Tzimenatos[1], J. Michael Dean[2], Nathan Kuppermann[13] for the TIC-TOC Collaborators of the Pediatric Emergency Care Applied Research Network

Study Design Go to

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	40 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Triple (Participant, Care Provider, Investigator)
Primary Purpose:	Treatment
Official Title:	Traumatic Injury Clinical Trial Evaluating Tranexamic Acid in Children (TIC-TOC): A Pilot and Feasibility Study
Actual Study Start Date :	March 4, 2019
Estimated Primary Completion Date :	June 2020
Estimated Study Completion Date :	June 2020

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Nishijima et al. Trials (2018) 19:593

TXA

- 15–30 mg/kg s následnou infúzí 2−10 mg/kg/h.
- 15 mg/kg s následnou infúzí 10 mg/kg/hod (Dadure 11)
- 50 mg/kg s následnou infúzí 5 mg/kg/h (Goobie 11)
- 15 mg/kg s následnou infúzí 2 mg/kg/hod po dobu 8 hodin (Royal College of Paediatrics and Child Health Evidence Statement. Major trauma and the use of tranexamic acid in children).

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Substituce

Initial coagulation resuscitation

Recommendation 24 In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies:

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

Spahn et al. Critical Care (2019) 23:98

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 Treml, Dieter Wally, Benjamin Treichl, Agnes Mayr, Christof Kranewitter, Elgar Oswald

- Monocentrická studie
- Polytraumatizovaní pacienti se známkami koagulopatie dle ROTEM
- FFP (15 ml/kg) vs CFC (primárně fibrinogen 50 mg/kg)
- Ukončená předčasně pro nadmíru vysoké selhání terapie ve skupině FFP

Lancet Haematol 2017; 4: e258–71

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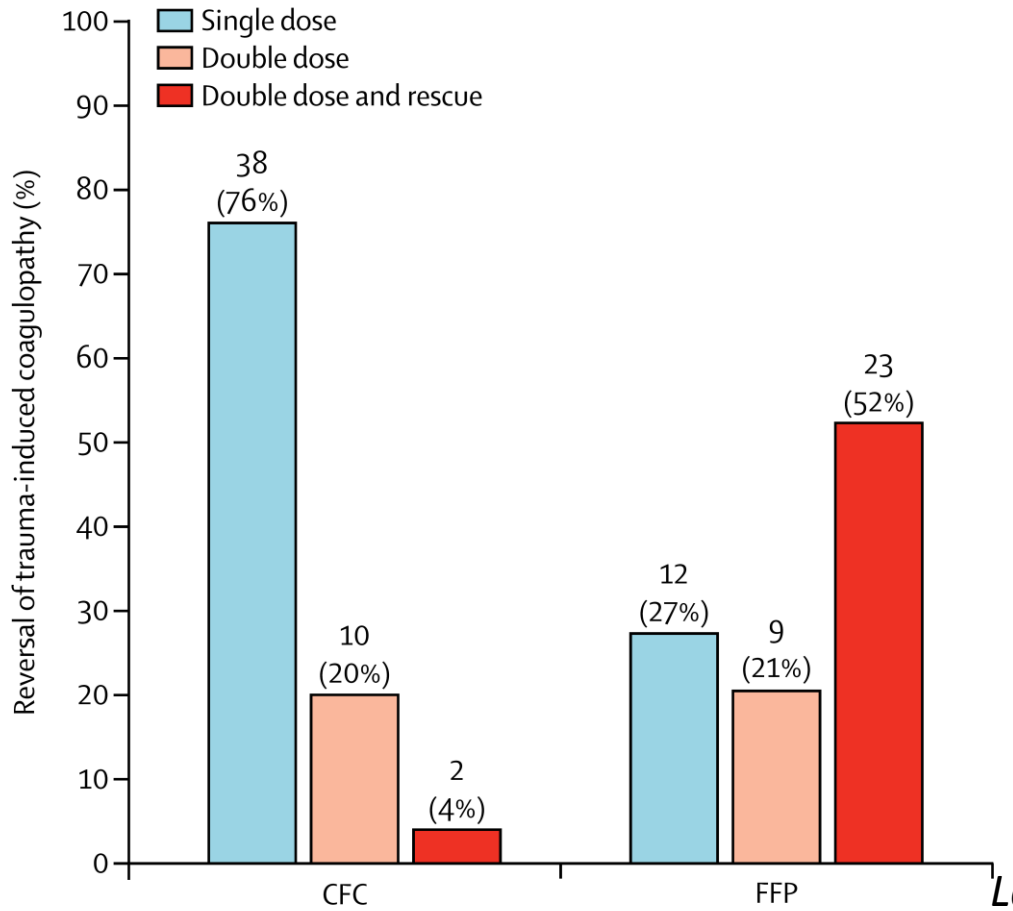

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- Vyšší riziko MODS (OR 3,13 [1,19–8,88], p=0,025).
- Vyšší ISS-adaptované SOFA score 0,16 (0,13-0,21) vs. 0,2 (0,15-0,27); p=0,19
- Více pacientů potřebovala masivní transfúzi

Lancet Haematol 2017; 4: e258–71

Proč zejména fibrinogen?

Table 24.2 The coagulation factors.

Factor	Plasma half-life (h)	Plasma concentration (mg/L)	Comments
II	65	100	Prothrombin group: vitamin K needed for synthesis; require Ca^{2+} for activation
VII	5	0.5	
IX	25	5	
X	40	10	
I	90	3000	Thrombin interacts with them; increase in inflammation, pregnancy, oral contraceptives
V	15	10	
VIII	10	0.1	
XI	45	5	
XIII	200	30	

Fibrinogen supplementation

Recommendation 28 We recommend treatment with fibrinogen concentrate or cryoprecipitate if major bleeding is accompanied by hypofibrinogenaemia (viscoelastic signs of a functional fibrinogen deficit or a plasma Clauss fibrinogen level ≤ 1.5 g/L). (Grade 1C)

We suggest an initial fibrinogen supplementation of 3–4 g. This is equivalent to 15–20 single-donor units of cryoprecipitate or 3–4 g fibrinogen concentrate. Repeat doses should be guided by VEM and laboratory assessment of fibrinogen levels. (Grade 2C)

Spahn et al. Critical Care (2019) 23:98

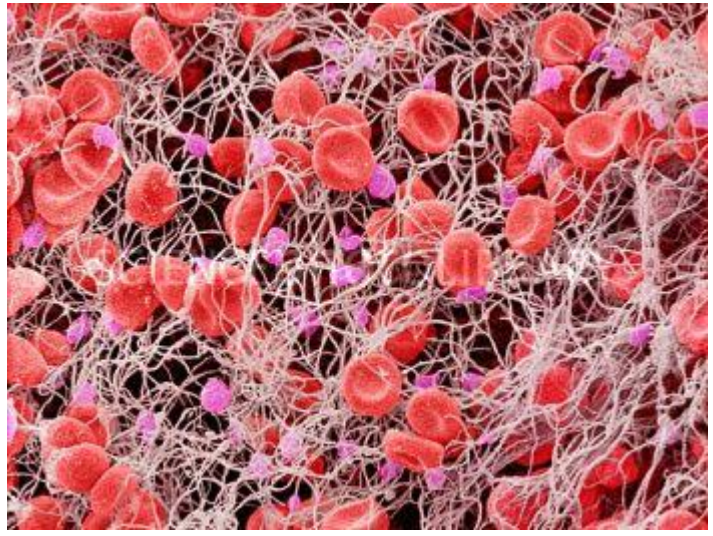
Substituce u dětí

- Není doporučení u traumat
- (20) 30- 50 mg / kg

Závěr

- TIC a zejména hypofibrinogenémie je důležitou příčinou mortality
- Viskoelastické metody nabízejí výhody oproti standardním koagulačním testům a dají se s výhodou kombinovat
- Tranexamová kyselina je indikovaná u každého pediatrického pacienta s možným masivním krvácením

Jak ideálně postupovat?



Děkuji za pozornost