Cílená hemosubstituční terapie pacientů s ŽOK v důsledku traumatu

Vaníčková Kateřina

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Klinika anesteziologie, resuscitace a intenzivní medicíny LF MU
a Fakultní nemocnice Brno

World Health Organization

19 June 2024

FAKULTNÍ NEMOCNICE BRNO

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- Injuries – both unintentional and violence-related – **take the lives of 4.4 million people around the world each year** and constitute nearly **8% of all deaths**.

- **For people age 5-29 years, 3 of the top 5 causes of death** are injury-related, namely road traffic injuries, homicide and suicide.

- Injuries and violence are responsible for an estimated **10% of all years lived with disability.**

- Injuries and violence place a massive burden on national economies, costing countries billions of US dollars each year in health care, lost productivity and law enforcement.

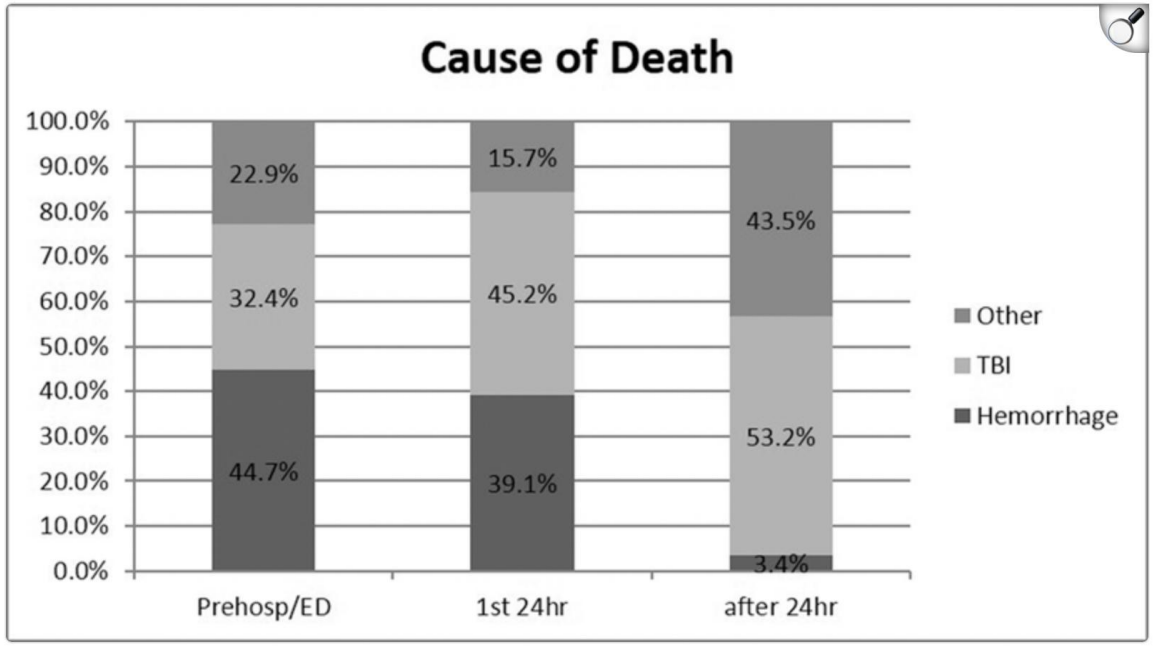
- Preventing injuries and violence will facilitate achievement of several Sustainable Development Goal (SDG) targets.

The why and how our trauma patients die:
A prospective Multicenter Western Trauma Association study

Callcut, Rachael A et al. *The journal of trauma and acute care surgery* vol. 86,5 (2019): 864-870. doi:10.1097/TA.0000000000002205

Primary Cause of Death

	Penetrating	Blunt	Total	p-value
TBI	154 (37.4%)	537 (47.8%)	691 (45.0%)	p=0.0003
Exsanguination	213 (51.7%)	140 (12.5%)	353 (23.0%)	p<0.0001
Early Physiologic Collapse	24 (5.8%)	125 (11.1%)	149 (9.7%)	p=0.0019
Late Physiologic Collapse	17 (4.1%)	222 (19.8%)	239 (15.6%)	p<0.0001
Airway	3 (0.73%)	20 (1.8%)	23 (1.5%)	p=0.1329
Sudden Unexpected Event	1 (0.24%)	14 (1.3%)	15 (0.98%)	p=0.076



healthcare MDPI

FAKULTNÍ NEMOCNICE BRNO

MUNI MED

Article

National Assessment of Opportunities for Improvement in Preventable Trauma Deaths: A Mixed-Methods Study

Junsik Kwon [1], Myeonggyun Lee [2] and Kyoungwon Jung [1,*]

3.3. Classification by Cause of Death

Among the 160 preventable trauma death cases, hemorrhage was the leading cause of death in 56 cases (35.0%), followed by sepsis or multiorgan failure and central nervous system injury. Additionally, in some cases the death was due to respiratory and cardiac issues, and in seven cases the cause of death was undetermined. In cases with preventable trauma deaths in 2017, although the causes of death showed a generally similar distribution, there was a difference in which central nervous system injury accounted for more deaths than sepsis/multiorgan failure (Table 3).

Table 3. Causes of mortality in cases with preventable trauma death.

Causes	2017 Number (%)	2019 Number (%)
Hemorrhage	117 (45.3)	56 (35.0)
Sepsis/multiorgan failure	43 (16.7)	43 (26.9)
Central nerve system injury	45 (17.4)	37 (23.1)
Respiratory issues	36 (14.0)	12 (7.5)
Cardiac issues	13 (5.0)	5 (3.1)
Undetermined	4 (1.6)	7 (4.4)
Total	258 (100.0)	160 (100.0)

Table 4. Opportunities for improvement by treatment stage for patients who died from hemorrhage.

Phase of Care	Inappropriate Care Related to	2017 Number (%)	2019 Number (%)
Prehospital	Inadequate hospital selection	15 (27.8)	8 (50.0)
	Fluid resuscitation	22 (40.7)	4 (25.0)
	Delay in transfer (to first hospital)	1 (1.9)	4 (25.0)
	Delay or miss in hemostatic procedures	8 (14.8)	0 (0.0)
	Airway management	8 (14.8)	0 (0.0)
	Total	54	16
Interhospital	Delay in transfer (to final hospital)	15 (19.0)	5 (22.7)
	Delay in transfusion	16 (20.3)	4 (18.2)
	Delay in hemostatic procedures	9 (11.4)	4 (18.2)
	Unsafe transfer	5 (6.3)	3 (13.6)
	Inadequate hospital selection	2 (2.5)	2 (9.1)
	Delay in procedures other than hemostasis	17 (21.5)	2 (9.1)
	Airway management	12 (15.2)	1 (4.5)
	Inappropriate diagnostic workup	3 (3.8)	1 (4.5)
	Total	79	22
Hospital	Delay in hemostatic procedures	66 (21.5)	46 (29.3)
	Delay in procedures other than hemostasis	75 (24.4)	42 (26.8)
	Delay in Transfusion	88 (28.7)	41 (26.1)
	Inappropriate diagnostic workup	29 (9.5)	17 (10.8)
	Airway and ventilation management	25 (8.1)	6 (3.8)
	Documentation	22 (7.2)	5 (3.2)
	Others	2 (0.6)	0 (0.0)
	Total	307	157

Healthcare ***2023****, 11, 2291. https://doi.org/10.3390/healthcare11162291*

UNDERSTANDING THE DISEASE

Trauma-induced coagulopathy

Derek J. B. Kleinveld[1,2], Sophie R. Hamada[3,4] and Claudio Sandroni[5,6*]

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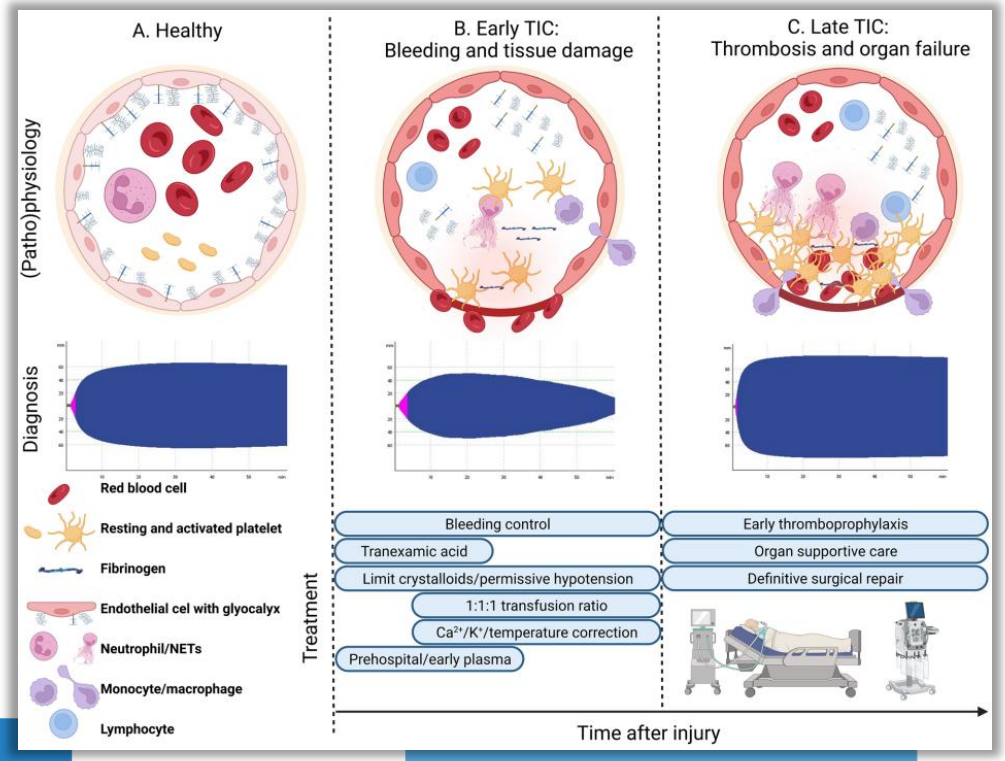
About **one-quarter of patients with severe trauma** develop a clotting disorder termed trauma-induced coagulopathy (TIC) which **is fatal in 30–50% of cases**.

TIC starts early after trauma and can be detected in the most severely injured patients, already **at the scene** of the accident.



Zdravotnická záchranná služba Jihomoravského kraje, p.o.
Kamenice 798/1d, 625 00 Brno
IČ: 00346292
IČP: 72901212

ZÁZNAM O VÝJEZDU **RV** PRI

Č. výjezdu: 092_01	Výzva: 10:01	25031010483625 Xy	
Datum: 10.3.2025	Výjezd: 10:02		999: neznámá identita, informován IP
Lékař: MUDr. OBORSKÁ Kateřina	Na místě: 10:13	Muž	
NLZP:	Transport: 10:34	Státní příslušnost: Česká republika	
Řidič: KNOBLOCH Lubomír	Přijezd ZZ: 10:38	Příbuzní/osoba blízká:	
Další:	Předání: 10:40	Heslo na info:	km:
	Na základně:	Místo zásahu: Brno, Studentská stavba biofarma,na bodě bude navigátor	
V. přijal: Bc. Kateřina Motyčková	Ukončení:		
V. zpracoval Ing. Kateřina Janeczková	Vozidlo: 25, 3BF 1144	Výjezdová základna: IV	
Indikace: ÚRAZ	Nal.: 1a	Místo výjezdu: IV	

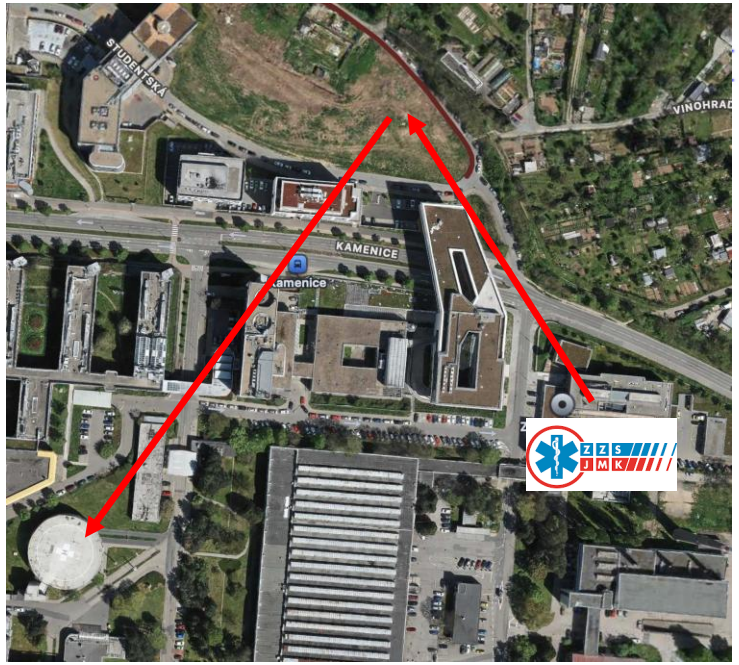
NO:
Propadl otvorem v podlaze 1.patra do přízemí, cca 4m na beton, hlava a P polovina těla, od počátku bezvědomí v poloze na P boku

Alergie:
nelze

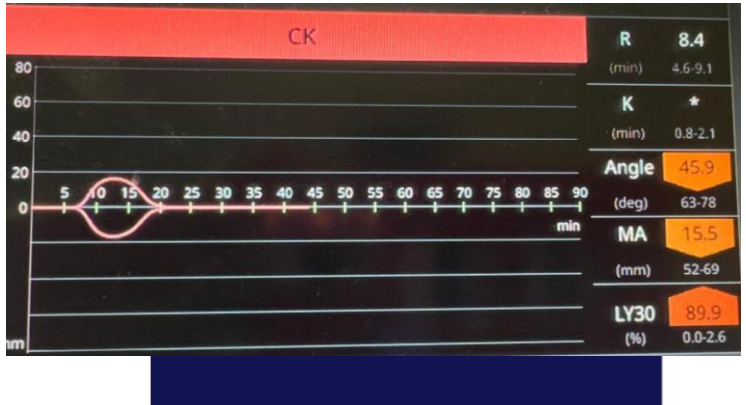
Anamnéza:
FA + OA: nelze

Objektivní nález:
Při příjezdu v polozena P boku, pod hlavou kaluž krve s koaguly cca 500-750ml ztráta, lapavé dýchání, otočen na záda
X- krvácení z P ucha a hlavy
A-neudrží, ambuing, masivně krvácí z ust odsáváno,
B- obtížně zajištěny DC, et 8,0 s bužií, pravý hrudník paradoxní dýchání, nestabilníprovedena torakostomie v 5.mezižebří, kapno 30, plíce se rozvíjí, saturace špatně měřitelná
C- TK neměřen, na místě velkémnožství krve, krátky dojezd do nemocnice, pulzace na periferii hmatné po celou dobu, CRT 3s
D- bezvědomí, široká mydriáza areaktivní, z P ucha krev a tkán
E- susp fr. PHK a poranění bérce LDK, pánev bez dislokace

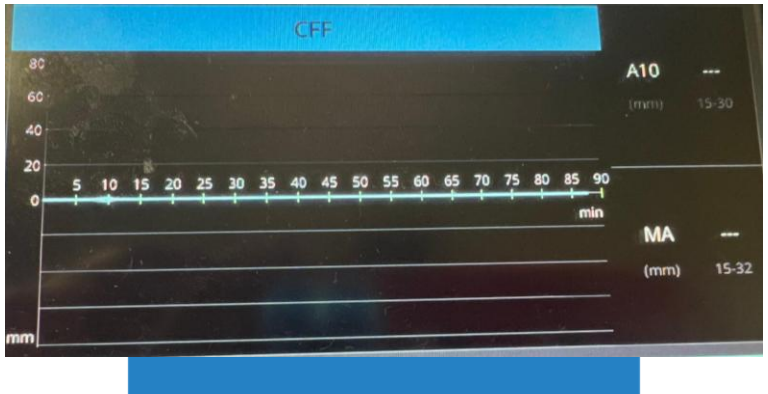
Dg polytrauma - hlava, hrudník PHK, PDK



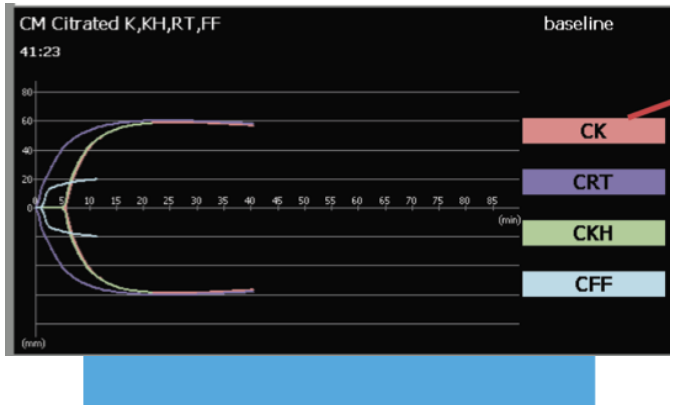
hyperfibrinolýza



deficit fibrinogenu



fyziologický tvar křivek



Pathophysiology of Trauma-Induced Coagulopathy

Herbert Schöchl [1], Felix C F Schmitt [2], Marc Maegele [3] [4]

Affiliations + expand

PMID: 38417803 DOI: 10.1055/a-2215-8936

Damage control haemostatic interventions are essential to halt TIC progression.

Endogenous factors TIC:

- combination of hypovolemic shock
- substantial tissue injury
- endothelial damage
- glycocalyx shedding
- upregulated fibrinolysis
- fibrinogen depletion
- altered thrombin generation
- platelet dysfunction

Exogenous factors

- minimise fluid infusion to avoid dilution of coagulation factors
- permissive hypotension
- correcting hypothermia
- correcting acidosis
- early administration of tranexamic acid

- replacing blood products
- replacing calcium

Journal of
Clinical Medicine

MDPI

Review

Whole Blood, Fixed Ratio, or Goal-Directed Blood Component Therapy for the Initial Resuscitation of Severely Hemorrhaging Trauma Patients: A Narrative Review

Mark Walsh [1,2], Ernest E. Moore [3,4], Hunter B. Moore [4], Scott Thomas [5], Hau C. Kwaan [6], Jacob Speybroeck [1], Mathew Marsee [1], Connor M. Bunch [1], John Stillson [1], Anthony V. Thomas [1], Annie Grisoli [1], John Aversa [7], Daniel Fulkerson [8], Stefani Vande Lune [9], Lucas Sjeklocha [10] and Quincy K. Tran [10,*]

FAKULTNÍ NEMOCNICE BRNO

MUNI MED

Table 2. Advantages and disadvantages of whole blood vs. fixed ratio vs. VET-guided BCT.

	Advantages	Disadvantages
Whole blood	- Simple protocols and uniform dosing - Easy to administer in prehospital and hospital setting - Provides all blood components; avoids hemodilution	- Not physiologically driven - Few RCTs - Unnecessary blood components may be given- Products currently not universally available; shorter shelf life - Requires AABB variances and additional cost
Fixed ratio	- Simple protocols and uniform dosing - Easy to administer in prehospital and hospital setting - More RCTs, but questionable validity regarding 1:1:1 vs. 1:1:2 - Blood components readily available	- Not physiologically driven - Unnecessary blood components may be given - Does not replenish fibrinogen effectively in early stages
VET-guided BCT	- Provides early physiologically driven resuscitation - Limits blood product waste - Blood components readily available	- Protocols not straight forward; accuracy operator dependent; steep learning curve - Cannot be used in prehospital setting - Few RCTs

J Clin Med. 2021 Jan 17;10(2):320. doi: 10.3390/jcm10020320. PMID: 33477257; PMCID: PMC7830337.

Intensive Care Med
https://doi.org/10.1007/s00134-022-06834-7

UNDERSTANDING THE DISEASE

Trauma-induced coagulopathy

Derek J. B. Kleinveld[1,2], Sophie R. Hamada[3,4] and Claudio Sandroni[5,6*]

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Early activation of massive transfusion protocols employing a balanced transfusion strategy of **1:1:1** red blood cells, plasma, and platelets. Based on pathophysiology, **replacing fbrinogen and calcium** as essential components of the coagulation cascade is also necessary.

Intensive Care Med https://doi.org/10.1007/s00134-022-06834-7

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Česká společnost anesteziologie resuscitace a intenzivní medicíny

V **úvodní etapě** léčby pacientů se ŽOK je doporučen jeden **ze dvou** následujících postupů:

- **použití jednotek FFP v poměru k ETP v poměru 1:2** *(1B)*
- podání fibrinogenu a ETP podle jejich aktuálních hodnot/hladin *(1C)*

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

Critical Care

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]

Initial coagulation resuscitation

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)***

https://doi.org/10.36290/aim.2024.022

Použití plné krve u pacientů se život ohrožujícím krvácením v důsledku traumatu: souhrn a konsenzus jednání mezioborového panelu

Bláha J.[1], Bohoněk M.[2,3], *Černý V.[4–10], Klugar M.[4], Kočí J.[11,12], Loužil J.[13], Řeháček V.[14], Truhlář A.[6,15,16], Zýková I.[8,17,18]

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Stanovisko 3
současný stav odborného poznání a vědeckých důkazů předmětné problematiky **neumožňuje označit podávání plné krve jako preferovanou metodu** v rámci postupu při masivních krevních ztrátách nebo v léčbě traumatem indukované koagulopatie.

Stanovisko 4
Podání plné krve je možnou alternativou ke stávajícím postupům léčby u pacientů se život ohrožujícím krvácením při závažném traumatu, zejména v podmínkách přednemocniční péče, případně na urgentních příjmech nemocnic.

Spahn *et al. Critical Care* 2013, **17**:R76
http://ccforum.com/content/17/2/R76

CRITICAL CARE

RESEARCH Open Access

Management of bleeding and coagulopathy following major trauma: an updated European guideline

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

Coagulation monitoring
We recommend that viscoelastic methods also be performed to assist in characterising the coagulopa-thy and in **guiding haemostatic therapy.**

Table 2. Advantages and disadvantages of whole blood vs. fixed ratio vs. VET-guided BCT.

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

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]

Initial coagulation resuscitation
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- **Fibrinogen concentrate or cryoprecipitate and pRBC**
  (Grade 1C)

Rossaint *et al. Critical Care* (2023) 27:80
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GUIDELINES Open Access

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

David et al. Critical Care (2023) 27:141
https://doi.org/10.1186/s13054-023-04421-w

Critical Care

RESEARCH Open Access

Thromboelastometry-guided haemostatic resuscitation in severely injured patients: a propensity score-matched study

Jean-Stéphane David[1,2*], Arthur James[3], Maxime Orion[1], Agathe Selves[3], Mélody Bonnet[1], Pauline Glasman[3], Charles-Hervé Vacheron[1,4,5] and Mathieu Raux[6]

FAKULTNÍ NEMOCNICE BRNO

MUNI MED

Abstract

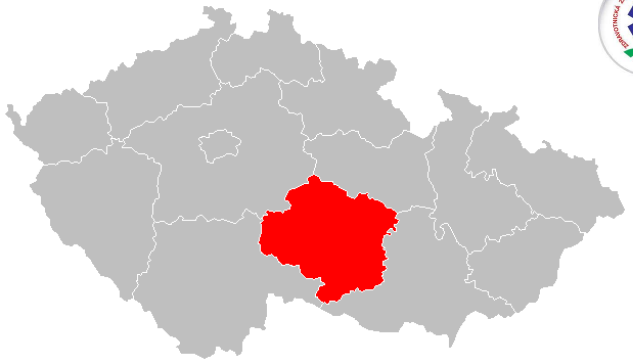
Background To accelerate the diagnosis and treatment of trauma-induced coagulopathy (TIC), viscoelastic haemo- static assays (VHA) are increasingly used worldwide, although their value is still debated, with a recent randomised trial showing no improvement in outcome. The objective of this retrospective study was to compare 2 cohorts of injured patients in which TIC was managed with either a VHA-based algorithm or a conventional coagulation test (CCT)-based algorithm.

Results From 2012 to 2019, **7250** patients were admitted in the 2 trauma centres, and among these 624 were included in the study (CCT group: 380; VHA group: 244). After propensity score matching, 215 patients remained in each study group without any significant difference in demographics, vital signs, injury severity, or laboratory analysis. **At 24 h, more patients were alive and free of MT in the VHA group (162 patients, 75%) as compared to the CCT group (112 patients, 52%; $p < 0.01$) and fewer patients received MT (32 patients, 15% vs. 91 patients, 42%, $p < 0.01$)**. However, no significant difference was observed for mortality at 24 h (odds ratio 0.94, 95% CI 0.59–1.51) or survival at day 28 (odds ratio 0.87, 95% CI 0.58–1.29). **Overall cost of blood products and coagulation factors was dramatically reduced in the VHA group as compared to the CCT group** (median [interquartile range]: 2357 euros [1108–5020] vs. 4092 euros [2510–5916], $p < 0.001$).

Conclusions : VHA-based strategy was associated with an increase of the number of patients alive and free of MT at 24 h together with an important reduction of blood product use and associated costs. However, that did not translate into an improvement in mortality.

Hemosubstituce na OUP

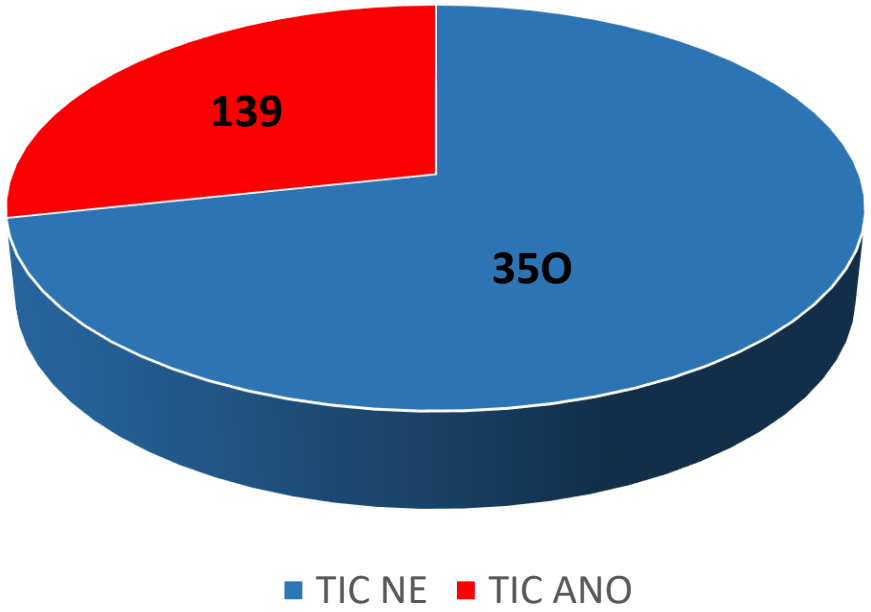
rok	počet pacientů přijatých na OUP celkem: ZZS JMK + ZZS KV	hemosubstituce na OUP: trauma ZZS JMK + ZZS KV	
2015	1899	65	3,4 %
2016	1586	60	3,7 %
2017	1408	96	6,8 %
2018	1541	134	8,7 %
2019	1387	83	6,0 %
2020	1406	95	6,8 %
2021	1570	102	6,5 %
2022	1602	114	7,1 %
2023	1616	119	7,4 %
2024	1880	126	6,7 %



∅ 6,3%

Vyhodnocení spolupráce ZZS KV a TC FN Brno Bohunice

2014-2024 **489** pacientů s ISS > 16
139 pacientů s TIC



ISS score	počet pacientů s TIC
16-20	11
21-30	40
31-40	31
41-50	34
51-60	4
61-75	19

Vyhodnocení spolupráce ZZS KV a TC FN Brno Bohunice - TIC

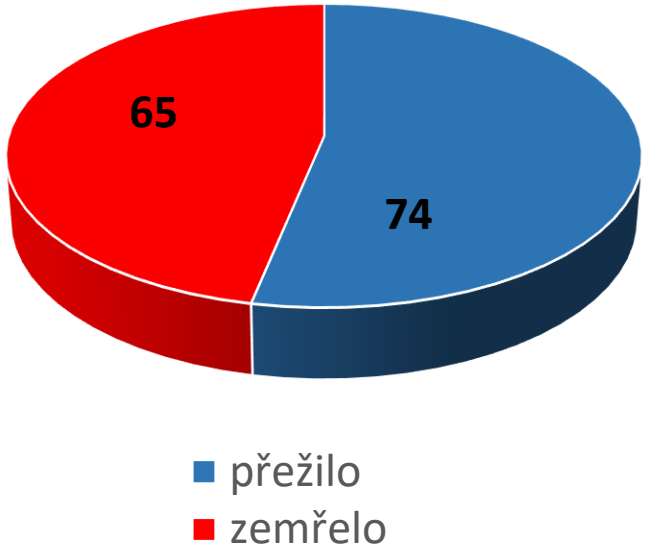
Established TIC upon emergency room admission is a prognostic indicator and is strongly associated with poor outcomes.

2014-2024	Počet pacientů Počet pacientů s TIC	Počet pacientů % Počet pacientů TIC %
ISS >16	489	100%
TIC	139	**28,4%**

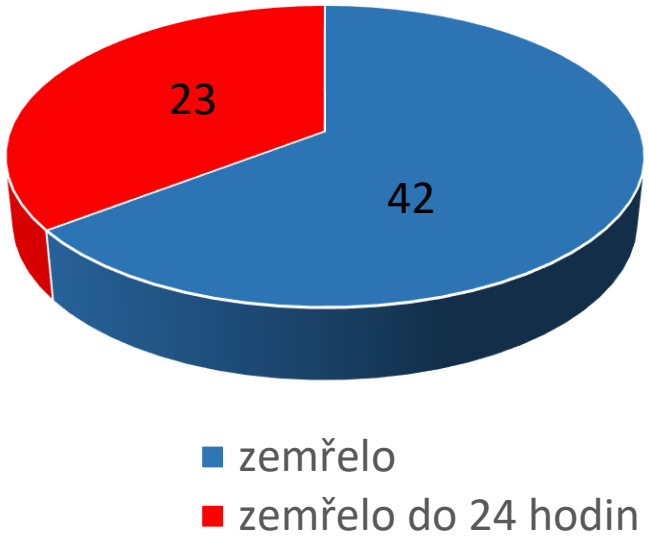
14/139 antikoagulační terapie

Vyhodnocení spolupráce ZZS KV a TC FN Brno Bohunice

TIC 139 pacientů



zemřelo 65 pacientů



do 24 hodin 23 pacientů
12 pacientů zemřelo na OUP
8 na KARIM
3 pacienti COS

mortalita TIC	**46,7%**
mortalita ISS > 16	13,2%

TIC is present in nearly one-third of all severely injured trauma patients and **carries a 50 % mortality rate**

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MUNI MED

Hemorrhage Control:
tourniquets
direct pressure
hemostatic dressings
REBOA

Reversal of:
hypothermia
acidosis
hypokalcemia
dilution due to crystalloid
and colloid fluid administration

Blood products:
plasma, RBCs and whole blood
thawed plasma
factors concentrates

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

Critical Care

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]

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I. Initial resuscitation and prevention of further bleeding

Pre-hospital blood product use

Recommendation 4

No clear recommendation or suggestion in favour or against the use of pre-hospital blood products can be provided at this time.

empirické podání fibrinogenu PP

- fibrinogen je kritickým proteinem hemostazy a krevního koagula
- substituce fibrinogenu je důležitou součástí multimodální terapie ŽOK

ČESKO-SLOVENSKÝ
MEZIOBOROVÝ DOPORUČENÝ POSTUP

DIAGNOSTIKA A LÉČBA ŽIVOT OHROŽUJÍCÍHO KRVÁCENÍ U DOSPĚLÝCH PACIENTŮ V INTENZIVNÍ A PERIOPERAČNÍ PÉČI

TIC SCORE		
Vitální funkce	měření	**body**
Tk systola	hodnota < 90	**5/0**
CR (lalůček,hrudník) - **pokud nelze Tk**	hodnota > 4	**0/5**
Pulz	hodnota > 100	**1**
Lokalizace krvácení	vyšetření	**body**
hrudník	nestabilita hrudníku	**1**
břicho	peritoneální dráždění	**1**
pánev	nestabilita	**2**
končetina levá dolní	zlomeny dlouhých kostí	**1**
končetina pravá dolní	zlomeny dlouhých kostí	**1**
aplikace FBR	**4g** – 2 balení	**> 7**

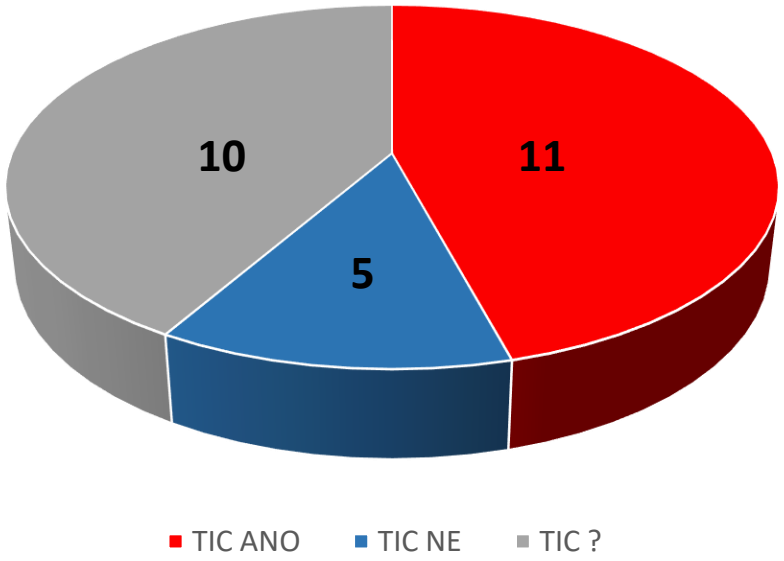
Při nemožnosti monitorování hladiny fibrinogenu a předpokladu jeho nízké hladiny doporučujeme podání koncentrátu fibrinogenu u pacientů se ŽOK co nejdříve i **bez znalosti jeho hladiny.**

empirické podání fibrinogenu PP

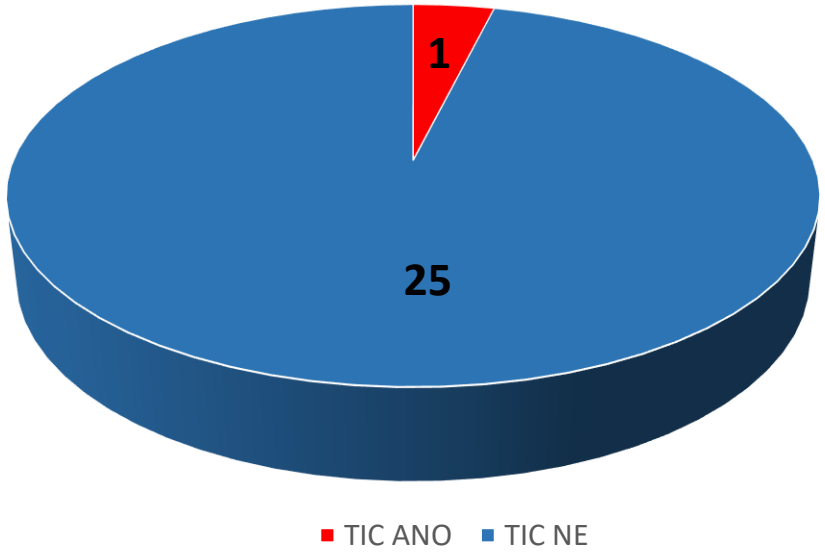
celkem **26** podání

ISS score	počet pacientů
16-20	2
21-30	9
31-40	5
41-50	5
51-60	0
61-75	3

odběr před aplikací FBG



odběr po aplikací FBG



Závěr

- nutná spolupráce mezi jednotlivých zdravotnickými zařízeními
- mezioborová shoda na vedení terapie
- vyhodnocení kvality a organizace zavedené terapie
- udržitelná terapie z hlediska budoucnosti

FAKULTNÍ NEMOCNICE BRNO

MUNI MED

Děkuji za pozornost…

Burt et al. Critical Care (2025) 29:49
https://doi.org/10.1186/s13054-025-05269-y

Critical Care

RESEARCH Open Access

Effect of early administration of fibrinogen replacement therapy in traumatic haemorrhage: a systematic review and meta-analysis of randomised controlled trials with narrative synthesis of observational studies

Tom Burt[1*], Ashley Guilliam[2], Elaine Cole[1] and Ross Davenport[1]

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Conclusion

This systematic review has highlighted the paucity of evidence to determine the effect of early fibrinogen replacement on mortality for trauma patients with severe bleeding.

This is especially evident in the early use of FgC in major haemorrhage.

After consideration of all the studies reviewed; **early fibrinogen therapy was not associated with reduced mortality, transfusion requirements or DVT incidence.**

This systematic review highlights the urgent need.

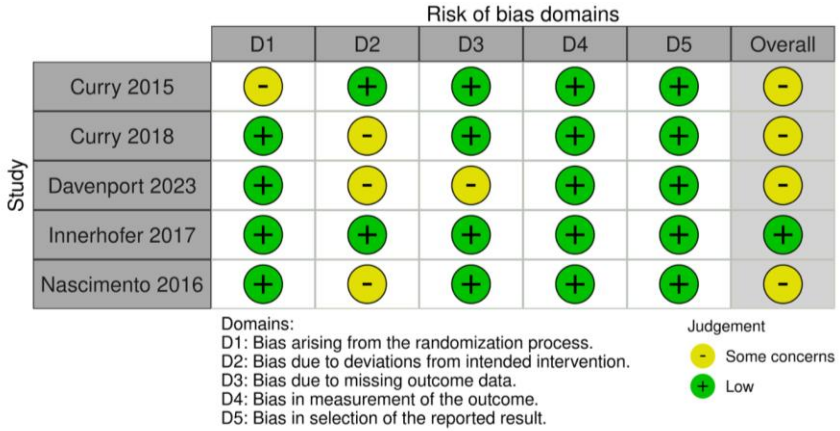

Fig. 6 Risk of Bias Summary RCTs. Risk of Bias Summary. RCTs only, using RoB2 tool

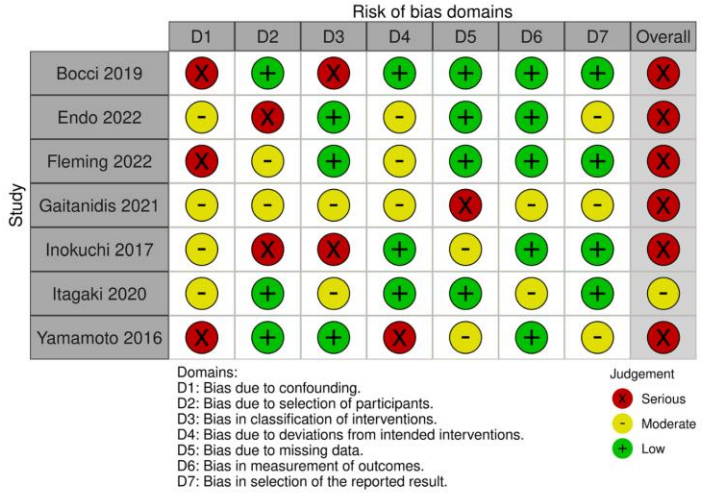

Fig. 7 Risk of Bias Summary Observational Studies. Risk of Bias Summary. Observational studies only using ROBINS-I tool