

From Guidelines to the ICU Bedside:

POC-Guided Haemostatic Resuscitation, Fluid Strategy and Thromboprophylaxis



JAN BLÁHA

KLINIKA ANESTEZIOLOGIE, RESUSCITACE A INTENZIVNÍ MEDICÍNY 



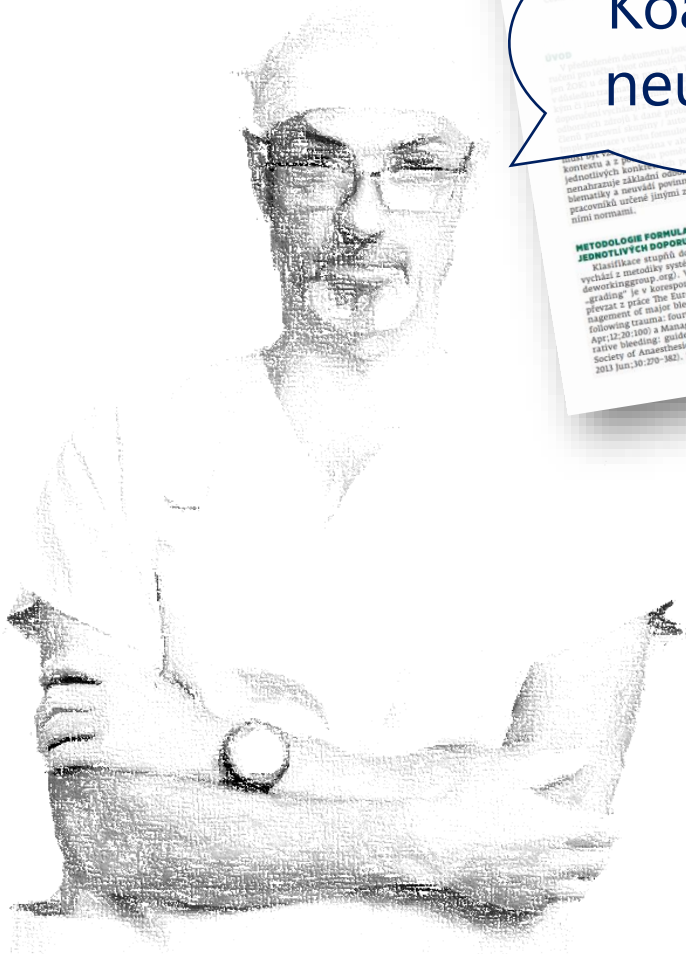
**1. LÉKAŘSKÁ
FAKULTA**
Univerzita Karlova



**VŠEOBECNÁ FAKULTNÍ
NEMOCNICE V PRAZE**

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CSL Behring



Koagulaci
neumím ...

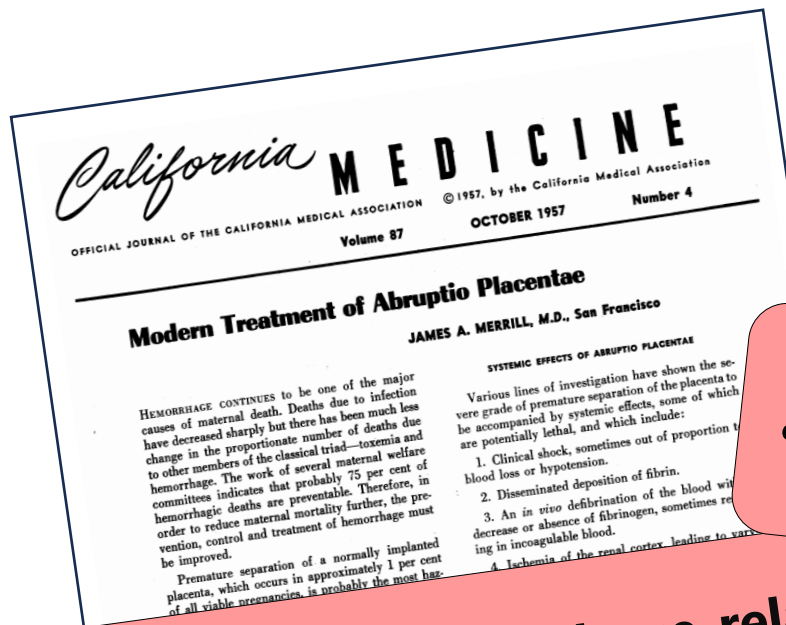
Potential conflict of interest: **CSL Behring**

AstraZeneca
octapharma

Tato prezentace vznikla s podporou společnosti CSL Behring.
Názory vyjádřené autorem v této prezentaci nemusí být v souladu s postoji společnosti CSL Behring.



1957



Delays in treatment in up to 90% of PPH cases

67% of maternal deaths in the USA and 85% in France were considered preventable

Up to 75% of hemorrhage-related deaths were potentially preventable



2022

We have studies. We have guidelines. We have expert recommendations.



A lot has changed ...

1990s

- **Volume resuscitation**
crystalloid-based fluid therapy
- **Liberal use of transfusions**
RBC; limited use of plasma and platelets
- **Expert opinions and personal experience**
- **Heparin, antithrombin !!!**

2000s

- **Guidelines**
locally adapted
- **Early use of TRF**
transfusion component ratios 1:2 (1:1:1)
- **Massive Transfusion Protocols**
enabling a rapid and standardised response
- **Novoseven®**

Today

- **Coagulation factors concentrates/ fibrinogen**
faster and safer than plasma
- **Tranexamic acid**
routinely administered based on the CRASH-2 / WOMAN trials
- **Octaplas**
immune-safer plasma
- **POC coagulation monitoring**
for targeted haemostatic therapy



We have

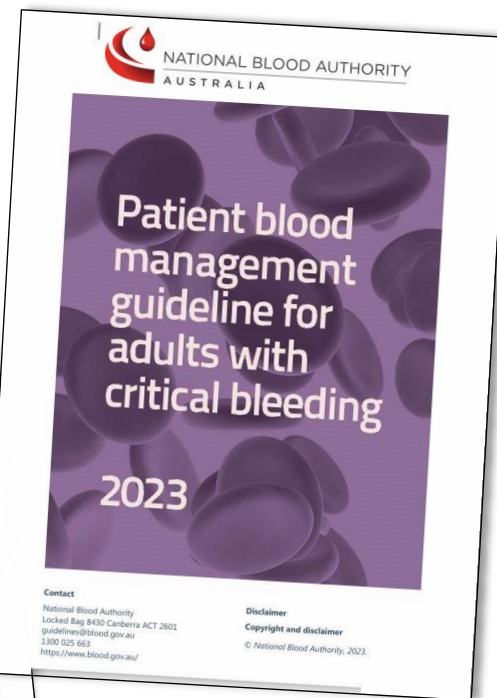
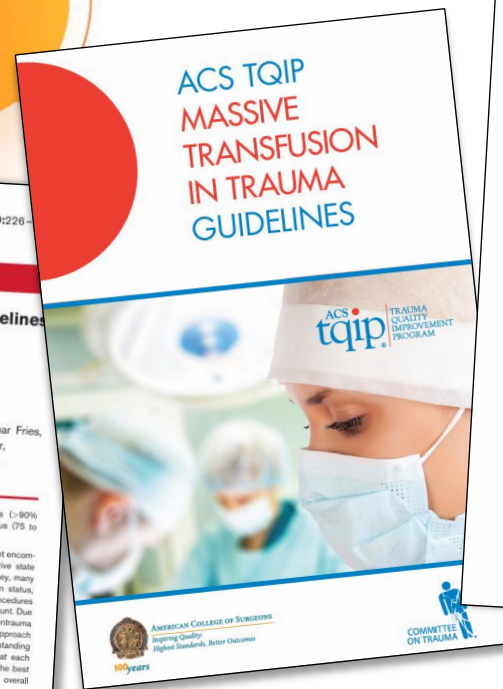
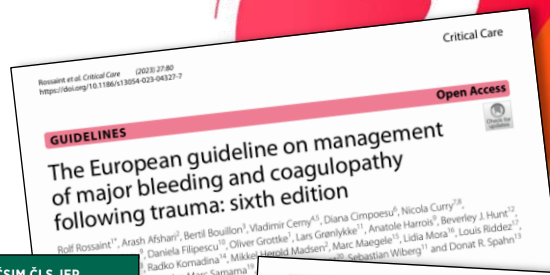
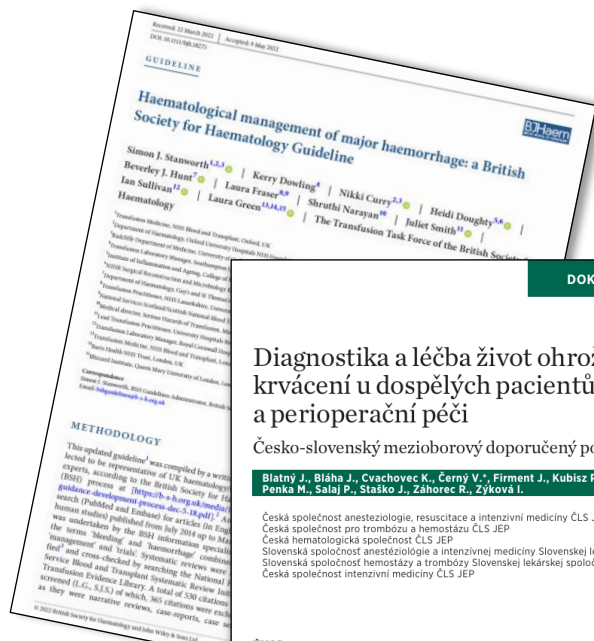
- better diagnostics
- safer blood products
- more effective drugs
- bedside monitoring

**We have
studies**

**We have expert
recommendations**

**We have
guidelines**

BUT TREATMENT IS STILL DELAYED...



Diagnostika a léčba život ohrožujícího krvácení u dospělých pacientů v intenzivní a perioperační péči

Česko-slovenský mezioborový doporučený postup

Blatný J., Bláha J., Cvachovec K., Černý V., Fírent J., Kubisz P., Kvasnička J., Masopust J., Penka M., Salaj P., Staško J., Záhořec R., Zýková I.

Česká společnost anesteziologie, resuscitace a intenzivní medicíny ČLS JEP
Česká společnost pro trombozu a hemostázu ČLS JEP
Česká hematologická společnost ČLS JEP
Slovenská společnost anesteziologie a intenzivní medicíny Slovenskej lekárskej spoločnosti
Slovenská společnost hemostázy a trombozy Slovenskej lekárskej spoločnosti
Česká společnost intenzivní medicíny ČLS JEP

Anest intenziv Med. 2017;28:263-269
*editor textu

ÚVOD

V předloženém dokumentu jsou uvedena doporučení pro léčbu život ohrožujícího krvácení (dále jen ŽOK) u dospělých pacientů, kde k ŽOK došlo v důsledku traumatu nebo v souvislosti s chirurgickým či jiným intervenčním výkonem. Jednotlivá doporučení vycházejí z dostupných publikovaných odborných zdrojů k dané problematice a názorů členů pracovní skupiny / autorského kolektivu. Implementace v textu formulovaných doporučení musí být vždy zvažována v aktuálním klinickém kontextu a z pohledu poměru přínosu a rizika jednotlivých konkrétních postupů. Dokument nenahrazuje základní odborné zdroje dané problematiky a neuvádí povinnosti zdravotnických pracovníků určené jinými zákonnými či profesními normami.

METODOLOGIE FORMULACE JEDNOTLIVÝCH DOPORUČENÍ

Klasifikace stupňů doporučení („grade“)

lovaný pracovní skupinou je označen symbolem „J“.

Klasifikace podle úrovně a kvality publikovaných prací:

0 = „doporučení nelze formulovat“.

1 = „silné doporučení“ (postup nebo intervence jsou doporučeny).

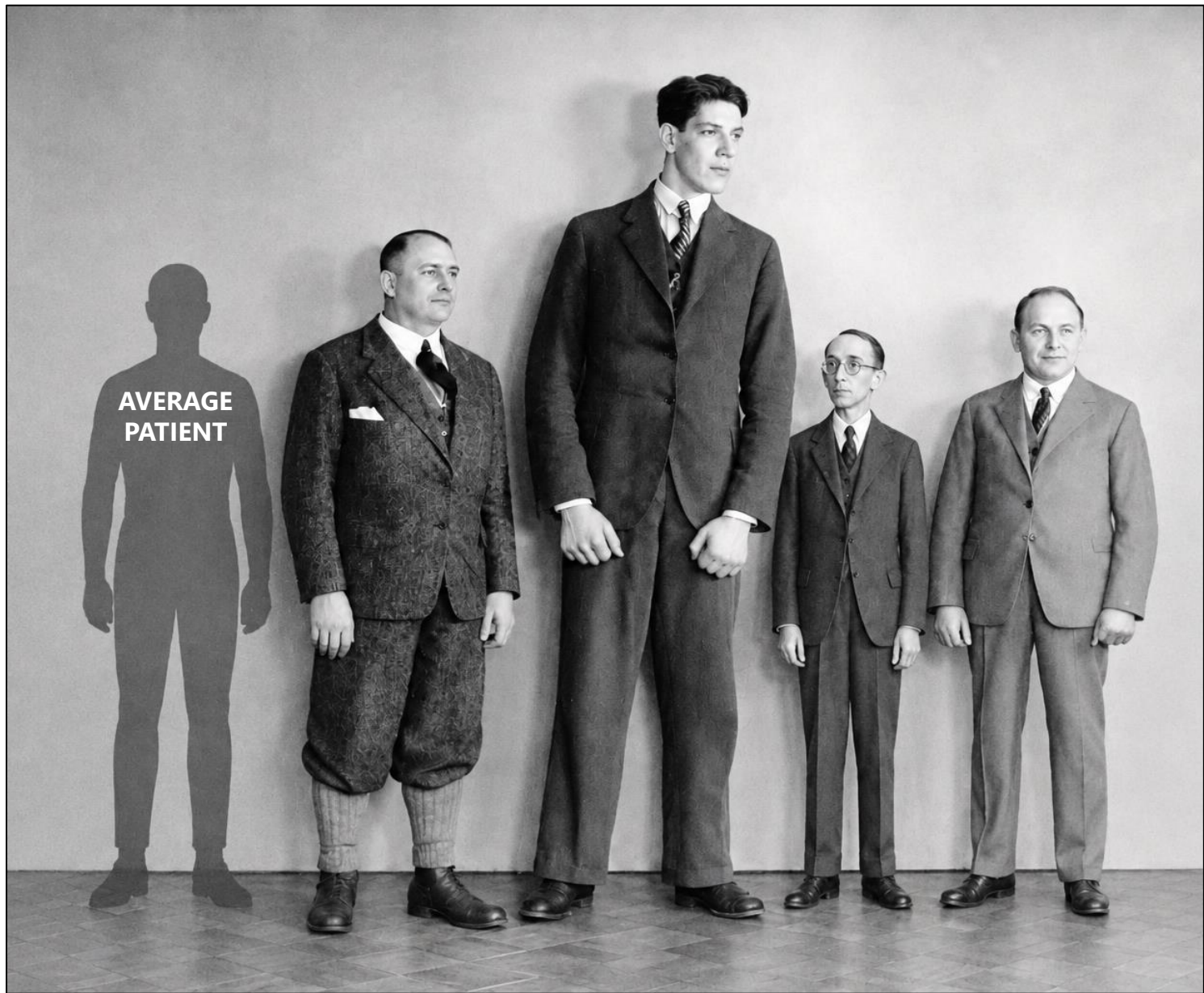
2 = „slabé doporučení“ (postup nebo intervence jsou ke zvážení).

Klasifikace podle názorů a zkušeností jednotlivých členů pracovní skupiny:
Poznámka: Pro formulaci doporučení muselo být dosaženo konsenzu všech členů autorského týmu.

1 = „silné doporučení“ (postup nebo intervence jsou doporučeny).

2 = „slabé doporučení“ (postup nebo intervence jsou ke zvážení).

But do we actually know how to read guidelines?



HEMOCOAGULATION MANAGEMENT

Read instructions and call for help early

0 CONTROLLED STABILIZATION

MASSIVE BLOOD LOSS

1 If you don't know, call for help

Call for help early. Activate multidisciplinary team.

2

Monitor vital signs and blood loss. Follow laboratory results (CBC, ABG, TEG/ROTEM). CAUTION Ca^{2+}

3

Administer balanced crystalloids, but start vasopressors early (norepinephrine, phenylephrine).

4

Initiate hemocoagulation = Exacyl, fibrinogen. Maintain temperature!

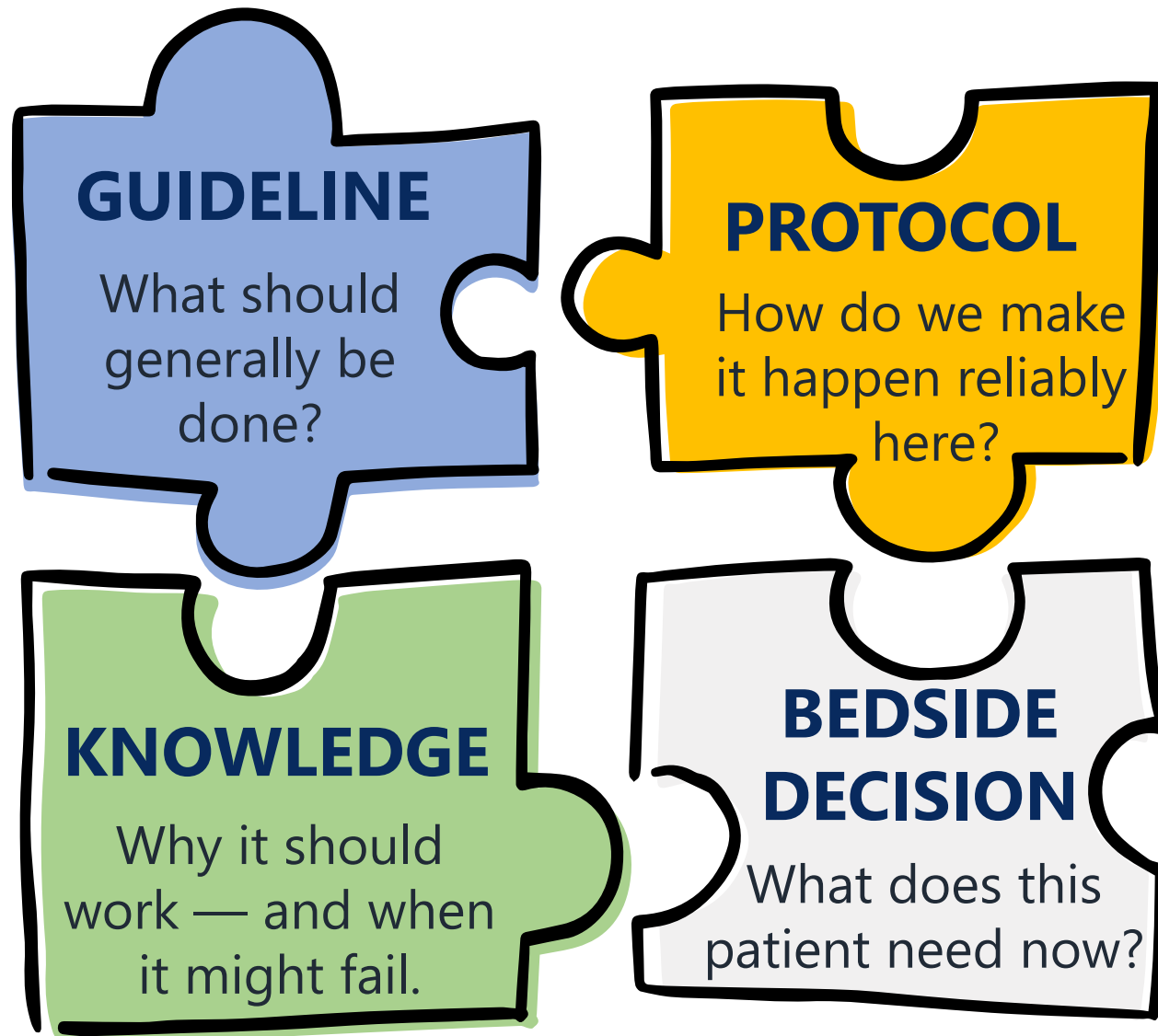
5

Consider plasma administration - prefer OCTAPLAS. Administer blood components, be restrictive.

Parts

2x 13x 1x Exacyl ampule Fibrinogen vial Octaplas bag Vials (CBC/ABG) Hot water bottle Vasopressor pump

Guideline ≠ protocol ≠ decision



Guidelines reduce **UNCERTAINTY**

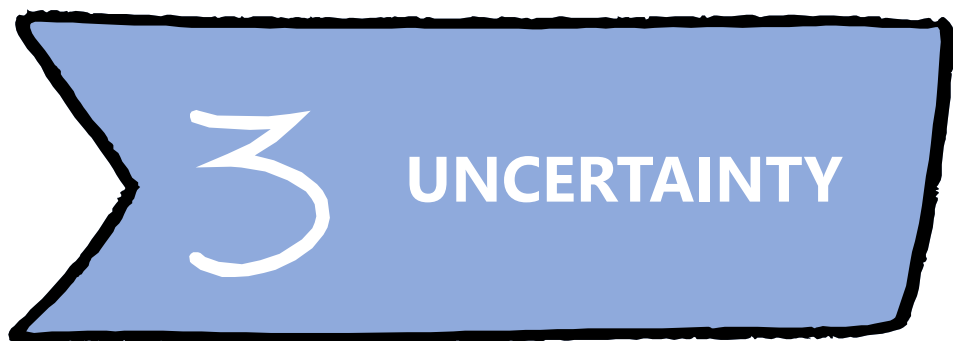
Protocols reduce **VARIABILITY**

Knowledge reveals their **LIMITS**

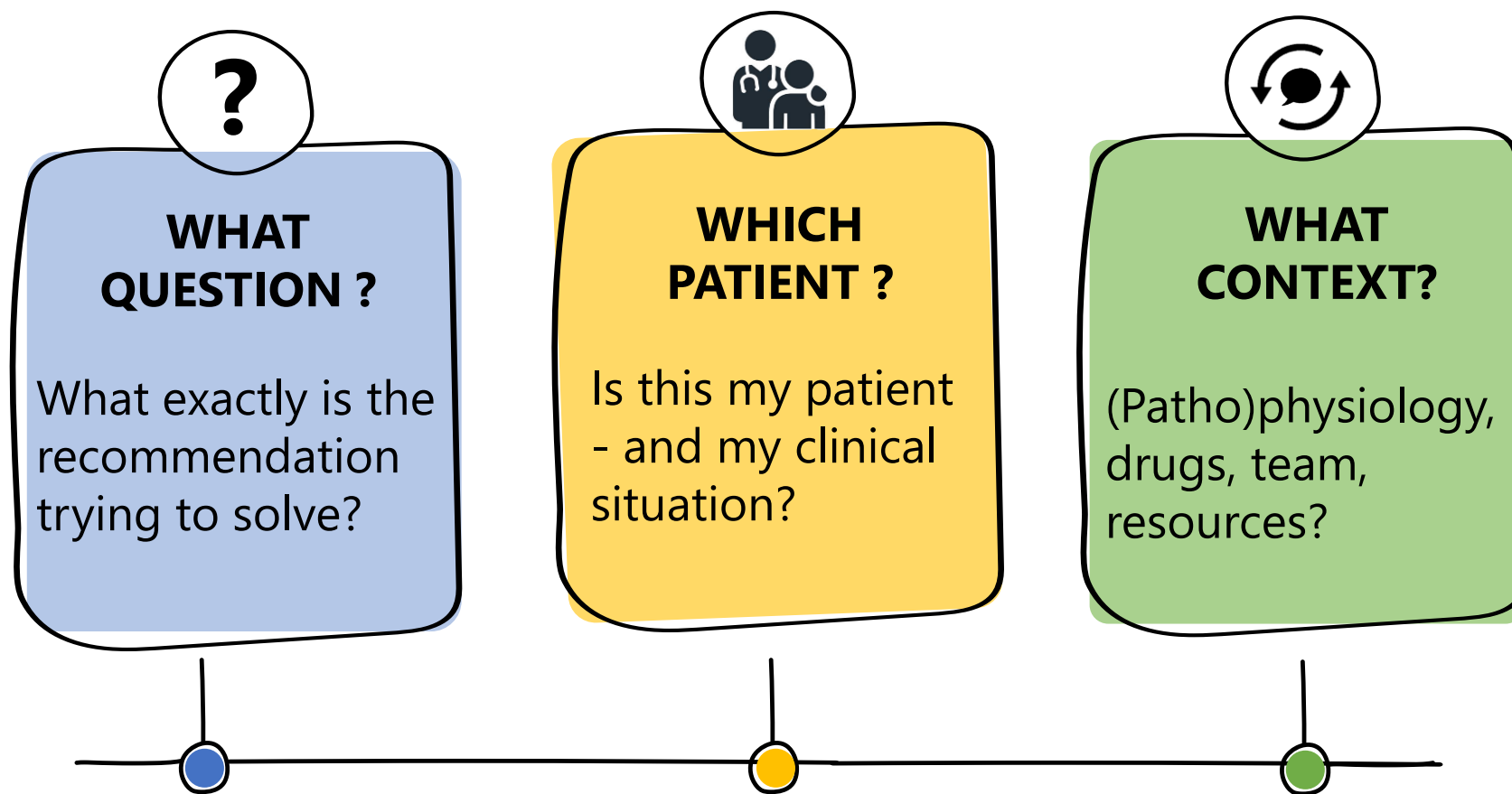
Clinical judgement **ADAPTS** them to the patient

THE DIFFICULT PART OF BLEEDING MANAGEMENT IS THE DECISION !

Because the bedside is different from the guideline.

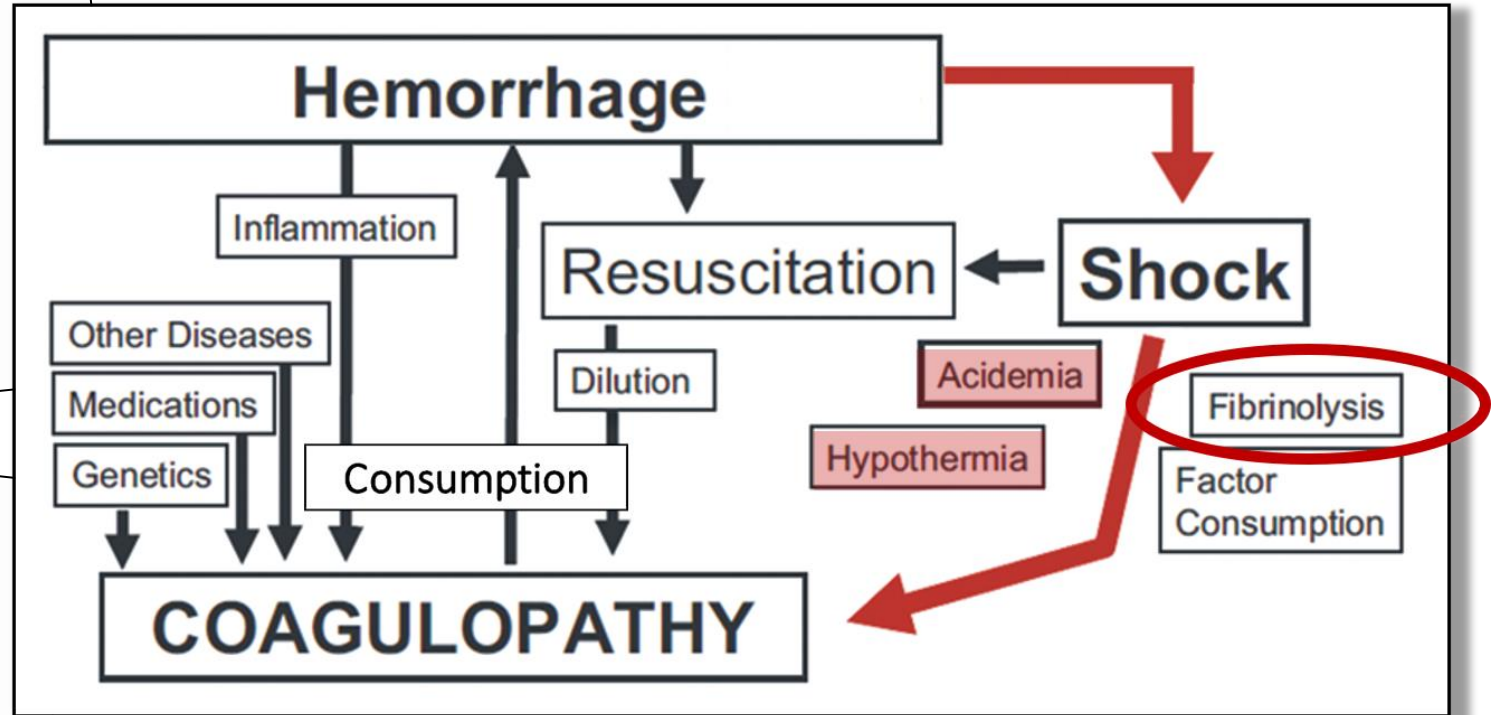


HOW TO READ A GUIDELINE AT THE BEDSIDE:



Guidelines cannot compensate for poor understanding of physiology, pharmacology and context.

Adapted from Hess et al. J Trauma. 2008;65:748-54



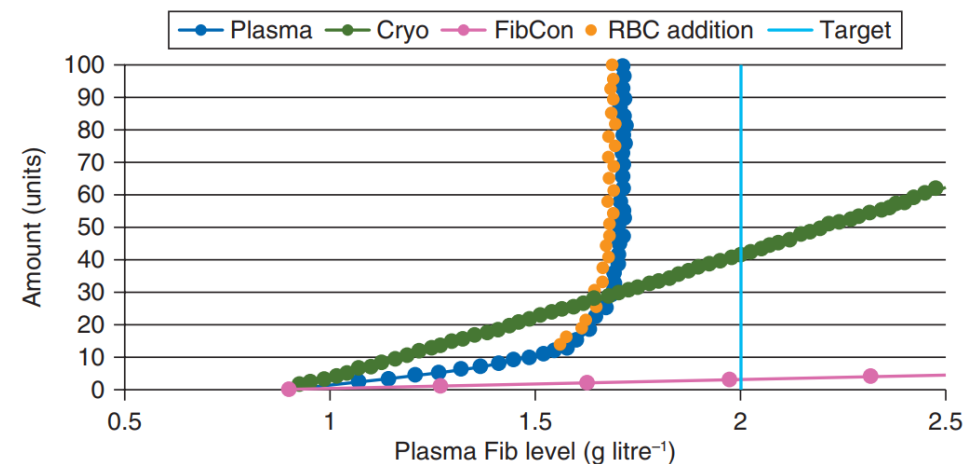
In massive bleeding, fibrinogen is the first factor to reach critically low levels!

Brenni M, et al. Acta Anaesthesiol Scand. 2010;54:111-117

Theoretical modelling of fibrinogen supplementation with therapeutic plasma, cryoprecipitate, or fibrinogen concentrate

P. W. Collins^{1*}, C. Solomon^{2,3}, K. Sutor⁴, D. Crispin⁴, G. Hochleitner⁵, S. Rizoli⁶, H. Schöchl^{7,8}, M. Schreiber⁹ and M. Ranucci¹⁰

Fib level graph



EJA

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

GUIDELINES

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

First update 2016

EJA

Eur J Anaesthesiol 2023; **40**:226–304

GUIDELINES

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

Second update 2022

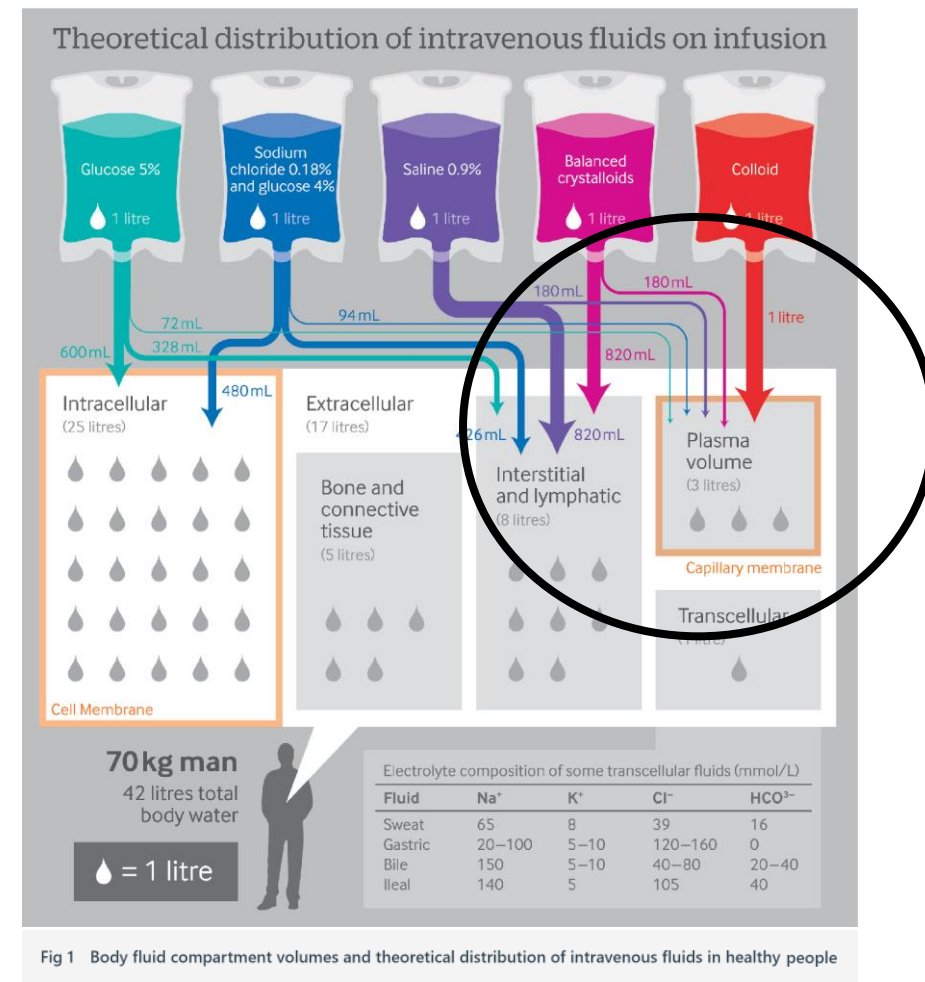
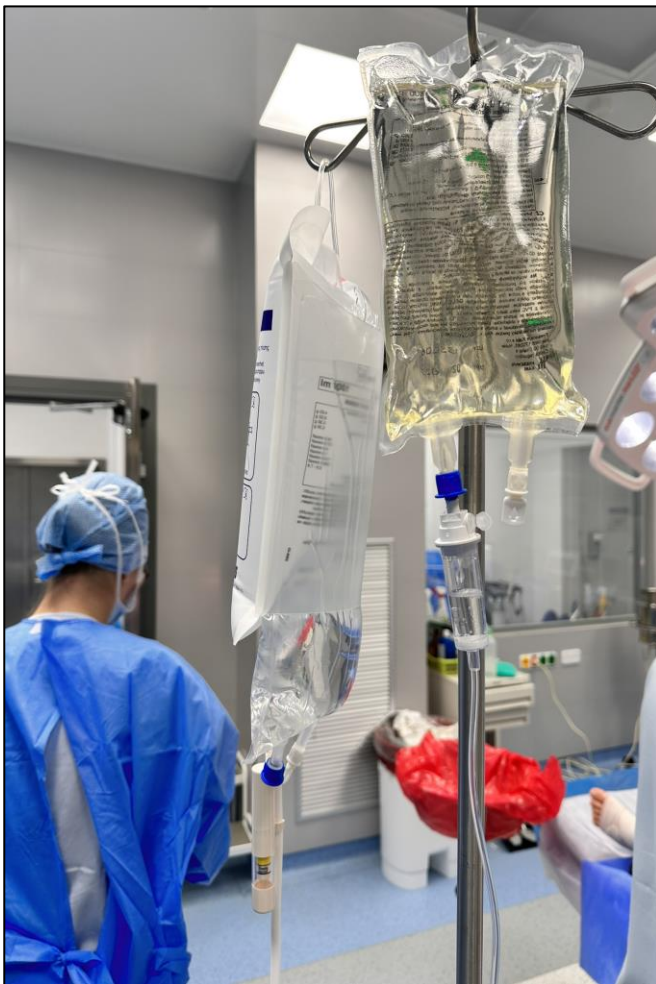
Plasma transfusion alone is not sufficient to correct hypo-fibrinogenaemia. **C**





FLUIDS

CRYSTALLOIDS OR COLOIDS ?



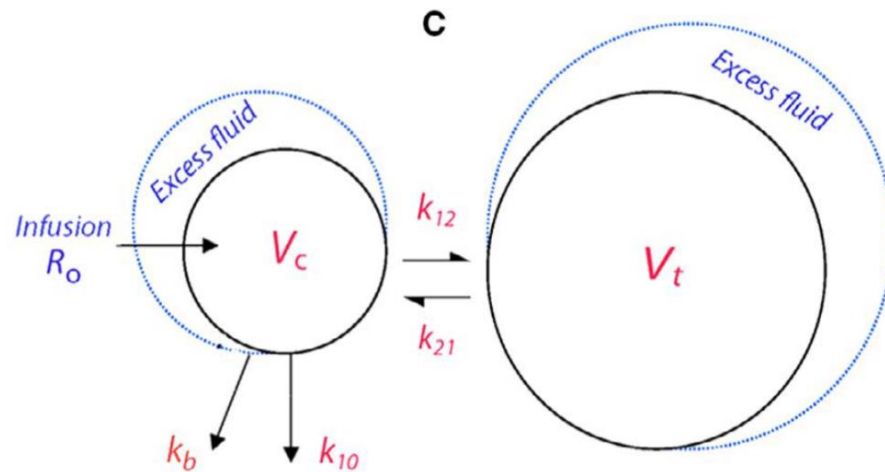
Frost. *BMJ* 2014;350:g7620 doi: 10.1136/bmj.g7620

RESEARCH

Open Access

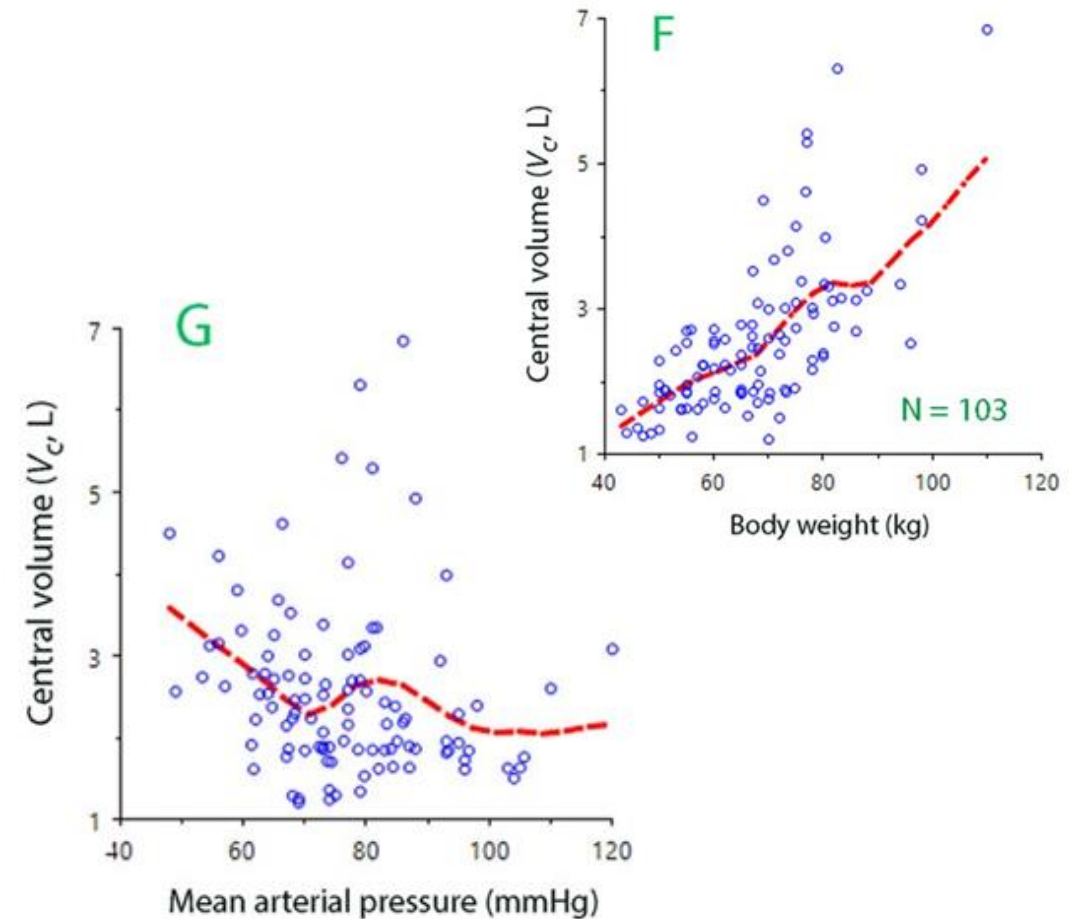
Attenuation of the plasma volume response to crystalloid fluid used for goal-directed fluid therapy

Robert G. Hahn^{1*} and Terry O'Brien¹



Crystalloid distribution depends on pressure, volume status, infusion rate and endothelial integrity

Crystalloid is not “intravascular or extravascular”. It is continuously moving between compartments.



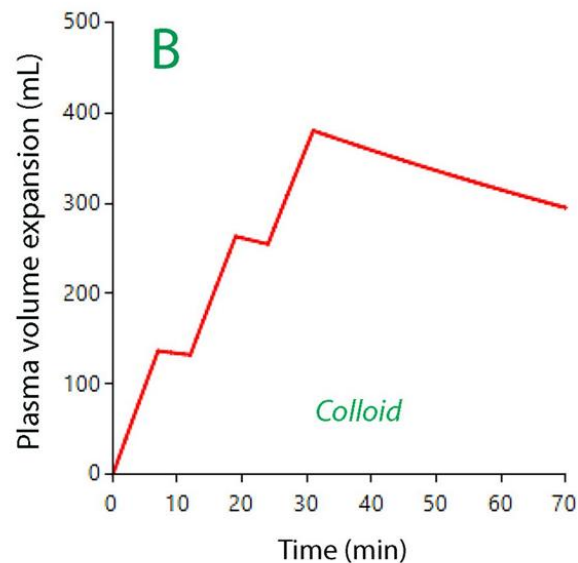
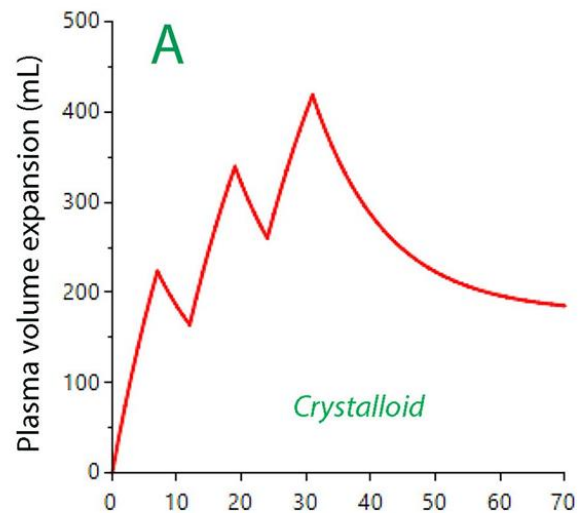


Fig. 2 Simulation of the plasma volume expansion following three successive bolus infusions during 7 min followed by a free interval of 5 min in a patient weighing 70 kg. **A** Crystalloid fluid 4 mL/kg in each bolus (Ringer solution). **B** Colloid fluid 2 mL/kg in each bolus (hydroxyethyl starch)

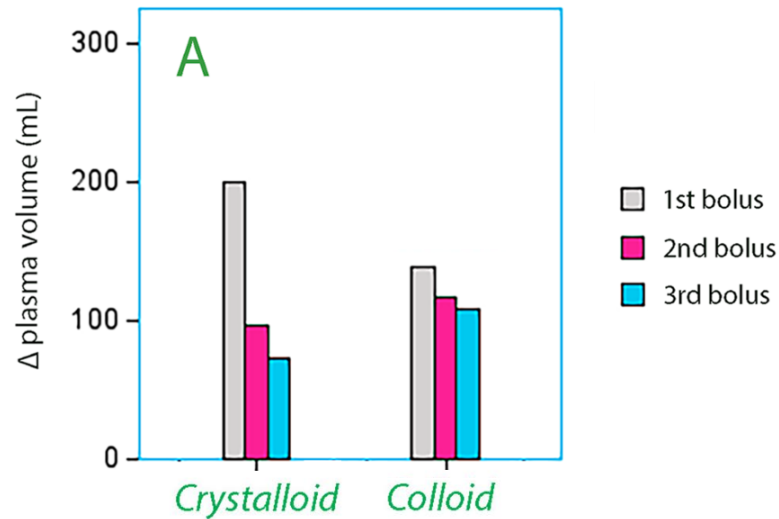


Fig. 3 Simulation of the plasma volume expansion following three successive bolus infusions during 7 min followed by a free interval of 5 min in a patient weighing 70 kg after a constant-rate infusion 5 mL/kg/h of crystalloid fluid infused over 60 min. **A** Crystalloid fluid 4 mL/kg in each bolus depending on body position and 2 mL/kg of colloid fluid in the flat recumbent position. **B** Bolus infusions of crystalloid fluid given a hemorrhage suddenly occurs at 60 min.

The same crystalloid bolus does not produce the same volume effect:

1st → 100 %

2nd → 51 %

3rd → 36 %

→ Repeated crystalloids become progressively inefficient

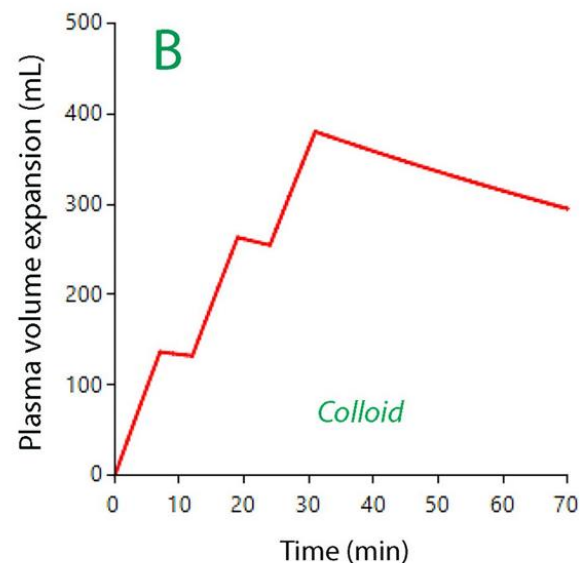
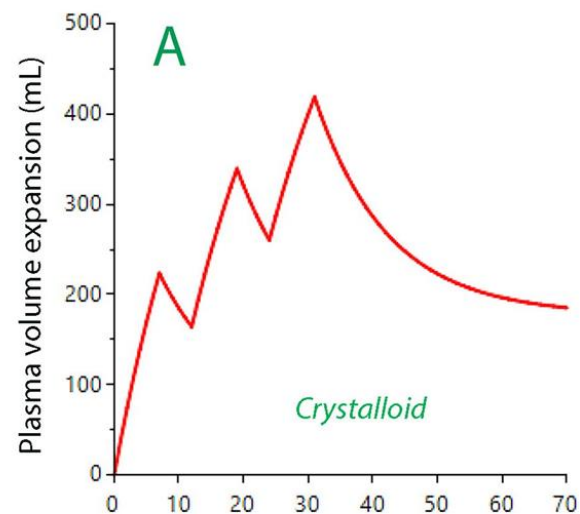


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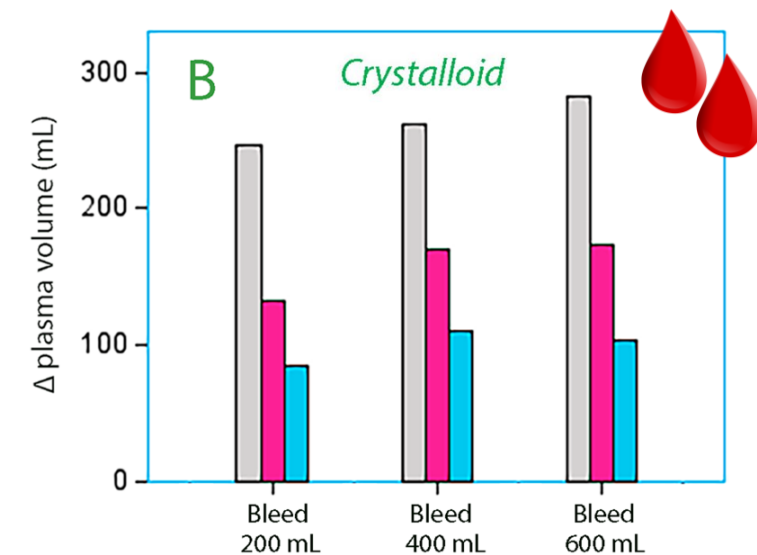
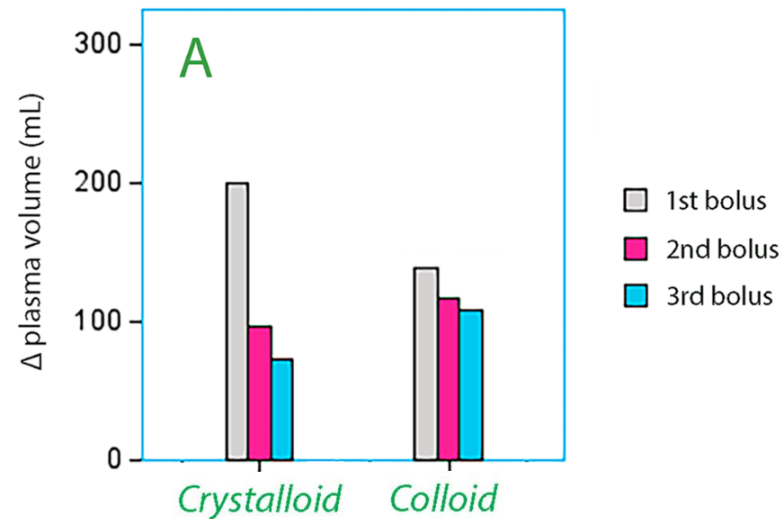


Fig. 3 Simulation of the plasma volume expansion following three successive bolus infusions during 7 min followed by a free interval of 5 min in a patient weighing 70 kg after a constant-rate infusion 5 mL/kg/h of crystalloid fluid infused over 60 min. **A** Crystalloid fluid 4 mL/kg in each bolus depending on body position and 2 mL/kg of colloid fluid in the flat recumbent position. **B** Bolus infusions of crystalloid fluid given a hemorrhage suddenly occurs at 60 min.

→ Repeated crystalloids become progressively inefficient

Initial assessment on the impact of crystalloids versus colloids during damage control resuscitation

Chrissy Guidry, DO,^{a,b} Elizabeth Gleeson, MD, MPH,^{a,c} Eric R. Simms, MD,^a Lance Stuke, MD, MPH,^d Peter Meade, MD, MPH,^a Norman E. McSwain Jr, MD,^a and Juan C. Duchesne, MD^{a,*}

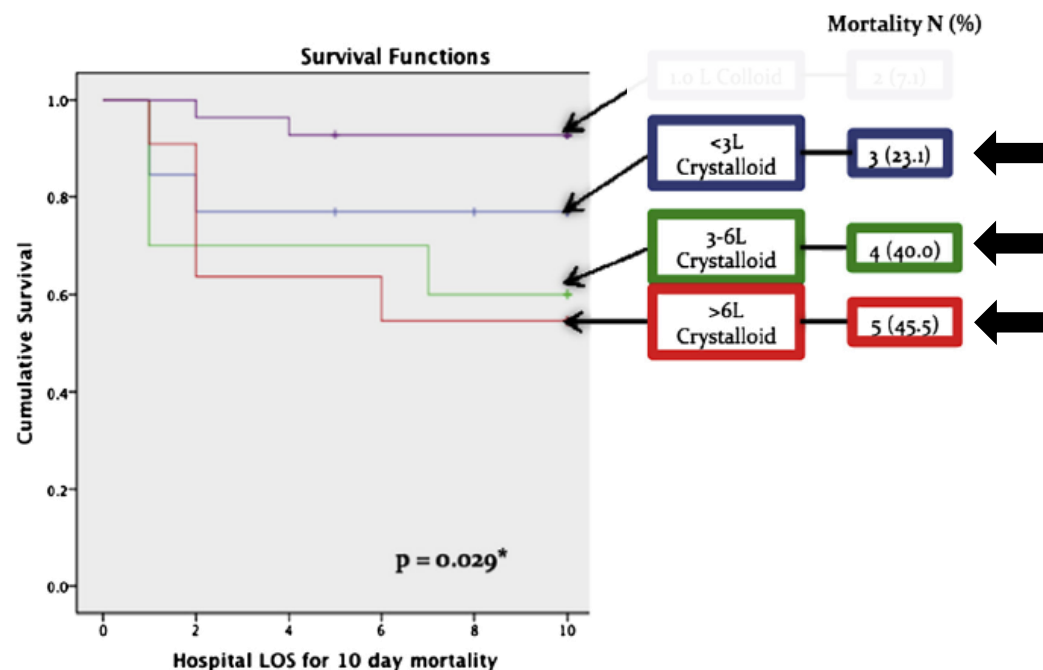


Fig. 2 – Kalpan-Meier curve, 10-d mortality, survivability for subgroup quantity analysis.

Endothelium and glycocalyx matter

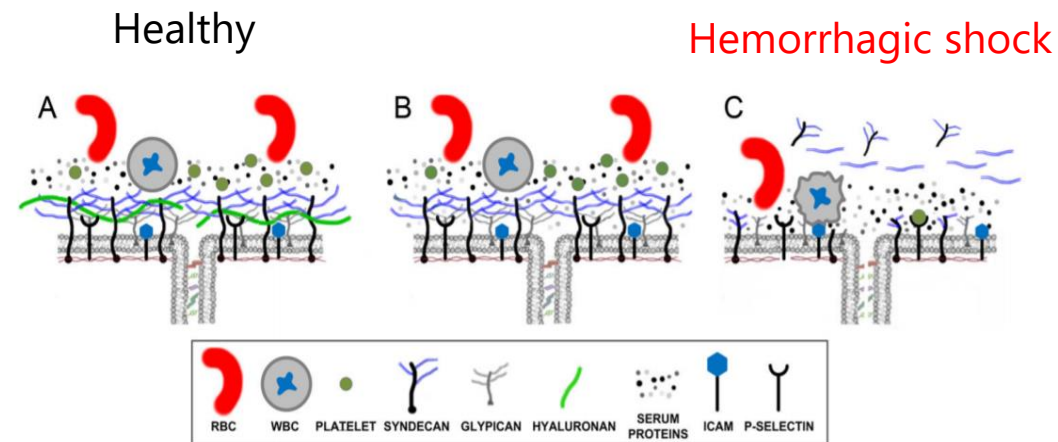
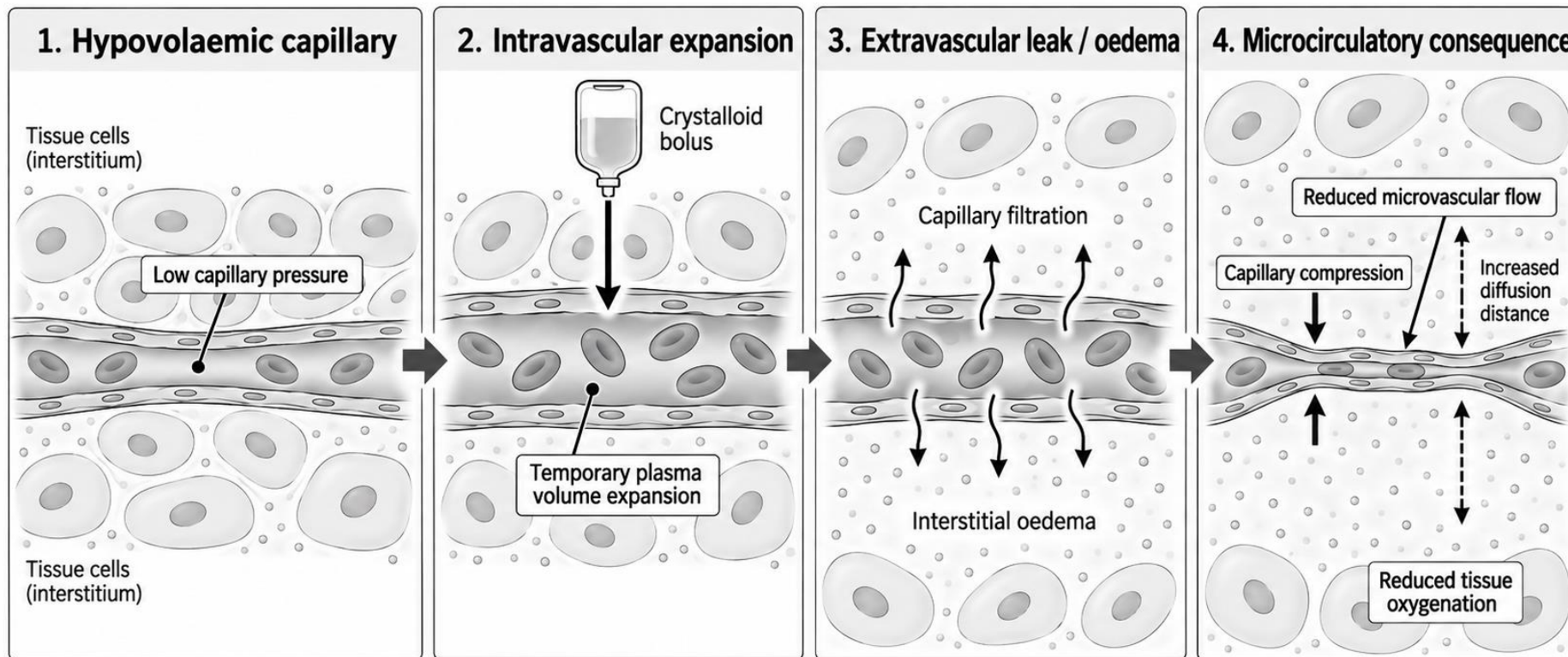


Figure 1.

A) An intact endothelial glycocalyx provides a barrier between the plasma compartment and the cell membrane and limits RBC, WBC and platelets from contacting the cell surface. The glycocalyx and associated immobile protein layer overlies the cell junction contributing to endothelial barrier properties for both water and protein flux. **B)** During mild to moderate inflammation, shedding and proteolytic cleavage of the glycocalyx (in this case removal of hyaluronan) increases the porosity of the glycocalyx. **C)** During severe inflammation and trauma, breakdown of the glycocalyx exposes ICAM and P-selectin resulting in increased WBC and platelet adhesion, respectively, and propagation of the inflammatory response. Note the presence of shed syndecans and heparan sulfates in the plasma that are hypothesized to contribute to auto-heparinization and the coagulopathy of trauma (see text for detail).



More fluid $\neq$ more perfusion

Macrohaemodynamics may improve while microcirculation gets worse.

Created by ChatGPT Eli, based on Torres et al. Critical Care 2017;21:160 and Ince C. Critical Care 2015;19(Suppl 3):S8.

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

Second update 2022

2.9 Intra-operative transfusion triggers and volume management

Recommendation 15

We recommend a target Hb concentration of 7 to 9 g dl⁻¹ during active bleeding. 1B

We recommend the replacement of extracellular fluid losses with isotonic crystalloids in a timely and protocol-based manner. 1B

Compared with crystalloids, colloids maintain micro-haemodynamic stability with less volume of isotonic fluid and less tissue edema. C

Micro and macrohemodynamic stability can be achieved more easily with colloids and with less tissue edema

Meta-analysis of colloids *versus* crystalloids in critically ill, trauma and surgical patients

S. H. Qureshi¹, S. I. Rizvi², N. N. Patel³ and G. J. Murphy¹

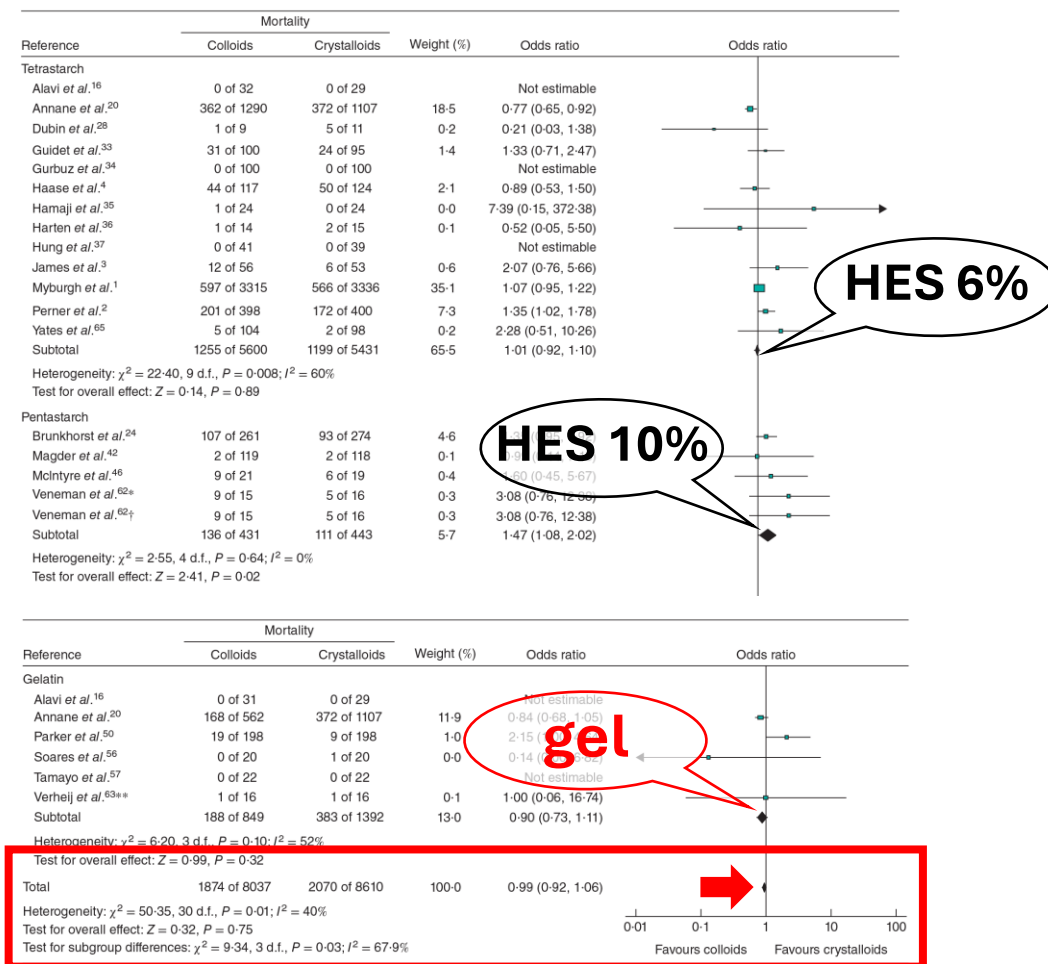


Fig. 2 Continued

Impact of experimental haemodilution on platelet function, thrombin generation and clot firmness: effects of different coagulation factor concentrates

Carolina Caballo¹, Gines Escolar¹, Maribel Diaz-Ricart¹, Irene Lopez-Vílchez¹, Miguel Lozano¹, Joan Cid¹, Marcos Pino¹, Joan Beltrán², Misericordia Basora², Arturo Pereira¹, Ana M. Galan¹

¹Haemotherapy-Haemostasis Department, Hospital Clinic, IDIBAPS; ²Department of Anaesthesiology, Hospital Clinic, Barcelona, Spain *Blood Transfus* 2013; **11**: 391-9

Table II - Effect of 60% haemodilution with different crystalloids and colloids on viscoelastic properties of forming clots.

	Baseline	Saline	Ringer lactate	Plasmalyte	HES 130/0.4	5% Albumin	Gelatin
CT (s)	60.9±2.0	88.6±3.0**	75.5±4.3*	70.3±3.2*	163.5±17.1**	111.3±4.6**	104.3±22.7*
CFT (s)	79.6±3.6	205.4±16.5**	202.9±15.4**	210.7±17.1**	457.9±42.5**	243.7±16.4**	344.0±63.2**
A10 (mm)	57.0±1.1	33.7±1.3**	34.3±1.1**	33.8±1.3**	23.6±1.3**	31.3±1.0**	28.7±3.5**
MCF (mm)	65.0±1.6	42.7±2.3**	44.7±2.3**	41.0±2.1**	36.5±3.5**	40.7±1.8**	40.8±2.3**

Legend Data are expressed as mean ± S.E.M. (n= 8). *: P <0.05; **: P <0.001 vs baseline.

CRYSTALLOIDS

mostly dilution

GELATIN

dilution + fibrin polymerisation
impairment often fibrinogen-responsive

HES

greater coagulation impairment
impairment poorly reversible

Impact of experimental haemodilution on platelet function, thrombin generation and clot firmness: effects of different coagulation factor concentrates

Carolina Caballo¹, Gines Escolar¹, Maribel Diaz-Ricart¹, Irene Lopez-Vílchez¹, Miguel Lozano¹, Joan Cid¹, Marcos Pino¹, Joan Beltrán², Misericordia Basora², Arturo Pereira¹, Ana M. Galan¹

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Diagnostika a léčba peripartálního krvácení, konsenzus mezioborové pracovní skupiny modifikovanou metodou ACCORD

Diagnosis and treatment of peripartum haemorrhage, consensus of the interdisciplinary working group by the modified ACCORD method

Editori: V. Černý^{1,2,3}, A. Pařízek²
 Autorský tým: J. Bláha¹, J. Blatný^{2,4}, V. Černý^{2,3}, P. Dulíček^{1,4}, J. Gumulec^{1,5}, P. Janků^{16,17}, M. Kacerovský^{1,8}, P. Křepelka^{19,20}, M. Lubešský²¹, J. Mannová²², A. Pařízek²³, D. Seidlová^{22,24}, O. Šimětka²⁵, P. Štourač^{22,26,27}

Stanovisko 20 (silné doporučení)

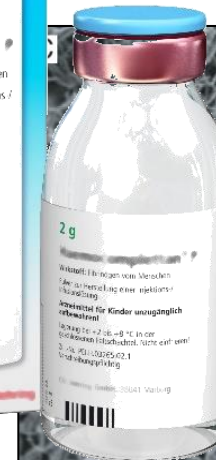
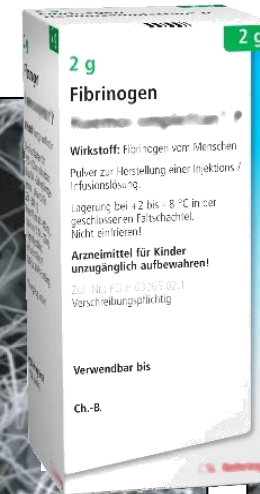
Doporučujeme u všech pacientek s PPH zahájit okamžitou tekutinovou resuscitaci. Pro zahájení tekutinové resuscitace doporučujeme použití **balancovaných roztoků krystaloidů** [35].

Stanovisko 21 (slabé doporučení)

Navrhujeme zvážit použití syntetických **koloidních roztoků s obsahem želatiny** při nedosažení nebo nedosahování hemodynamických cílů tekutinové resuscitace použitím krystaloidních roztoků a při trvající potřebě tekutin.

Efficacy of fibrinogen and prothrombin complex concentrate used to reverse dilutional coagulopathy—a porcine model

D. Fries^{1*}, T. Haas³, A. Klingler³, W. Streif⁴, G. Klima⁵, J. Martini¹,
H. Wagner-Berger² and P. Innerhofer²



A

Balanced crystalloids versus normal saline for trauma resuscitation: A systematic review and meta-analysis

Hany A. Zaki^{a,b}, Hussam Elmelliti^{b,*}, Amira Shaban^c, Ahmed Shaban^c, Ali Elkandow^b, Mohamed Gafar Abdelrahim^b, Wadah Musaad^b, Eman E. Shaban^d

Conclusions: In trauma patients with TBI, NS was associated with lower mortality and more ventilator-free days than balanced crystalloids, whereas no significant difference was noted in trauma populations without TBI. Moreover, there was no significant difference between NS and balanced crystalloids in terms of AKI incidence, need for RRT, and ICU stay, suggesting that balanced crystalloids remain a safe and reasonable option for trauma resuscitation.

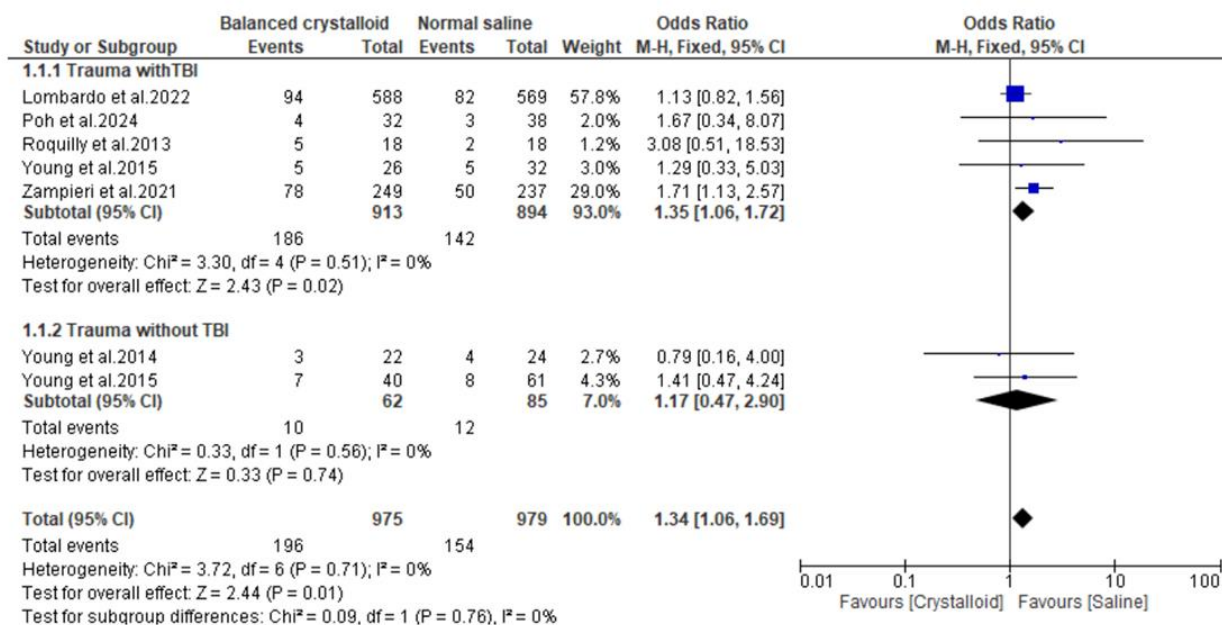


Fig. 2. Mortality rate in trauma patients receiving balanced crystalloids or normal saline.

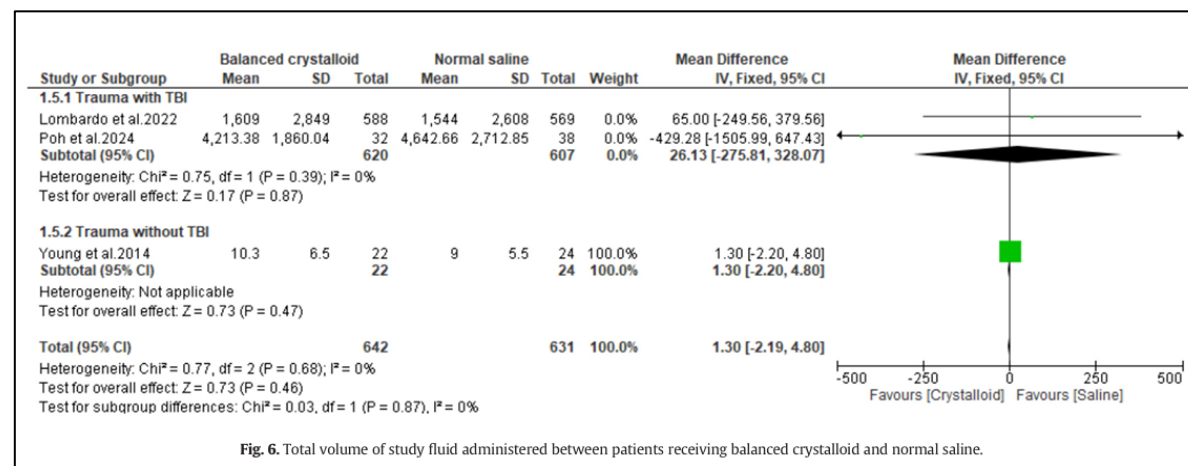


Fig. 6. Total volume of study fluid administered between patients receiving balanced crystalloid and normal saline.

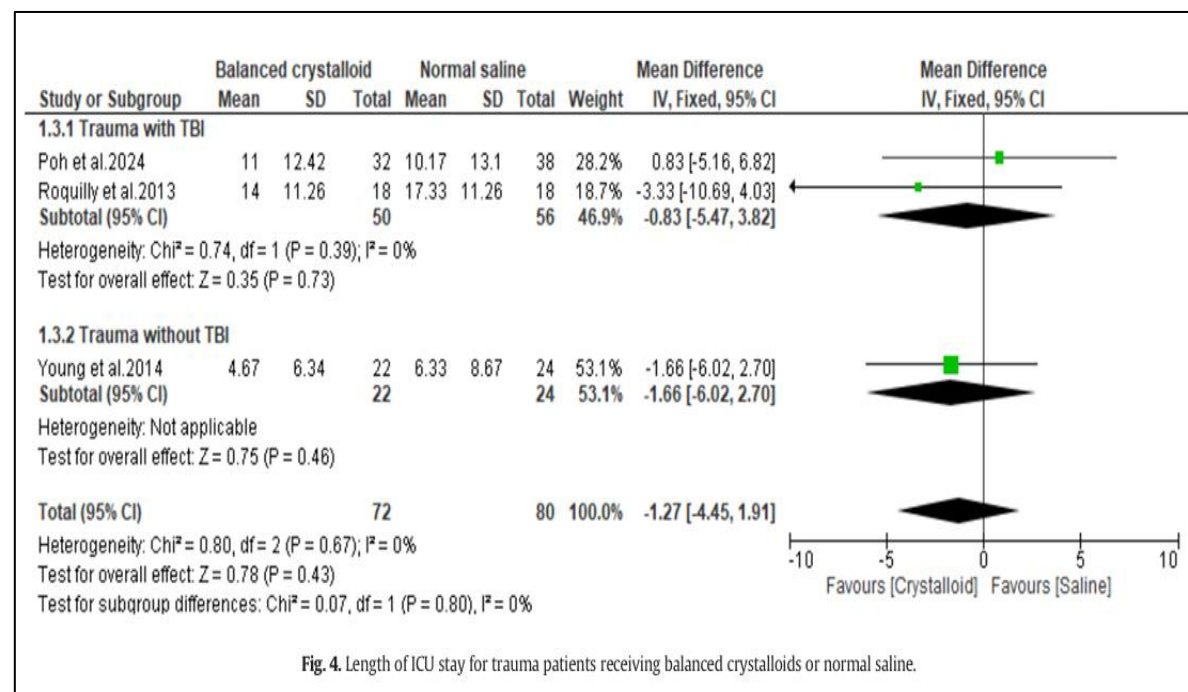


Fig. 4. Length of ICU stay for trauma patients receiving balanced crystalloids or normal saline.

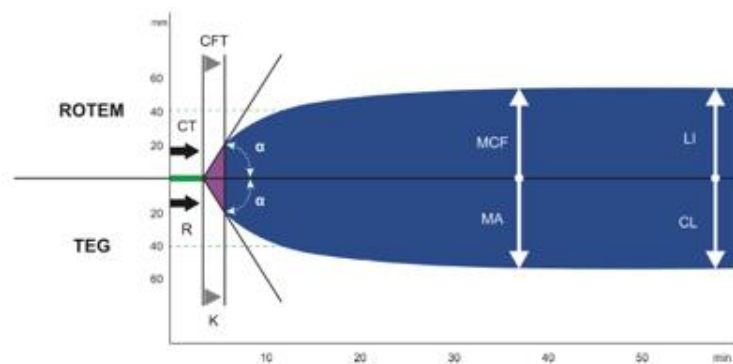


FIGURE 1

The difference in the terminology of the most important results between ROTEM and TEG. ROTEM parameters: CT, clotting time; CFT, clot formation time; α , α angle; MCF, maximum clot firmness; LI (30/60), lysis index 30 and 60 min after CT. TEG parameters: R, reaction time; k, kinetics; α , α angle; MA, maximum amplitude; CL (30/60), clot lysis after 30 and 60 min (99). With reprint permission by Georg Thieme Verlag KG.

POC

WHY VISCOELASTIC TESTING CHANGED BLEEDING MANAGEMENT ?

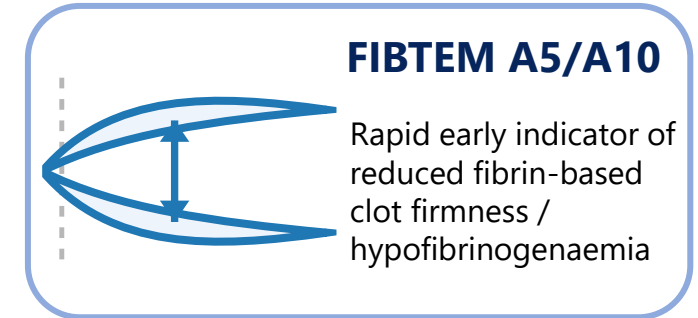
It makes individualised haemostatic treatment standardisable.

Conventional coagulation tests (PT/aPTT)

45–60 min
historical information

Viscoelastic testing (ROTEM/TEG)

10–15 min
dynamic picture

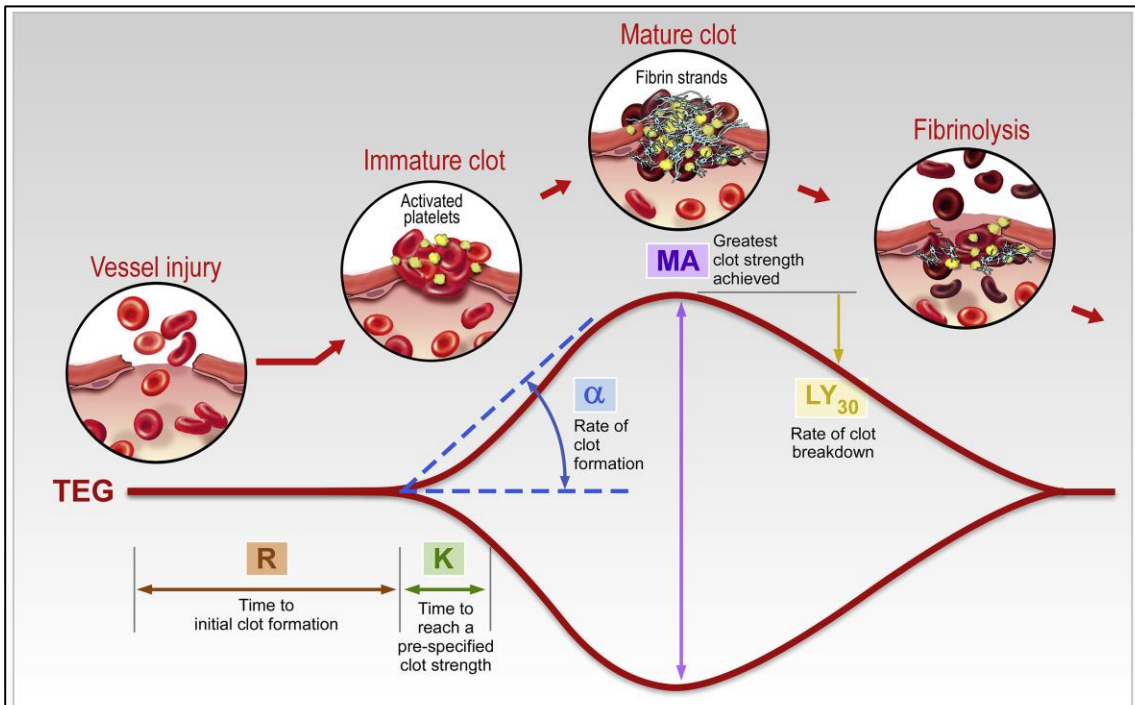


CONVENTIONAL COAGULATION TESTS

- isolated plasma
- mainly initiation of fibrin formation
- static result
- limited haemostatic pattern information

VISCOELASTIC TESTING

- whole blood
- rapid haemostatic pattern information
- clot formation as a process
- Initiation → propagation → strength → lysis

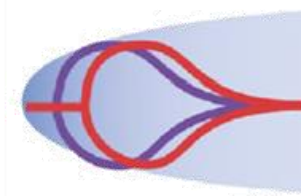


	R-time (R)	K-time (K)	Alpha angle (α)	Maximum Amplitude (MA)	Lysis % at 30 mins. (LY30)
Definition	Time to first deviation from baseline	Time for tracing to reach 20 mm amplitude	Angle between baseline and tangent line that intersects initial deviation	Maximum deviation of tracing from baseline	Decrease in curve amplitude (relative to MA) at 30 minutes
Controlling Pathways	Coagulation cascade	Fibrinogen cleavage Fibrin polymerization	Fibrinogen cleavage Fibrin polymerization	Fibrinogen activity Platelet count / quality	Fibrinolysis
Interpretation	$\uparrow$ = hypocoagulable $\downarrow$ = hypercoagulable		$\downarrow$ = hypocoagulable $\uparrow$ = hypercoagulable		
Therapeutic Implications	$\uparrow$ = administer fresh frozen plasma	If K time is $\uparrow$ or alpha angle is $\downarrow$, then: administer cryoprecipitate or fibrinogen concentrate		$\downarrow$ = administer platelets	$\downarrow$ = administer tranexamic acid



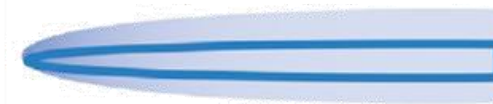
Tyler et al. Ann Emerg Med. 2021;77:357–366

THROMBOELASTOGRAPHY



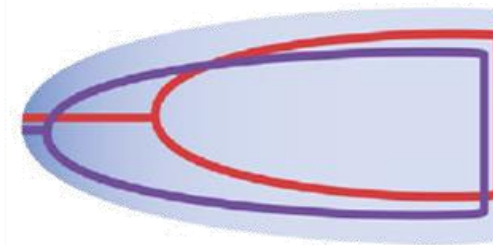
HYPERFIBRINOLYSIS

- $Ly30_{CK} > 4\%$ or $Ly30_{CRT} > 3\%$
- **EARLY TREATMENT** (clinical suspicion)
- **Tranexamic Acid 1g iv**



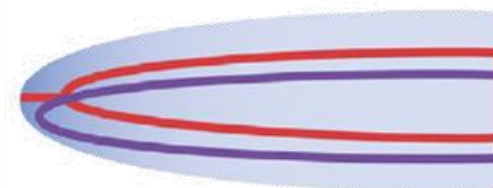
HYPOFIBRINOGENEMIA

- $MA_{CFF} < 15mm$ ($A10_{CK} < 45mm$)
- $\alpha_{CRT} < 60^\circ$ or $K_{CRT} > 2.5 min$
- **OBJECTIVE 18-20mm**
- **Fibrinogen concentrate or cryoprecipitate**



THROMBIN GENERATION DEFICIENCY

- $R_{CK} > 9min$ or $R_{CRT} > 1min$
- $ATC_{CRT} > 150''$ or $\alpha_{CRT} < 45^\circ$
- **PCC or plasma / protamine**
- (Consider AC / CKH)



THROMBOCYTOPENIA

- $A10_{CK} < 45mm$ ($MA_{CFF} > 15mm$)
- **Platelets pool**

1 BLEEDING + ABNORMAL

Does it explain the bleeding?
→ targeted intervention may help

2

BLEEDING + NEAR-NORMAL

Think beyond the tracing
→ source, drugs, vWF/platelets

3

NO BLEEDING + ABNORMAL

Does this require treatment at all?

POC-GUIDED ≠ POC-DRIVEN

**Treat a clinical problem
— not an abnormal tracing.**

Better information ≠ automatically better outcome.

**POC SHOULD ANSWER A
CLINICAL QUESTION
— NOT CREATE ONE.**

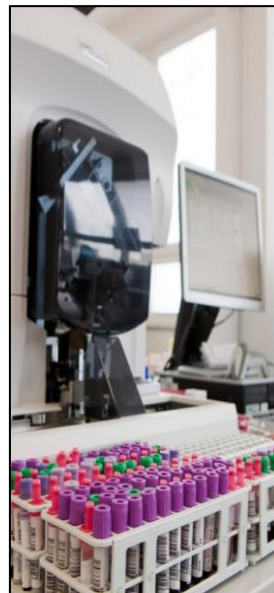


12

REMEMBER
TIME LOST

CANNOT BE
REGAINED

6



Výsledek: (82...)

Režim Mixer Data Zobrazení Filtry Typy událostí Potvrzování Zpřístupňování Konfigurace

Třídy a metody	28/06/11 11:49	28/06/11 12:01	28/06/11 12:03	28/06/11 12:31
Diabetický profil				
Glukóza	8,3 ^			
ABR - krev				
Hemoglobin	63			
pH	7,306			
PCO2	5,04			
HCO3 aktuální	18,3			
HCO3 standardní	18,8			
Base excess aktuální	-6,8			
PO2	30,0			
O2 saturovaný	98,9			
CO2 celkový	18,1			
Typ krve	Arterial			
Plná krev				
Laktát			2,80	
Sodík			126	
Draslík			5,0	
Chloridy			108	
Vápník ionizovaný			0,62	
Krevní obraz-perifer				
Leukocyty		8,20		
Erytrocyty		2,74		
Hemoglobin		80		
Hematokrit		0,245		
Stř.obj.erytr.		89,4		
Barvivo erytr.		29,2		
Stř.barev.kon.		327		
Distr.křiv.ery		14,8		
Trombocyty		69		
Stř.obj.trombo		10,3		
Destičkový hematokrit		0,070		
Distr.křiv.tr.		18,9		
Koagulační vyšetření				
Quickův test INR				1,05
APTT				30,3
Trombinový čas				17,1
Fibrinogen koagul.				2,7
Etanol gelifik.test				
Antitrombin III				78
D-dimery				1830

ORIGINAL RESEARCH ARTICLE

Circulation. 2016;134:1152–1162. DOI: 10.1161/CIRCULATIONAHA.116.023956

Point-of-Care Hemostatic Testing in Cardiac Surgery

A Stepped-Wedge Clustered Randomized Controlled Trial

Keyvan Karkouti, MD
Jeannie Callum, MD
Duminda N. Wijeyesundera, MD
Vivek Rao, MD, PhD
Mark Crowther, MD
Hilary P. Grocott, PhD
Ruxandra Pinto, PhD
Damon C. Scales, MD, PhD
TACS Investigators

Clinical Perspective

What Are the Clinical Implications?

- We found that implementation of point-of-care hemostatic testing within the context of a simple, integrated transfusion algorithm reduced red blood cell transfusions, platelet transfusions, and major bleeding following cardiac surgery.
- Our findings suggest that the use of point-of-care hemostatic testing improves the management of coagulopathy in cardiac surgery and support their broader adoption into clinical practice.

Circulation. 2016;134:1152–1162. DOI: 10.1161/CIRCULATIONAHA.116.023956



Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

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

Ask Daffy Kvisselgaard^{1,2a}, Signe Amalie Wolthers^{3,4b}, Anne J. Wikkelsø^{4,5c}, Lars Brokso Holst^{6d}, Bergitte Drivenes⁷, Arash Afshari^{4,6e}
Cochrane Database of Systematic Reviews 2026, Issue 5. Art. No.: CD007871.
DOI: 10.1002/14651858.CD007871.pub4.

Authors' conclusions

TEG-/ROTEM-guided transfusion algorithms may reduce the risk of mortality, bleeding volume, and the need for fresh frozen plasma, platelets, and surgical re-intervention, but the evidence is very uncertain. Furthermore, the results were primarily based on the adult population undergoing elective cardiac surgery. Hence, the conclusion remains unchanged from the previous update of this review.

There is a need for large, low risk of bias randomised controlled trials evaluating TEG/ROTEM across diverse clinical settings, including paediatric and neonatal populations, sepsis, trauma, obstetrics, and high-risk surgical and critically ill cohorts requiring major transfusion. Future studies should be adequately powered and prioritise patient-centred outcomes such as long-term survival, adverse events, cost-effectiveness, and the role of TEG/ROTEM in coagulopathy and severe haemorrhage.

PLAIN LANGUAGE SUMMARY

Key messages

- It is possible that TEG (thromboelastography) and ROTEM (thromboelastometry, which give guidance on the need for transfusion, **may reduce the risk of death, amount of blood lost and the need for blood products, as well as additional surgery**, but this is very unclear. This finding mainly applied to people undergoing heart surgery
- We had **no information on unwanted events** from this guidance.
- The evidence is very uncertain, and more studies are needed in a greater number of people, particularly children and people in other settings than heart surgery.

ORIGINAL

Viscoelastic haemostatic assay augmented protocols for major trauma haemorrhage (ITACTIC): a randomized, controlled trial

K. Baksaas-Aasen¹, L. S. Gall², J. Stensballe³, N. P. Juffermans⁴, N. Curry⁵, M. Maegele⁶, A. Brooks⁷, C. Rourke², S. Gillespie², J. Murphy⁸, R. Maroni⁸, P. Vulliamy², H. H. Henriksen³, K. Holst Pedersen³, K. M. Kolstadbraaten¹, M. R. Wirtz⁴, D. J. B. Kleinvelde⁴, N. Schäfer⁶, S. Chinna⁷, R. A. Davenport², P. A. Naess¹, J. C. Goslings⁴, S. Eaglestone², S. Stanworth^{5,9}, P. I. Johansson³, C. Gaarder¹ and K. Brohi^{2*}

Abstract

Purpose: Contemporary trauma resuscitation prioritizes control of bleeding and uses major haemorrhage protocols (MHPs) to prevent and treat coagulopathy. We aimed to determine whether augmenting MHPs with Viscoelastic Haemostatic Assays (VHA) would improve outcomes compared to Conventional Coagulation Tests (CCTs).

Methods: This was a multi-centre, randomized controlled trial comparing outcomes in trauma patients who received empiric MHPs, augmented by either VHA or CCT-guided interventions. Primary outcome was the proportion of subjects who, at 24 h after injury, were alive and free of massive transfusion (10 or more red cell transfusions). Secondary outcomes included 28-day mortality. Pre-specified subgroups included patients with severe traumatic brain injury (TBI).

Results: Of 396 patients in the intention to treat analysis, 201 were allocated to VHA and 195 to CCT-guided therapy. At 24 h, there was no difference in the proportion of patients who were alive and free of massive transfusion (VHA: 67%, CCT: 64%, OR 1.15, 95% CI 0.76–1.73). 28-day mortality was not different overall (VHA: 25%, CCT: 28%, OR 0.84, 95% CI 0.54–1.31), nor were there differences in other secondary outcomes or serious adverse events. In pre-specified subgroups, there were no differences in primary outcomes. In the pre-specified subgroup of 74 patients with TBI, 64% were alive and free of massive transfusion at 24 h compared to 46% in the CCT arm (OR 2.12, 95% CI 0.84–5.34).

Conclusion: There was no difference in overall outcomes between VHA- and CCT-augmented-major haemorrhage protocols.

Take-home message

When standard of care is delivered with empiric balanced haemostatic therapy and intensive conventional coagulation testing, viscoelastic haemostatic assays did not improve clinical outcomes in the intention to treat cohort.

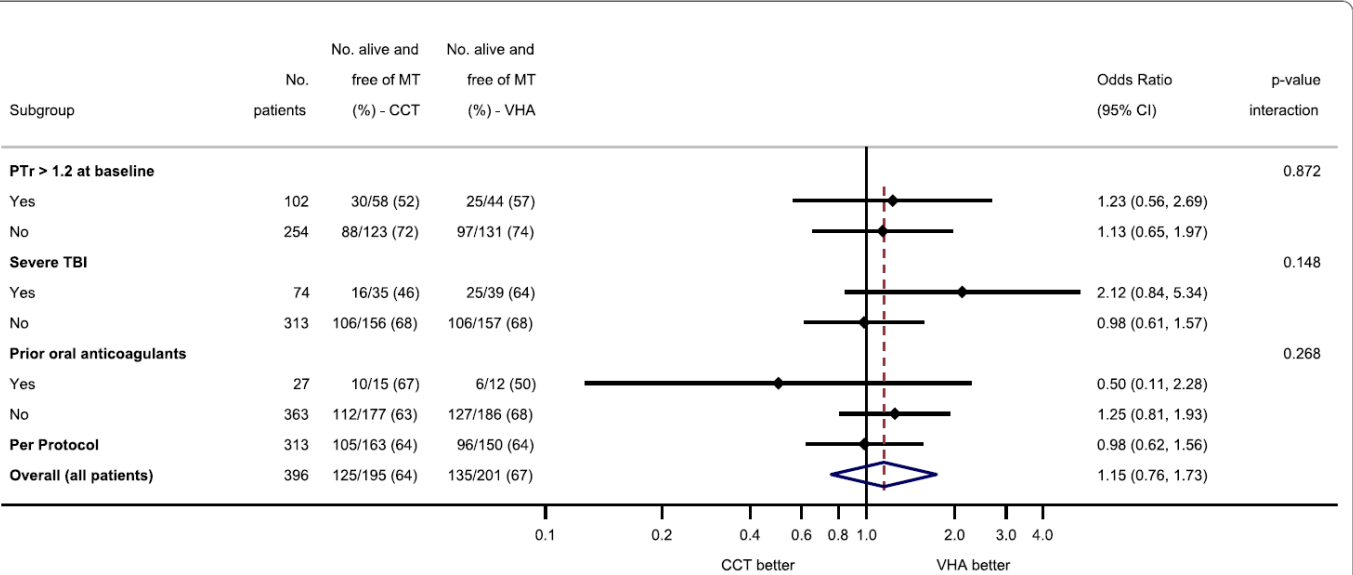


Fig. 2 Primary outcome (alive and free of massive transfusion at 24 h) in pre-specified subgroups. Odds ratios for the primary outcome (alive and free of massive transfusion at 24 h) in the subgroups of coagulopathic patients at baseline (defined as PTtr > 1.2), patients with severe TBI, patients with prior oral anticoagulants, the Per Protocol and Intention-To-Treat (Overall) populations. Odds ratios were calculated using the VHA arm as the exposed group. The solid black line indicates an odds ratio of 1, equivalent to no difference between study groups. The vertical red dashed line indicates the overall odds ratio for the ITT population. Subgroup allocation criteria were missing for some patients, so some subgroups do not add up to 396 patients. In particular, the following patients had missing data in their records: 40 did not have a PTtr value at baseline, 9 did not have a TBI score, 6 did not have a record for prior oral anticoagulants. Post-hoc analysis: the p-values for the interaction between study arm and each subgroup were calculated using a logistic regression with “being alive and free of massive transfusion at 24 h” as the outcome. CI confidence interval, CCT conventional coagulation test, VHA viscoelastic haemostatic assay, PTtr prothrombin time ratio, TBI traumatic brain injury, ITT intention-to-treat

ORIGINAL

Viscoelastic haemostatic assay augmented protocols for major trauma haemorrhage (ITACTIC): a randomized, controlled trial

K. Baksaas-Aasen¹, L. S. Galli², J. Stensballe³, N. P. Juffermans⁴, N. Curry⁵, M. Maegele⁶, A. Brooks⁷, C. Rourke², S. Gillespie², J. Murphy⁸, R. Maroni⁸, P. Vulliamv², H. H. Henriksen³, K. Holst Pedersen³, K. M. Kolstadbraaten¹.

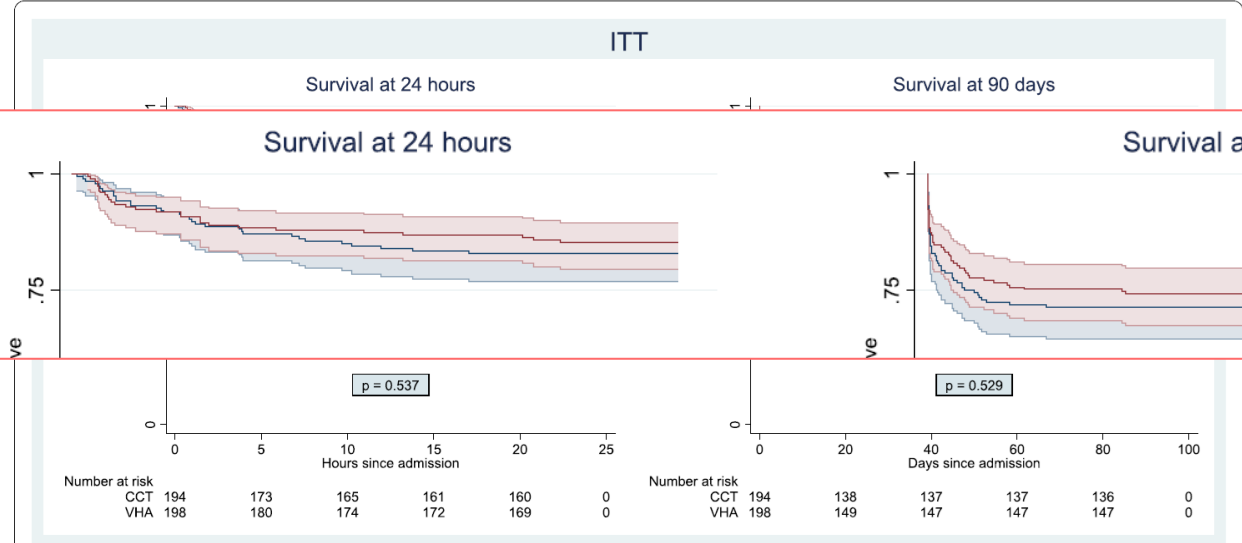


Fig. 3 Survival curves at 24 h and 90 days. Survival curves with 95% confidence intervals at 24 h and 90 days for the Intention-To-Treat (ITT) population. Blue: CCT-guided and Red: VHA-guided. The *p* values shown are the result of the log-rank test. 4 patients in the ITT population had missing date/time of events and were therefore not included in the survival curve. CCT conventional coagulation test, VHA viscoelastic haemostatic assay

Take-home message

When standard of care is delivered with empiric balanced haemostatic therapy and intensive conventional coagulation testing, viscoelastic haemostatic assays did not improve clinical outcomes in the intention to treat cohort.

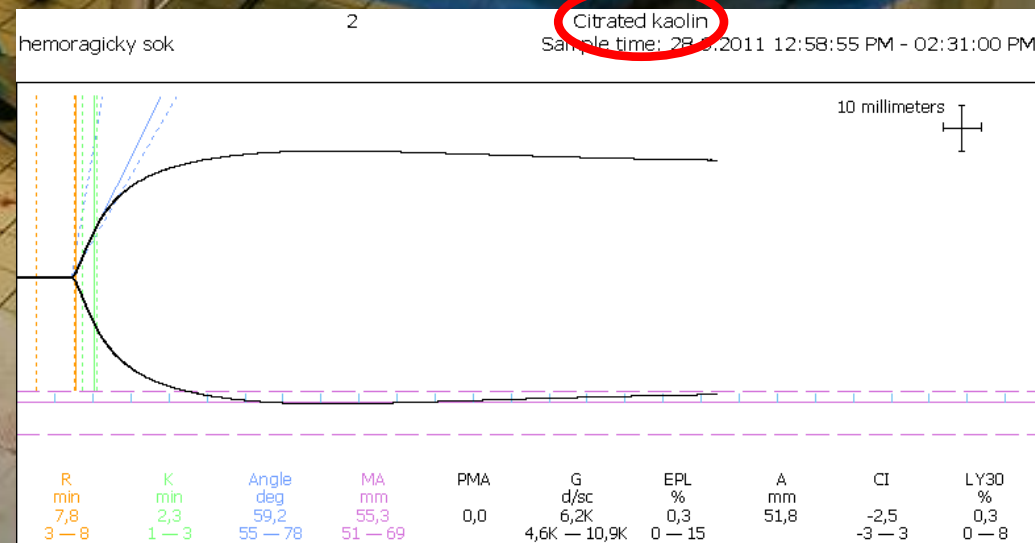
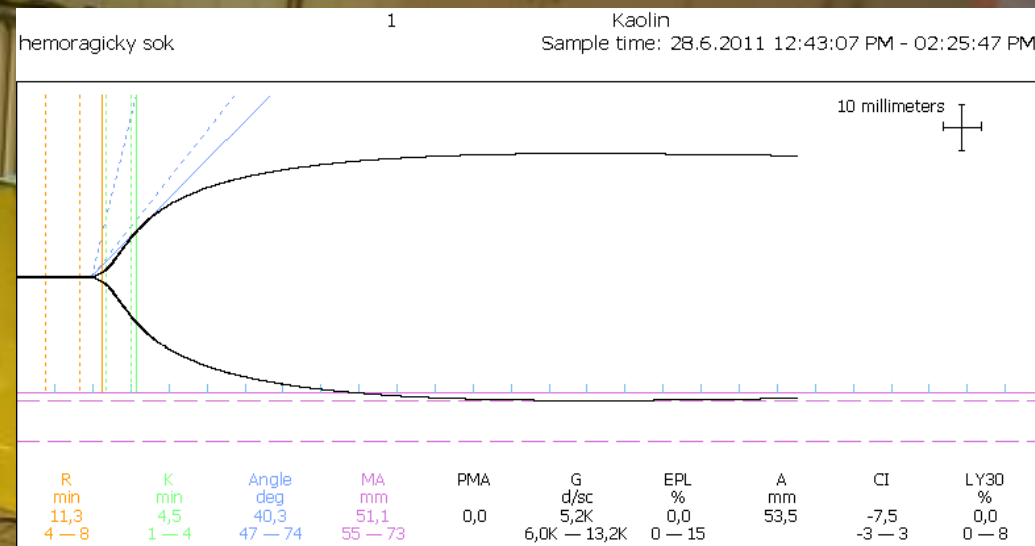
Table 2 Secondary outcomes for the intention-to-treat population

	CCT (n = 195)	VHA (n = 201)	p value
Mortality at 6 h—no. (%)	22/195 (11%)	22/201 (11%)	0.915
TE ^{^^} —no. (%)	33/195 (17%) ↑	29/201 (14%)	0.495
Myocardial infarction—no. (%)	55/194 (28%) ↑	50/201 (25%)	0.435
Stroke—no. (%)	56/177 (31%) ↑	53/179 (29%)	0.678
Reoperation—no. (%)	17/56 (30%) ↑	13/51 (25%)	0.576
Thrombocytopenia—no. (%)	24/54 (44%) ↑	19/50 (38%)	0.505
Massive transfusion at 24 h—no. (%)	55/195 (28%) ↑	53/201 (26%)	0.682
Patients with symptomatic TE ^{^^} —no. (%)	27/195 (14%) ↑	17/201 (9%)	0.088
Patients with MODS ^{^^^} —no. (%)	134/159 (84%)	141/164 (86%)	0.668
Median 28-day ventilator-free days (IQR)	20 (0–26), n = 192	17 (0–25), n = 198	0.422
Median 28-day ICU-free days (IQR)	15 (0–23), n = 192	13 (0–23), n = 198	0.691

CCT conventional coagulation test, VHA viscoelastic haemostatic assay, TE thromboembolic events, MODS multiple organ dysfunction syndrome, ICU intensive care unit, LOS length of stay

^{^^}Myocardial infarction and Embolic strokes are included in thromboembolic events

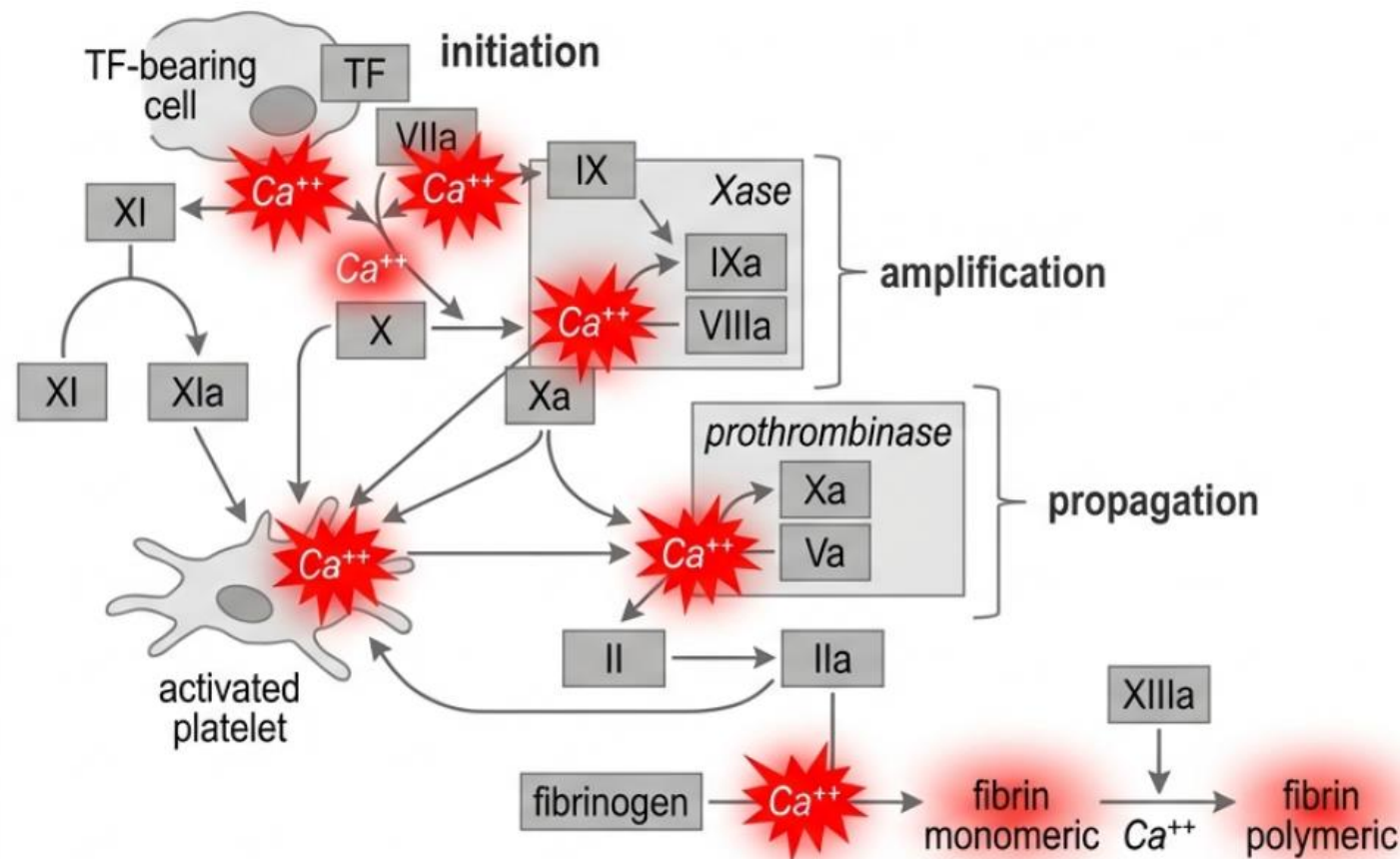
Výsledky: (825)				
Režim	Mixer	Data	Zobrazení	Filtry
Typy událostí	Potvrzování	Zpřístupňování	Konfigurace	
Třídy a metody	28/06/11	28/06/11	28/06/11	28/06/11
	11:49	12:01	12:03	12:31
Diabetický profil				
Glukóza	8,3 ^			
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HCO3 standardní	18,8			
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Laktát			2,80	
Sodík			126	
Draslík			5,0	
Chloridy			100	
Vápník ionizovaný			0,62	
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Stř. barev. kon.	327			
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Trombocyty	69			
Stř. obj. trombo	10,3			
Destičkový hematokrit	0,070			
Distr. křiv. tr.	18,9			
Koagulační vyšetření				
Quickův test INR			1,05	
APTT			30,3	
Trombinový čas			17,1	
Fibrinogen koagul.			2,7	
Etanol gelifík. test				
Antitrombin III				78
D-dimery				



Ca^{2+} is a coagulation factor !

Ionizované kalcium je nezbytným kofaktorem pro stabilizaci a funkci koagulační kaskády.

- **Iniciace & Propagace:** Ca^{2+} je nutné pro vazbu faktorů na povrch destiček.
- **Kritický bod:** Nízká hladina Ca^{2+} brání tvorbě sraženiny, i když jsou ostatní faktory přítomny.





THROMBO PROPHYLAXIS

ACTIVE BLEEDING

- source control
- haemostatic resuscitation
- correct reversible deficits
- avoid worsening haemodilution

REASSESS

BLEEDING CONTROL

- immobility
- inflammation / end
- trauma / surgery
- prothrombotic recov

VTE PREVENTION

REASSESS

BLEEDING CONTROL IS NOT THE END OF HAEMOSTATIC MANAGEMENT !

A. TBI

- Karmur et al. Neurocrit Care 2026;44:427–444
- Shuja et al. J Clin Neurosci 2025;132:110936
- Dengler et al. J Neurosurg 2025;142:1046–1057
- Byrne et al. JAMA Surg 2022;157:e215794
- Byrne et al. J Am Coll Surg 2016;223:621–631.e5
- Byrne et al. J Am Coll Surg 2026;242:401–413
- Ratnasekera et al. J Am Coll Surg 2021;250:289–298
- Coleman et al. J Surg Res 2021;250:289–298
- Al-Dorzi et al. Ann Thorac Med 2022;88:18
- Rivas et al. Am Surg 2022;88:18
- Störmann et al. World J Surg 20
- Phelan et al. J Trauma Acute Care
- Meyer et al. J Neurosurg 2017
- Jiang et al. Semin Thromb Hem
- ...

C. Major surgery

- Klonis et al. Ann Surg 2023;277:904–911
- PROTECTinG investigators . World J Surg 2023;47:1174–1183
- VERITAS Collaborative. World J Surg
- McAlpine et al. J Am Coll Surg 2021;233:619–631.e14
- Kakkar et al. Ann Surg 2014;259:1073–1079
- Zaghiyan et al. Ann Surg 2016;264:632–639
- ...

B. Blunt trauma / blunt solid-org

- Schellenberg et al. J Trauma Acute Care Surg 20
- Anteby et al. J Surg Res 2023;282:270–279
- Lamb et al. World J Emerg Surg 2022;17:19
- Murphy et al. Eur J Trauma Emerg Surg 2022;48:2039
- Gaitanidis et al. J Trauma Acute Care Surg 2021;90:14
- Schellenberg et al. World J Surg 2019;43:2797–2803
- Sumislawski et al. J Trauma Acute Care Surg 2018;85:9
- Chapman et al. J Surg Res 2013/2014
- Joseph et al. Am J Surg 2015;209:194–198
- Rostas et al. Am J Surg 2015
- Kwok et al. Am J Surg 2016
- Murphy et al. Can J Surg ...

D. Postpartum / PPH

- Freedman et al. Blood Coagul Fibrinolysis 2008;19:55–59
- Blondon et al. BJOG 2025;132:35–43
- Bruno et al. Am J Perinatol 2026
- Bruno et al. Am J Obstet Gynecol 2024;231:128.e1–128.e11
- Bruno et al. Obstet Gynecol 2025
- NATA PBM consensus, Blood Transfus 2019;17:112–136
- RCOG Green-top 37a
- local thromboprophylaxis cohorts
- national obstetric thromboprophylaxis guidelines
- ...

Evidence for timing of pharmacological thromboprophylaxis



Original Investigation

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

James P. Byrne, MD, PhD¹; Christopher D. Witiw, MD, MS²; James M. Schuster, MD, PhD³; [et al](#)

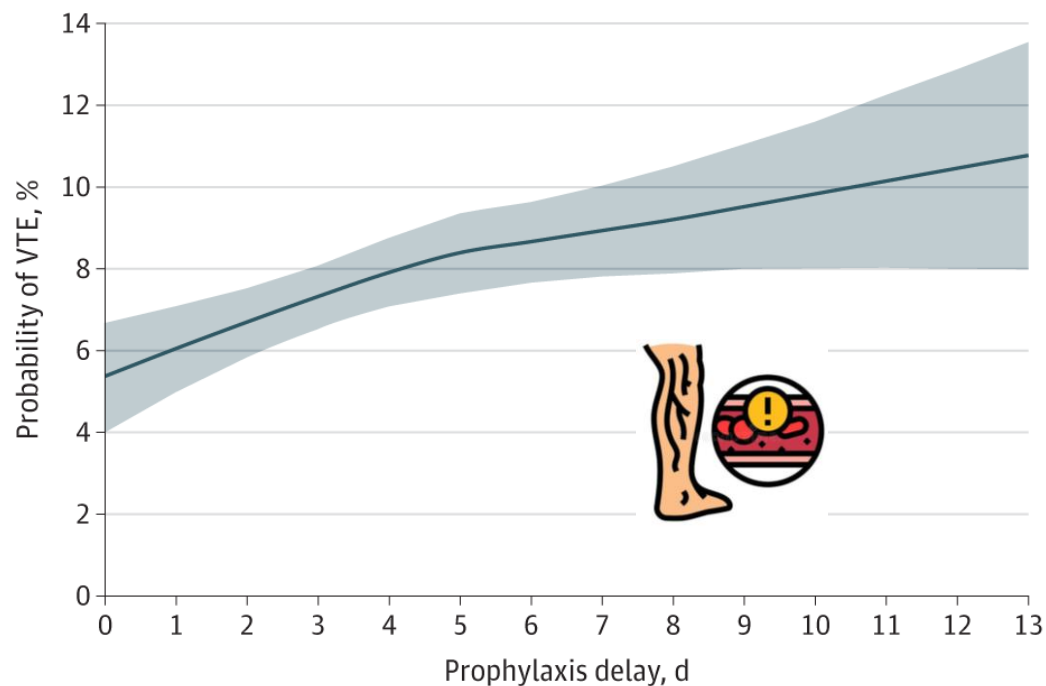
JAMA Surg

Published Online: December 15, 2021

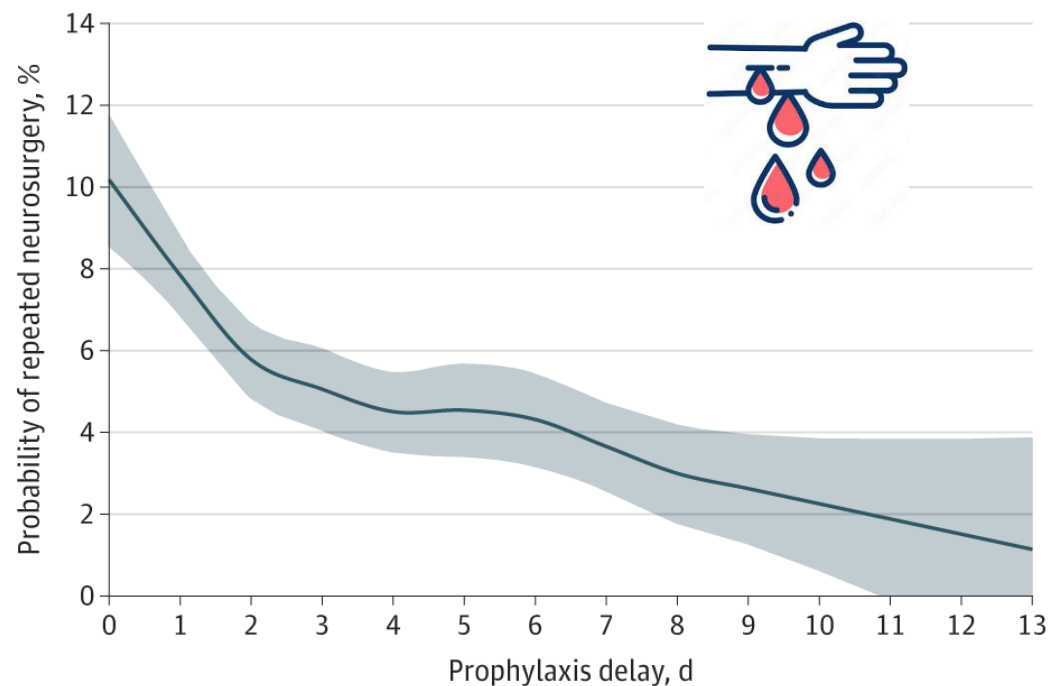
2022;157;(3):e215794.

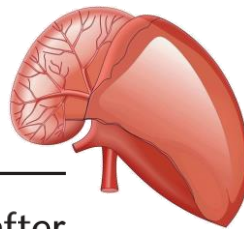
doi:10.1001/jamasurg.2021.5794

A Probability of VTE



B Probability of neurosurgical intervention





When is it safe to start venous thromboembolism prophylaxis after blunt solid organ injury? A prospective American Association for the Surgery of Trauma multi-institutional trial

Morgan Schellenberg, MD, MPH, Natthida Owattanapanich, MD, Brent Emigh, MD, Jan-Michael Van Gent, DO, Tanya Egodage, MD, Patrick B. Murphy, MD, MPH, Chad G. Ball, MD, Audrey L. Spencer, MD, Kelly N. Vogt, MD, PhD, Jessica A. Keeley, MD, Stephanie Doris, DO, Marissa Beiling, MD, Megan Donnelly, MD, Mira Ghneim, MD, Thomas Schroepel, MD, James Bradford, Connor S. Breinholt, MD, Raul Coimbra, MD, PhD, Allison E. Berndtson, MD, Catherine Anding, Michael S. Charles, MD, William Rieger, MD, Kenji Inaba, MD, and The AAST VTE Prophylaxis Study Group, Los Angeles, California

RESULTS: In total, 1,173 patients satisfied the study criteria with 571 liver (49%), 557 spleen (47%), and 277 kidney injuries (24%). The median patient age was 34 years (interquartile range, 25–49 years), and 67% (n = 780) were male. The median Injury Severity Score was 22 (interquartile range, 14–29) with Abbreviated Injury Scale Abdomen score of 3 (interquartile range, 2–3), and the median American Association for the Surgery of Trauma grade of solid organ injury was 2 (interquartile range, 2–3). Early VTEp patients (n = 838 [74%]) had significantly lower rates of VTE (n = 28 [3%] vs. n = 21 [7%], $p = 0.008$), comparable rates of nonoperative management failure (n = 21 [3%] vs. n = 12 [4%], $p = 0.228$), and lower rates of post-VTEp blood transfusion (n = 145 [17%] vs. n = 71 [23%], $p = 0.024$) when compared with Late VTEp patients (n = 301 [26%]). Late VTEp was independently associated with VTE (odds ratio, 2.251; $p = 0.046$).

CONCLUSION: Early initiation of VTEp was associated with significantly reduced rates of VTE with no increase in bleeding complications. Venous thromboembolism chemoprophylaxis initiation ≤ 48 hours is therefore safe and effective and should be the standard of care for patients with blunt solid organ injury. (for the Surgery of Trauma.)

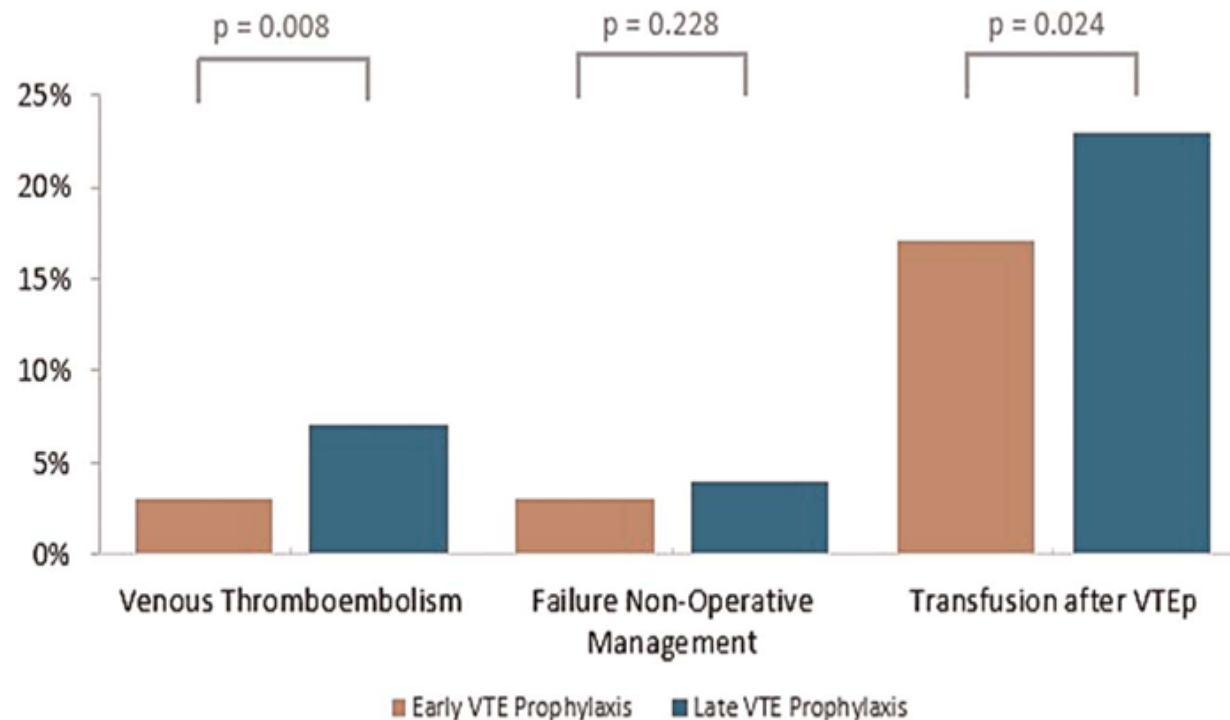


Figure 1. Primary and key secondary outcomes between Early versus Late VTEp patients.

When to start thromboprophylaxis?

Control of bleeding is a clinical and anatomical state — not a laboratory threshold.



CLINICAL JUDGEMENT
GIVES THE GREEN LIGHT



What should guide the decision

- Source controlled
- No ongoing clinically relevant bleeding
- Haemodynamically stable (~~for 12–24 h~~)
- No ongoing transfusion requirement
- Stable haemoglobin trajectory (~~over 12–24 h~~)
- Stable relevant imaging when applicable



What should NOT guide the decision

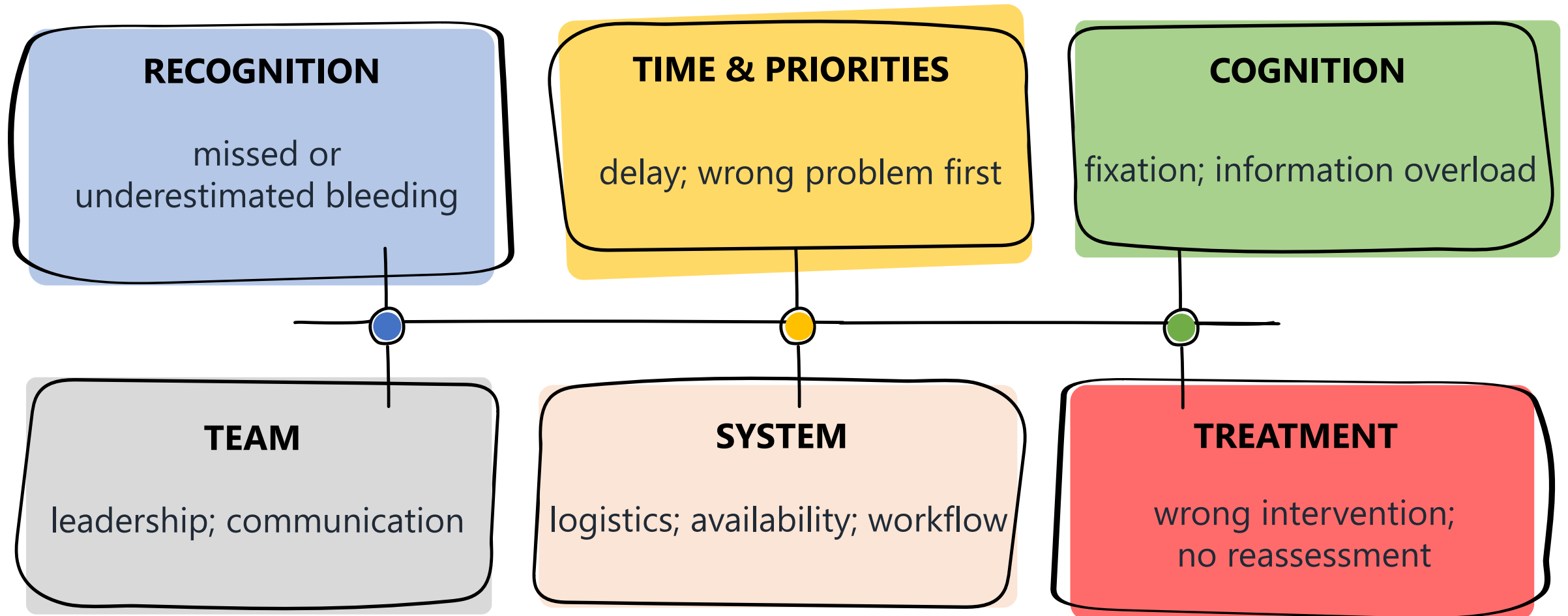
- Waiting for “normal” PT / aPTT
- Waiting for “normal” fibrinogen
- Normal ROTEM / TEG
- Hypercoagulable ROTEM / TEG
- Platelet count alone as a positive trigger
- One universal hour threshold

ROTEM/TEG may show a shift toward hypercoagulability, but they do not measure endothelial integrity and cannot confirm that the bleeding source is safely sealed.

From haemostasis to thromboprophylaxis: the decision is dynamic, not chronological.

BLEEDING MANAGEMENT OFTEN FAILS BEFORE COAGULATION FAILS

Haemostatic therapy is only one part of the problem.



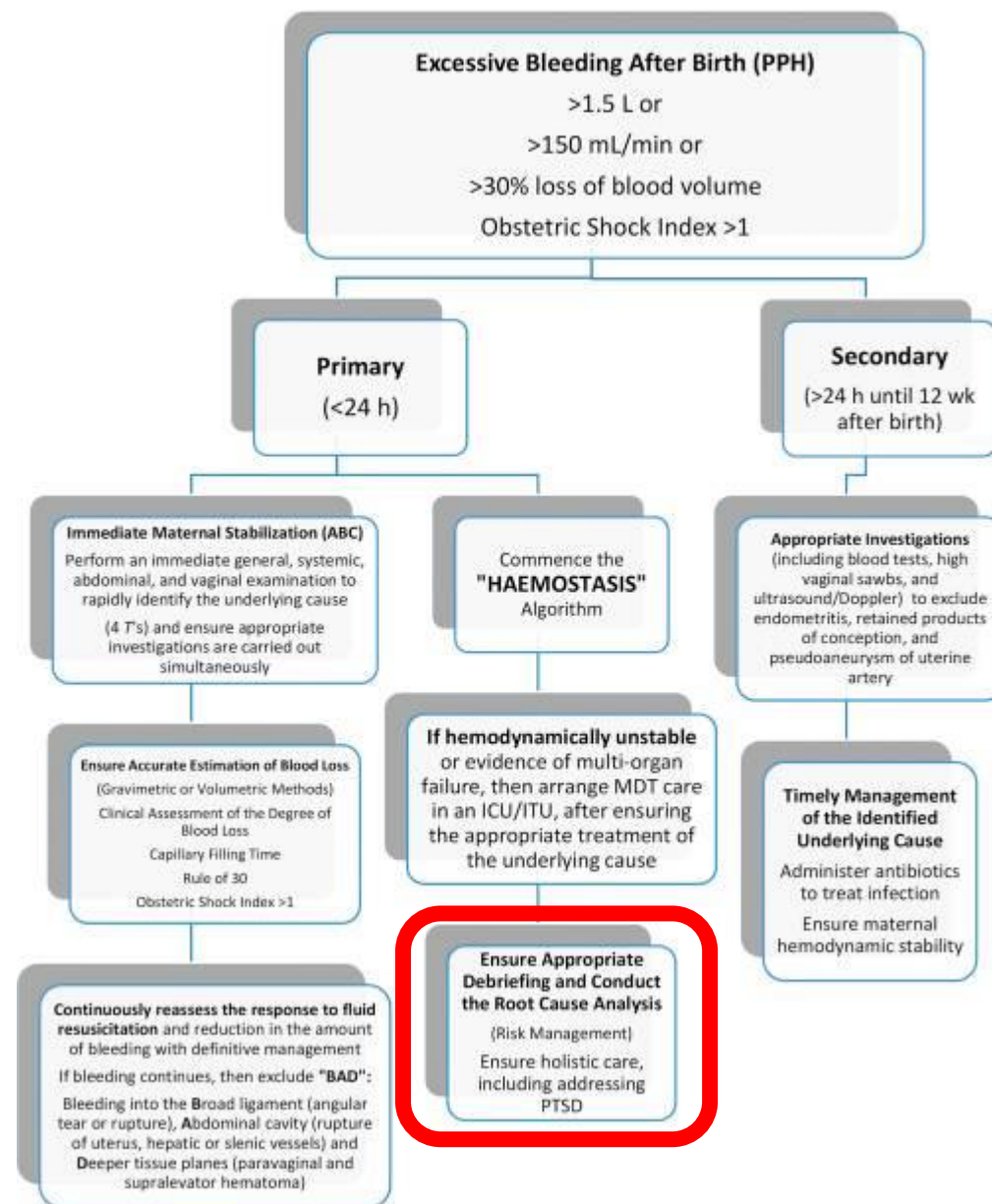
Recognition and Management of Postpartum Hemorrhage

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Abstract

Postpartum hemorrhage (PPH) is an obstetric emergency and refers to excessive blood loss after birth. Loss of blood volume and oxygen-carrying capacity may lead to maternal hypovolemia and hypotension resulting in tissue hypoxia, the onset of anaerobic metabolism, and multiorgan failure. If timely and appropriate action is not taken, cardiac arrest and maternal death may occur. If the amount of blood loss exceeds 500 mL following a vaginal birth or 1000 mL during or following a cesarean section, it is termed PPH. Similar to any other surgical hemorrhage, PPH is classified into primary PPH (occurs within 24 hours of birth) or secondary PPH (between 24 hours and 12 weeks postpartum). PPH is a major contributor to maternal deaths worldwide, and it is estimated that a person dies because of PPH approximately every 5 minutes. Therefore, measures should be directed at prevention and early detection of PPH with prompt management. The prevalence of PPH varies globally and is influenced by location, socioeconomic factors, and the availability and quality of health care. The World Health Organization reported that PPH accounts for a quarter of global maternal deaths. The Mothers and Babies Reducing Risks through Audits and Confidential Enquiries report from the United Kingdom (2023) highlighted that despite rare mortality due to hemorrhage, the number of people dying of obstetric hemorrhage is not decreasing, particularly among people with abnormally invasive placentation. Additionally, substandard care was found to be responsible for more than 50% of deaths due to PPH in the United Kingdom. Therefore, it is vital that adequate healthcare infrastructure, trained and competent healthcare professionals, and immediate access to resources, interventions, and multidisciplinary teams are essential both in well-resourced and resource-restrained healthcare systems. Healthcare professionals must identify the potential risk factors for PPH and initiate preventive measures whenever possible. Additionally, they must respond swiftly if PPH occurs and ensure a multidisciplinary, multilayered approach for a synchronized response to optimize outcomes. This review article emphasizes the etiopathogenesis, diagnosis, and management of PPH based on current scientific evidence as well as international best practice recommendations.

Keywords: Postpartum Hemorrhage; Hemostasis; PPH Management; Triple P Procedure





Modern bleeding management does not fail because we lack knowledge, technology or treatment options.

It fails when we use them without understanding the problem we are trying to solve.

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