SALA CONCORDIA C

PIANETA TRAUMA

Moderatori: **Geminiano Bandiera – Mario Rugna**

Vanessa Agostini

Quando c’è la coagulopatia da trauma

XII congresso nazionale
simeu
RICCIONE 13-15 MAGGIO 2022

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico

QUANDO C'E' LA COAGULOPATIA DA TRAUMA

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U.O. Medicina Trasfusionale IRCCS Policlinico San Martino Genova
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Struttura Regionale per il Coordinamento Attività Trasfusionali-Regione Liguria

XII congresso nazionale
simeu
RICCIONE 13-15 MAGGIO 2022

Dichiarazione di trasparenza

In qualità di relatore

dichiaro

che negli ultimi due anni ho avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

- CSL Behring
- Vifor Pharma
- Baxter
- Sanofi
- Novonordisk

Hemorrhagic blood failure: Oxygen debt, coagulopathy and endothelial damage

Article *in* Journal of Trauma and Acute Care Surgery · March 2017

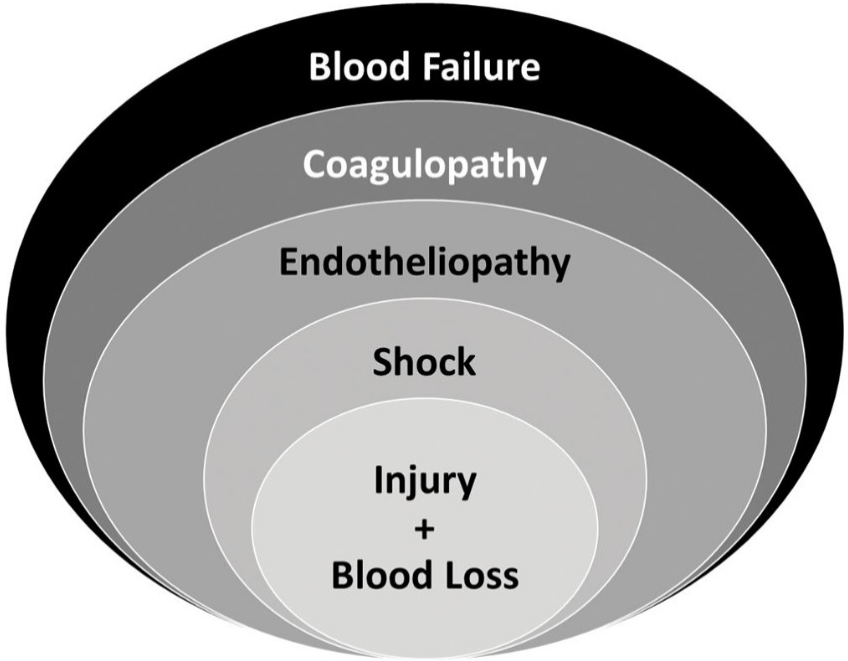


Figure 1.
Schematic representing the components of hemorrhagic blood failure.

Major bleeding following severe trauma continues to represent a global public health issue

Immediate treatment is vital as up to 80 per cent of deaths in the **first hour**, and more than 50 per cent of deaths in the prehospital setting, are due to hemorrhage.

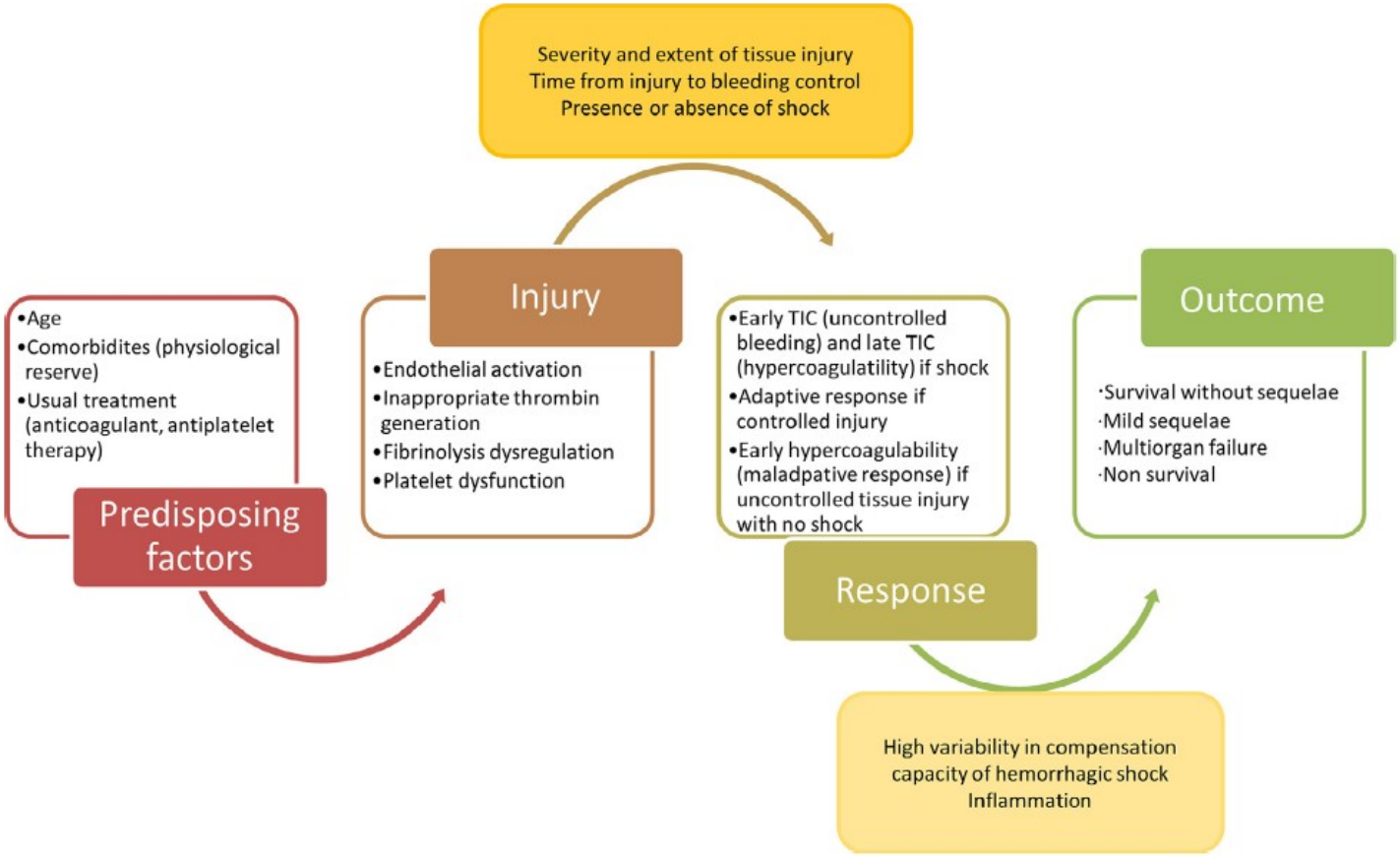
Eur J Trauma Emerg Surg. 2019 Feb;45(1):115-124.

Trauma-Induced Coagulopathy upon Emergency Room Arrival: Still a Significant Problem Despite Increased Awareness and Management?

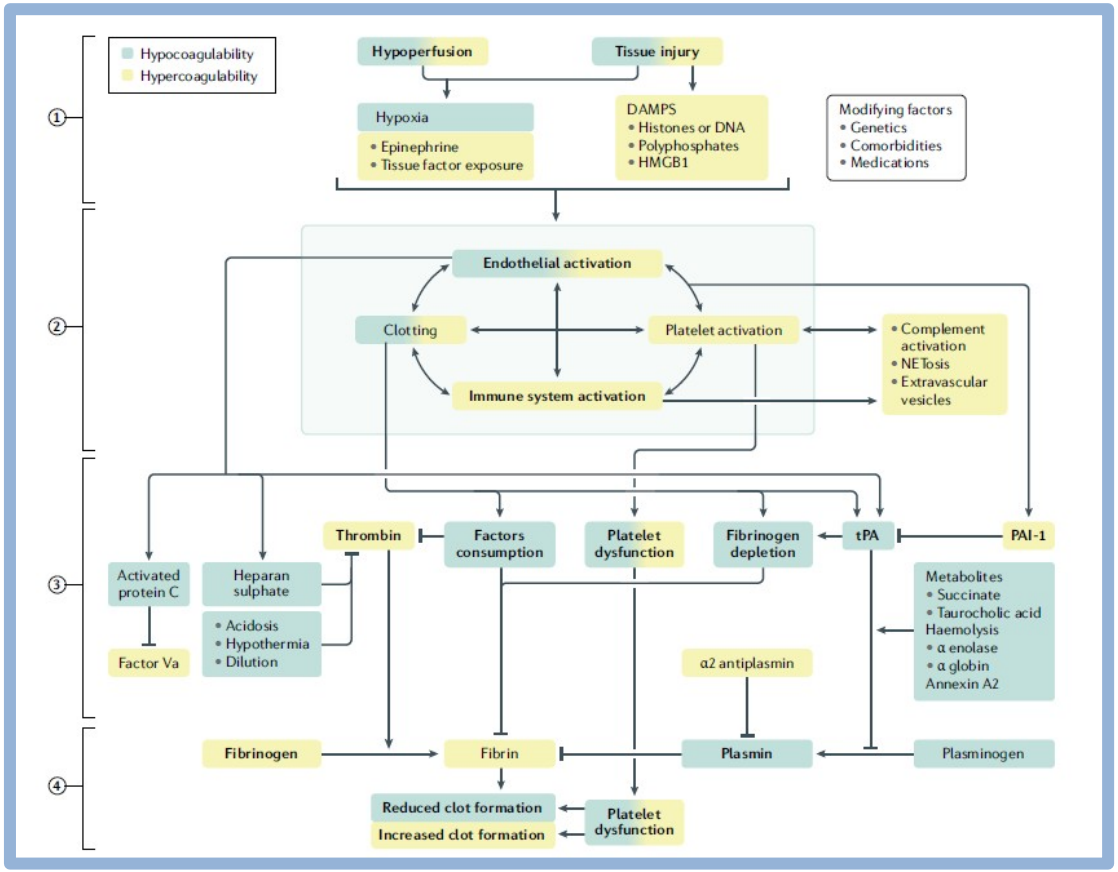
Fröhlich M, Mutschler M, Caspers M, Nienaber U, Jäcker V, Driessen A, Bouillon B, Maegele M; TraumaRegister DGU.

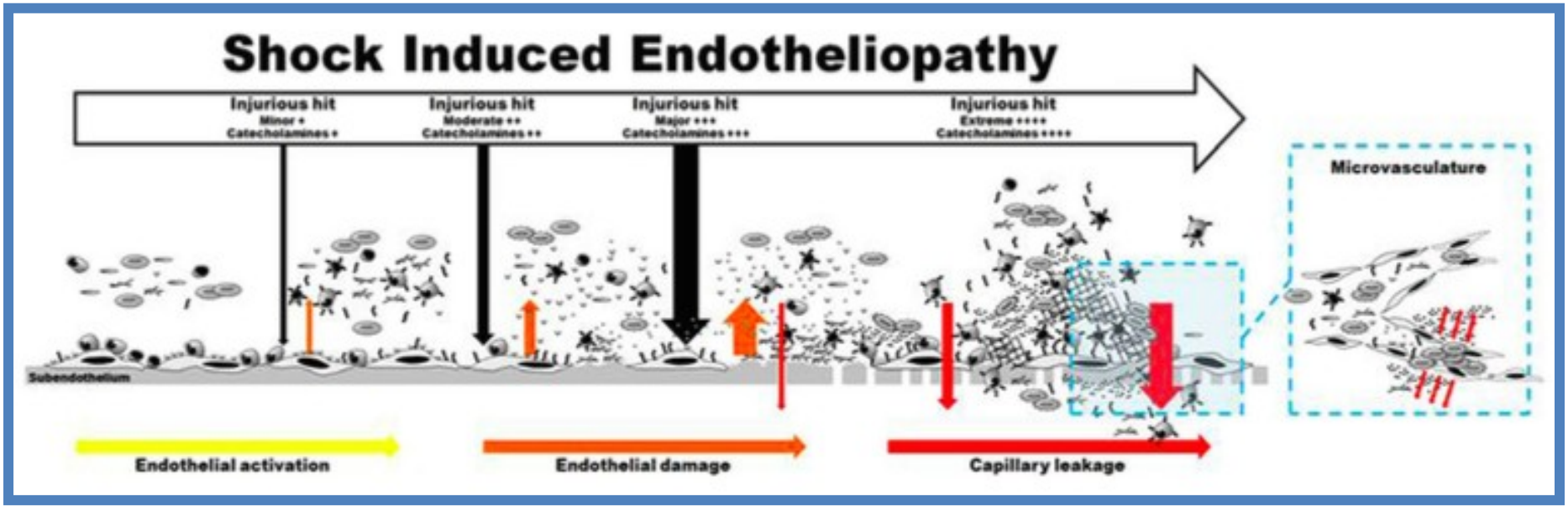
Results: **Coagulopathy upon ER admission** was present in **24.5% of all trauma patients.**

TIC IS A DYNAMIC PROCESS



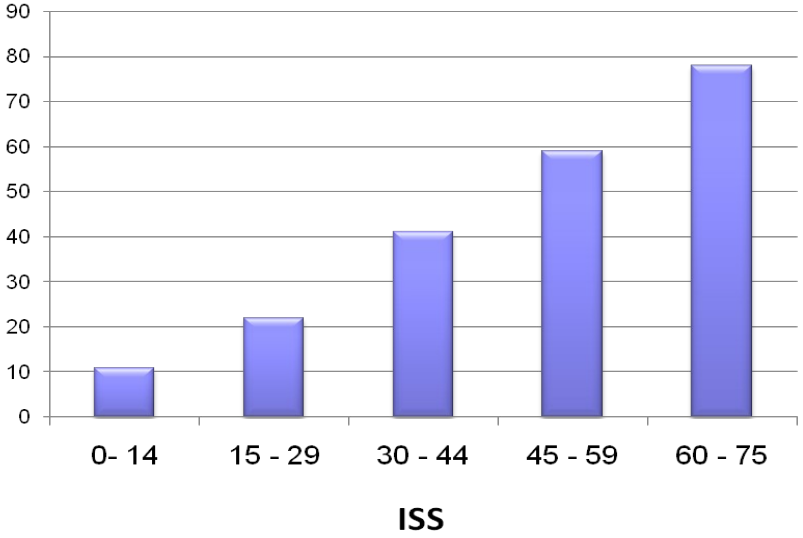
Trauma-induced coagulopathy

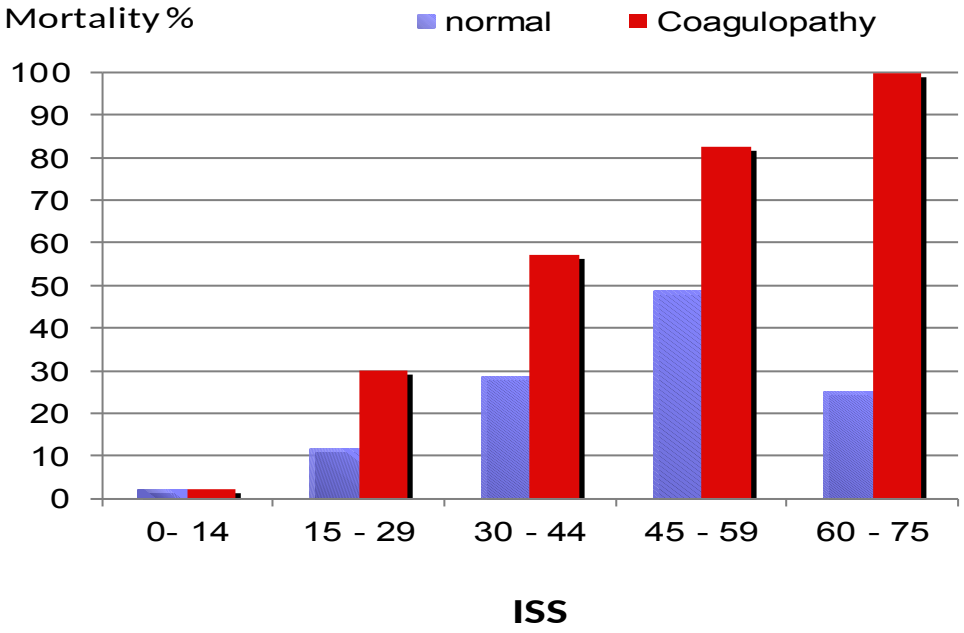



Shock Induced Endotheliopathy
Injurious hit
Minor +
Catecholamines +
Injurious hit
Moderate ++
Catecholamines ++
Injurious hit
Major +++
Catecholamines +++
Injurious hit
Extreme ++++
Catecholamines ++++
Microvasculature
Subendothelium
Endothelial activation
Endothelial damage
Capillary leakage

Acute Traumatic Coagulopathy

Karim Brohi, BSc, FRCS, FRCA, Jasmin Singh, MB, BS, BSc, Mischa Heron, MRCP, FFAEM, and Timothy Coats, MD, FRCS, FFAEM





ACUTE TRAUMATIC COAGULOPATHY (ATC)

There are two main clotting abnormalities in ATC:

1. increased clot breakdown (fibrinolysis)
2. low fibrinogen levels

Variations and obstacles in the use of coagulation factor concentrates for major trauma bleeding across Europe: outcomes from a European expert meeting

Vladimir Černý[1] · Marc Maegele[2] · Vanessa Agostini[3] · Dietmar Fries[4] · Santiago R. Leal-Noval[5] · Gábor Nardai[6] · Giuseppe Nardi[7] · Anders Östlund[8] · Herbert Schöchl[9]

Definition of TIC

Severity level	Definition
TIC 1	Fibrinogen level < 1.5 g/L
TIC 2	Fibrinogen level < 1.5 g/L *and* INR > 1.5
TIC 3	Fibrinogen level < 1.5 g/L *and* INR > 1.5 with platelet count < $100{,}000 \times 10^9$/L

INR, international normalized ratio; TIC, trauma-induced coagulopathy

Criteria for coagulation and resuscitation therapy. ALL should be met.

1. Severe bleeding and clinical and/or laboratory signs of hypoperfusion/haemorrhagic shock;
2. Base excess – 6 mmol/L;
3. Haemoglobin ≤ 9 g/dL;
4. Blood pressure abnormalities (e.g. mean arterial pressure < 65 mmHg or systolic blood pressure < 100 mmHg), and
5. FIBTEM A5 < 10 mm.

FIBRINOLYSIS

Hyperfibrinolysis After Major Trauma: Differential Diagnosis of Lysis Patterns and Prognostic Value of Thrombelastometry

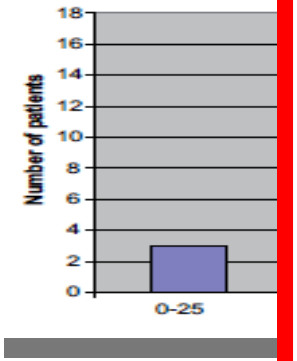
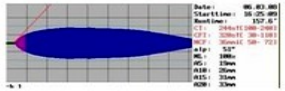


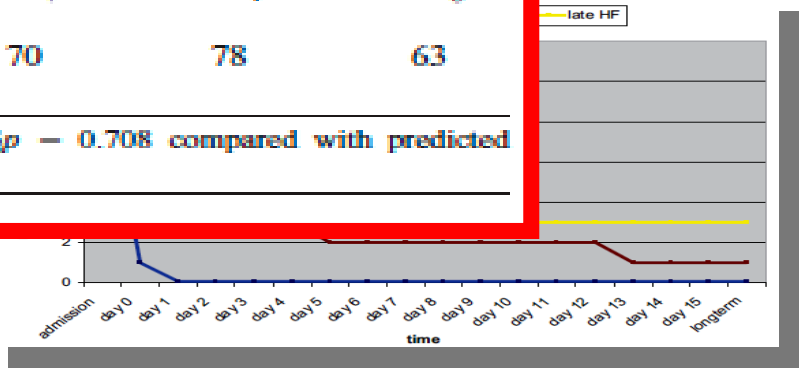
TABLE 2. Basic Characteristics, ISS Score, Observed and Predicted (TRISS) Mortality Overall and in the Hyperfibrinolysis Groups Fulminant (Group A), Intermediate (Group B), and Late (Group C)

	Overall	Fulminant	Intermediate	Late
Number of patients	33	11	11	11
Age (median/range)	45/20–88	45/20–74	44/24–80	48/22–88
Male (%)	67	73	64	64
ISS (Mean ± SD)	[illegible] ± 14	48 ± 14	52 ± 10	42 ± 16
Mean observed mortality (%)	88*	100†	91‡	73§
Mean predicted mortality (TRISS, %)	70	70	78	63

*p — 0.039; †p — 0.065; ‡p — 0.499; §p — 0.708 compared with predicted mortality.

- **fulminant HF**
  - immediate breakd
    the clot within 30
- **intermediate HF**
  - breakdown of the
    between 30 – 60
- **late HF**
  - complete clot lysis after more than 60 min





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

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)

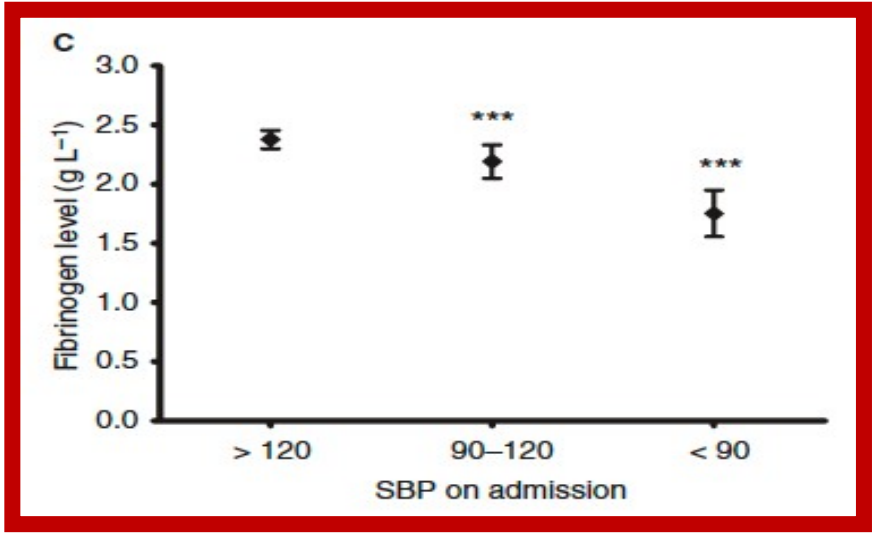
We recommend that protocols for the management of bleeding patients consider administration of the first dose of TXA en route to the hospital. (Grade 1C)

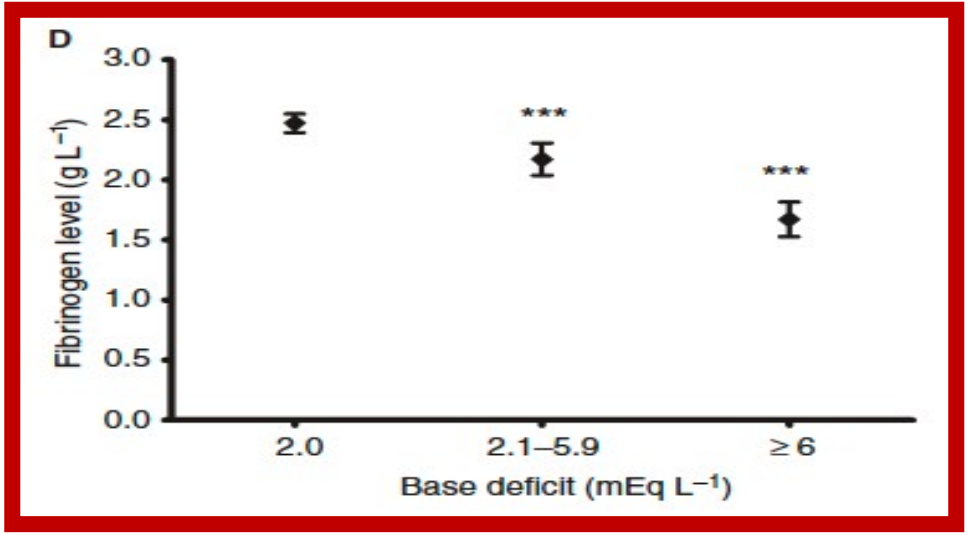
We recommend that the administration of TXA not await results from a viscoelastic assessment. (Grade 1B)

Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes

C. ROURKE,*[1] N. CURRY,†[1] S. KHAN,* R. TAYLOR,† I. RAZA,* R. DAVENPORT,* S. STANWORTH† and K. BROHI*

*Trauma Sciences, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London; and † National Health Service Blood & Transplant/Haematology, John Radcliffe Hospital, Oxford, UK





41% dei pazienti ipotesi (PAS<90 mmHg) hanno livelli di fibrinogeno<1,5g/L

Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes

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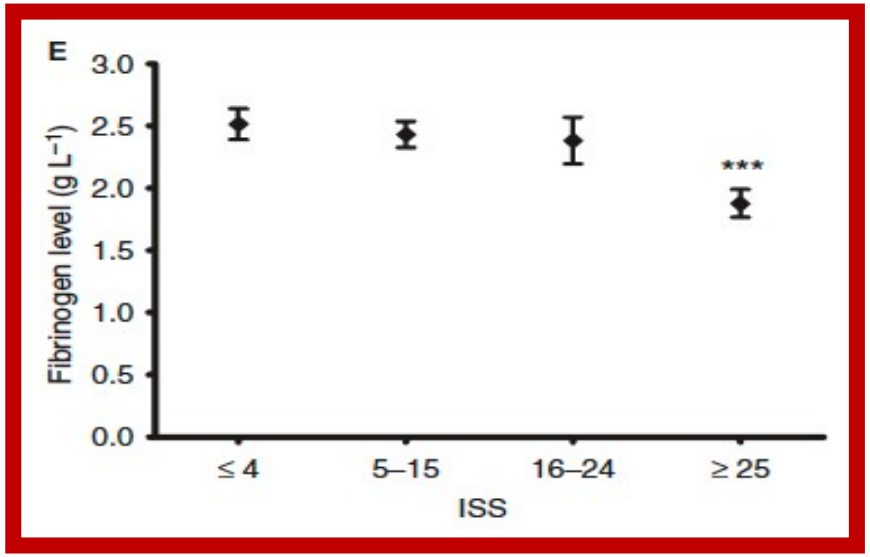

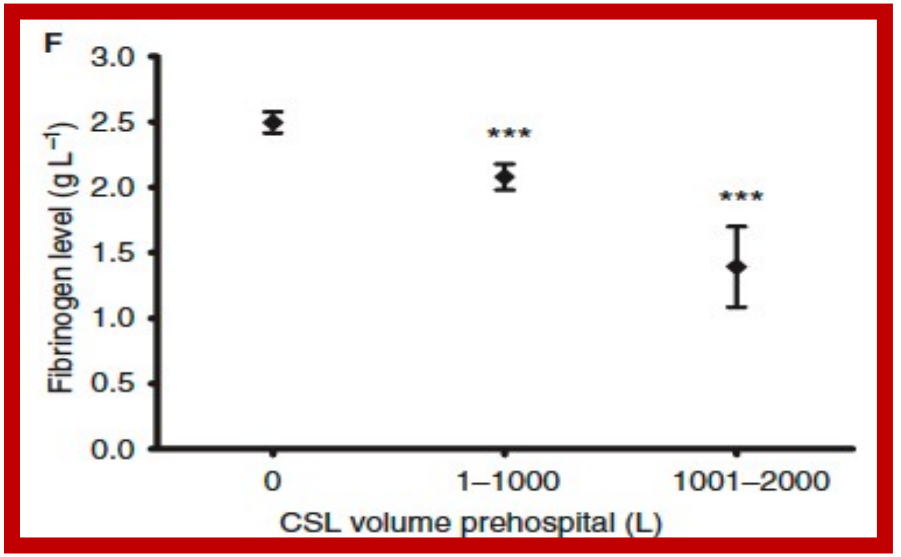

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Fibrinogen supplementation

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)

Recommendation 10

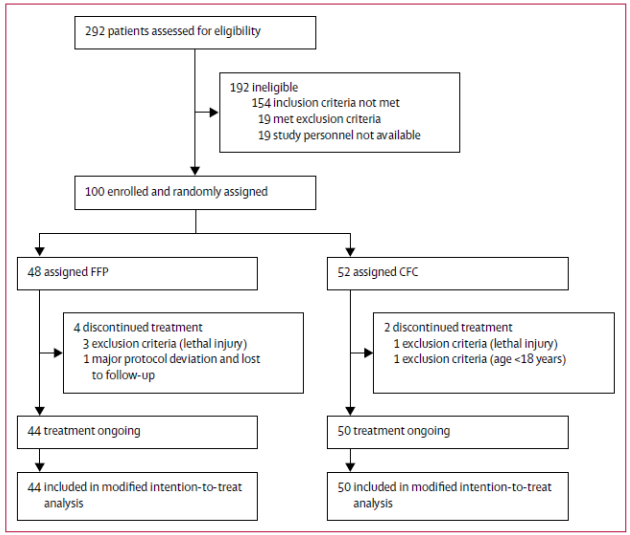
We recommend that routine practice include the early and repeated monitoring of haemostasis, using either a combined traditional laboratory determination [prothrombin time (PT), platelet counts and Clauss fibrinogen level] and/or point-of-care (POC) PT/international normalised ratio (INR) and/or a viscoelastic method (VEM) (Grade 1C).

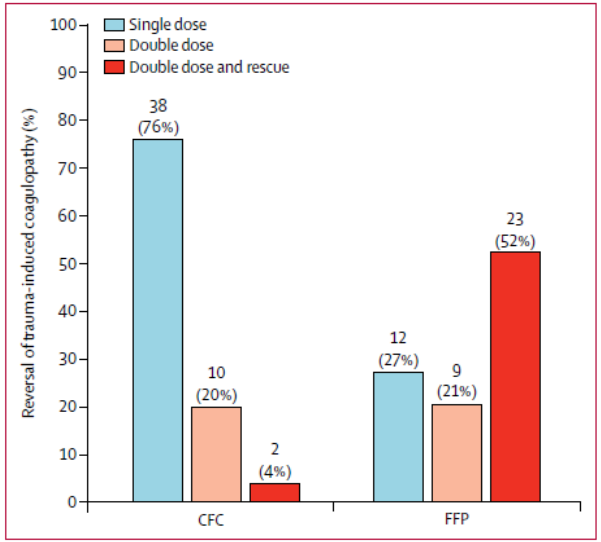
We recommend laboratory screening of patients treated or suspected of being treated with anticoagulant agents (Grade 1C).

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).

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





FFP 15mL/Kg

FC 50mg/Kg
± 4 factor PCC
± factor XIII

CONCLUSION

This randomised trial is the first to our knowledge to compare first-line use of FFP and CFC for treatment of coagulopathy and associated bleeding in major blunt trauma. The study aimed to compare the efficacy of haemostatic treatment in correcting trauma-induced coagulopathy, consequently arising blood loss-associated transfusion requirements, and clinical outcome. The trial was terminated early after randomisation of 100 patients, as the a-priori planned interim analysis showed an unacceptably high incidence of treatment failure and increased risk for massive transfusion for patients randomly allocated to the FFP group. However, the available sample size appears sufficient to make some conclusions that first-line CFC is superior to FFP.

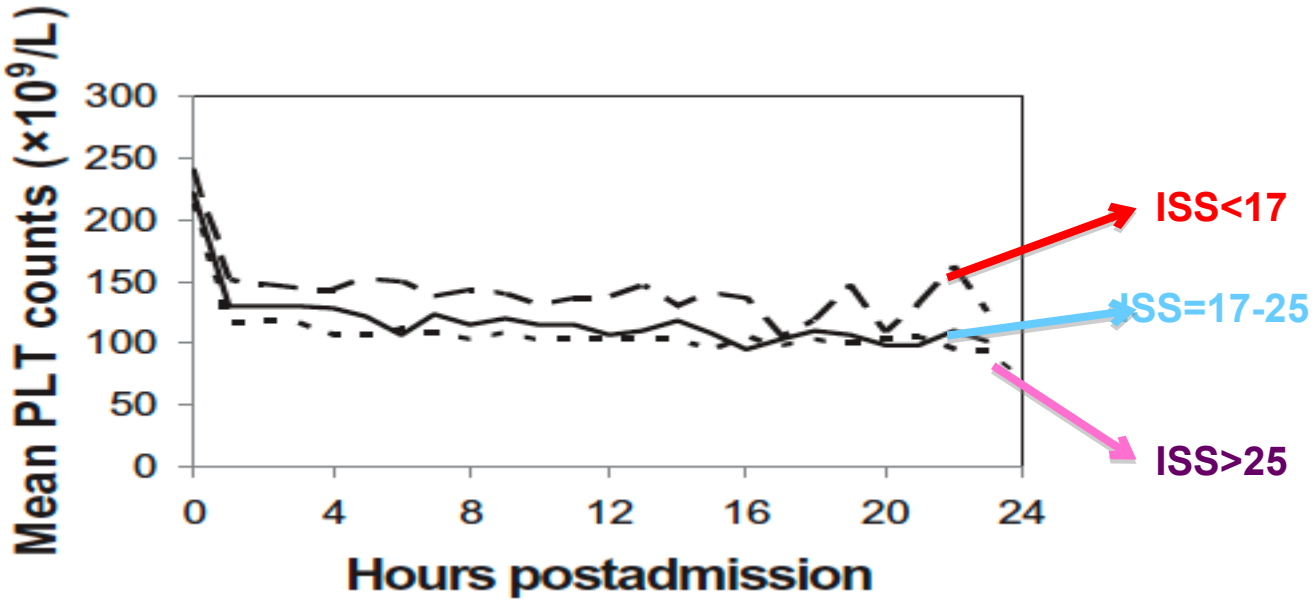
In conclusion, our results underline the importance of early fibrinogen supplementation for severe clotting failure in multiple trauma. A CFC-based algorithm guided by viscoelastic tests is considerably superior to FFP transfusion. Correction of trauma-induced

First randomised trial that compare FFP vs CFC in trauma

Terminated early due to an high incidence of treatment failure and increased risk for massive transfusion (FFP group)

A CFC-based algorithm guided by viscoelastic tests is superior to FFP transfusion

The clinical significance of platelet counts in the first 24 hours after severe injury



TIC e FATTORI DELLA COAGULAZIONE

	ATC (CA5 ≤35mm)	Non-ATC (CA5 >35mm)	p value
Patients (n)	50	250	
Median ISS	23 (10-34)	9 (4-22)	<0.001
Temperature (°C)	35.9 ± 0.2	35.2 ± 0.5	0.010
pH	7.4 ± 0	7.3 ± 0	<0.001
Lactate (mmol/L)	2.4 ± 0.3	4.4 ± 1.2	0.003
BD mmol/L	5.2 ± 1.6	1.5 ± 0.5	<0.001
Platelets	195 ± 19	249 ± 8	<0.001
Fibrinogen (g/L)	1.35 ± 0.16	2.23 ± 0.07	<0.001
II	79 ± 5	98 ± 2	<0.001
V	70 ± 10	103 ± 3	<0.001
VII	88 ± 7	102 ± 4	0.001
VIII	267 ± 44	289 ± 16	0.355
IX	97 ± 8	120 ± 3	<0.001
X	83 ± 6	102 ± 2	<0.001
XI	91 ± 9	111 ± 3	<0.001

Davenport *et al.* In Press

Spahn et al. Critical Care (2019) 23:98
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Variations and obstacles in the use of coagulation factor concentrates for major trauma bleeding across Europe: outcomes from a European expert meeting

Vladimír Černý[1] · Marc Maegele[2] · Vanessa Agostini[3] · Dietmar Fries[4] · Santiago R. Leal-Noval[5] · Gábor Nardai[6] Giuseppe Nardi[7] · Anders Östlund[8] · Herbert Schöchl[9]

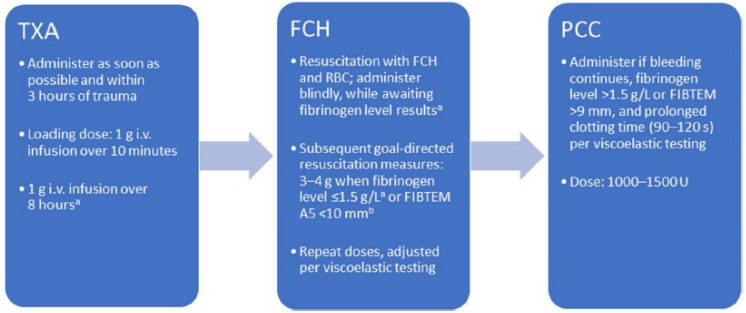
Recommendation 27

If a CFC-based strategy is used, we recommend treatment with factor concentrates based on standard laboratory coagulation parameters and/or viscoelastic evidence of a functional coagulation factor deficiency (Grade 1C).

Provided that fibrinogen levels are normal, we suggest that PCC is administered to the bleeding patient based on evidence of delayed coagulation initiation using VEM (Grade 2C).

We suggest that monitoring of FXIII be included in coagulation support algorithms and that FXIII be supplemented in bleeding patients with a functional FXIII deficiency (Grade 2C).

Overall, impaired thrombin generation is not considered a problem in the early stages of trauma-related bleeding management, as thrombin levels are often increased following trauma. Indeed, studies have found greater thrombin generation in trauma patients compared with healthy controls



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Critical Care **23**, Article number: 98 (2019) | Cite this article

MT

Tranexamic acid
Fibrinogen

PFC
Fibrinogen
PPC

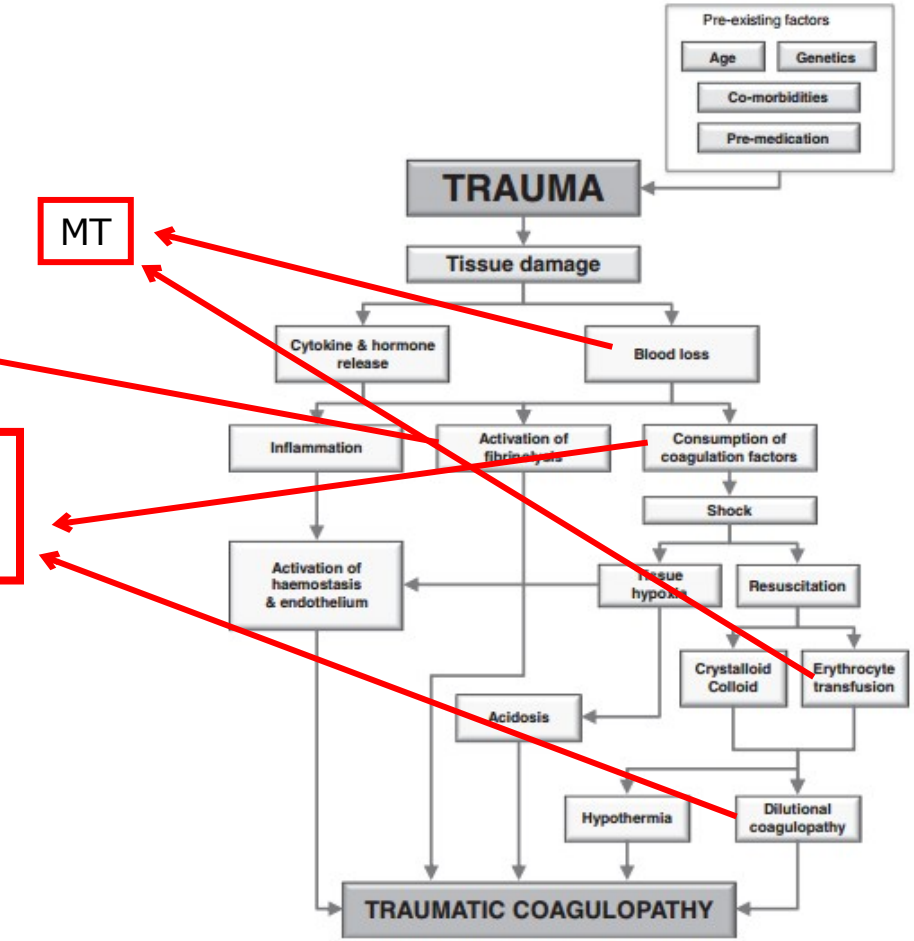

Fig. 1 Schematic drawing of the factors, both pre-existing and trauma-related, that contribute to traumatic coagulopathy. Adapted from [18, 19, 34]


FFP
CRYO
FIBRINOGEN
?
rFVIIa
PCC
PLATELETS
DDAVP
TXA

TIME IS THE ISSUE

J Trauma Acute Care Surg. 2019 Aug;87(2):342-349.

Earlier Time to Hemostasis is Associated with Decreased Mortality and Rate of Complications: Results from the Pragmatic Randomized Optimal Platelet and Plasma Ratio Trial

Chang R, Kerby JD, Kalkwarf KJ, Van Belle G, Fox EE, Cotton BA, Cohen MJ, Schreiber MA, Brasel K, Bulger EM, Inaba K, Rizoli S, Podbielski JM, Wade CE, Holcomb JB; PROPPR Study Group.

RESULTS: **Every 15-minute decrease in time to hemostasis was associated with decreased 30-day mortality (RR, 0.97;** 95% CI, 0.94-0.99),
AKI (RR, 0.97; 95% CI, 0.96-0.98),
ARDS (RR, 0.98; 95% CI, 0.97-0.99),
MOF (RR, 0.94; 95% CI, 0.91-0.97), and
sepsis (RR, 0.98; 95% CI, 0.96-0.99), but not
venous thromboembolism (RR, 0.99; 95% CI, 0.96-1.03).

Every minute counts: Time to delivery of initial massive transfusion cooler and its impact on mortality

Delays in the activation of MTP and delays in the delivery of the first blood product cooler were both associated with increased time to hemostasis and increased mortality. In the PROPPR dataset, every minute of delay between the activation of MTP and the arrival of the first blood cooler regardless of ratio, resulted in a 5% increase in the odds of mortality. In fact, it appears that decreasing the time to blood product administration is one of the modifiable risk factors that affect mortality in the exsanguinating trauma patient. Every effort should be made to decrease the time to recognition of the need for MTP and the time to administration of the first blood product.

STRATEGIE TRASFUSIONALI

- **Formula driven (1:1:1-concept):**
  PRBC - FFP - Platelets - rFVIIa

- **Lab-driven (Pts, PT, aPTT, Fib)**

- **Individualized POC-driven:**
  Fibrinogen/Cryo - Plt - PCC/FFP

Early Goal-directed Coagulation Management

www.oegari.at

Trauma Update Network:
Early Coagulation Support (ECS) protocol

Un protocollo di intesa dell'Italian Trauma Update Research Group per la prevenzione e il trattamento della coagulopatia indotta dal trauma (TIC)

Algoritmo decisionale | Protocollo ECS | Terapia guidata da ROTEM/TEG

Algoritmo decisionale

Il paziente presenta emorragia significativa oppure è a rischio di emorragia?

SI

Prelievo per:
- Emocromo con piastrine
- Coag (PT-INR, PTT, FIB)
- EGA con lattati
- Gruppo sanguigno
- **ROTEM/TEG** → prelievo in provetta da coagulazione da consegnare all'anestesista. Identificarla come BASALE

Acido tranexamico (1 gr e.v. + 1 gr in 8 h)

Assume anticoagulanti/antiaggreganti?

NO

Presenta un'emorragia massiva (non controllabile) + almeno uno dei seguenti segni
- PAS <100 mmHg
- BE <-6 o pH <7,2
- Lattati ≥ 5 mmol/l o 45 mg/l
- FAST ++++
- (INR >1,5)

SI

Attiva protocollo ECS

NO

Trattamento standard

NO

No ECS

Intensive Care Med (2021) 47:49–59
https://doi.org/10.1007/s00134-020-06266-1

ORIGINAL

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

Enrolled patients will be block randomized per centre to either study arm:

- CCT: Haemostatic resuscitation, based on a MTP aiming at ratio 1:1:1 of blood components (RBC 1: plasma 1: platelets 1) and CCT to guide further resuscitation with blood products and procoagulant factors.
- VHA: Haemostatic resuscitation, based on a MTP aiming at ratio 1:1:1 of blood components (RBC 1: plasma 1: platelets 1) and VHA-guiding further resuscitation with blood products and procoagulant factors.

CCT arm Algorithm

FIBRINOGEN
If Fibrinogen <2g/L
Give additional 4g equivalent of fibrinogen
(As Cryoprecipitate or Concentrate)

PLATELETS
If Platelets <100 x10^9/L
Give 1 additional pool of platelets

PLASMA
If INR >1.2 **AND** Fibrinogen ≥2g/L
Give 4 additional units of plasma

VHA Algorithm RoTEM ®

FIBRINOGEN
If FIBTEM CA5 < 10mm
Give additional 4g equivalent of fibrinogen
(As Cryoprecipitate or Concentrate)

PLATELETS
If (EXTEM CA5 - FIBTEM CA5) < 30mm
Give 1 additional pool of platelets

PLASMA
If EXTEM CA5 ≥40mm **AND** EXTEM CT >80s
Give 4 additional units of plasma

TRANEXAMIC ACID
If EXTEM LI30 <85%
Give additional 1g IV bolus of tranexamic acid

Intensive Care Med (2021) 47:49–59
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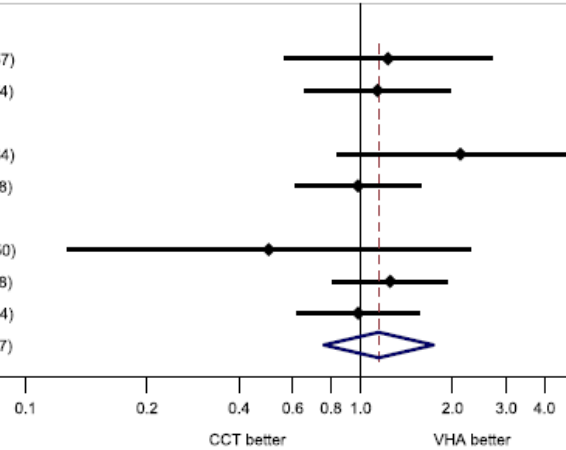
ORIGINAL

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

Subgroup	No. patients	No. alive and free of MT (%) - CCT	No. alive and free of MT (%) - VHA	Odds Ratio (95% CI)	p-value interaction
PTr > 1.2 at baseline					0.872
Yes	102	30/58 (52)	25/44 (57)	1.23 (0.56, 2.69)	
No	254	88/123 (72)	97/131 (74)	1.13 (0.65, 1.97)	
Severe TBI					0.148
Yes	74	16/35 (46)	25/39 (64)	2.12 (0.84, 5.34)	
No	313	106/156 (68)	106/157 (68)	0.98 (0.61, 1.57)	
Prior oral anticoagulants					0.268
Yes	27	10/15 (67)	6/12 (50)	0.50 (0.11, 2.28)	
No	363	112/177 (63)	127/186 (68)	1.25 (0.81, 1.93)	
Per Protocol	313	105/163 (64)	96/150 (64)	0.98 (0.62, 1.56)	
Overall (all patients)	396	125/195 (64)	135/201 (67)	1.15 (0.76, 1.73)	



Schlimp *et al. Critical Care* 2013, **17**:R137
http://ccforum.com/content/17/4/R137

CRITICAL CARE

RESEARCH Open Access

Estimation of plasma fibrinogen levels based on hemoglobin, base excess and Injury Severity Score upon emergency room admission

Christoph J Schlimp[1], Wolfgang Voelckel[2], Kenji Inaba[3], Marc Maegele[4], Martin Ponschab[5] and Herbert Schöchl[1,2*]

In the first five minutes we have to recognize patients at risk

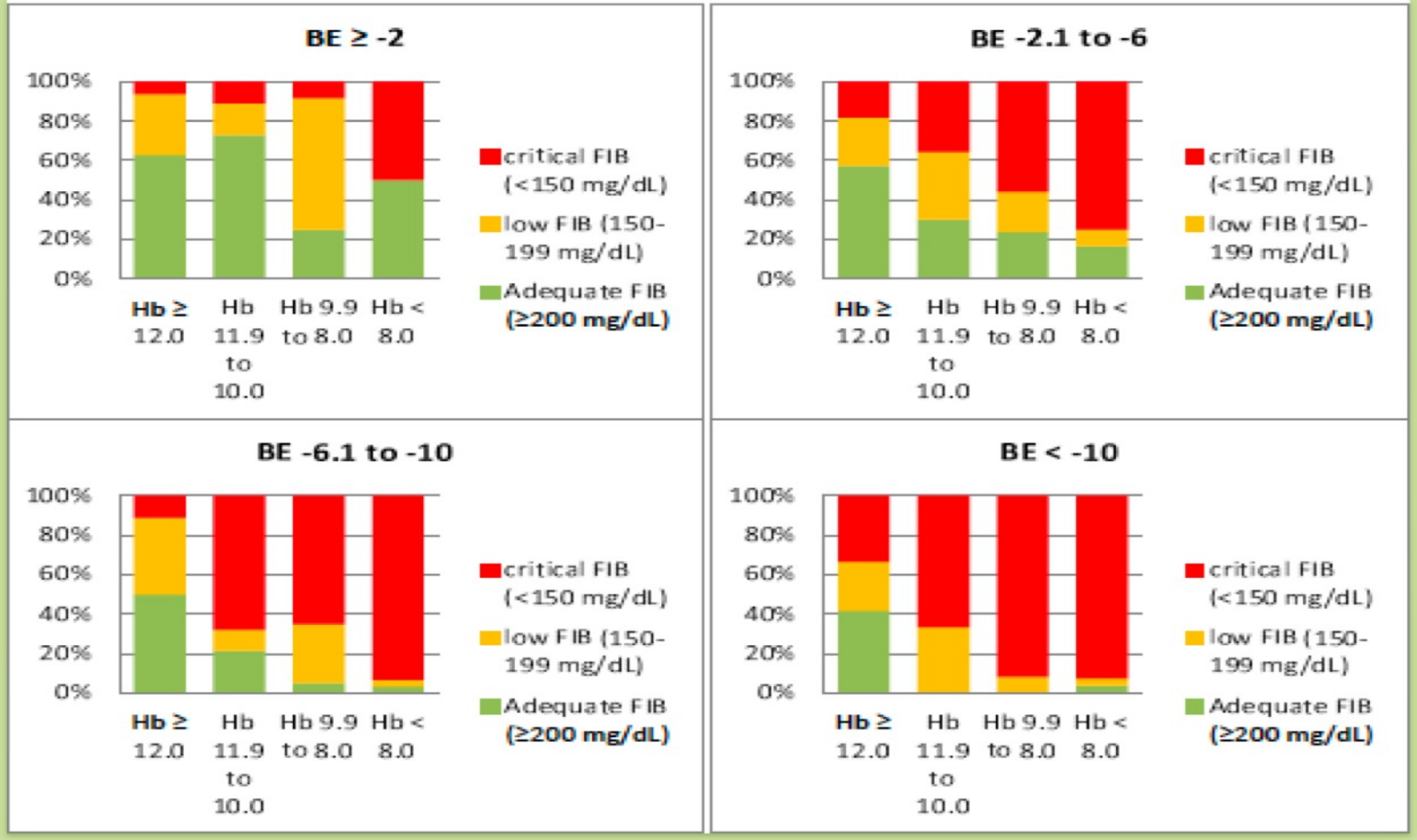
Bleeding	Hemoglobin < 9 mg/dL
Shock	SBP < 100 mmHg
Acidosis	BE < −6 Lactate > 5 mEq/L

ABL825 R0848N005 PS dx 15.50 14/08/2013
REFERTO PAZIENTE Siringa - S 195uL Campione 22897

Identificazioni			
ID paziente			
Cognome paziente	TRAUMA		
Nome paziente			
Tipo di campione	Arterioso		
T	37,0 °C		
$FO_2(I)$	70,0 %		
Valori gas ematici			
?↓ pH	7,307		[7,350 - 7,450]
↓ pCO_2	29,3	mmHg	[35,0 - 45,0]
↓ pO_2	79,8	mmHg	[80,0 - 100]
$pO_2(a,T$	114	mmHg	
Valori ossimetrici			
↓ ctHb	6,2	g/dL	[11,5 - 17,4]
sO_2	97,2	%	[75,0 - 99,0]
FO_2Hb	95,3	%	[95,0 - 99,0]
FCOHb	1,7	%	[0,0 - 2,5]
FHHb	2,7	%	[1,0 - 5,0]
↓ FMetHb	0,3	%	[0,4 - 1,5]
Valori elettroliti			
cK^+	4,0	mmol/L	[3,5 - 4,5]
cNa^+	138	mmol/L	[135 - 148]
cCa^{2+}	1,25	mmol/L	[1,12 - 1,32]
↑ cCl^-	113	mmol/L	[98 - 107]
Valori metaboliti			
↑ cGlu	318	mg/dL	[60 - 110]
↑ cLac	5,3	mmol/L	[0,4 - 2,2]
Valori corretti con la temperatura			
? pH(*T*)	7,307		
$pCO_2(T)$	29,3	mmHg	
$pO_2(T)$	79,8	mmHg	
Stato di ossigenazione			
ctO_2,c	8,5	Vol%	
? p50,e	28,22	mmHg	
Stato Acido Base			
? cBase(Ecf),c	-10,9	mmol/L	
? $cHCO_3^-$(P,st),c	15,7	mmol/L	
$pO_2(a,T$	114	mmHg	
mOsm,c	294,1	mmol/kg	
? Anion Gap,c	10,9	mmol/L	
Hct,c	19,5	%	

Estimation of plasma fibrinogen levels based on hemoglobin, base excess and ISS upon emergency room admission

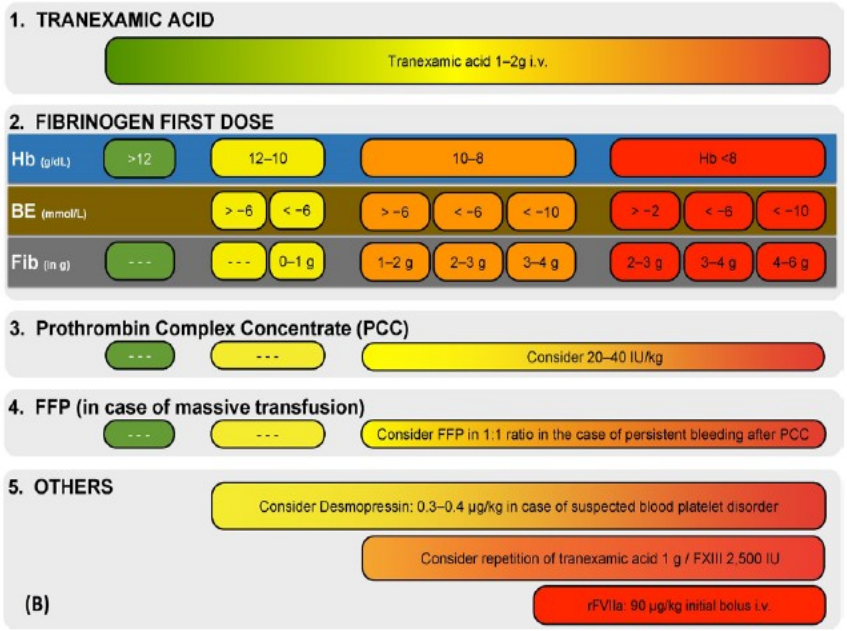
Critical Care 2013, **17**:R137 doi:10.1186/cc12816



Trauma Surgery
& Acute Care Open

Simplified treatment algorithm for the management of trauma-induced hemorrhage without viscoelastic testing

Basics	1. Oxygen & fluid management 2. Laboratory blood testing (depending on local protocol) 3. Logistics for further diagnostics, therapy and transport
Maintain!	1. pH >7.2 2. T >35°C 3. Ca_i >0.9mmol/L
Medical history	Increased bleeding tendency? Antiplatelet agents? Oral anticoagulation? Antidote therapy possible?
Tranexamic acid	Consider *early* 1–2 g i.v.
Fibrinogen	2–6 g (30 mg/kg body weight) or in accordance with Base Excess (BE) and hemoglobin (Hb); target range: >150–200 mg/dL (decision tree detailed overleaf)
Prothrombin complex concentrate (PCC)	20–40 IU/kg body weight
In case of massive blood transfusion	Consider early: Fresh Frozen Plasma (FFP):erythrocyte concentrate in 1:1 ratio
Platelets	Target range: >50/nL respectively >100/nL in case of brain injury or upon suspicion of acquired or hereditary failure of platelet function
Ultima ratio	1. Repeat tranexamic acid 2. FXIII (1,250–2,500 IU) 3. rFVIIa (90 micrograms per kg) Off-label use! Pay attention to requirements!



Recommendation 1

We recommend that severely injured patients be transported directly to an appropriate trauma facility (Grade 1B).

INTERNATIONAL PRE-HOSPITAL BLOOD PRODUCT

- Australia
  - PRBC
  - Not using TXA routinely
- New Zealand (Auckland)
  - whole blood
- USA
  - PRBC
  - Thawed plasma trials
  - Low titre O whole blood
- Europe
  - Austria – fibrinogen (FinTIC)
  - France, Germany, Denmark, UK – lyophilised / thawed plasma
  - Norway – plasma, low titre O WB
- Military
  - US – whole blood (Afghanistan)
  - UK MERT – PRBC & thawed plasma
  - Israel – low titre whole blood
  - Norway special forces – warm whole blood

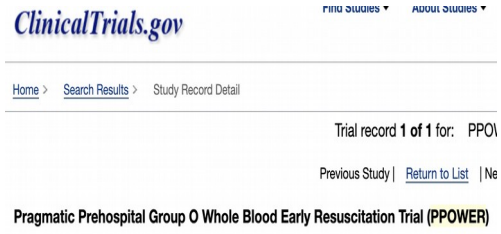
BLOOD on BOARD

Volume and Concentrations Between Component Therapy vs. Warm Whole Blood

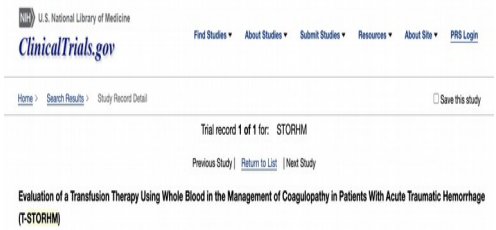
VS

Component therapy (675 mL)	Whole blood (500 mL)
1 unit of pRBC = 335 mL with hematocrit of 55%	Hematocrit of 38–50%
1 unit of PLTs = 50 mL with 88 K platelets	Platelet count of 150–400 K
1 unit of FFP = 275 mL with 80% coagulation activity	Plasma coagulation factors = 100%
1 unit of cryoprecipitate = 15 mL with 150 mg of fibrinogen	Fibrinogen = 1000 mg
Thus, 1 unit of pRBC + 1 unit of PLTs + 1 unit of FFP + 1 unit of cryoprecipitate = 675 mL with hematocrit of 29%, platelet count of 88 K and coagulation activity of 65% compared with WB	

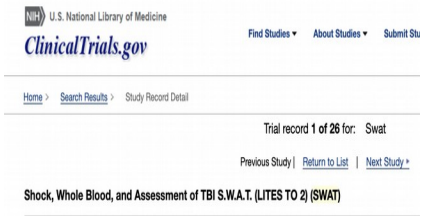
pRBC packed red blood cells, *PLTs* platelets, *FFP* fresh frozen plasma, *WB* whole blood.



Single center prospective randomized pilot trial of LTOWB leukocyte-reduced: 6 unit of WB followed by TEG-guided resuscitation



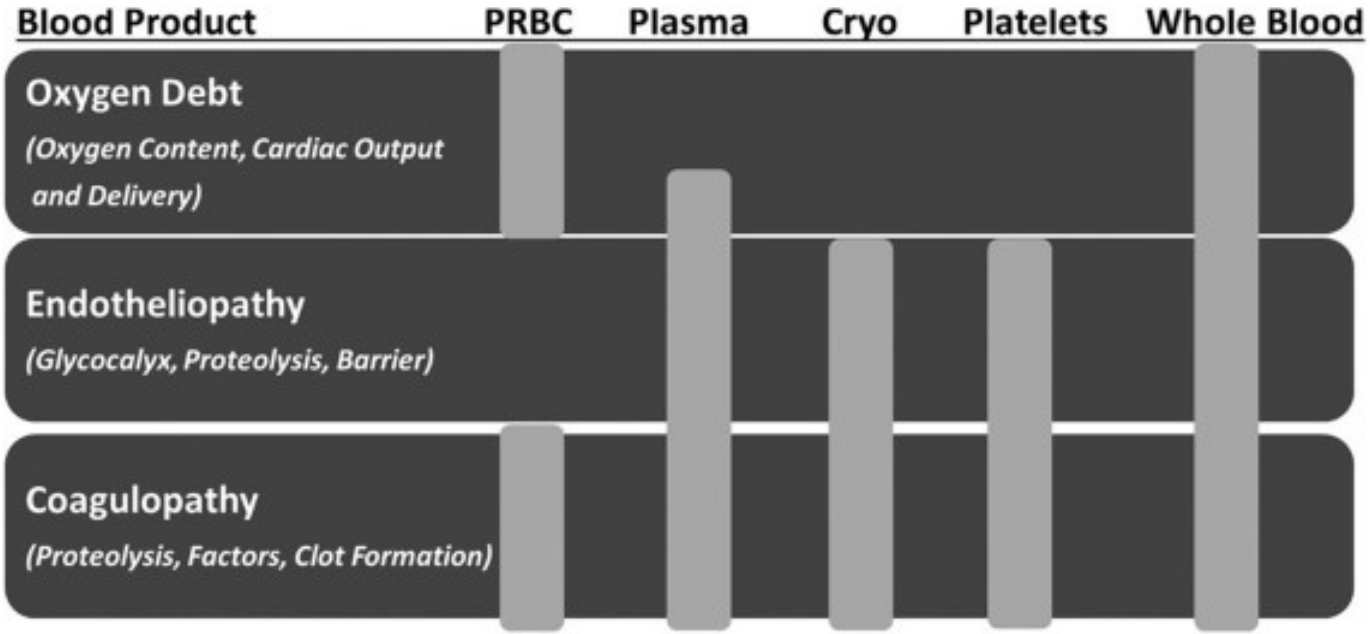
French study is still planning as a non inferiority study to compare LTLR WB to 1:1:1 fixed ratio. End point mortality and TEG parameters



Consortium of trauma centers that conduct prospective, multicenter study to compare WB to BCT

Hemorrhagic blood failure: Oxygen debt, coagulopathy and endothelial damage

Article *in* Journal of Trauma and Acute Care Surgery · March 2017




GRAZIE PER
L'ATTENZIONE