Segítség.... vérzik a betegem....

Kritikus vérzés és Masszív transzfúzió

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SZTE Aneszteziológiai és Intenzív Terápiás Intézet

Szeged, 2013. szeptember 20-21.

Definíciók

Kritikus vérzés: masszív transzfúzióhoz vezető és/vagy dedikált helyen (intrakraniális, intraspinális) történő kisebb volumenű vérzés, mely életveszélyes állapotot erdeményez

National Blood Authority. Australia Patient Blood Management 2011.

Masszív transzfúzió: egyszeres vércsere 24 óra alatt

félszeres vércsere 4 óra alatt

Hewitt PE et al.: BMJ 1990; 300(6717): 107–109.

150 ml/perc vérvesztés

Mitra B et al.: Injury 2007; 38(9):1023–1029.

10 vagy több egység vvt konc. transzfúziója

Stainsby D et al.:BJH 2006 135(5):634–641.

Dzik *et al. Critical Care* 2011, 15:242
http://ccforum.com/content/15/6/242

REVIEW

Clinical review: Canadian National Advisory Committee on Blood and Blood Products – Massive Transfusion Consensus Conference 2011: report of the panel

Walter H Dzik[1]*, Morris A Blajchman[2,3], Dean Fergusson[4], Morad Hameed[5], Blair Henry[6], Andrew W Kirkpatrick[7], Teresa Korogyi[8], Sarvesh Logsetty[9], Robert C Skeate[10], Simon Stanworth[11], Charles MacAdams[12†] and Brian Muirhead[13†]

„ the panel recommended that all hospitals in Canada that supply blood transfusion services should have a local procedure in place for urgent blood transfusion. Panel consensus: strong agreement.”

http://www.nba.gov.au/guidelines/module1/contents/contents.html

Patient Blood Management Guidelines: Module 1

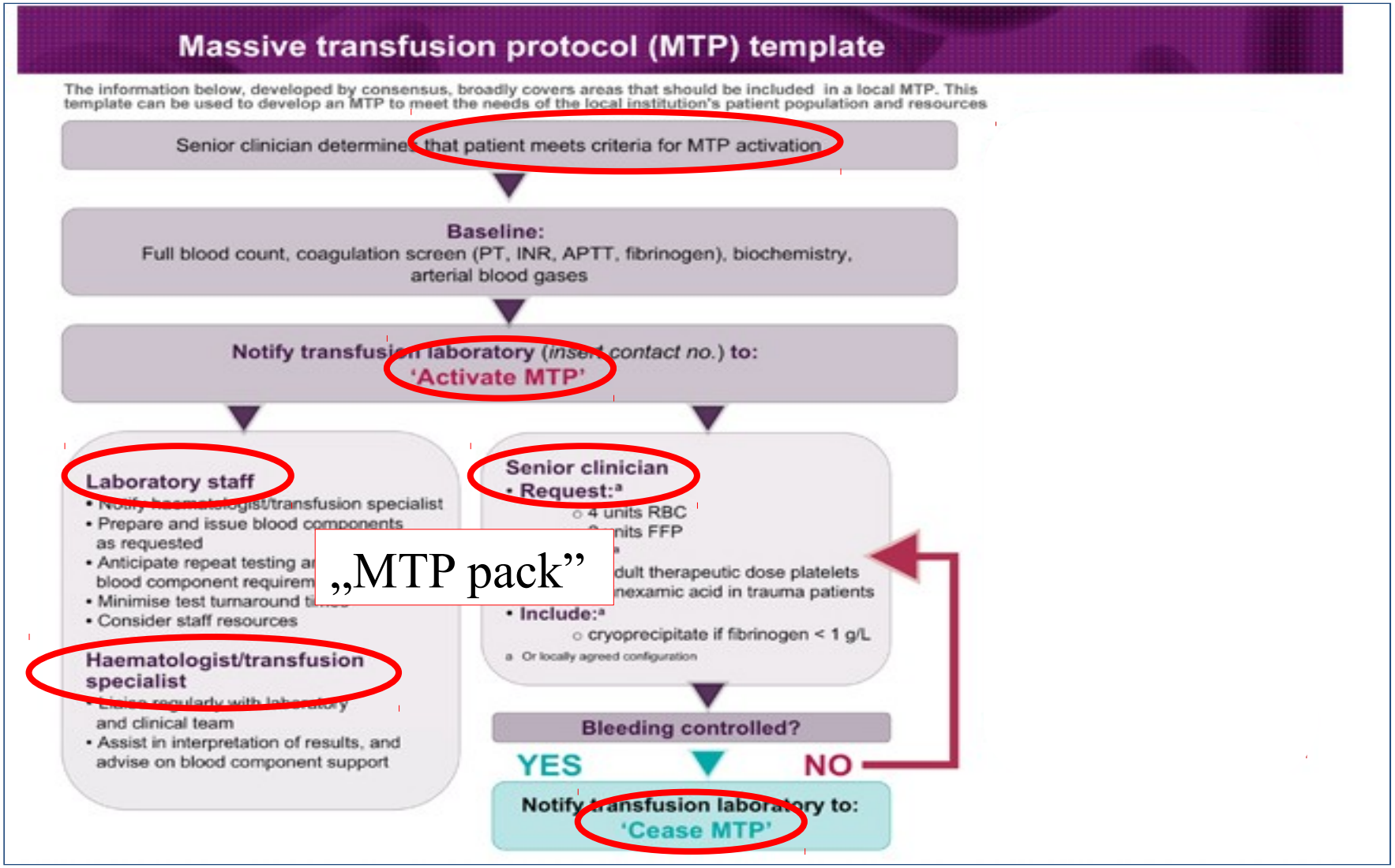
Critical Bleeding Massive Transfusion

National Blood Authority Australia

„It is recommended that institutions develop an MTP that includes the dose, timing and ratio of blood component therapy for use in trauma patients with, or at risk of, critical bleeding requiring massive transfusion (Grade C)".

Masszív Transzfúziós Protokoll

National Blood Authority. Australia Patient Blood Management.2011



„MTP pack”

Időfaktor!

Riskin et al.: J Am Coll Surg 2009(209).2,198-205

- Stanford School of Medicine – Level I Trauma Center
- 2005 július új MTP – hatékonyabb kommunikáció ill. rendszer
- 4 éves retrospektív analízis (2 év előtte – 2 utána)
- ≥10 E vvt/24 óra - 40 ill. 37 beteg
- az első választott vér kézhez vételéhez szükséges idő (4 E csoportazonos vvt konc. elérhető a sürgősségin)

Table 4. Mortality Rates Between Cohorts

Variable	Pre-MTP	Post-MTP	p Value
Patients, n	40	37	
Deaths, n	18	7	
Mortality, %	45	19	0.02*

*Statistically significant; $p \leq 0.05$.
MTP, massive transfusion protocol.

„The improved efficiency of process resulting in decreased time to transfusion, in turn leading to rapid correction of coagulopathy...”

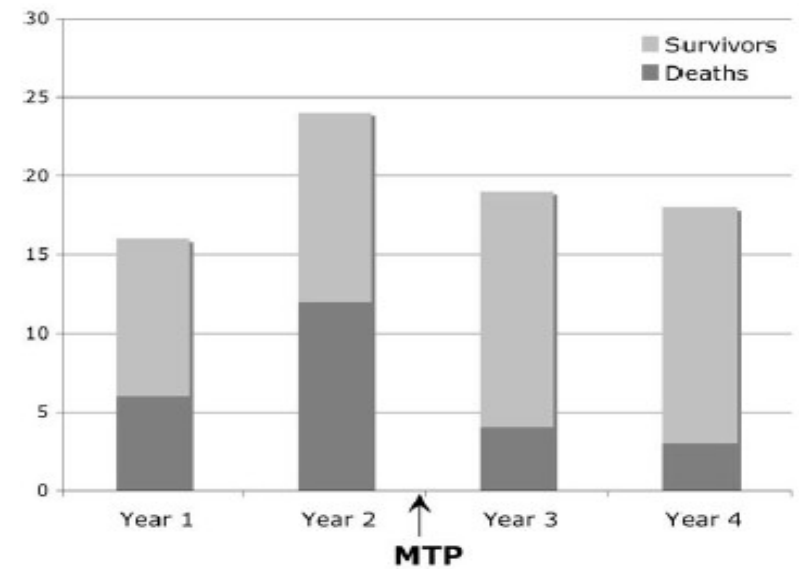


Figure 2. Patient survival by year. MTP, massive transfusion protocol.

Masszív Transzfúziós Protokoll

MTP csomag

Első világháború – nincs reszusztitáció

Második világháború – krisztalloid

Vietnámi háború – krisztalloid + teljes vér (1:3)

Moore FA et al Lancet. 2004; 363(9425):1988-96.

„Bloody lethal trias”: hipothermia, acidózis, koagulopathia

Shapiro MB et al J Trauma. 2000; 49(5):969-78.

1970-1980: teljes vér – komponens terápia – VVT konc. és FFP megjelenése

2003: „a proactive, rather than reactive approach”

Hirshberg A et al J Trauma. 2003; 54(3):454-63.

MTP csomag – optimális FFP/RBC arány?

Table 2: Predetermined blood product administration in massive transfusion in trauma victims. A sample protocol

Package no.	RBC units	elets	Cryoprecipitate
1	6		
2	6	1	
3	6		20 units
4	6	1	
5	6		10 units
6	6	1	
7	6		10 units

Transfusion. 2010 Jul;50(7):1545-51. doi: 10.1111/j.1537-2995.2010.02587.x. Epub 2010 Feb 11.

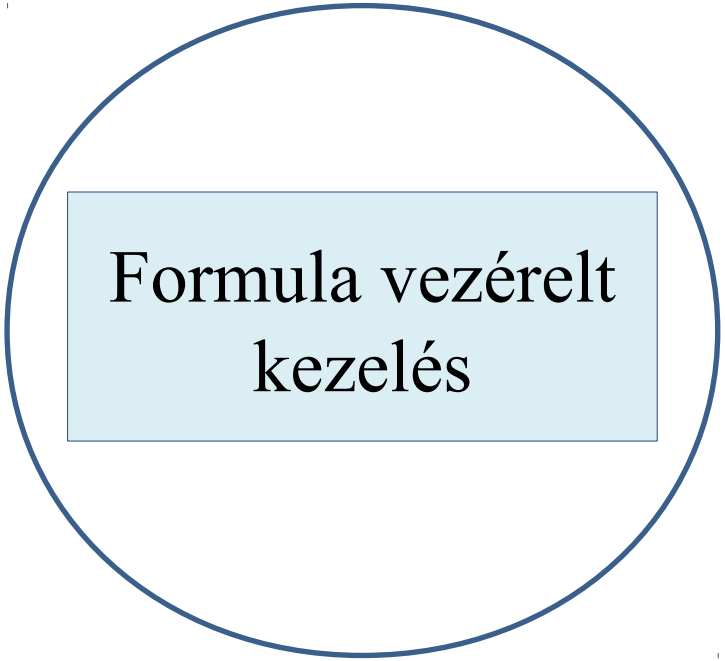
The status of massive transfusion protocols in United States trauma centers: massive transfusion or massive confusion?

Schuster KM, Davis KA, Lui FY, Maerz LL, Kaplan LJ.

Department of Surgery, Section of Trauma, Surgical Critical Care and Surgical Emergencies, Yale University School of Medicine, New Haven, Connecticut 06520-8062, USA.
kevin.schuster@yale.edu

Hemosztázis rendezésének lehetőségei

Dzik et al. Critical Care 2011, 15:242



katonai bizonyítékok → civil terület

· betegpopuláció
· sérülések mechanizmusa

„Túltranszfundálás” veszélyei

National Blood Authority. Australia Patient Blood Management.2011

Transfusion risk	Estimated rate [a] (highest to lowest risk)
Transfusion-associated circulatory overload (iatrogenic)	Up to 1 in 100 transfusions
Haemolytic reactions	Delayed: 1 in 4,000–9,000 Acute: 1 in 12,000–77,000
Anaphylaxis (IgA deficiency)	1 in 20,000–50,000
Bacterial sepsis: platelets	1 in 75,000
Bacterial sepsis: RBCs	1 in 500,000
Transfusion-related acute lung injury	1 in 5,000–190,000
Hepatitis B	1 in 739,000
HIV	1 in 5.4 million
Hepatitis C	1 in 2.7 million
Malaria	1 in 4.9 million – 10.2 million
Variant CJD (not tested)	Never reported in Australia
Transfusion-associated graft-versus-host disease	Rare
Transfusion-related immunomodulation	Not quantified

Calman Chart a (UK risk per one year)

Rate	Example
< 1 in 1,000,000	Death from lightning strike
1 in 100,000–1,000,000	Death from train accident
1 in 10,000–100,000	Death from an accident at work
1 in 1,000–10,000	Death from a road accident
> 1 in 1,000	Transmission of chicken pox to susceptible household contacts

Formula vezérelt kezelés

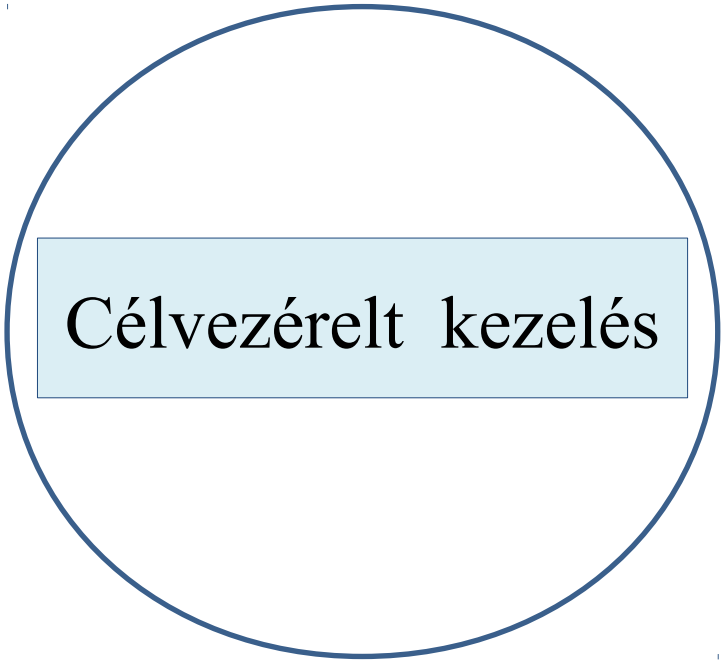
Table 1 Massive transfusion: the main differences between elective surgery and trauma

J.-F. Hardy et al.:Vox Sanguinis (2005)89, 123–127

	Elective surgery	Trauma
Tissue trauma	Controlled	Massive and uncontrolled
Initiation of massive transfusion	No delay between haemorrhage and initiation of treatment	The interval between haemorrhage and treatment can vary widely
Volume status/shock	Normovolemia is maintained and shock is avoided	Hypovolemia and shock are frequent
Temperature	Normothermia is maintained	Hypothermia is frequent
Monitoring of haemostasis	Ongoing. Anticipation of haemostatic defects is possible	Late. Laboratory tests are obtained when coagulopathy is installed
Coagulopathy	More often related to decreased coagulation factors	Often related to disseminated intravascular coagulation
Treatment of coagulopathy	Correction of anaemia FFP and platelets as determined by laboratory tests (FFP should probably be administered first)	Correction of tissue hypoperfusion Correction of hypothermia Correction of anaemia Platelets and FFP as determined by laboratory tests (platelets first?)

Hemosztázis rendezésének lehetőségei

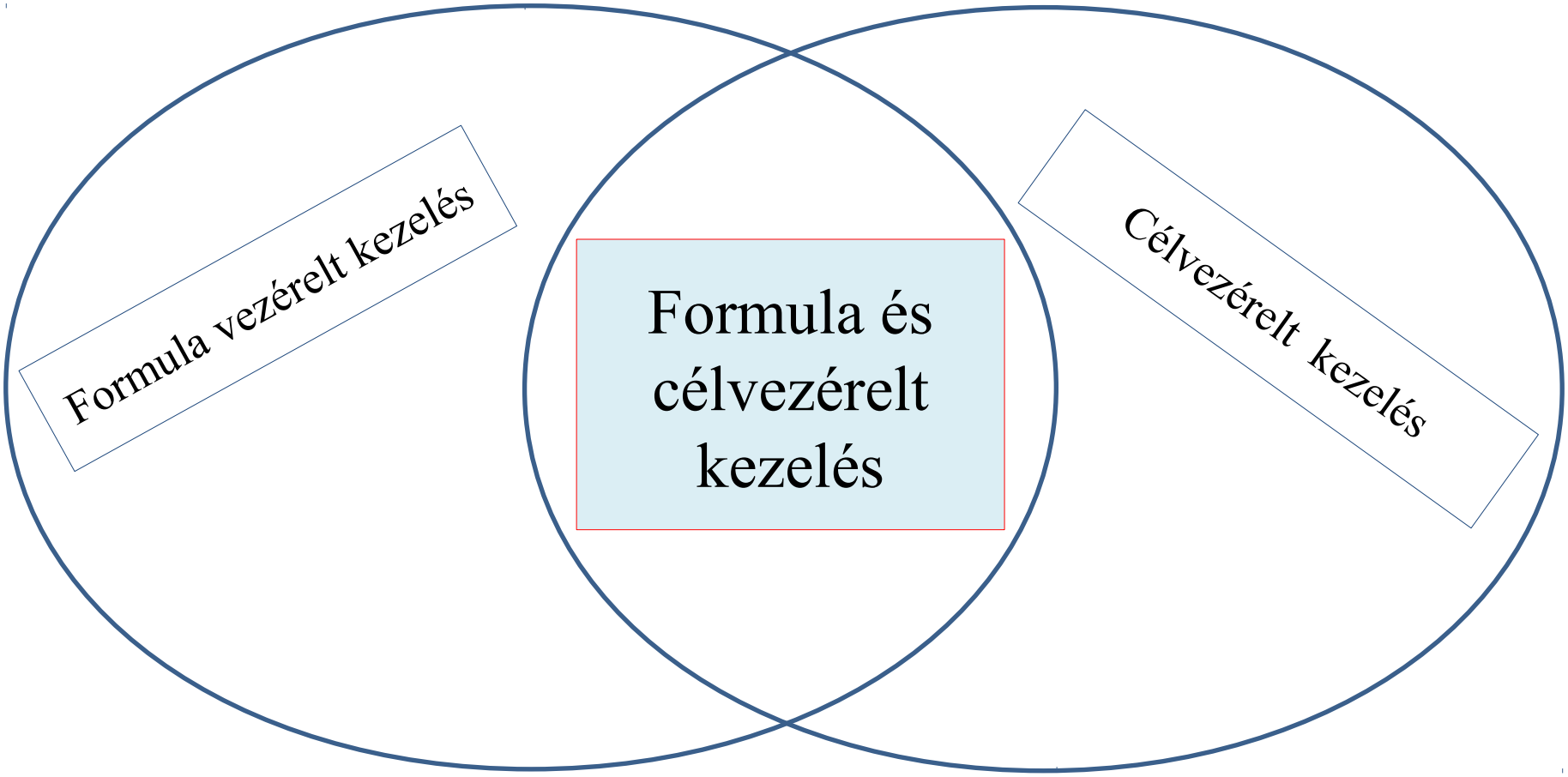
Dzik et al. Critical Care 2011, 15:242



- tesztek alacsony szenzitivitása rossz prediktív értéke
- késedelem

Hemosztázis rendezésének lehetőségei

Dzik et al. Critical Care 2011, 15:242



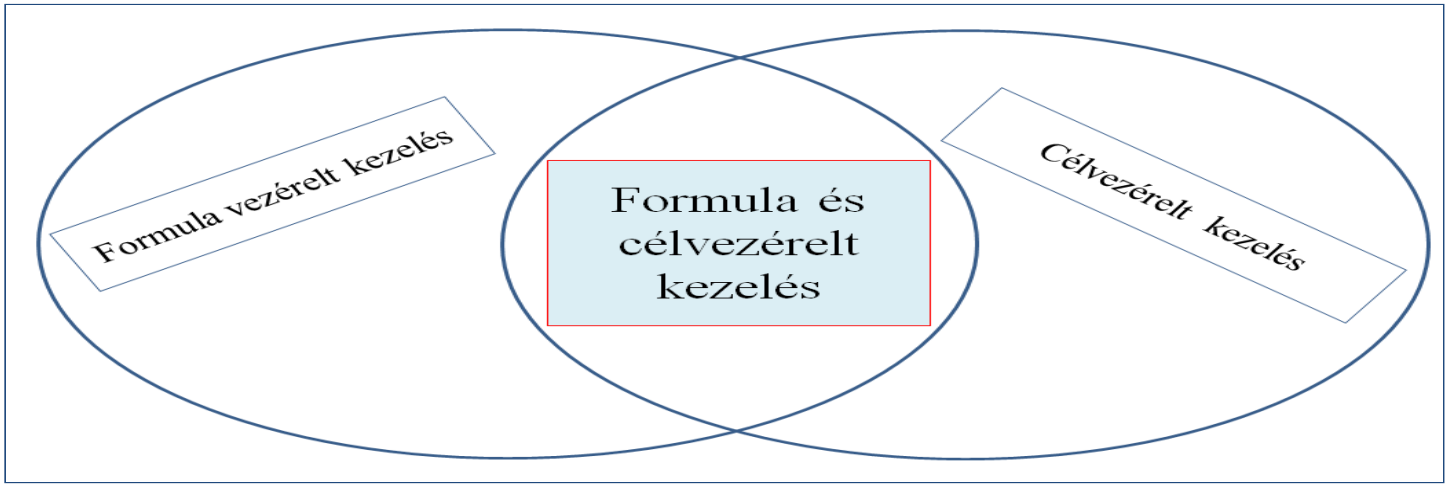
Formula és célvezérelt kezelés

Dzik et al. Critical Care 2011, 15:242

1. Tranexámsav 1 gr + 1gr/8 óra (traumás beteg esetén)

2. Azonnali formula vezérelt kezelés (pl. 1:1,5 – 1:2 FFP:VVT arány)

3. Célvezérelt hemostasis kontroll (pl. standard plazmatikus tesztek vagy tromboelasztografia alapján)



Formula és célvezérelt kezelés

National Blood Authority. Australia Patient Blood Management.2011

Tranexámsav (trauma esetén) 1 gr 10 perc alatt, majd 1 gr 8 óra alatt

Fibrinogén < 1.0 gr/l FFP 15 ml/kg vagy Fibrinogén konc. 3-4 gr.

INR > 1.5 FFP 15 ml/kg

Warfarin hatás K vitamin 10 mg iv. Faktorkészítmény 25 E/kg

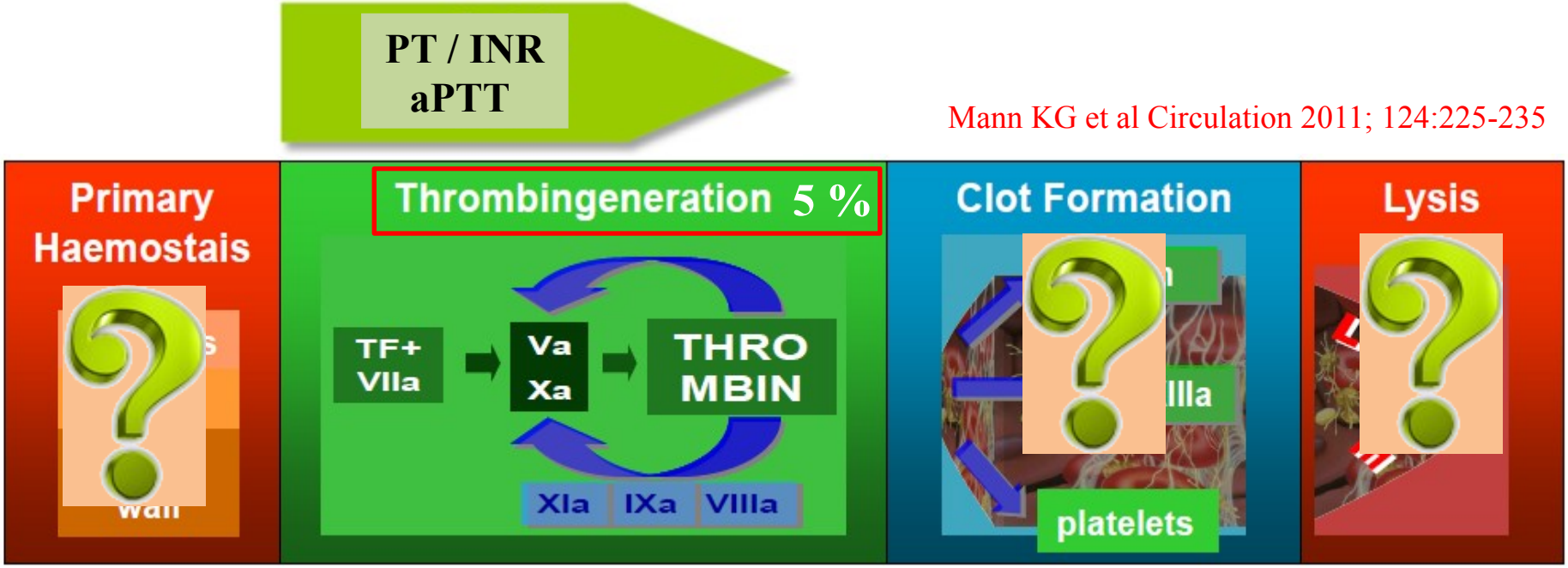
Trombocitaszám < 50 G/l Tct szuszp. 0.1 E/kg

Formula és **célvezérelt** kezelés

Tauber H et al. BJA 2011, 15:242

Prevalence of abnormal coagualtion tests in patients with isolated brain injury (n=60) and multiple trauma (n=274)

Standard plazmatikus tesztek



Mann KG et al Circulation 2011; 124:225-235

Davenport R et al Crit Care Med 2011; 39:2652-2658,2011

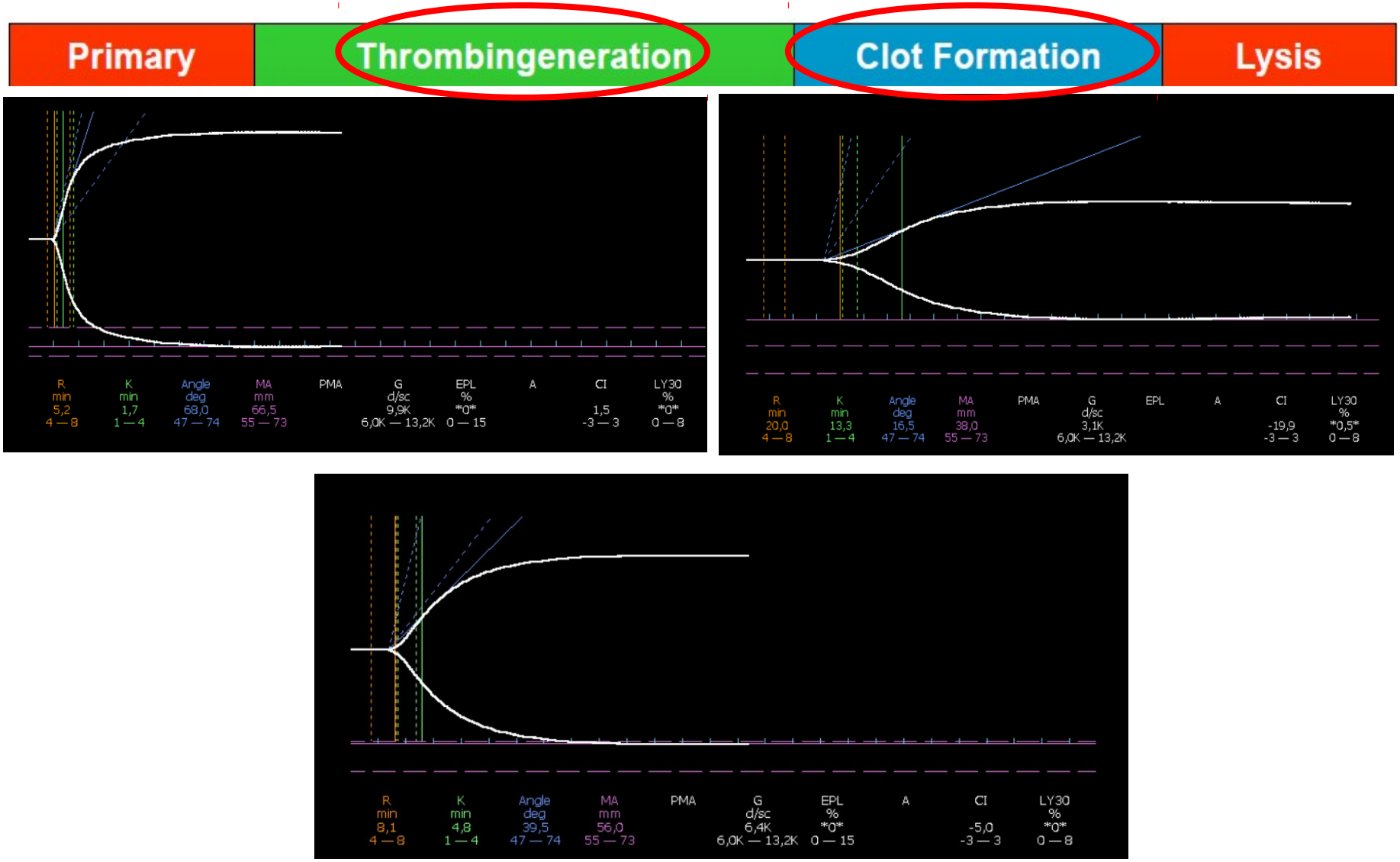
- megbízhatatlanok alacsony fibrinogén (< 1 gr/l) esetén

Tanaka KA et al Anesth Analg 2009; 108:1433-1446

- késedelmes tesztek

Toulon P et al Thromb Haemost 2009;101:394-401

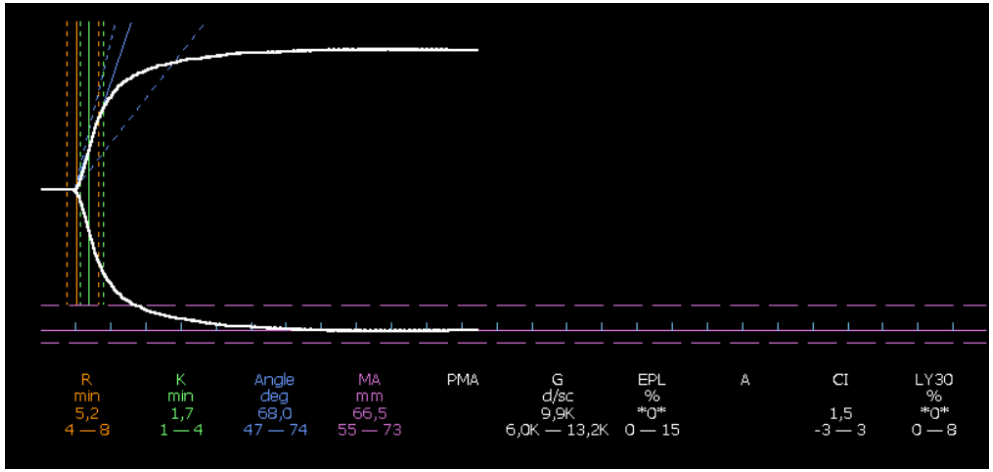
Viszkoelasztikus tesztek (TEG, ROTEM)

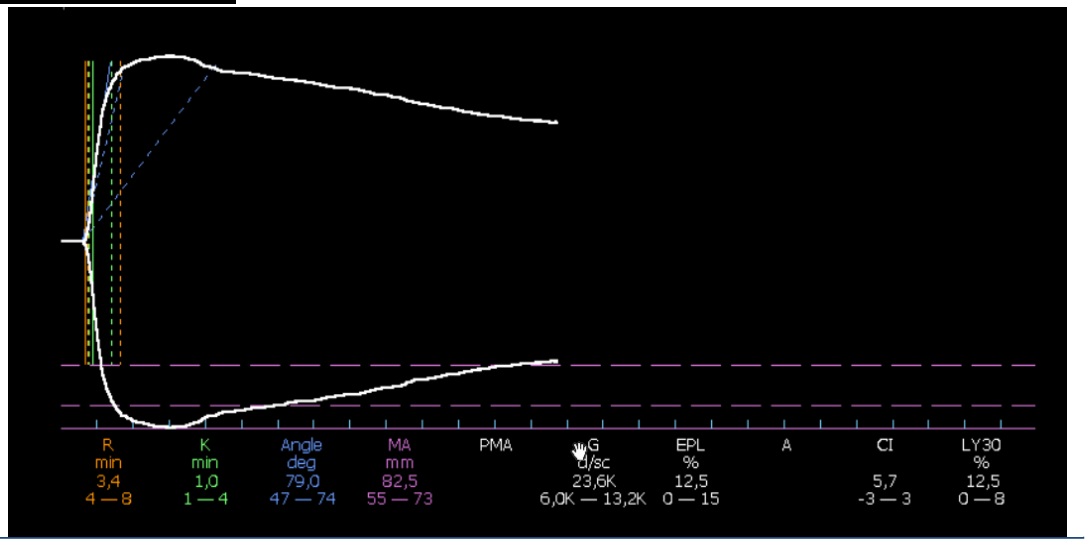


Schöchl et al. J Cardiothor and Vasc Anesth 2013; l27, 35–43

Viszkoelasztikus tesztek (TEG, ROTEM)

Primary	Thrombingeneration	Clot Formation	Lysis





Schöchl et al. J Cardiothor and Vasc Anesth 2013; l27, 35–43

Segítség.... vérzik a betegem....

1. Interdiszciplináris párbeszéd:klinikus, hematológus, laboros, transzfúziológus

3. Saját rendszerre adaptált MTP kialakítása – logisztikai kérdések

4. Formula és célvezérelt kezelés

5. Viszkoelasztikus tesztek ?

Korai célvezérelt koaguloterápia ?

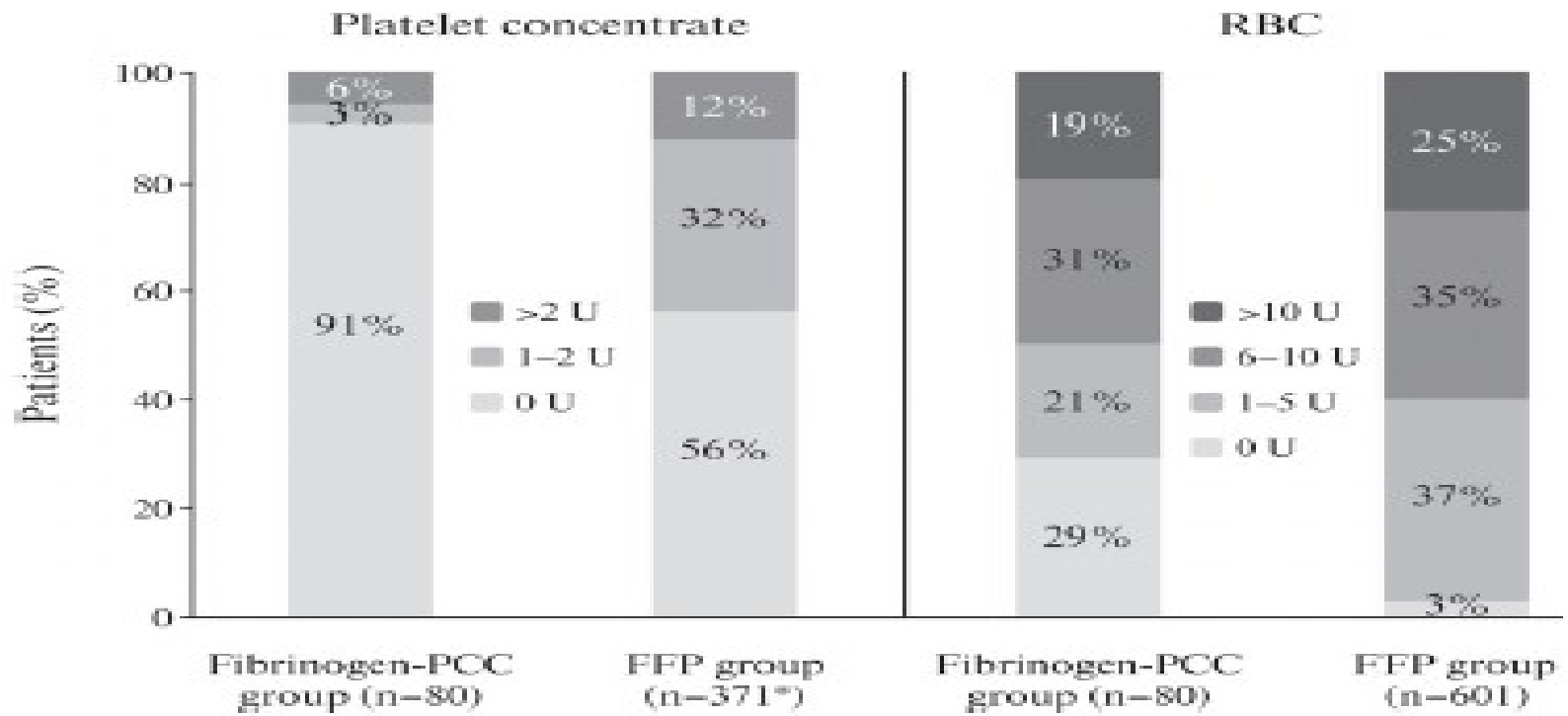


Figure 1 Platelet concentrate and red blood cell (RBC) transfusion in the emergency room and during surgery.
*Platelet concentrate transfusion only reported for 371 of 601 patients from the trauma registry of the German Society for Trauma Surgery (TR-DGU). FFP, fresh frozen plasma; PCC, prothrombin complex concentrate.

Schöchl et al. Critical Care 2011, 15:R83

Köszönöm a figyelmet!

Masszív Transzfúziós Protokoll – dosing

Initial management of bleeding

- Identify cause
- Initial measures:
  - compression
  - tourniquet
  - packing
- Surgical assessment:
  - early surgery or angiography to stop bleeding

Specific surgical considerations

- If significant physiological derangement, consider damage control surgery or angiography

Cell salvage

- Consider use of cell salvage where appropriate

Dosage

Platelet count < 50 x 10^9/L	1 adult therapeutic dose
INR > 1.5	FFP 15 mL/kg[a]
Fibrinogen < 1.0 g/L	cryoprecipitate 3–4 g[a]
Tranexamic acid	loading dose 1 g over 10 min, then infusion of 1 g over 8 hrs

CRASH-2.Lancet 2010; 376: 23–32.

Resuscitation

"lethal triad"

- Avoid hypothermia, institute active warming
- Avoid excessive crystalloid
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled
- Do not use haemoglobin alone as a transfusion trigger

Moore E, et al.:Am J Surg 1996;172:405–410.

Special clinical situations

- Warfarin:
  - add vitamin K, prothrombinex/FFP
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate
- Head injury:
  - aim for platelet count > 100 × 10^9/L
  - permissive hypotension contraindicated

Considerations for use of rFVIIa[b]

The *routine* use of rFVIIa in trauma patients is not recommended due to its lack of effect on mortality (Grade B) and variable effect on morbidity (Grade C). Institutions may choose to develop a process for the use of rFVIIa where there is:

- uncontrolled haemorrhage in salvageable patient, and
- failed surgical or radiological measures to control bleeding, and
- adequate blood component replacement, and
- pH > 7.2, temperature > 34°C.

Discuss dose with haematologist/transfusion specialist

[b] rFVIIa is not licensed for use in this situation; all use must be part of practice review.

ABG	arterial blood gas	FFP	fresh frozen plasma	APTT	activated partial thromboplastin time
INR	international normalised ratio	BP	blood pressure	MTP	massive transfusion protocol
DIC	disseminated intravascular coagulation	PT	prothrombin time	FBC	full blood count
RBC	red blood cell	rFVIIa	activated recombinant factor VII		

National Blood Authority. Australia Patient Blood Management.2011

Table 1 Inclusion criteria

	Fibrinogen-PCC group (Salzburg Trauma Centre)	FFP group (TR-DGU)
Type of therapy	ROTEM-guided administration of coagulation factor concentrates	According to local protocols
ISS	≥ 16	
AIS thorax, abdomen, extremities	At least in one region, one injury with severity degree ≥3, $AIS_{head/neck} < 5$	
Age (years)	18-70	
Base deficit at admission	≥2 mmol/L	
FFP administered	No FFP	≥2 units FFP
Fibrinogen/PCC administered	≥1 g fibrinogen; ≥ 500 U PCC	No fibrinogen or PCC
Investigated time period	2005-2009	2005-2008
Patients included in database	353	21263
Patients fulfilling inclusion criteria	80	601

Table 2 Patient demographic and clinical data

	Fibrinogen-PCC group (*n* = 80)	FFP group (*n* = 601)
Age (years)	37.3 ± 14.5	39.1 ± 14.5
Male *n* (%)	63 (79)	442 (74)
Systolic blood pressure on admission at ER (mmHg)	95 ± 30	108 ± 30**
Heart rate on admission at ER (beats/minute)	105 ± 26	99 ± 24*
ISS	35.5 ± 10.5	35.2 ± 12.5
GCS	12.2 ± 3.4	11.3 ± 4.4*
AIS Head	1.1 ± 1.5	1.6 ± 1.7*
AIS Chest	2.1 ± 2.0	3.1 ± 1.7**
AIS Abdomen	2.5 ± 2.1	2.1 ± 1.8
AIS Extremity	2.9 ± 1.8	2.9 ± 1.4
TASH	13.9 ± 6	12.6 ± 5*
RISC	6.9 (2.4, 16.2)	8.5 (3.3, 24.8)
TRISS	13 (3, 38)	7 (2, 38)
Death	6 (7.5)	60 (10)