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NENÍ PLNÁ KREV,
V DOBĚ KONCENTRÁTŮ KOAGULAČNÍCH FAKTORŮ,
CESTA DO PRAVĚKU?

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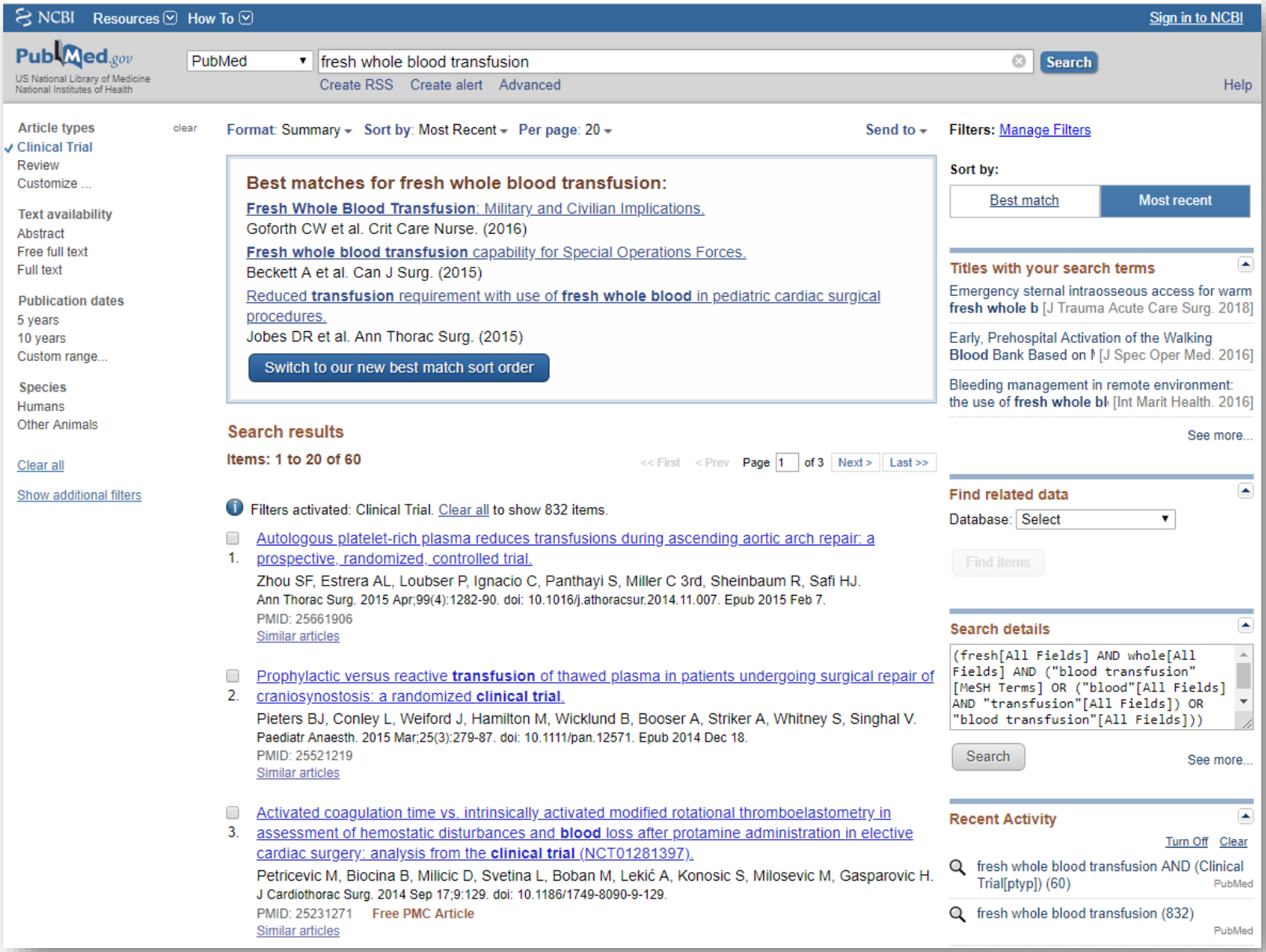

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The Journal of **TRAUMA**® *Injury, Infection, and Critical Care*

J Trauma. 2009;66:S69–S76.

Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries

Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Alec C. Beekley, MD, and John B. Holcomb, MD

Warm fresh whole blood transfusion for severe hemorrhage: U.S. military and potential civilian applications

Philip C. Spinella, MD

How do I implement a whole blood program for massively bleeding patients?

Mark H. Yazer,[1] Andrew P. Cap,[2] Philip C. Spinella,[3] Louis Alarcon,[4] and Darrell J. Triulzi[1]

Vox Sanguinis (2018)

DOI: 10.1111/vox.12677

INTERNATIONAL FORUM

Vox Sanguinis International Forum on the use of prehospital blood products and pharmaceuticals in the treatment of patients with traumatic hemorrhage

M. H. Yazer, P. C. Spinella, S. Allard, D. Roxby, C. So-Osman, M. Lozano, K. Gunn, A. W. Shih, J. Stensballe, P. I. Johansson, M. Bagge Hansen, M. Maegele, H. Doughty, N. Crombie, D. H. Jenkins, A. C. McGinity, R. M. Schaefer, C. Martinaud, E. Shinar, R. Strugo, J. Chen & H. Russcher

SHOCK, Vol. 41, Supplement 1, pp. 76–83, 2014

EMERGENCY WHOLE-BLOOD USE IN THE FIELD: A SIMPLIFIED PROTOCOL FOR COLLECTION AND TRANSFUSION

Geir Strandenes,*† Marc De Pasquale,‡ Andrew P. Cap,§ Tor A. Hervig,† Einar K. Kristoffersen,† Matthew Hickey,‖ Christopher Cordova,¶ Olle Berseus, Håkon S. Eliassen,† Logan Fisher,†† Steve Williams,‡‡ and Philip C. Spinella§,§§**

**Norwegian Naval Special Operation Commando; and; †Department of Immunology and Transfusion Medicine, Haukeland University Hospital, and Institute of Clinical Science, University of Bergen, Bergen, Norway; ‡Deployment Medicine International, Gig Harbor, Washington; §US Army Institute of Surgical Research, Fort Sam Houston, Texas; ‖Naval Special Warfare Command, San Diego, California; ¶Specialist Corps, US Army, Keller Army Community Hospital, West Point, New York; **Department of Transfusion Medicine, Örebro University Hospital, Orebro, Sweden; ††NSWDG US Navy, Virginia Beach, Virginia; ‡‡Medical Operations Royal Caribbean Cruises Ltd.; and §§Department of Pediatrics, Division of Critical Care, Washington University in St. Louis, St. Louis, Missouri*

Use of Freeze-Dried Plasma in French Intensive Care Unit in Afghanistan

Christophe Martinaud, MD, Sylvain Ausset, MD, Anne Virginie Deshayes, PharmD, Amandine Cauet, Nicolas Demazeau, MD, and Anne Sailliol, MD

Meeting blood requirements following terrorist attacks: the Israeli experience

Eilat Shinar[a], Vered Yahalom[a] and Barbara G. Silverman[b]

MILITARY MEDICINE, 183, 9/10:44, 2018

Whole Blood Transfusion

COL Andrew P. Cap, MC USA; LTC Andrew Beckett, MC CAF; MAJ Avi Benov, MC IDF; LTC Matthew Borgman, MC USA; LTC Jacob Chen, MC IDF; LTC Jason B. Corley, MSC USA; COL (ret) Heidi Doughty, MC UK; MAJ Andrew Fisher, SP USA; COL Elon Glassberg, MC IDF; COL (ret) Richard Gonzales, MSC USA; COL Shawn F. Kane, MC USA; LTC (ret) Wilbur W. Malloy, MSC USA; COL Shawn Nessen, MC USA; COL Jeremy G. Perkins, MC USA; MAJ Nicolas Prat, MC France; LTC Jose Quesada, MSC USA; COL Michael Reade, MC ADF; MG Anne Sailliol, MC France; PROF Philip C. Spinella, US; CAPT Zsolt Stockinger, MC USN; CDR Geir Strandenes, MC Norway; COL Audra Taylor, MSC USA; PROF Mark Yazer, MD US; PROF Barbara Bryant, MD; COL Jennifer Gurney, MC USA

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.*, Firment J., Kubisz P., Kvasnička J., Masopust J., Penka M., Salaj P., Staško J., Záhorec R., Zýková I.

Česká společnost anesteziologie, resuscitace a intenzivní medicíny ČLS JEP
Česká společnost pro trombózu a hemostázu ČLS JEP
Česká hematologická společnost ČLS JEP
Slovenská spoločnosť anestéziológie a intenzívnej medicíny Slovenskej lekárskej spoločnosti
Slovenská spoločnosť hemostázy a trombózy 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.

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DIAGNOSIS AND THERAPY OF LIFE-THREATENING PERIPARTUM HAEMORRHAGE

Czech-Slovak interdisciplinary guidelines

České gynekologické a porodnické společnosti (ČGPS)
České lékařské společnosti Jana Evangelisty Purkyně (ČLS JEP)
Slovenské gynekologicko-porodnické společnosti (SGPS)
Slovenské lékařské společnosti (SLS)

Pracovní skupina: Pařízek A.[1], Binder T.[2], Bláha J.[3], Blatný J.[4], Buršík M.[5], Feyereisl J.[6], Janků P.[7], Kokrdová Z.[1], Křepelka P.[6], Kvasnička J.[8], Lubušký M.[9], Seidlová D.[10], Šimetka O.[11, 12], Štourač P.[13], Černý V.[14, 15, 16, 17]

[1]Gynekologicko-porodnická klinika 1. LF UK a VFN, Praha, Česká republika
[2]Gynekologicko-porodnická klinika, Univerzita J. E. Purkyně, Masarykova nemocnice, Ústí nad Labem, Česká republika
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[4]Oddělení dětské hematologie, Centrum pro trombózu a hemostázu, FN a LF MU, Brno, Česká republika
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[10]II. ARO, Klinika anesteziologie, resuscitace a intenzivní medicíny, FN a LF MU, Brno, Česká republika
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[14]Klinika anesteziologie, perioperační a intenzivní medicíny, Univerzita J. E. Purkyně, Masarykova nemocnice, Ústí nad Labem, Institut postgraduálního vzdělávání ve zdravotnictví Praha, Česká republika
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[17]Dept. of Anesthesia, Pain Management and Perioperative Medicine, Dalhousie University, Halifax, Canada

Materiál je konsenzuálním stanoviskem sekcí ČGPS ČLS JEP

Oponenti: výbor Sekce perinatologie a fetomaternální medicíny ČGPS ČLS JEP
výbor ČGPS ČLS JEP
výbor SGPS SLS

Revize doporučeného postupu ČGPS ČLS JEP z roku 2008, publikovaného v Čes. Gynek., 2009, 74, supplementum, s. 28-31, revize mezioborového konsenzuálního stanoviska z roku 2011, publikovaného v Čes. Gynek., 2013, 78, supplementum, s. 38-40
Schváleno výborem ČGPS ČLS JEP dne 5. 12. 2017
Čes. Gynek. 2018, 83, č. 2, s. 151–158

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.*, Firment J., Kubisz P., Kvasnička J., Masopust J., Penka M., Salaj P., Staško J., Záhorec R., Zýková I.

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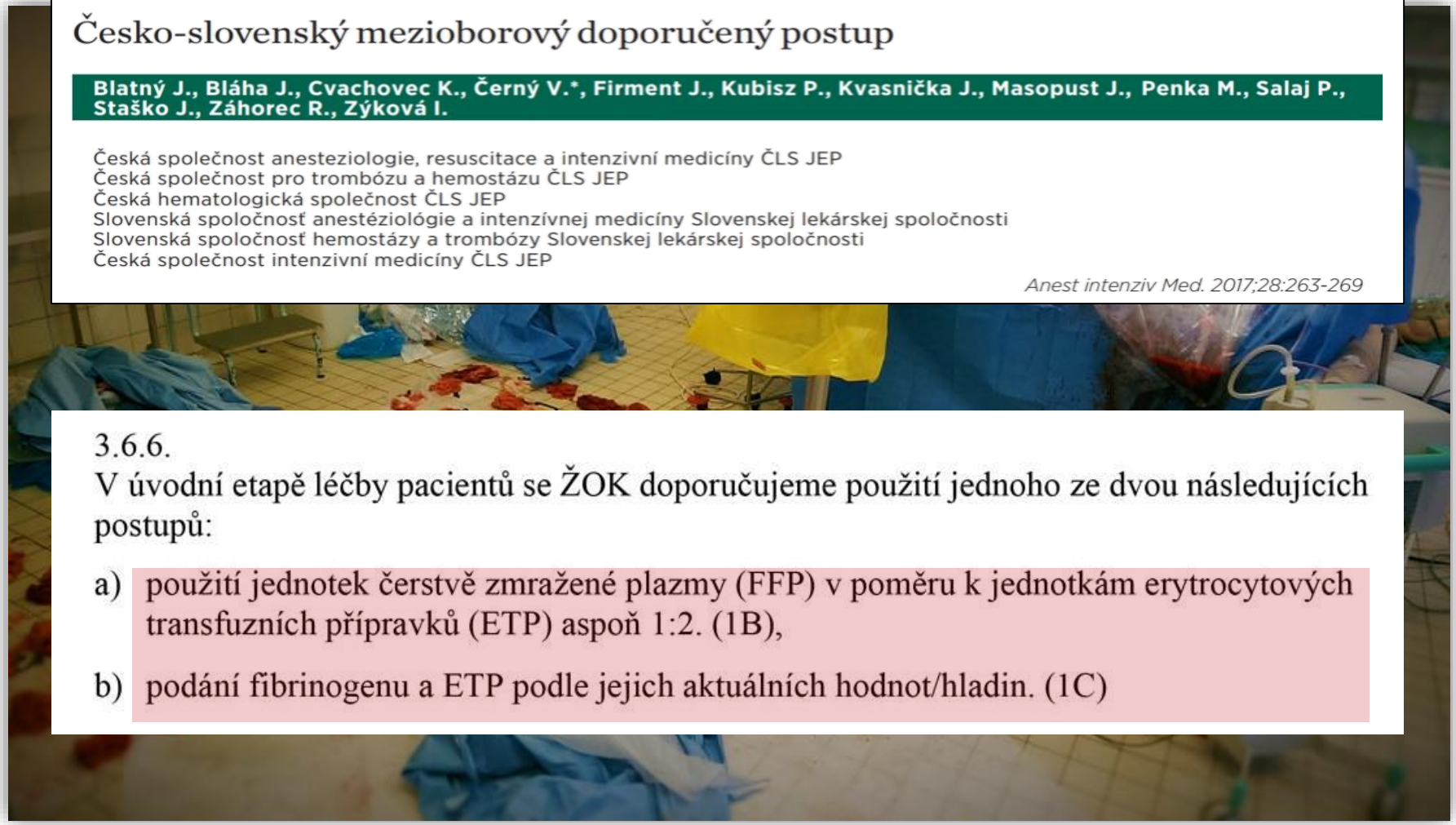
Česká společnost intenzivní medicíny ČLS JEP

Anest intenziv Med. 2017;28:263-269



3.6.6.
V úvodní etapě léčby pacientů se ŽOK doporučujeme použití jednoho ze dvou následujících postupů:

a) použití jednotek čerstvě zmražené plazmy (FFP) v poměru k jednotkám erytrocytových transfuzních přípravků (ETP) aspoň 1:2. (1B),

b) podání fibrinogenu a ETP podle jejich aktuálních hodnot/hladin. (1C)

Rossaint *et al. Critical Care* (2016) 20:100
DOI 10.1186/s13054-016-1265-x

Critical Care

RESEARCH Open Access

The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Timothy J. Coats[7], Jacques Duranteau[8], Enrique Fernández-Mondéjar[9], Daniela Filipescu[10], Beverley J. Hunt[11], Radko Komadina[12], Giuseppe Nardi[13], Edmund A. M. Neugebauer[14], Yves Ozier[15], Louis Riddez[16], Arthur Schultz[17], Jean-Louis Vincent[18] and Donat R. Spahn[19*]

EJA

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

GUIDELINES

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

First update 2016

Sibylle A. Kozek-Langenecker, Aamer B. Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Guidrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V.L. Pitarch, Susan Mallett, Jens Meier, Zsolt L. Molnar, Niels Rahe-Meyer, Charles M. Samama, Jakob Stensballe, Philippe J.F. Van der Linden, Anne J. Wikkelsø, Patrick Wouters, Piet Wyffels and Kai Zacharowski

Initial coagulation resuscitation

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

- Plasma (FFP or pathogen-inactivated plasma) in a plasma–RBC ratio of at least 1:2 as needed. (Grade 1B)
- Fibrinogen concentrate and RBC according to Hb level. (Grade 1C)


EVIDENCE
BASED MEDICINE !
PLASMA
A

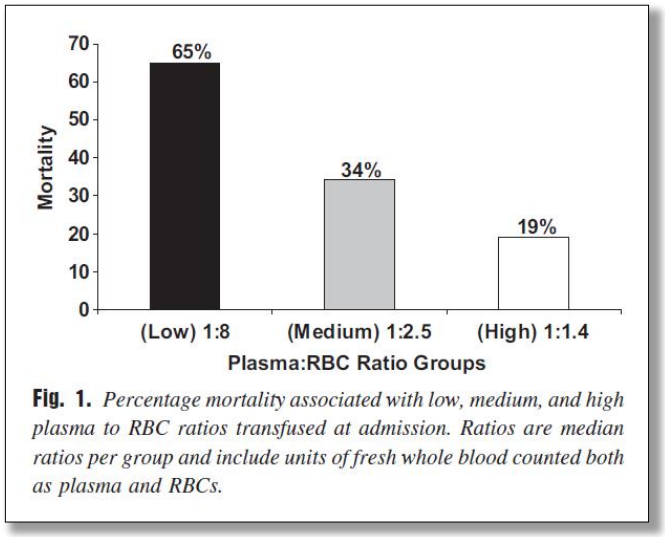
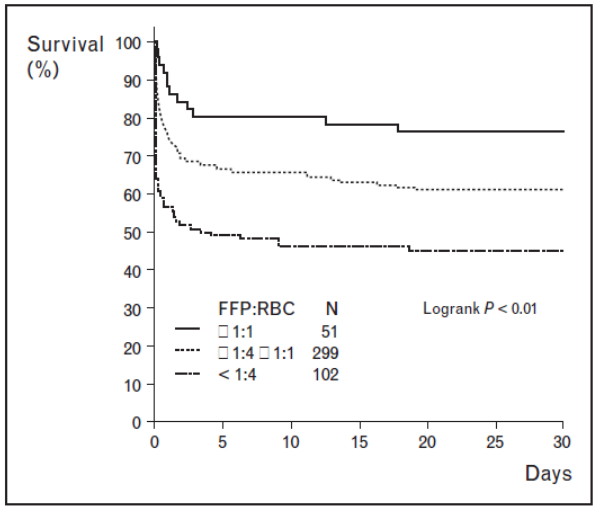


Fig. 1. *Percentage mortality associated with low, medium, and high plasma to RBC ratios transfused at admission. Ratios are median ratios per group and include units of fresh whole blood counted both as plasma and RBCs.*

Borgman et al. J Trauma. 2007;63:805–813.

Figure 1 Survival curves for each category of fresh frozen plasma : packed red blood cell ratio



The lowest mortality was observed in the category of patients who received a ratio of fresh frozen plasma : packed red blood cells (FFP : PRBCs) equal to or greater than 1 : 1. Most of the separation of the survival curves occurred immediately after the injury. Data from [16].

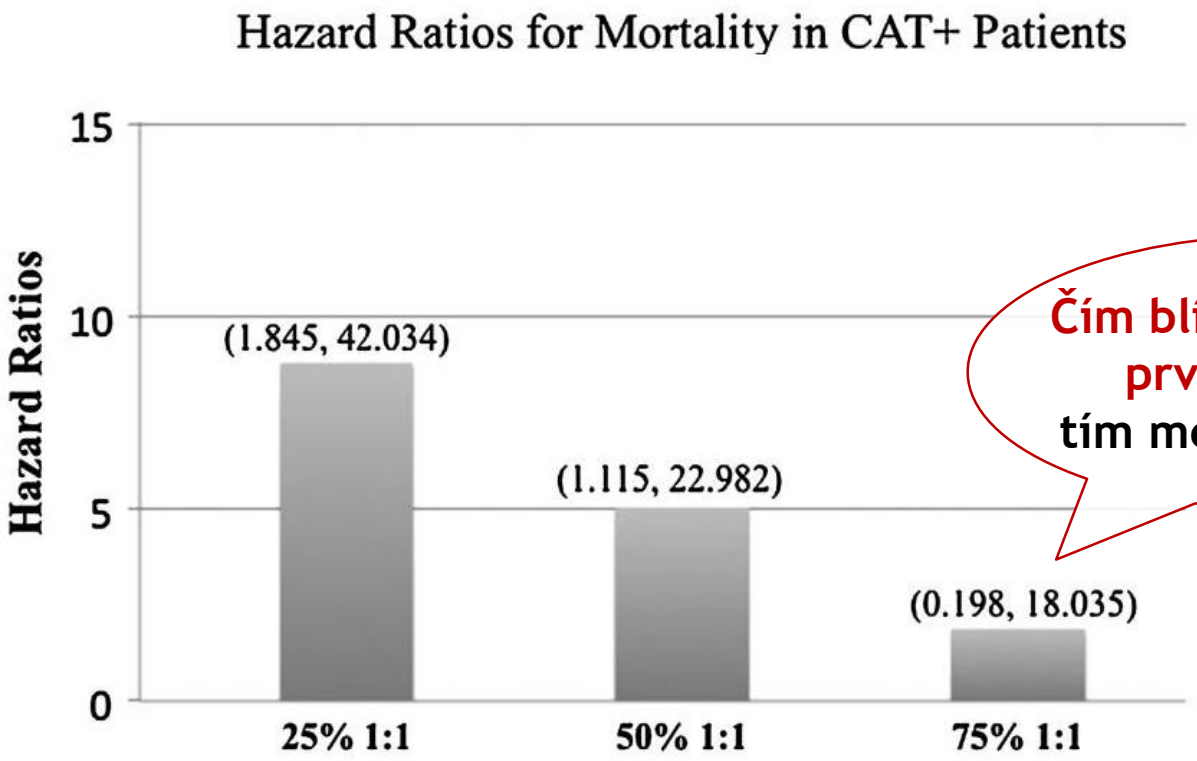
Griffee et al. Current Opinion in Anaesthesiology 2010,23:263–268

Time matters in 1:1 resuscitations: Concurrent administration of blood:plasma and risk of death

Stephanie A. Savage, MD, Ben L. Zarzaur, MD, Martin A. Croce, MD,
and **Timothy C. Fabian, MD,** *Memphis, Tennessee*

J Trauma Acute Care Surg 2014; Volume 77, Number 6

Critical Administration Threshold
= 3 TU krve/hod



Čím blíže 1:1 během prvních hodin, tím menší mortalita!

The closer to 1:1 in the first hours, the lower mortality!

Reconstructing Deconstructed Blood for Trauma

I hear the train a comin'[1]
—Johnny Cash, Folsom Prison Blues, 1956

ceived as not needed, while furnishing them for patients who do need them. Although this strategy

"The logical question that should arise is that if a ratio of transfused red cells to plasma of 1:1 is beneficial, then why not transfuse whole blood, thus reducing substantially recipient exposure to donors?"

utive Scientific Advisor at Novo Nordisk A/S (Bagsvaerd, Denmark) 2005–2007.

survivor bias in observational studies on fresh frozen plasma: Erythrocyte ratios in trauma requiring massive transfusion. ANESTHESIOLOGY 2012; 116:716–28.


2 g
N1
Fibrinogen
Wirkstoff: Fibrinogen vom Menschen
Pulver zur Herstellung einer Injektions-/Infusionslösung.
Arzneimittel für Kinder unzugänglich aufbewahren!
Verwendbar bis
Ch.-B.

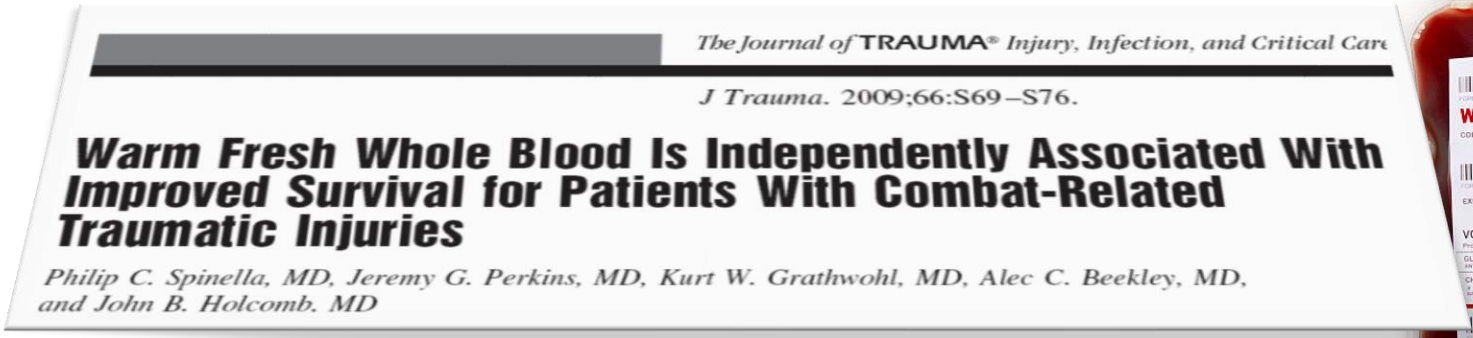

2 g


Kozek-Langenecker et al. Critical Care 2011, 15:R239
http://ccforum.com/content/15/5/R239
CRITICAL CARE
Open Access
RESEARCH
Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review
Sibylle Kozek-Langenecker[1*], Benny Sørensen[2,3], John R Hess[4] and Donat R Spahn[5]


Beriplex P/N 500


FXIII Concentrate (Human)

versus


The Journal of TRAUMA® Injury, Infection, and Critical Care
J Trauma. 2009;66:S69–S76.
Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries
Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Alec C. Beekley, MD, and John B. Holcomb, MD


WHOLE BLOOD
COLLECTION DATE:
O
Rh NEGATIVE
EXPIRES:
VOLUNTEER DONOR
GLOBAL HEALTH BLOOD
CHECK FOR TEMPERATURE ABUSE

EVIDENCE …

Table 1 Grading of recommendations after [24] (reprinted with permission)

Grade of Recommendation	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A			
Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations (overwhelming evidence from obser studies	ommendation, can ost patients in most ces without
1B			
Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inc results, methodological flaws, indire imprecise) or exceptionally strong e observational studies	ommendation, can ost patients in most ces without
1C			
Strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A			
Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B			
Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C			
Weak recommendation, Low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks and burden; benefits, risk and burden may be closely balanced	Observational studies or case series	Very weak recommendation; other alternatives may be equally reasonable

Cochrane Library
Cochrane Database of Systematic Reviews

Fibrinogen concentrate in bleeding patients (Review)

Wikkelsø A, Lunde J, Johansen M, Stensballe J, Wetterslev J, Møller AM, Afshari A

Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD008864

Analysis 1.1. Fibrinogen concentrate versus any comparator, Mortality

Review: Fibrinogen concentrate in bleeding patients Comparison: 1 Fibrinogen concentrate versus any comparator

Study or subgroup	Fibrinogen n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Karlsson 2009	0/10	0/10			Not estimable
Rahe-Meyer 2013	1/29	4/32			0.28 [0.03, 2.33]
Subtotal (95% CI)	**0**	**0**			**0.0 [0.0, 0.0]**

Total events: 1 (Fibrinogen), 4 (Control)
Heterogeneity: not applicable
Test for overall effect: Z = 0.0 (P < 0.00001)

0.01 0.1 1 1 100
Favours fibrinogen Favours control

Analysis 1.2. Fibrinogen concentrate versus any comparator, ICU stay (hours).

Review: Fibrinogen concentrate in bleeding patients Comparison: 1 Fibrinogen concentrate versus any comparator

Study or subgroup	Fibrinogen N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Cui 2010	17	137 (40.37)	14	173.1 (251.48)		0.7 %	-36.10 [-169.22, 97.02]
Karlsson 2009	10	13.7 (7.78)	10	24.9 (17.1)		86.0 %	-11.20 [-22.84, 0.44]
Rahe-Meyer 2013	29	45.6 (69.336)		45.6 (44.448)		13.3 %	0.0 [-29.56, 29.56]
Total (95% CI)	**56**		**56**			**100.0 %**	**-9.87 [-20.67, 0.93]**

Heterogeneity: Chi² = 0.63, df = 2 (P = 0.73); I² =0.0%
Test for overall effect: Z = 1.81 (P = 0.070)

-200 -100 0 100 200
Favours fibrinogen Favours control

Analysis 1.4. Fibrinogen concentrate versus any comparator, Stay in hospital (days).

Review: Fibrinogen concentrate in bleeding patients Comparison: 1 Fibrinogen concentrate versus any comparator

Study or subgroup	Fibrinogen N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Cui 2010	17	21 (10.74)	14	32 (11.85)		19.9 %	-11.00 [-19.04, -2.96]
Karlsson 2009	10	6 (1.76)	10	5 (0.94)		44.6 %	1.00 [-0.24, 2.24]
Rahe-Meyer 2013	28	14 (7.778)		15.5 (6.667)		35.6 %	-1.50 [-5.29, 2.29]
Total (95% CI)	**55**		**52**			**100.0 %**	**-2.28 [-7.04, 2.48]**

Heterogeneity: Tau² = 12.84; Chi² = 9.56, df = 2 (P = 0.01); I² =79%
Test for overall effect: Z = 0.94 (P = 0.35)

-100 -50 0 50 100
Favours fibrinogen Favours control

2017

Blood Transfus 2017; **15**: *318-24* DOI 10.2450/2017.0094-17

REVIEW

The use of fibrinogen concentrate for the management of trauma-related bleeding: a systematic review and meta-analysis

Carlo Mengoli[1], Massimo Franchini[1,2], Giuseppe Marano[1], Simonetta Pupella[1], Stefania Vaglio[1,3], Marco Marietta[4], Giancarlo M. Liumbruno[1]

[1]Italian National Blood Centre, National Institute of Health, Rome; [2]Department of Haematology and Transfusion Medicine, "Carlo Poma" Hospital, Mantua; [3]Department of Clinical and Molecular Medicine, "Sapienza" University of Rome, Rome; [4]Department of Oncology, Haematology and Respiratory Diseases, University Hospital, Modena, Italy

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Haemorrhage following injury is associated with significant morbidity and mortality. The role of fibrinogen concentrate in trauma-induced coagulopathy has been the object of intense research in the last 10 years and has been systematically analysed in this review. A systematic search of the literature identified six retrospective studies and one prospective one, involving 1,650 trauma patients. There were no randomised trials. **Meta-analysis showed that fibrinogen concentrate has no effect on overall mortality** (risk ratio: 1.07, 95% confidence interval: 0.83-1.38). Although the metaanalytic pooling of the current literature evidence suggests no beneficial effect of fibrinogen concentrate in the setting of severe trauma, the quality of data retrieved was poor and the final results of ongoing randomised trials will help to further elucidate the role of fibrinogen concentrate in traumatic bleeding.

...podávání fibrinogenu nemá žádný vliv na mortalitu!

...není žádná evidence pozitivního efektu !


ONEMAN
SHOW
CREW
ONEMAN
SHOW
CREW
ONEMAN
SHOW
CREW


1 / 10

REVIEW Blood Transfus 2017; 15: 318-24 DOI 10.2450/2017.0094-17

The use of fibrinogen concentrate for the management of trauma-related bleeding: a systematic review and meta-analysis

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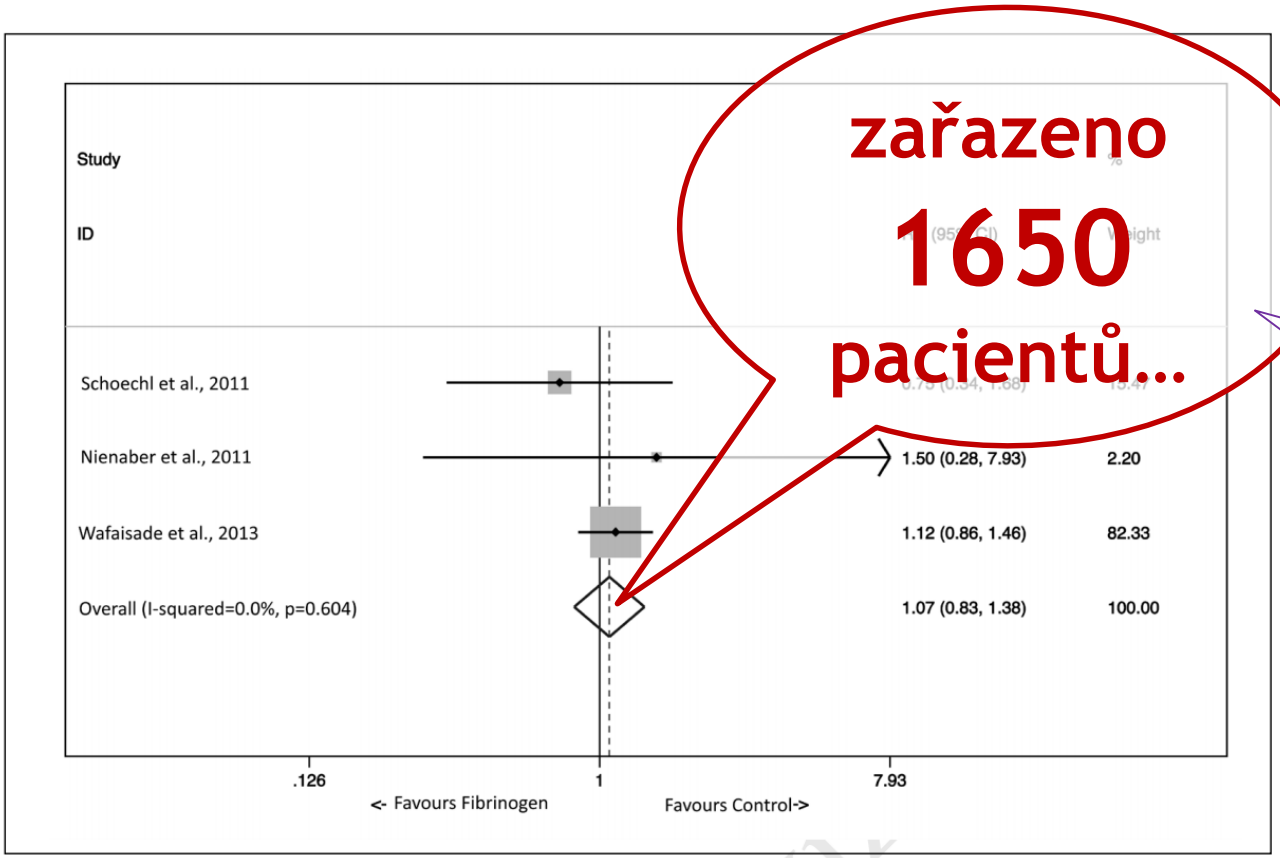

Figure 2 - Effect of fibrinogen concentrate on overall in-hospital mortality.
The effect was measured comparatively as the risk ratio (RR) in three studies amenable to meta-analytical pooling. Squares denote RR, with size proportional to the weight assigned to the study. Horizontal bars indicate 95% confidence intervals (CI) for each study. The diamond represents the aggregate effect, with the width representing the 95% confidence interval of the total effect.

REVIEW

Curr Opin Anesthesiol 2015, 28:275–284

CURRENT OPINION

Transfusion and coagulation management in major obstetric hemorrhage

Alexander J. Butwick[a] *and Lawrence T. Goodnough*[b,c]

INTRODUCTION

Obstetric hemorrhage is a leading cause of maternal death and morbidity worldwide. In Africa and Asia, obstetric hemorrhage accounts for more than 30% of all maternal deaths [1]. By comparison, obstetric hemorrhage is responsible for lower rates of maternal death in the developed world: 3.4% in the UK between 2006 and 2008 and 11.4% in the USA between 2006 and 2010 [2].

ClinCalc.com

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Sample Size Calculator

Determines the minimum number of subjects for adequate study power

ClinCalc.com » Statistics » Sample Size Calculator

Study Group Design

Two independent study groups	One study group vs. population

Two study groups will each receive different treatments.

Primary Endpoint

Dichotomous (yes/no)	Continuous (means)

The endpoint is **binomial** - only two possible outcomes.
Eg, mortality (dead/not dead), pregnant (pregnant/not)

Anticipated Incidence

Group 1	3.4	%
Group 2	2.55	%
	Incidence	
Enrollment ratio	1	

Type I/II Error Rate

Alpha	0.05
Power	80%

Reset | Calculate

RESULTS

Dichotomous Endpoint, Two Independent Sample Study

Sample Size	
Group 1	6270
Group 2	6270
Total	**12540**

Study Parameters	
Incidence, group 1	3.4%
Incidence, group 2	2.55%
Alpha	0.05
Beta	0.2
Power	0.8

View Power Calculations

EVIDENCE …?

Table 1. Current Licensing Status of Fibrinogen Concentrate Manufactured by CSL Behring.

Product Name	Availability[a]	Date of First Approval
Haemocomplettan® P[b]		
	Argentina	August 2012
	Austria	June 1994
	Brazil	March 1963 (March 2008[c])
	Bulgaria	January 2009
	Czech Republic	March 1993
	Germany	March 1966 (March 2005[c])
	Hungary	June 1998
	Iran	January 2010
	Kuwait	October 2003
	Lebanon	December 2013
	Netherlands	March 1997
	Portugal	January 1978
	Romania	July 1999
	Switzerland	November 1992
	Taiwan	March 1970 (January 1987[c])
	Tunisia	April 2013
	Turkey	October 1997
	Uruguay	October 2013
	Israel	August 2009
RiaSTAP®		
	Australia	August 2010
	Belgium	October 2010
	Canada	September 2012
	Cyprus	January 2012
	Denmark	August 2010
	Finland	September 2010
	France	October 2010
	Germany	December 2009
	Greece	May 2011
	Iceland	August 2010
	Ireland	September 2010
	Italy	April 2012
	Luxembourg	February 2011
	Malta	February 2012
	Mexico	January 2013
	New Zealand	May 2011
	Norway	November 2010
	Poland	June 2011
	Puerto Rico	December 2009
	Slovakia	October 2010
	Slovenia	June 2011
	Spain	March 2011
	Sweden	October 2010
	United Kingdom	August 2010
	United States	January 2009

[a]Additional countries received licenses to use the product that are no longer active, for example, pre-1985 (Colombia, Jamaica, Pakistan) and post-1985 (Croatia, India).
[b]Other trade names have been used for this product during the licensing history and in other countries, for example, FIBRINOGENIO HUMANO LIOF, Fibrinogenio Humano, Fibrinogenio, Haemocomplettan, Haemocomplettan HS, Human-Fibrinogen Behringwerke Konzentrat.
[c]Approval date of current license.

OPEN

The Clinical Efficacy of Fibrinogen Concentrate in Massive Obstetric Haemorrhage with Hypofibrinogenaemia

Received: 09 January 2017
Accepted: 24 March 2017
Published: 24 April 2017

Shigetaka Matsunaga[1], Yasushi Takai[1], Eishin Nakamura[1], Sumiko Era[1], Yoshihisa Ono[1], Koji Yamamoto[2], Hiroo Maeda[2] & Hiroyuki Seki[1]

	Abruption F + F (n = 8)	Abruption F (n = 18)	*P*-value
Hb (g/dl)	7.27 ± 1.39	7.0 [illegible]	>0.05
PT%	58.5 ± 16.6	[illegible]	>0.05
Fibrinogen (mg/dl)	83.6 ± 20.9	82.5 ± 33.0	>0.05
Estimated blood loss (ml)	2504.6 ± 1306	2988.1 ± 1365	>0.05
RCC (unit)	7.00 ± 1.85	6.88 ± 2.19	>0.05
FFP (unit)	9.75 ± 2.91	19.0 ± 9.40	0.0122
FFP/RCC	1.47 ± [illegible]	2.96 ± 1.60	0.0187

LOWER BLOOD LOSS
MENŠÍ KREVNÍ ZTRÁTA
LESS PLASMA
MÉNĚ PLASMY
LEPŠÍ FFP/RBC
BETTER FFP/RBC

Table 4. Comparison of fibrinogen levels and other haemostatic parameters before treatment, and blood product usage in the groups of early-stage placental abruption requiring ≤10 units of red blood cell concentrate. Hb, haemoglobin concentration; PT%, prothrombin time activity percentage; RCC, red cell concentrate; FFP, fresh frozen plasma; F + F, fresh frozen plasma and fibrinogen concentrate; F, fresh frozen plasma alone.

Matsunaga et al. Scientific Reports volume 7, Article number: 46749 (2017)

Terminated early for high proportion of patients in the FFP group requiring rescue therapy

Reversal of trauma-induced coagulopathy using first-line coagulation factor concentrates or fresh frozen plasma (RETIC): a single-centre, parallel-group, open-label, randomised trial

Petra Innerhofer, Dietmar Fries, Markus Mittermayr, Nicole Innerhofer, Daniel von Langen, Tobias Hell, Gottfried Gruber, Stefan Schmid, Barbara Friesenecker, Ingo H Lorenz, Mathias Ströhle, Verena Rastner, Susanne Trübsbach, Helmut Raab, Benedikt Treml, Dieter Wally, Benjamin Treichl, Agnes Mayer, Christof Kranewitter, Elgar Oswald

less TRF with factors

more MOF with plasma

s faktory méně TRF

s plasmou více MOF

Findings

The study was terminated early for futility and safety reasons because of the high proportion of patients in the FFP group who required rescue therapy compared with those in the CFC group (52% in the FFP group *vs* 4% in the CFC group) and increased needed for massive transfusion (30% in the FFP group *vs* 12% in the CFC group) in the FFP group.

Multiple organ failure occurred in 66% patients in the FFP group and in 50% pati

koagulační faktory jsou superiorní

Interpretation

The available sample size in our study appears sufficient to make some conclusions that first-line CFC is superior to FFP.


PATHOPHYSIOLOGY !
PLASMA
A

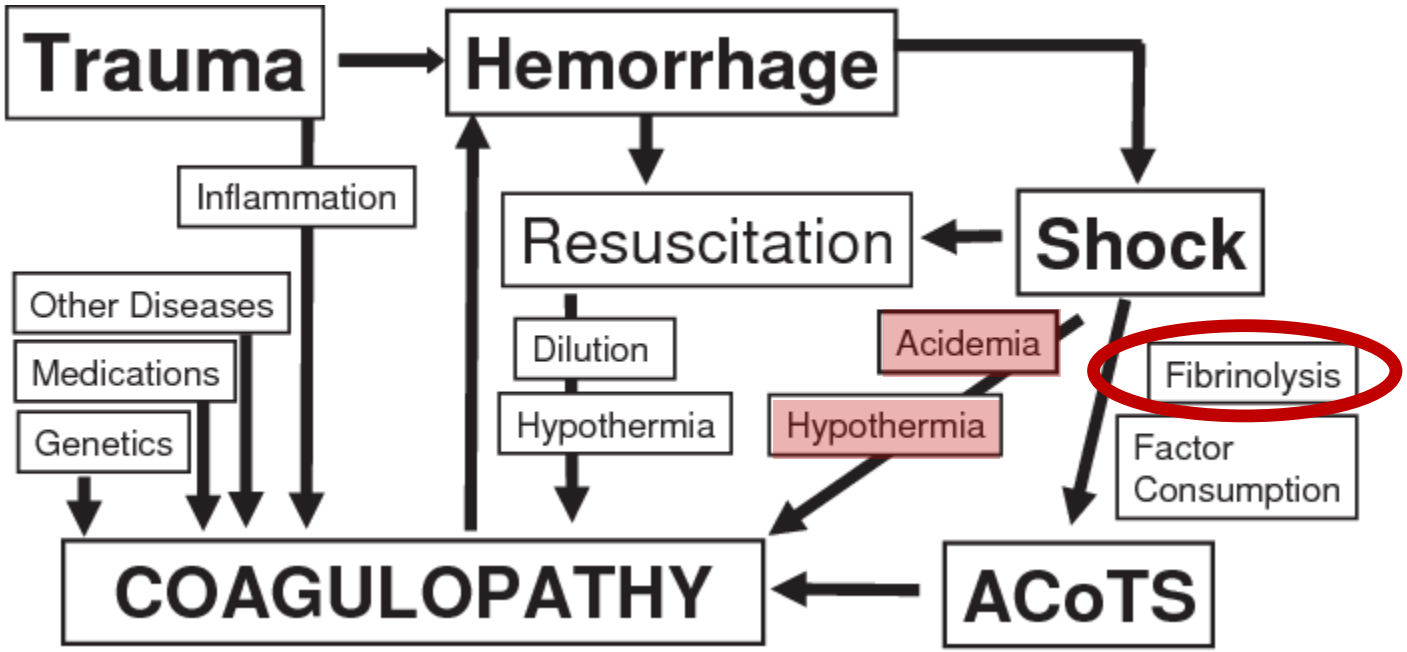
Dries *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2010, **18**:63
http://www.sjtrem.com/content/18/1/63

SCANDINAVIAN JOURNAL OF
trauma, resuscitation
& emergency medicine

REVIEW Open Access

The contemporary role of blood products and components used in trauma resuscitation

David J Dries



Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

Published Online
April 26, 2017
http://dx.doi.org/10.1016/
S0140-6736(17)30638-4

*WOMAN Trial Collaborators**

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

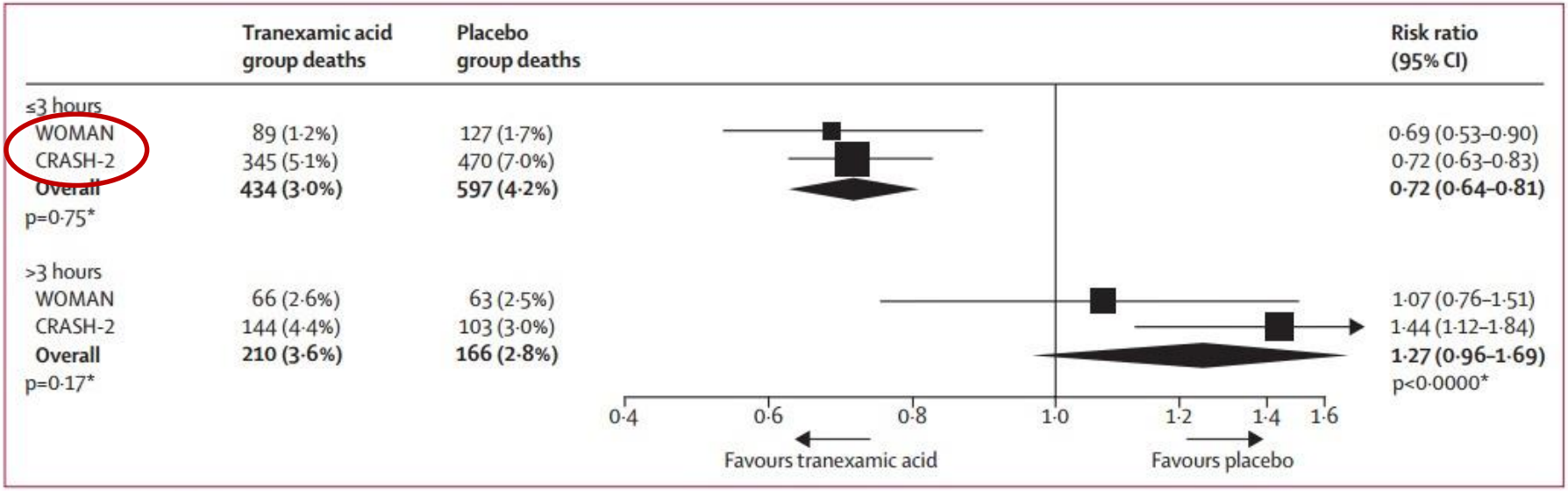
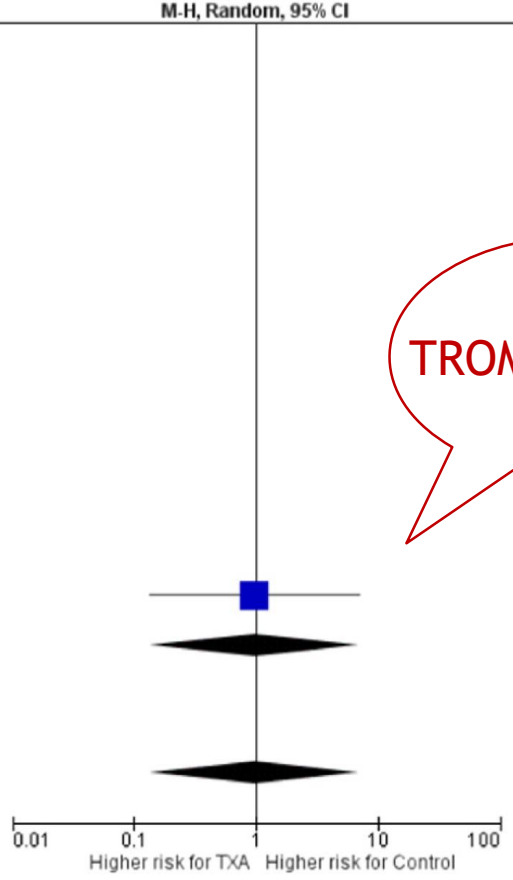


***Figure 5*: Time to treatment**
*Heterogeneity p value.

Prophylactic Use of Tranexamic Acid for Postpartum Bleeding Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Asim Alam [a,*], Stephen Choi [a,b]

Study or Subgroup	TXA Events	TXA Total	Placebo/No treatment Events	Placebo/No treatment Total	Weight	Odds Ratio M-H, Random, 95% CI
1.7.1 Vaginal Birth						
Gungorduk 2013	0	220	0	219		Not estimable
Subtotal (95% CI)		**220**		**219**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.7.2 Cesarian Section						
Abdel-Aleem 2013	0	373	0	367		Not estimable
Ahmed 2014	0	64	0	64		Not estimable
Gai 2004	0	91	0	89		Not estimable
Gobbur 2014	0	50	0	50		Not estimable
Goswami 2013	0	60	0	30		Not estimable
Gungorduk 2010	0	330	0	330		Not estimable
Mayur 2007	0	50	0	50		Not estimable
Movafegh 2011	0	50	0	50		Not estimable
Ramani 2014	0	60	0	60		Not estimable
Rashmi 2012	0	50	0	50		Not estimable
Sekhavat 2009	0	45	0	45		Not estimable
Senturk 2013	0	101	0	122		Not estimable
Shahid 2013	0	38	0	36		Not estimable
Singh 2014	0	100	0	100		Not estimable
Xu 2013	2	88	2	86	100.0%	0.98 [0.13, 7.09]
Yehia 2014	0	106	0	106		Not estimable
Subtotal (95% CI)		**1656**		**1635**	**100.0%**	**0.98 [0.13, 7.09]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (*P* = .98)						
Total (95% CI)		**1876**		**1854**	**100.0%**	**0.98 [0.13, 7.09]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.02 (*P* = .98)						
Test for subgroup differences: Not applicable						



TROMBEMBOLIE

Fig 8. Forest plot demonstrating effects of TXA on the incidence of thromboembolic side effects. Sample size, number of events, ORs, and the pooled estimate of the OR are shown according to subgroup. 95% CIs are indicated as lines for each study and diamonds for pooled estimates.

U masivního krvácení je fibrinogen prvním faktorem, který dosáhne kriticky nízké hladiny!

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

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

significant change on TEG when the fibrinogen falls under 100-150 mg/dl

významná změna na TEG při poklesu fibrinogenu pod 100-150 g/l

Table 2

FI concentration–response via thrombelastography.

mg dl^{-1}	R	α
75	237 (198–261)	33.6 (32.4–34.8)
100	156 (141–168)*	49.4 (46.2–53.2)*
150	144 (138–159)*	63.2 (60.7–65.6)*†
200	138 (135–156)*	71.6 (70.2–74.0)*†‡
250	132 (126–144)*	75.8 (75.3–76.9)*†‡ §
300	141 (135–147)*	78.6 (77.9–79.9)*†‡§¶
345	156 (141–165)*	79.8 (78.4–80.4)*†‡§¶

Values are expressed as median (1st–3rd quartiles).
All conditions were the results of eight separate experiments.
*$P < 0.05$ vs. 75 mg dl^{-1},
†$P < 0.05$ vs. 100 mg dl^{-1},
‡$P < 0.05$ vs. 150 mg dl^{-1},
§$P < 0.05$ vs. 200 mg dl^{-1},
¶$P < 0.05$ vs. 250 mg dl^{-1}.

Table 3

FII activity–response via thrombelastography.

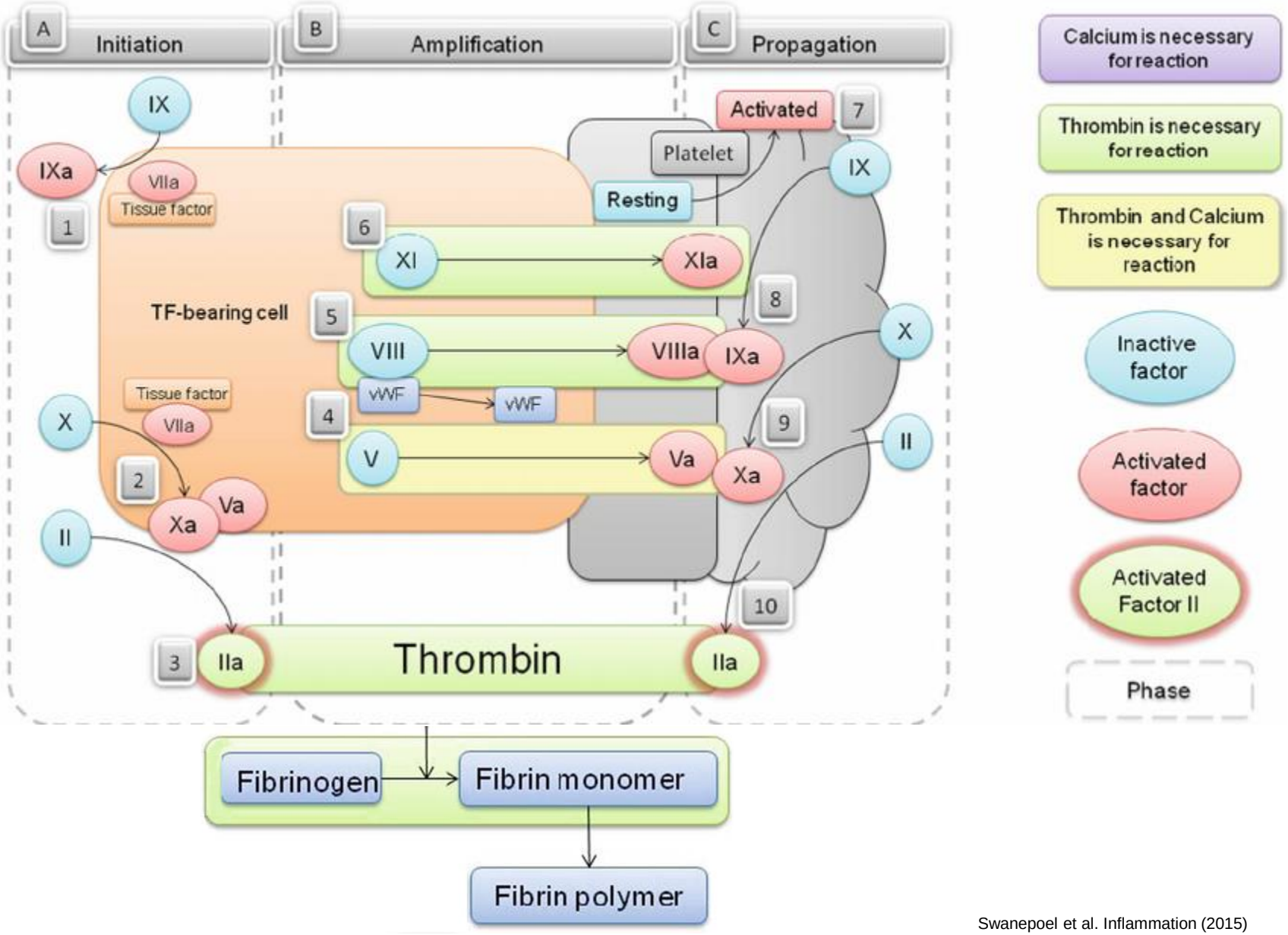
%	R	α
1	297 (279–318)	56.6 (55.8–58.4)
6.25	144 (138–156)*	67.3 (65.2–69.2)*
12.5	141 (129–144)*†	67.4 (66.2–69.4)*
25	129 (120–138)*†	72.2 (67.8–72.5)*
50	138 (123–144)*†	75.8 (74.7–77.0)*†‡§
100	156 (141–165)*†‡§¶	79.8 (78.4–80.4)*†‡§¶

Values are expressed as median (1st–3rd quartiles).
All conditions were the results of eight separate experiments.
*$P < 0.05$ vs. 1%,
†$P < 0.05$ vs. 6.25%,
‡$P < 0.05$ vs. 12.5%,
§$P < 0.05$ vs. 25%
¶$P < 0.05$ vs. 50%.

významná změna na TEG při poklesu trombinu pod 5% aktivity

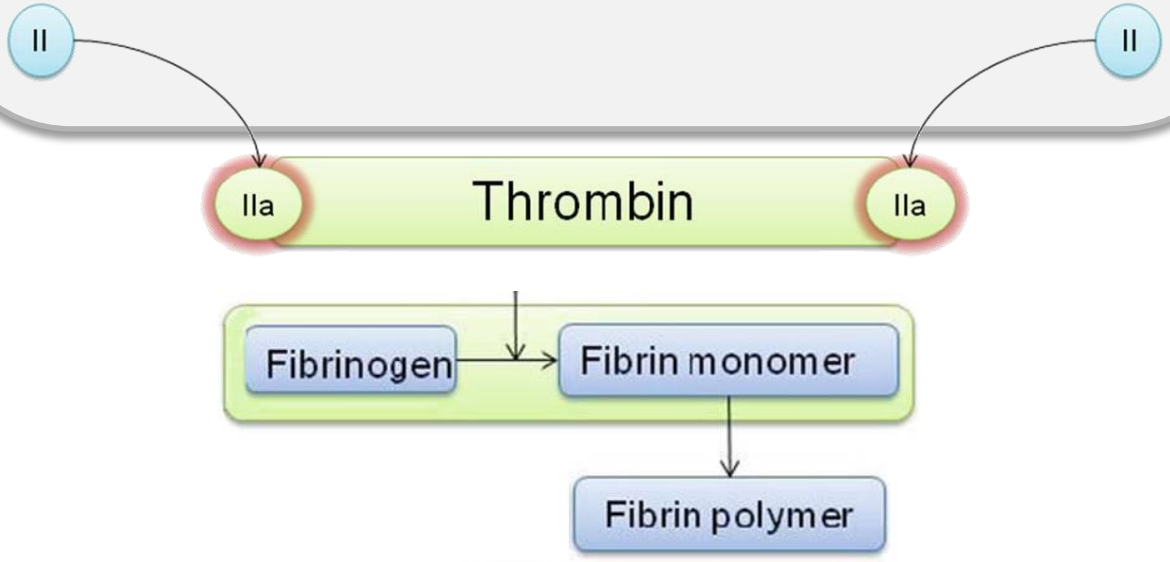
significant change on TEG when thrombin falls under 5% of activity

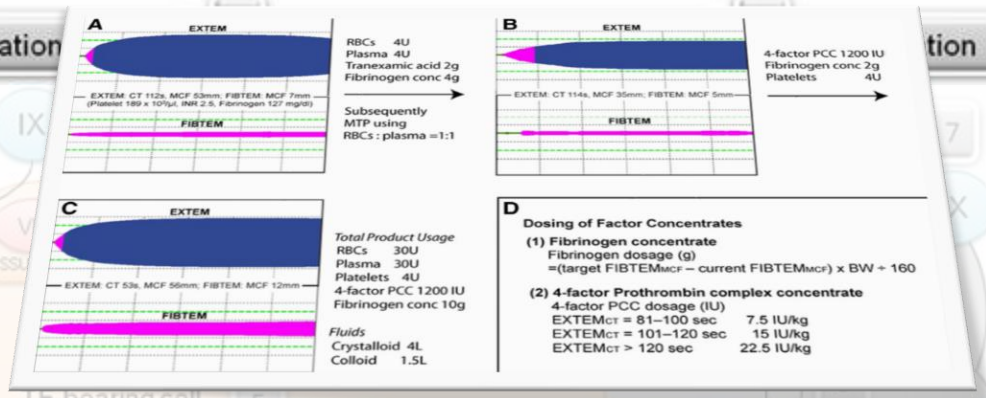
Nielsen VG et al. Acta Anaesthesiol Scand. 2005 Feb;49(2):222-31

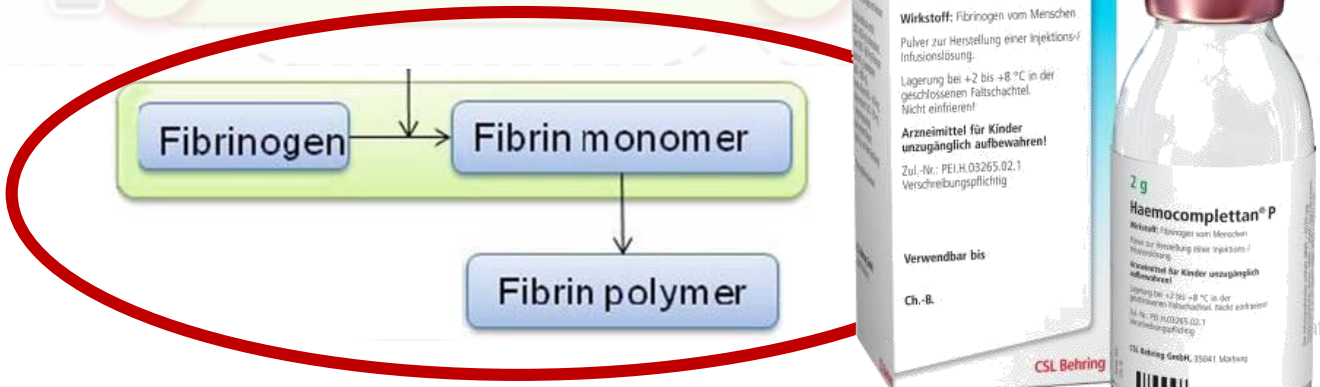


Swanepoel et al. Inflammation (2015)

HIC SUNT LEONES







flammation (2015)

Transfusion Medicine, 2012, **22**, 350–355

National audit of the use of fibrinogen concentrate to correct hypofibrinogenaemia

N. D. Gollop,[1] J. Chilcott,[2] A. Benton,[3] R. Rayment,[2] J. Jones[4] & P. W. Collins[2]

[1]The School of Medicine, [2]Department of Haematology, University Hospital of Wales and School of Medicine, Cardiff University Cardiff, [3]Department of Haematology, Singleton Hospital, Swansea University Swansea, and [4]Welsh Blood Service Cardiff UK

Table 2. Effect of fibrinogen infusion on fibrinogen levels

	Fibrinogen ($g\,L^{-1}$) before infusion	Fibrinogen ($g\,L^{-1}$) after infusion	Absolute increment in fibrinogen ($g\,L^{-1}$)	Adjusted increment in fibrinogen ($g\,L^{-1}$ increase per $mg\,kg^{-1}$ infused)
Bleeding patients ($n = 46$)	1·0 (0·7–1·3) 0·4–3·4	2 (1·4–2·4) 0·5–4·3	0·9 (0·5–1·3) −0·6 to 2·6	0·02 (0·01–0·03) −0·01 to 0·1
Non-bleeding patients ($n = 17$)	0·9 (0·5–1·2) 0·3–1·7	1·7 (1·3–2·5) 0·9–3·7	0·8 (0·6–1·5) 0·1–3·2	0·02 (0·01–0·03) 0–0·08

Fibrinogen levels and observed increment are shown. Data are median, (IQR) and range.

pro zvýšení o 1 g/l
je nutná dávka
60 mg/kg

a dose of **60 mg/kg**
is required to
increase by **1 g/l**

EJA

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

GUIDELINES

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

First update 2016

Sibylle A. Kozek-Langenecker, Aamer B. Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Guidrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V.L. Pitarch, Susan Mallett, Jens Meier, Zsolt L. Molnar, Niels Rahe-Meyer, Charles M. Samama, Jakob Stensballe, Philippe J.F. Van der Linden, Anne J. Wikkelsø, Patrick Wouters, Piet Wyffels and Kai Zacharowski

We suggest an initial fibrinogen concentrate dose of 25 to 50 mg kg^{-1}. **2C**

Plasma transfusion alone is not sufficient to correct hypofibrinogenaemia. **C**

Whole Blood

A unit of whole blood is produced from a whole blood donation that does not undergo any processing steps.

Volume: 513 ± 45 ml (includes anticoagulant)

Anticoagulant: CPD

Storage temperature: 2 °C to 6 °C

Shelf life: 21 days

Indications: Anaemia, severe haemorrhage, volume replacement, exchange transfusion in neonates.

Not indicated for: Conditions responsive to specifc components.

Special precautions: Compatibility testing must be performed; do not add any fluids or drugs; calcium containing fluids should not be used with citrated whole blood. Clotting factor and platelet function deteriorate rapidly with storage.

Rate of infusion: Administer through a standard blood recipient set. Infuse as fast as the patient can tolerate for severe blood loss.


REMEMBER
TIME LOST
CANNOT BE
REGAINED


We order blood derivates
Objednáme krevní deriváty,
odešleme koagulační vyšetření
will sent coagulation tests
a budeme čekat… !!!
and will wait…!!!

.Výsledky: [redacted] (82[redacted])

Režim Mixer Data Zobrazení Filtry Typy událostí Potvrzování Zpřístupňování Konfigurace

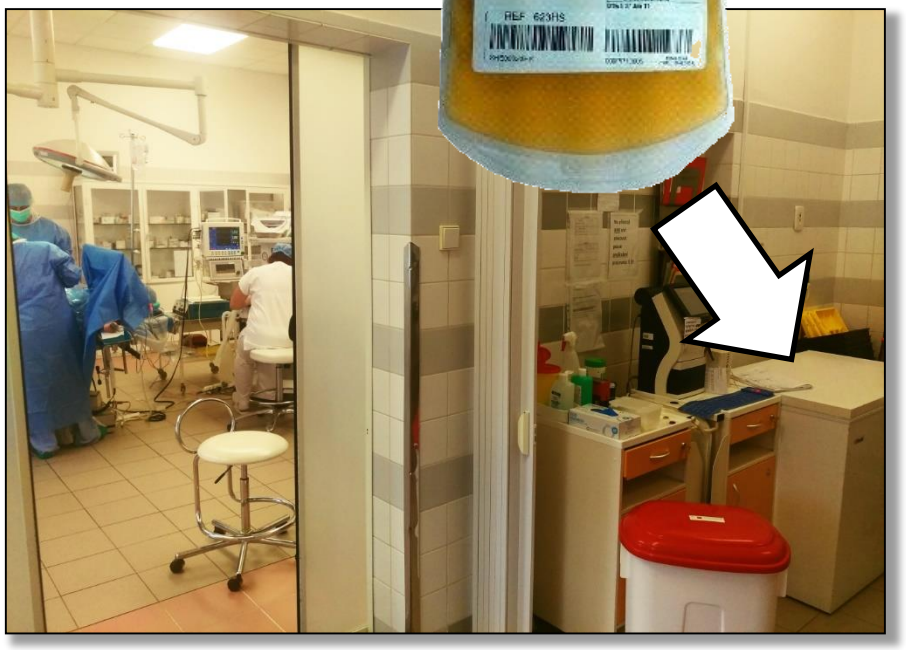
Třídy a metody	28/06/11 11:49	28/06/11 12:01	28/06/11 12:03	28/06/11 12:31
Diabetický profil				
Glukóza	8,3			
ABR - krev				
Hemoglobin	63			
pH	[redacted]			
PCO2	5,04			
HCO3 aktuální	18,3			
HCO3 standardní	18,8			
Base excess aktuální	-6,8			
PO2	30,0			
O2 saturovaný	98,9			
CO2 celkový	18,1			
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				Txt+His
Antitrombin III				78
D-dimery				1830


PLASMA
A
Rh POSITIVE
VOLUNTEER DONOR


PLASMA
AB
Rh POSITIVE
VOLUNTEER DONOR
For Instructional Use Only / Not For Human or Animal Use

= 35 minut


AB
Rh D POSITIVE
REF 623HS




ATROPIN Biotika
0,5 mg
Adrenalin Léčiva
Mesocain


2 g
N1
Fibrinogen
Haemocomplettan® P
CSL Behring

35 minut

= 8 minut

The effect of prehospital transport time, injury severity, and blood transfusion on survival of US military casualties in Iraq

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BACKGROUND: Reducing time from injury to care can optimize trauma patient outcomes. A previous study of prehospital transport of US military casualties during the Afghanistan conflict demonstrated the importance of time and treatment capability for combat casualty survival.

METHODS: A retrospective descriptive analysis was conducted to analyze battlefield data collected on US military combat casualties during the Iraq conflict from March 19, 2003, to August 31, 2010. All casualties were analyzed by mortality outcome (killed in action, died of wounds, case fatality rate) and compared with Afghanistan conflict. Detailed data for those who underwent prehospital transport were analyzed for effects of transport time, injury severity, and blood transfusion on survival.

RESULTS: For the total population, percent killed in action (16.6% vs. 11.1%), percent died of wounds (5.9% vs. 4.3%), and case fatality rate (10.0 vs. 8.6) were higher for Iraq versus Afghanistan ($p < 0.001$). Among 1,692 casualties (mean New Injury Severity Score, 22.5; mortality, 17.6%) with detailed data, the injury mechanism included 77.7% from explosions and 22.1% from gunshot wounds. For prehospital transport, 67.6% of casualties were transported within 60 minutes, and 32.4% of casualties were transported in greater than 60 minutes. Although 97.0% of deaths occurred in critical casualties (New Injury Severity Score, 25–75), 52.7% of critical casualties survived. Critical casualties were transported more rapidly ($p < 0.01$) and more frequently within 60 minutes ($p < 0.01$) than other casualties. Critical casualties had lower mortality when blood was received ($p < 0.01$). Among critical casualties, blood transfusion was associated with survival irrespective of transport time within or greater than 60 minutes ($p < 0.01$).

CONCLUSION: Although data were limited, early blood transfusion was associated with battlefield survival in Iraq as it was in Afghanistan.
(*J Trauma Acute Care Surg.* 2018;85: S112–S121.

Table 6. Difference in Mortality by Number of Units Transfused

Units Transfused	No.	Mortality, %		*P* Value*
		Survived (n = 2422)	Died (n = 614)	
0	1896	85.1	14.9	<.01
1	157	84.1	15.9	
2	377	79.6	20.4	
3	157	70.7	29.3	
4	130	69.2	30.8	
>4	319	55.2	44.8	

*Numbers do not total 3534 because of missing data (some forms incomplete). $\chi^2 = 171.46$.

ABC Study: Jama 2002; 288:1499–1507

Impact of Plasma Transfusion in Trauma Patients Who Do Not Require Massive Transfusion

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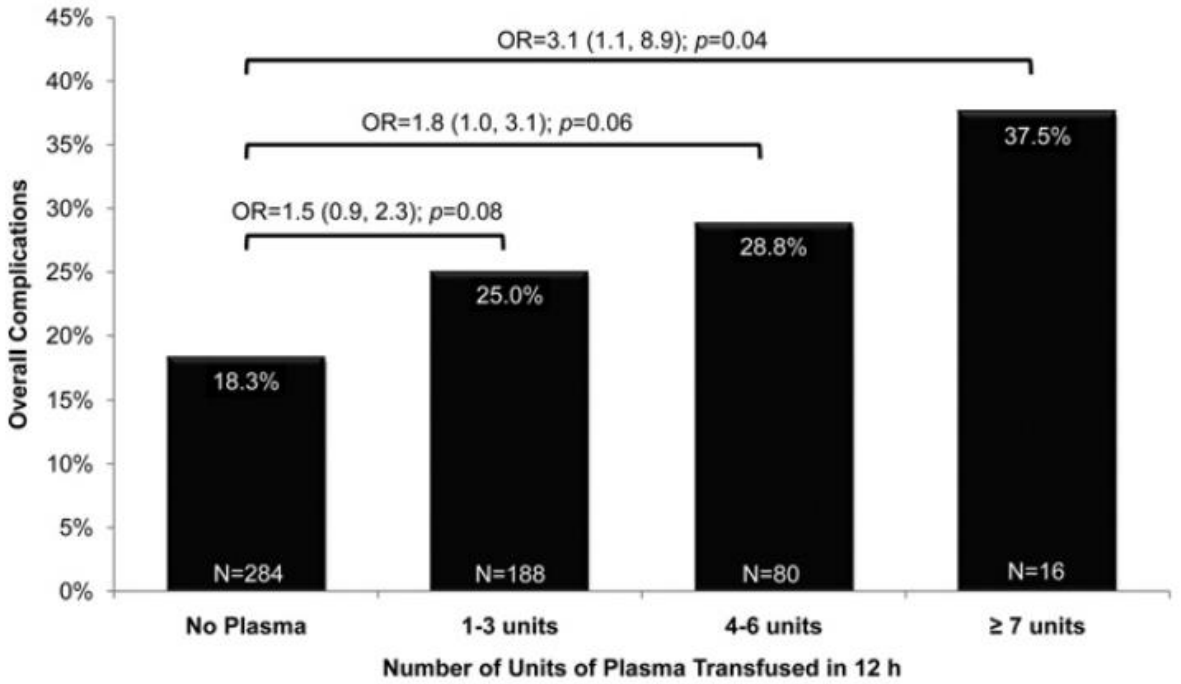

Figure 2. Overall complication rates stratified by the number of units of plasma transfused in 12 hours. OR, odds ratio (95% confidence interval); p-values were derived from McNemar's chi-square test.

Table 1. Transfusion-related risks, modified according to Marcucci and colleagues (1)

Type of Risk	Estimate of Current Risk (Infection Rate Per Unit)	
	High HDI Countries	Low HDI Countries
Infections		
Viruses		
HIV	1:1,468,000 (53)–1:4,700,000 (10)	1:50 (54)–1:2,578 (55)
HBV	1:31,000 (10)–1:205,000 (53)	1:74–1:1,000 (56)
HCV	1:1,935,000 (53)–1:3,100,000 (10)	1:2,578 (55)
Bacteria	1:2,000–1:8,000 (platelet pools) 1:28,000–1:143,000 (red cells) (10)	?
Parasites		
Malaria	1:4,000,000 (10)	≤1:3 (57)
Prions		
vCJD	First two cases (4,5)	?
Immunological reactions		
Hemolytic transfusion reactions		
Acute hemolytic	1:13,000 (10)	?
Delayed hemolytic	1:9,000 (10)	?
Alloimmunization	1:1,600 (10)	?
Immunosuppression	1:1 (58,59)	?
TRALI	1:4,000–1:557,000[a] (60)	?
Mistransfusion	1:14,000–1:18,000 (2)	?

HDI, human development index, an index based on life expectancy, literacy, enrollment in scholarly education, and per capita income; HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; vCJD, variant Creutzfeld-Jacob disease; TRALI, transfusion-related acute lung injury. Values in parentheses are reference numbers.

Madjdpour et al. Crit Care Med 2006; 34:S102–S108

Transfusion of sex-mismatched and non–leukocyte-depleted red blood cells in cardiac surgery increases mortality

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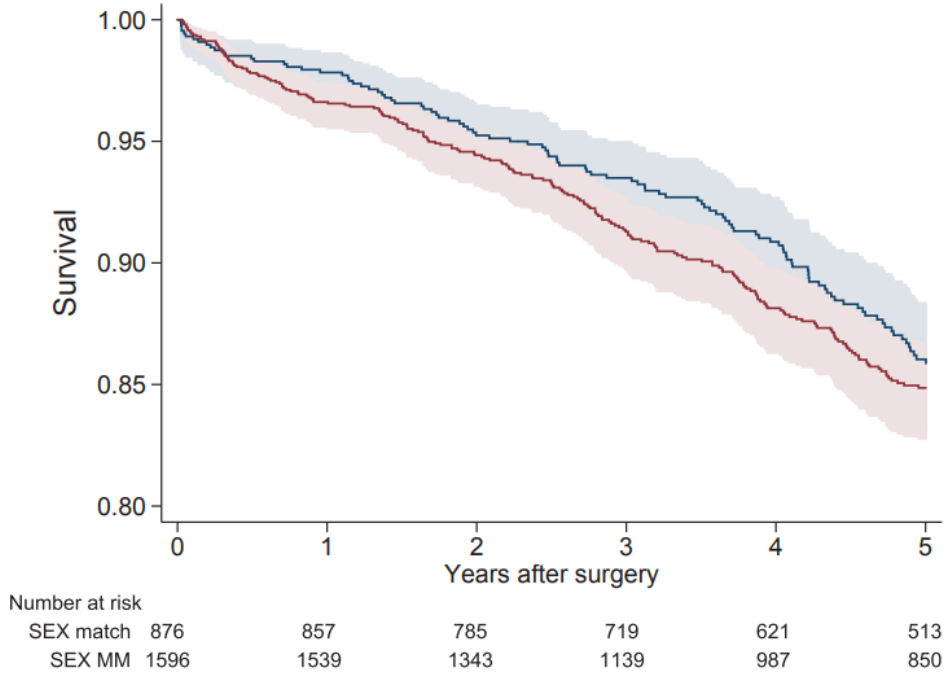

FIGURE 1. Kaplan-Meier curve comparing patients receiving only sex-matched blood (*blue line*) with only sex mismatched red blood cells (*red line*). Shaded area represents 95% confidence interval.

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Original Investigation October 17, 2017

Association of Blood Transfusion From Female Donors With and Without a History of Pregnancy With Mortality Among Male and Female Transfusion Recipients

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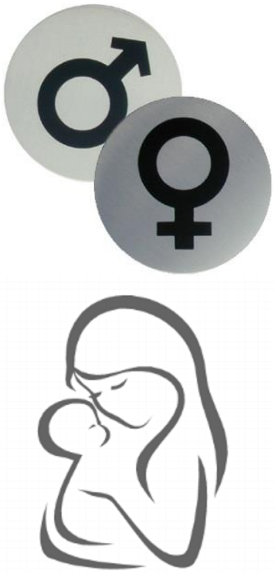

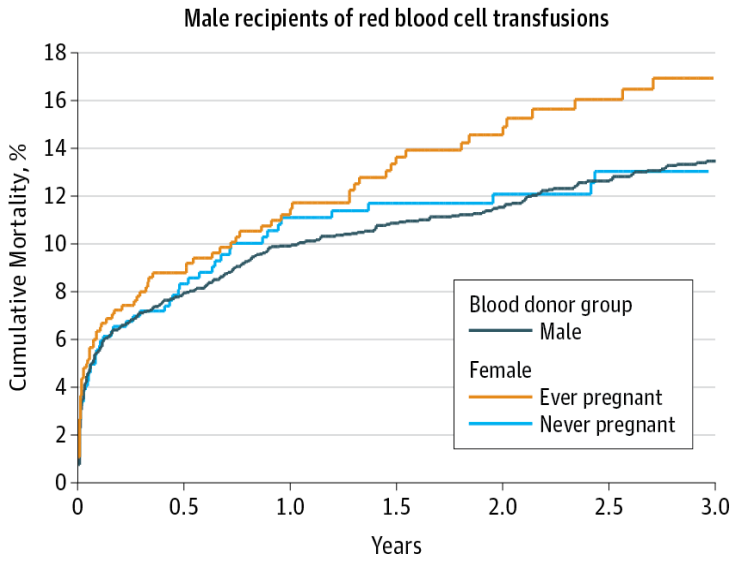

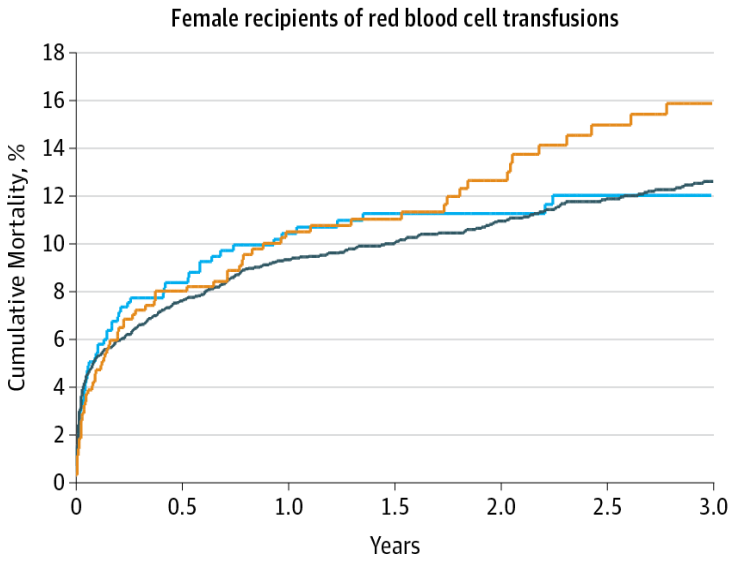

No. at risk by donor group														
Male	6189	2408	2102	1833	1624	1421	1236	6243	2598	2296	1990	1726	1484	1278
Female														
Ever pregnant	1190	438	367	305	245	197	163	1160	456	371	303	243	197	166
Never pregnant	1084	393	331	279	225	177	146	1093	425	353	294	255	211	172

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Despite efforts to educate care providers and limit the number of inappropriate and/or ineffective plasma transfusions, the annual usage of plasma products grew from 3.3 million units in 1998 to 4.5 million units in 2009.[1] The majority of these plasma transfusions are administered in the perioperative period, particularly in the setting of cardiac surgery.[2] Importantly, historic estimates suggest 25-30 percent of plasma units are transfused without evidence-based indications.[3] In addition, concerns related to the liberal use of plasma products, including life-threatening complications such as transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO), have been increasingly appreciated.[4] In addition to the need for ongoing transfusion education, these data have resulted in increased interest in safe and effective alternatives to plasma transfusion.

1. The 2009 National Blood Collection and Utilization Survey Report. US Department of Health and Human Services, 2011.
2. Abdel-Wahab OI, et al. Transfusion. 2006;46(8):1279-1285.
3. Wilson K et al. Transfusion. 2002;42(9):1224-1229.

Tab. 1 Attributes of different sources of fibrinogen concentrate available for the management of perioperative bleeding, modified according to Soerensen B et al. (91)

	FFP	cryoprecipitate	fibrinogen concentrate
content of fibrinogen	inconsistent and donor dependent	variable fibrinogen content	constant amount of fibrinogen in each vial
side effects, risk of immunological reactions	• ABO group matching required • transfusion related lung injury • acute lung injury • transfusion related cardiac overload • sepsis • multi organ failure	• ABO group matching required • low risk (because resuspended in small volume of plasma) of – transfusion related lung injury – severe anaphylactic reactions	negligible risk of immunological reactions (because purification steps during preparation and removal of donor antibodies)
risk of viral / pathogen transmission	low risk for quarantined plasma and SD plasma	potential risk of pathogen transmission – not virally inactivated	pasteurization and filtration steps minimize the risk of pathogen transmission
number of Units / vials required to provide a 4 g dose	6–8 Units	29 Units (based on 140 mg/U)	4 vials
time to administration	has to be thawed prior to use		immediately available

Schöchl H. Hämostaseologie 2014; 34: 29–39

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