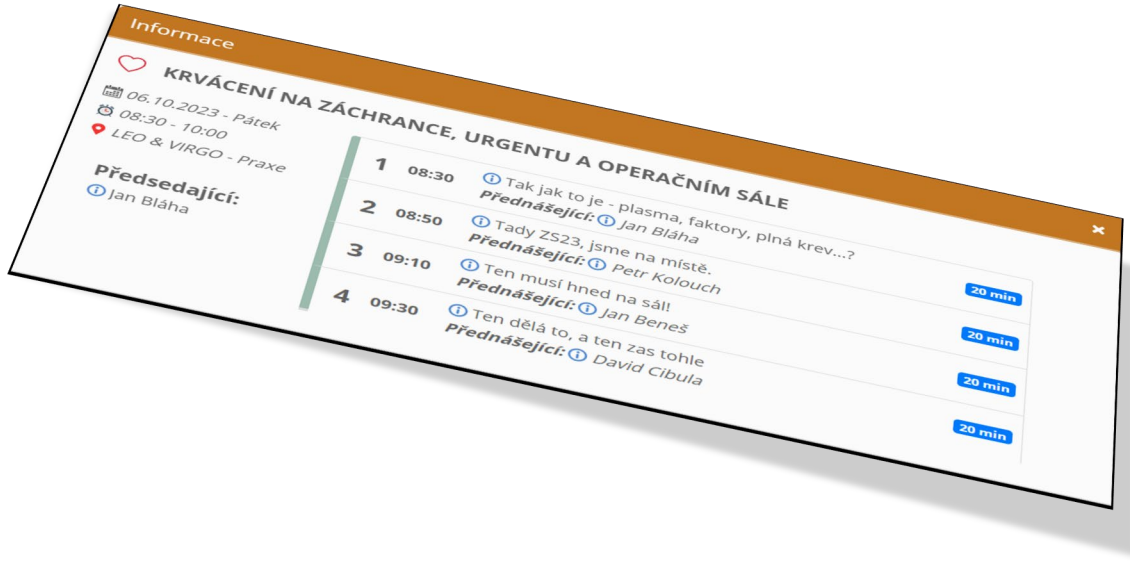
TAK JAK TO JE

- plasma, faktory, plná krev…?



JAN BLÁHA

KLINIKA ANESTEZIOLOGIE, RESUSCITACE A INTENZIVNÍ MEDICÍNY

1. LÉKAŘSKÁ FAKULTA
Univerzita Karlova

VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

jan.blaha@vfn.cz

Prosíme, vyplňte dotazník
Patient Blood Management

Pár minut Vašeho času = data pro budoucnost

Možný konflikt zájmů: CSL Behring AstraZeneca octapharma

California MEDICINE

OFFICIAL JOURNAL OF THE CALIFORNIA MEDICAL ASSOCIATION

Volume 87 OCTOBER 1957 Number 4

Modern Treatment of Abruptio Placentae

JAMES A. MERRILL, M.D., San Francisco

HEMORRHAGE CONTINUES to be one of the major causes of maternal death. Deaths due to infection have decreased sharply but there has been much less change in the proportionate number of deaths due to other members of the classical triad—toxemia and hemorrhage. The work of several maternal welfare committees indicates that probably 75 per cent of hemorrhagic deaths are preventable. Therefore, in order to reduce maternal mortality further, the prevention, control and treatment of hemorrhage must

75% úmrtí na krvácení je pravděpodobně preventabilních

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of abruptio placentae that causes death, the mortality rate associated with this grade approximates 10 per cent. Fortunately, the severe form is not common, occurring in about 15 per cent of cases of premature separation. Often the only evidence of premature separation is that found by pathologic examination of the placenta. Moreover, diagnosis and treatment of abruptio placentae are frequently linked with another complication of pregnancy—toxemia.

From the Department of Obstetrics and Gynecology, University of California School of Medicine, San Francisco 22.

Presented before the Section on Obstetrics and Gynecology at the 86th Annual Session of the California Medical Association, Los Angeles, April 28 to May 1, 1957.

SYSTEMIC EFFECTS OF ABRUPTIO PLACENTAE

Various lines of investigation have shown the severe grade of premature separation of the placenta to be accompanied by systemic effects, some of which are potentially lethal, and which include:

1. Clinical shock, sometimes out of proportion to blood loss or hypotension.

2. Disseminated deposition of fibrin.

3. An *in vivo* defibrination of the blood with a decrease or absence of fibrinogen, sometimes resulting in incoagulable blood.

4. Ischemia of the renal cortex, leading to varying degrees of necrosis.

5. Activation of a fibrinolysin in the plasma.

Zpoždění léčby až u 90% případů krvácení (PPH)

Best Practice & Research Clinical Anaesthesiology
Volume 36, Issues 3–4, December 2022, Pages 325-339

Epidemiology and definition of PPH worldwide

Jan Bláha (Associate Professor), Tereza Bartošová Anaesthetist

Department of Anaesthesiology and Intensive Care Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague, U Nemocnice 2, 128 08, Prague 2, Czech Republic

Available online 10 December 2022.

In the United States, during the period from 1993 through 2014, the rate of PPH (defined as blood loss >1000 ml) requiring a blood transfusion increased from approximately 8 to 40 per 10 000 deliveries [103]. An increase in high-risk groups such as higher maternal age, obesity, more frequent and serious comorbidities, especially cardiovascular, or increased cesarean section rates cannot fully explain this rise [104,105]. The increasing incidence of PPH suggests an incomplete implementation of guidelines [106–108], resulting in treatment delays or suboptimal care, which are increasingly being reported in 30–90% of PPH cases [109–112]! Moreover, reports from confidential inquiries have shown that as many as 67% of the deaths in the United States and 85% of those in France are avoidable, resulting as they have from either delayed or inadequate treatment [113–115]. Delays in diagnosing and treating PPH are believed to directly affect the severity of bleeding, the development of complications such as coagulopathy, and result in higher morbidity and mortality. Delays are reported to be caused by misinterpretation of the extent of blood loss and its physiological effects, failure to recognize hidden bleeding, and failure to escalate care to more senior colleagues [116–118].

67% v USA a 85% ve Francii úmrtí bylo preventabilních !!!

Proper Estimation of Blood Loss on Scene of Trauma: Tool or Tale?

Matthias Frank, MD, Uli Schmucker, MD, Dirk Stengel, MD, PhD, Lutz Fischer, MD, Joern Lange, MD, Rico Grossjohann, Dipl. Phys., Axel Ekkernkamp, MD, PhD, and Gerrit Matthes, MD, PhD

(*J Trauma.* 2010;69: 1191–1195)

The Journal of **TRAUMA®** *Injury, Infection, and Critical Care* • Volume 69, Number 5, November 2010 *Proper Estimation of Blood Loss on Scene of Trauma*

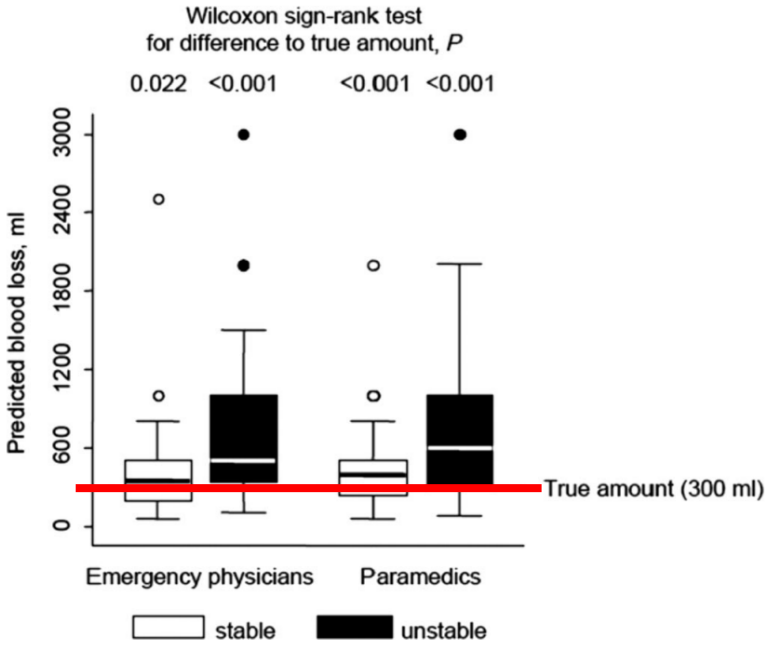


Figure 1. Estimation of blood loss by emergency physicians and paramedics for stable and unstable patients. Given *p* values indicate the statistical significance of the difference to the actual blood loss of 300 mL.

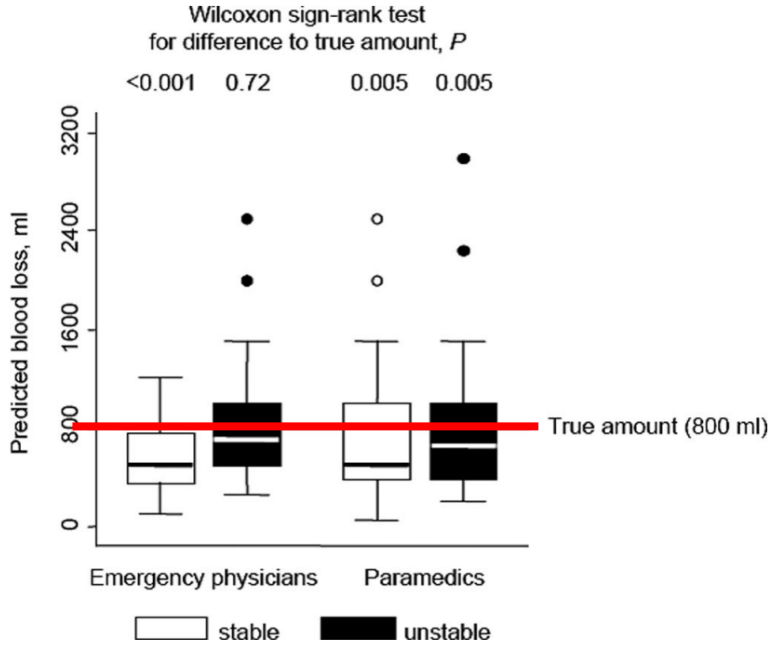


Figure 2. Estimation of blood loss by emergency physicians and paramedics for stable and unstable patients. Given *p* values indicate the statistical significance of the difference to the actual blood loss of 800 mL.

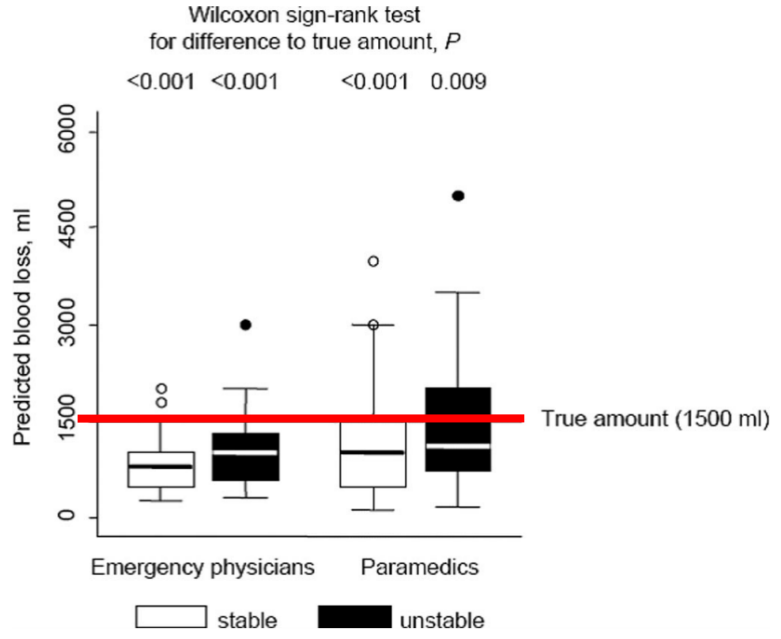
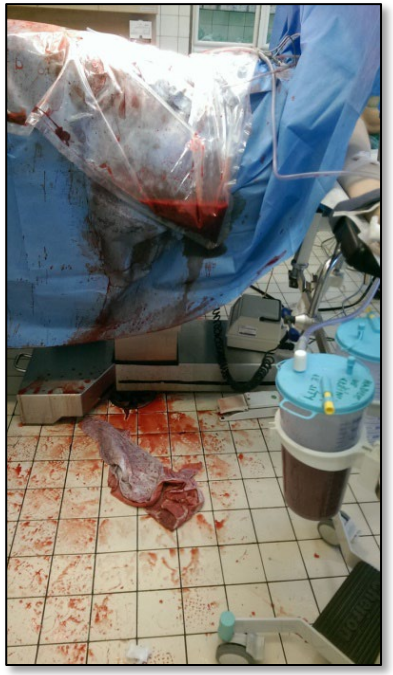
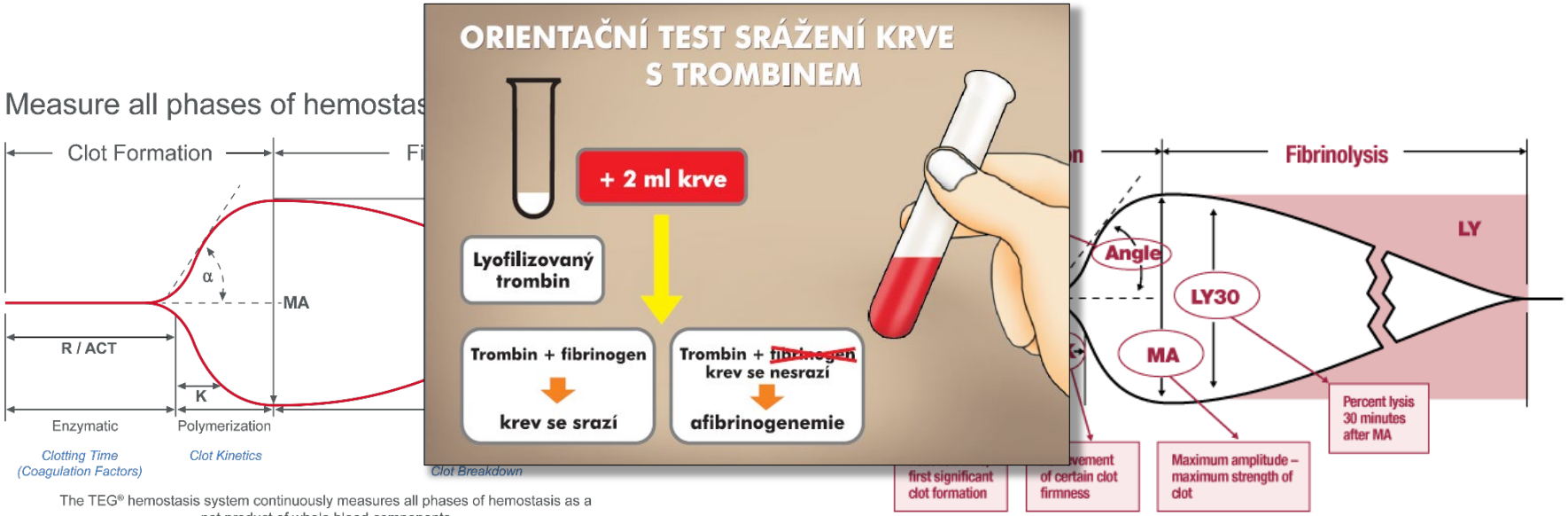


Figure 3. Estimation of blood loss by emergency physicians and paramedics for stable and unstable patients. Given *p* values indicate the statistical significance of the difference to the actual blood loss of 1,500 mL.

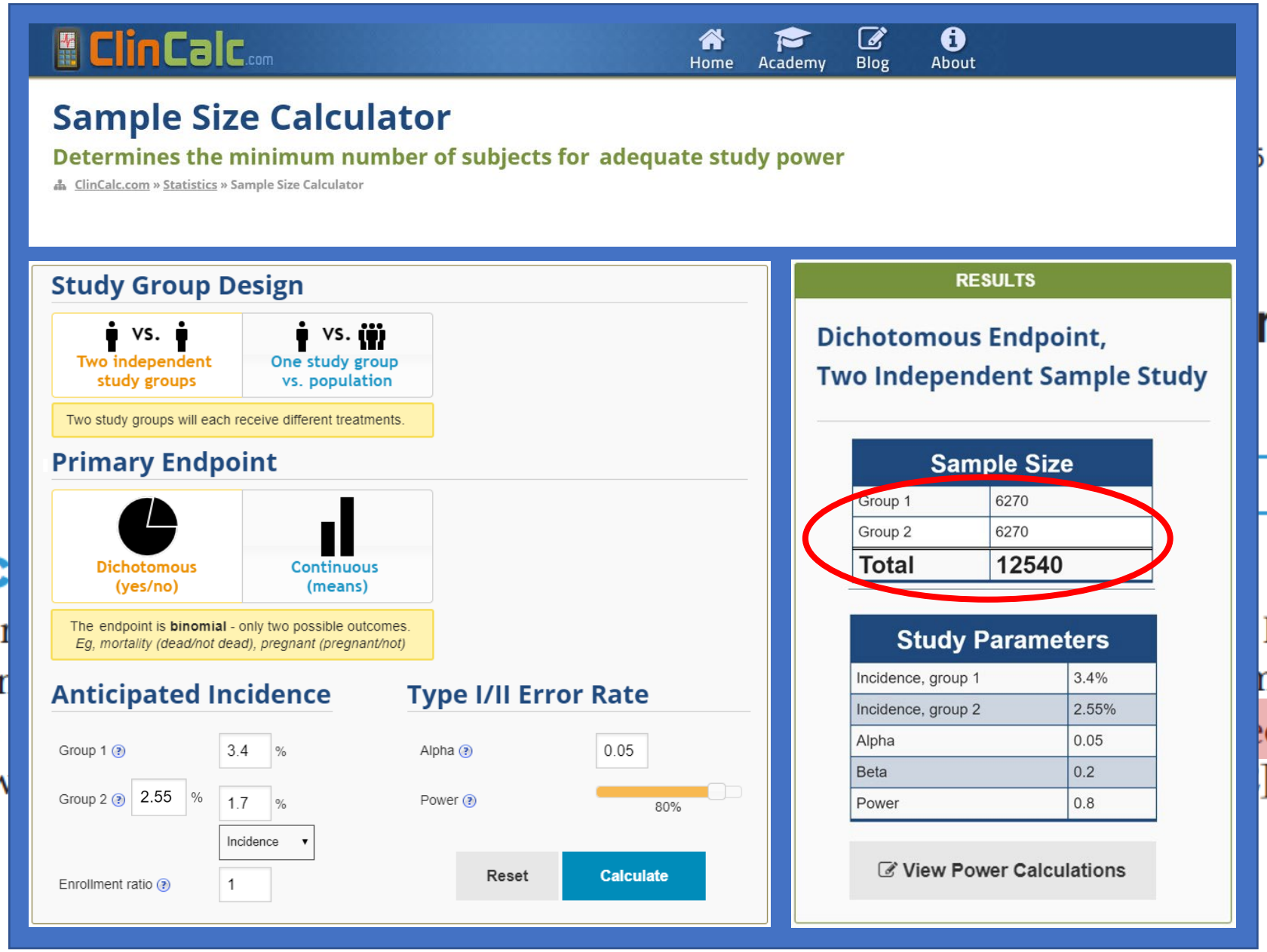




The TEG® hemostasis system continuously measures all phases of hemostasis as a net product of whole blood components.

EMINENCE-BASED

EVIDENCE-BASED



INTRODUC

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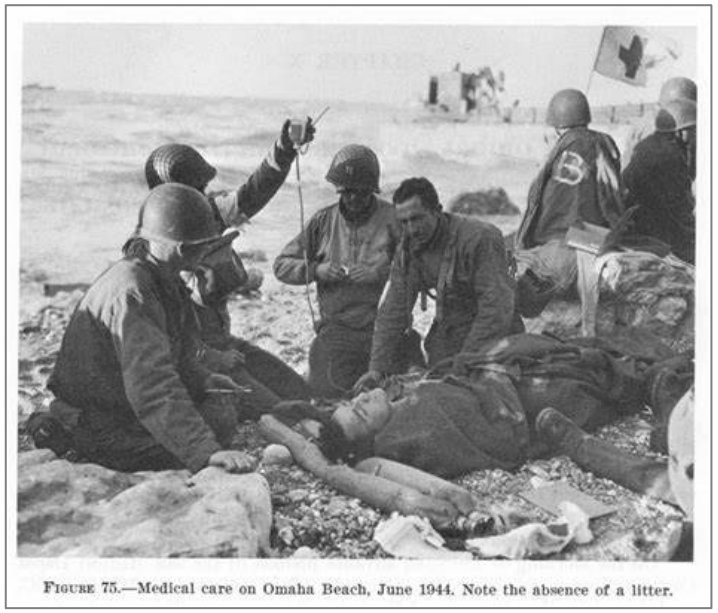


FIGURE 75.—Medical care on Omaha Beach, June 1944. Note the absence of a litter.

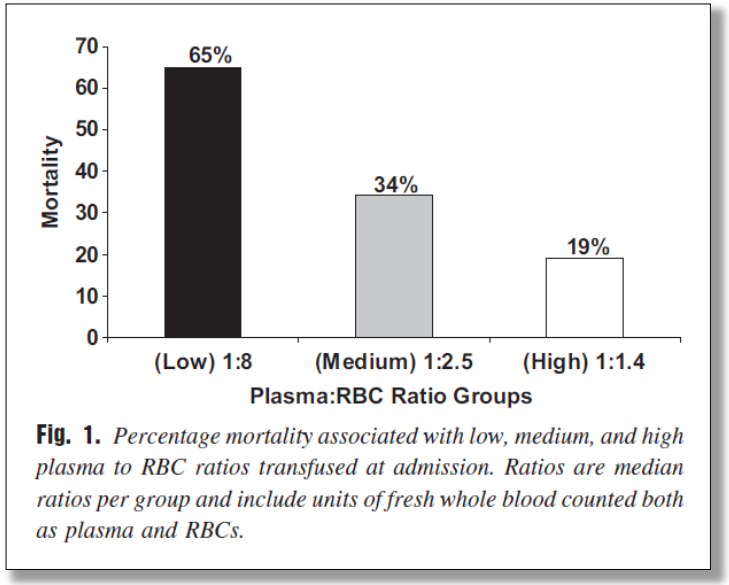
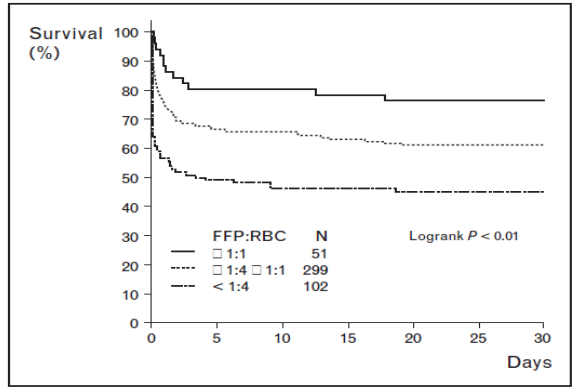


Fig. 1. *Percentage mortality associated with low, medium, and high plasma to RBC ratios transfused at admission. Ratios are median ratios per group and include units of fresh whole blood counted both as plasma and RBCs.*

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



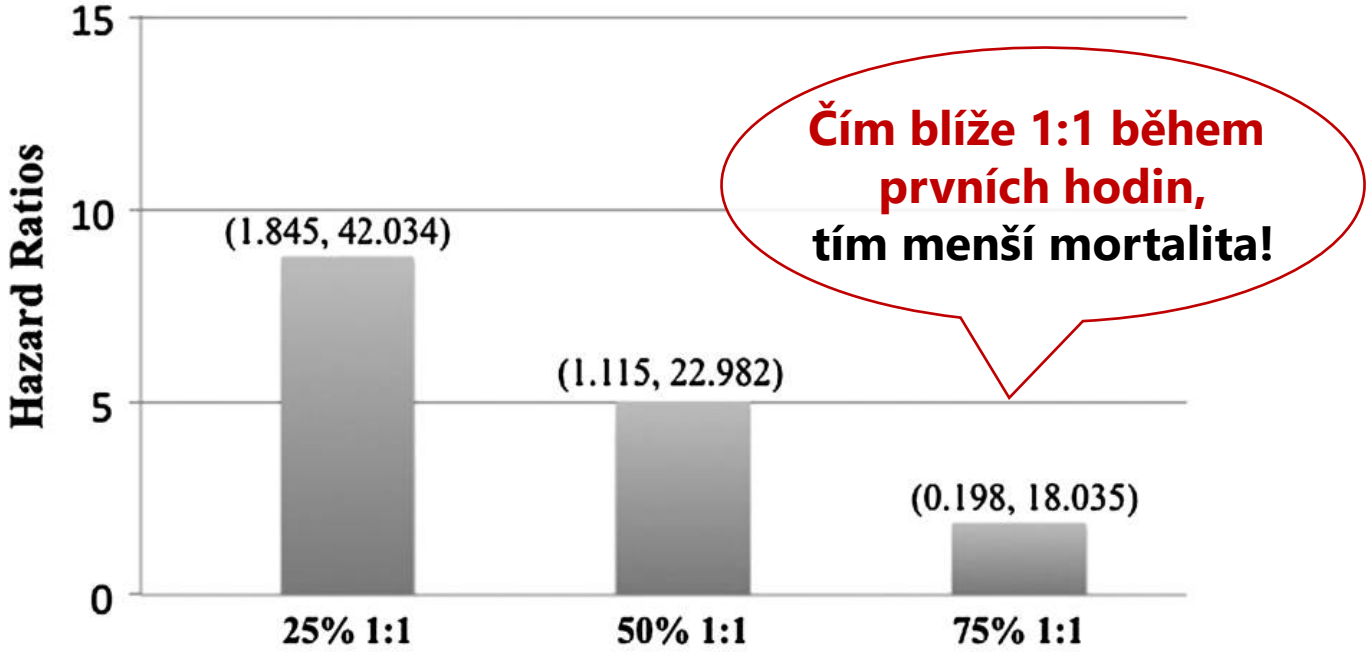
The lowest mortality was observed in the category of patients who received a ratio of fresh frozen plasma : packed red blood cells (FFP : PRBCs) equal to or greater than 1 : 1. Most of the separation of the survival curves occurred immediately after the injury. Data from [16].

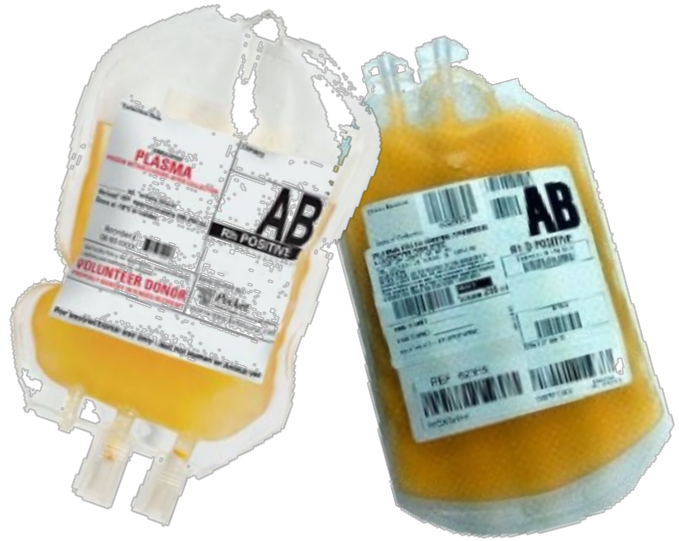
Griffee et al. Current Opinion in Anaesthesiology 2010,23:263–268

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*

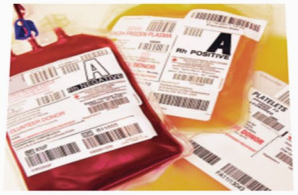
J Trauma Acute Care Surg 2014; Volume 77, Number 6





Reconstructing Deconstructed Blood for Trauma

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



Military medicine has been, and continues to be, at the forefront of many important medical developments and innovations, especially in the area of the care of traumatic injury. The advances made for combat casualty care have had important and lasting impacts on the care of civilian trauma. Included in these have been the treatment of hemorrhagic shock, fluid resuscitation, and transfusion of blood and blood components. In this issue of Anesthesiology, Ho *et al.*[2] examine the evidence for the increased use of plasma in treating major hemorrhage, a practice that began in the U.S. military and that has been embraced in U.S. civilian practice, as well.

"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?"

The ability to separate whole blood into components began with Cohn's separation of plasma into fractions ("fractionation") and his suggestion that they be "explored . . . to determine their possible value in therapy."[3] This eventually created an entire fractionation industry with the ability to isolate various "fractions" with significant therapeutic efficacy for specific disorders. The development of the plastic storage bag and other technological advances, such as component-specific storage/preservation, contributed importantly to the development of component therapy, as well.[4] Thus, clinicians have been able to provide patients with the specific components required, without simultaneously transfusing components that are perceived as not needed, while furnishing them for patients who do need them. Although this strategy has been successful for those circumstances of a deficiency of one specific component, the overall efficacy of this strategy for patients needing more than one, or all components of blood, is questionable and untested. The almost ubiquitous separation of all blood collected in the United States, Canada, and Europe into red cells and plasma (for freezing or further fractionation) proceeded well beyond Cohn's original suggestion, abetted by the development of regional blood centers, rather than individual hospitals, as the major collectors of blood. The few who objected cited the additional cost and effort to transfuse both plasma and packed red cells (PRBC) for those in need of whole blood, especially for massive hemorrhage,[5,6] implying that collection agencies were motivated by aims other than clinical care.[5] However, the need for whole blood was challenged as unsupported by some at the American Red Cross,[7] the largest collector of donated blood in the United States. Patients who bleed sufficient quantities of whole blood require all components contained therein. For the past several decades this has required separate transfusion of PRBCs, plasma, and platelets. Several medical specialty societies, the American Society of Anesthesiologists included, have recommended that plasma be transfused only when there are clinical data/diagnoses to support the need for augmentation of coagulation factors.[8,9]

Based on database analyses of the combat injured,[10] the U.S. military recommends greater use of plasma[11] than has been recommended previously.[9] Consequently, in military in-theater practice the ratio of transfused PRBCs to fresh frozen plasma (FFP) has approached their recommended 1:1

◆ This Editorial View accompanies the following article: Ho AMH, Dion PW, Yeung JHH, Holcomb JB, Critchley LAH, Ng CSH, Karmakar MK, Cheung CW, Rainer TR: Prevalence of survivor bias in observational studies on fresh frozen plasma: Erythrocyte ratios in trauma requiring massive transfusion. Anesthesiology 2012; 116:716–28.

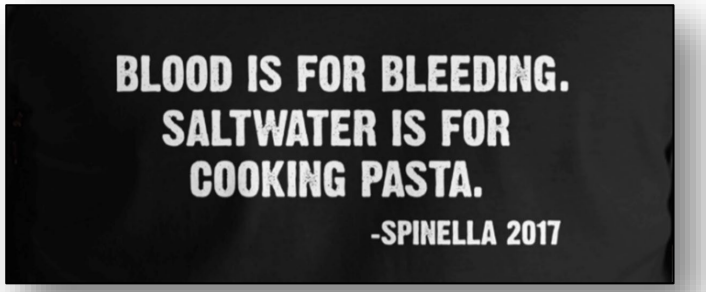
Photograph: J. P. Rathmell.

Accepted for publication October 27, 2011. The author has a relationship with or consults for the following companies and organizations that have an interest in erythrocyte and/or plasma transfusion: US Food and Drug Administration (Rockville, Maryland), US National Heart, Lung, and Blood Institute/National Institutes of Health (Bethesda, Maryland), US Department of Defense (Washington, D.C.), CaridianBCT (Lakewood, Colorado), CSLBehring (King of Prussia, Pennsylvania), Entegrion (Research Triangle, North Carolina), OPK Biotech (Cambridge, Massachusetts), and Sangart Inc. (San Diego, California). The author was project/corp VP and Executive Scientific Advisor at Novo Nordisk A/S (Bagsvaerd, Denmark) 2005–2007.

 Anesthesiology 2012; 116:518–21

M*A*S*H 4077TH

Koncept „WALKING BLOOD BANK“



Red blood cell processing methods and in-hospital mortality: a transfusion registry cohort study

Nancy M Heddle, Donald M Arnold, Jason P Acker, Yang Liu, Rebecca L Barty, John W Eikelboom, Kathryn E Webert, Cyrus C Hsia, Sheila F O'Brien, Richard J Cook

Lancet Haematol 2016
Published Online
March 4, 2016

Summary

Background Quality of red blood cells (RBCs) varies depending on the method of processing the whole blood donation, and the method of processing might affect outcomes in patients transfused RBCs. We aimed to establish whether an association exists between in-hospital mortality and RBC processing method and duration of storage.

Methods We did a retrospective registry cohort study using data from three a
Canada, and Canadian Blood Services over a 6-year period (2008–14). Adult pati
hospital and who received RBC transfusions were included in the study. All tr
the method of processing (red cell filtered or whole blood filtered) and storage a
old 36–42 days). The primary outcome was in-hospital mortality. We used Cox
time-dependent stratification variables and fixed stratification variables, and co

Findings Between April 1, 2008, and March 31, 2014, 91 065 RBC transfusions
included in the analyses. When storage duration was included in the model, i
increased with fresh whole blood filtered units compared with the referen
units (hazard ratio 2·19, 95% CI 1·09–4·42; p=0·033). Differences between
were not significant.

Interpretation The potential effect of whole blood processing methods on p
investigation, since adverse outcomes could be reduced by minor changes to blo
management policies.

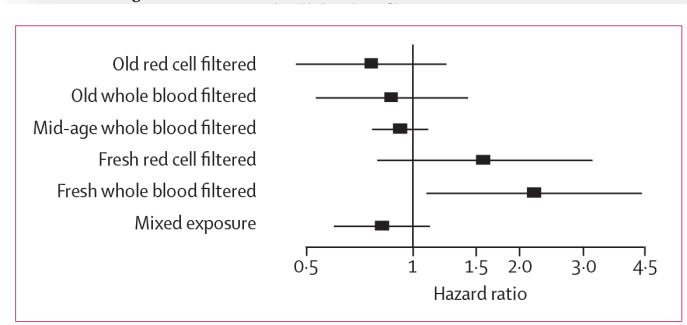


Figure 3: **Forest plot for in-hospital mortality**
Cox regression model for in-hospital mortality for the six categories of red blood cells exposure compared with the reference category. Hazard ratios >1 are associated with a higher risk of death.

Transfusion Medicine Reviews 32 (2018) 28–35

Exploring donor and product factors and their impact on red cell post-transfusion outcomes

Shuoyan Ning [a], Nancy M. Heddle [a,b,*], Jason P. Acker [c,d]

[a] *Department of Medicine, McMaster University, Hamilton, ON, Canada*
[b] *Centre for Innovation, Canadian Blood Services, Hamilton, ON, Canada*
[c] *Centre for Innovation, Product and Process Development, Canadian Blood Services, Edmonton, AB, Canada*
[d] *Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada*

ARTICLE INFO

Available online 31 July 2017

Keywords:
Blood transfusion
Blood donors
Storage
Red blood cells
Outcomes

ABSTRACT

The impact of donor characteristics, red cell a
emerging area of research. Knowledge gener
to change the way donors are selected and h
and operational impact. Recently, donor char
and ethnicity have been shown to affect prod
chemical and immunological changes that occu
ents after 14 randomized clinical trials. However
safety of blood stored for a shorter duration. W
linked to inferior recipient outcomes when comp
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units of red cells are quite the same. This review
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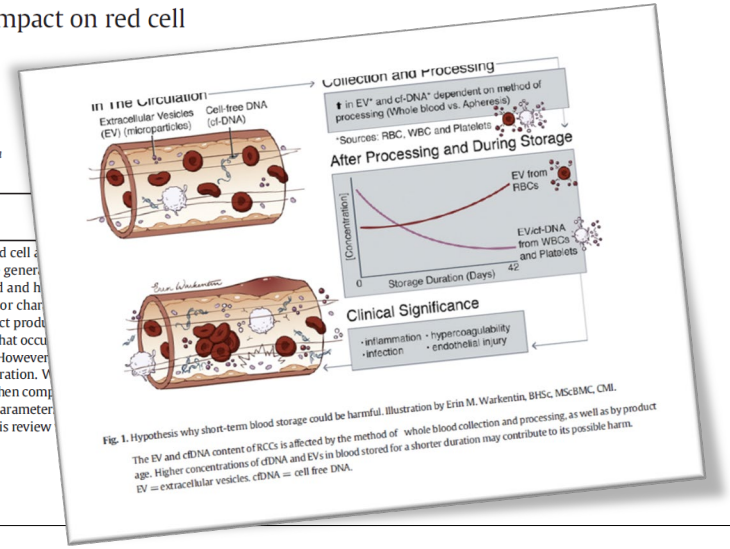


Fig. 1. Hypothesis why short-term blood storage could be harmful. Illustration by Erin M. Warkentin, BHSc, MScBMC, CMI.
The EV and cfDNA content of RCCs is affected by the method of whole blood collection and processing, as well as by product age. Higher concentrations of cfDNA and EVs in blood stored for a shorter duration may contribute to its possible harm. EV = extracellular vesicles. cfDNA = cell free DNA.

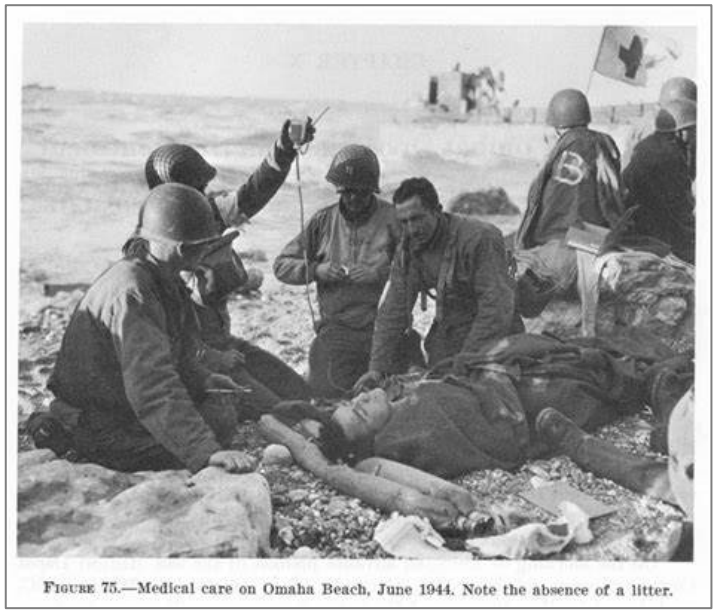


FIGURE 75.—Medical care on Omaha Beach, June 1944. Note the absence of a litter.

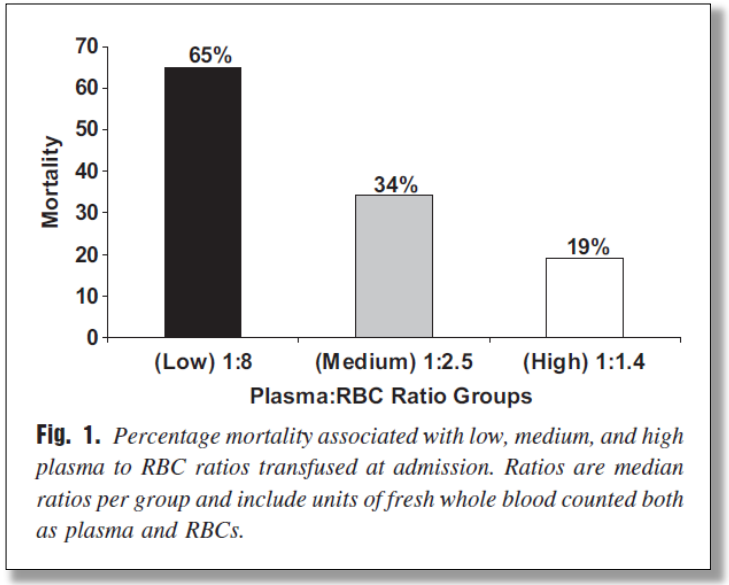
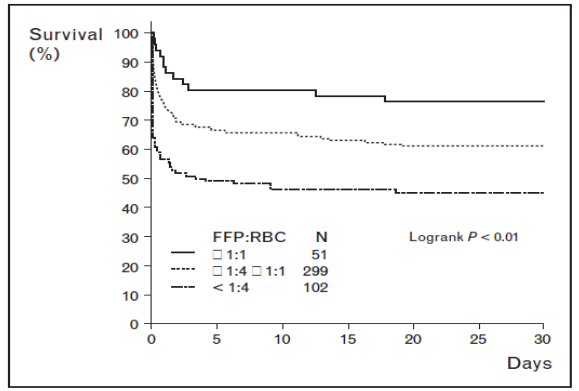


Fig. 1. *Percentage mortality associated with low, medium, and high plasma to RBC ratios transfused at admission. Ratios are median ratios per group and include units of fresh whole blood counted both as plasma and RBCs.*

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

Transport Time and Preoperating Room Hemostatic Interventions Are Important: Improving Outcomes After Severe Truncal Injury

John B. Holcomb, MD, FACS

Holcomb. *Crit Care Med* 2018; 46:447–453

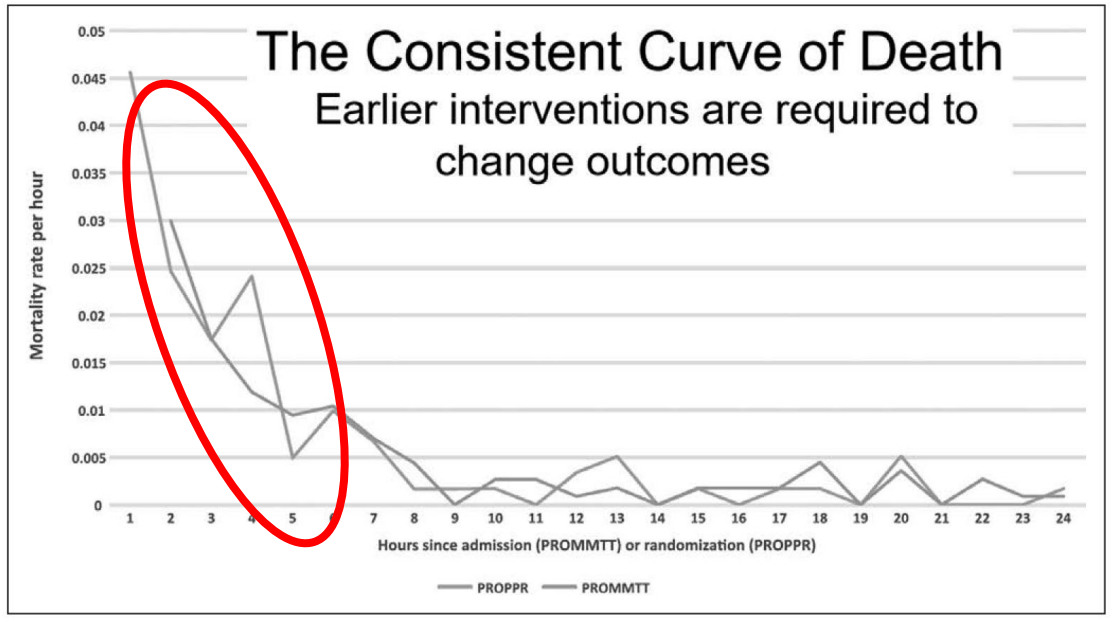


Figure 2. After admission, PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) and Pragmatic Randomized Optimal Platelet and Plasma Ratio (PROPPR) patients die early and at a very reproducible rate, $n = 1{,}925$. Modified from Fox et al (22).

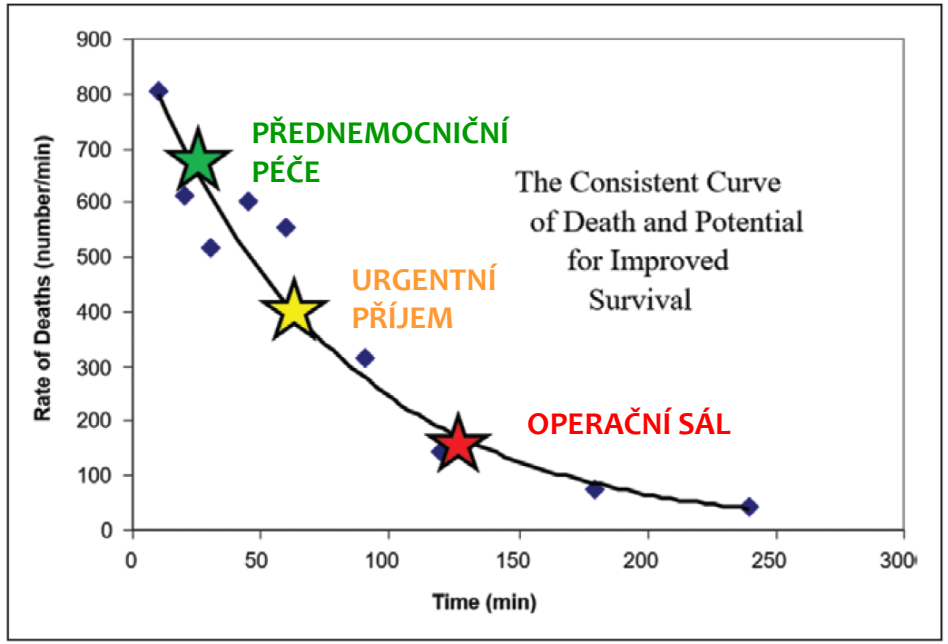


Figure 3. Death versus time: U.S. vehicle-related fatalities from 2003 to 2005. $n = 55{,}537$. Modified from Champion et al (23). ★ Prehospital intervention, ★ emergency department intervention, ★ operating room definitive hemostasis.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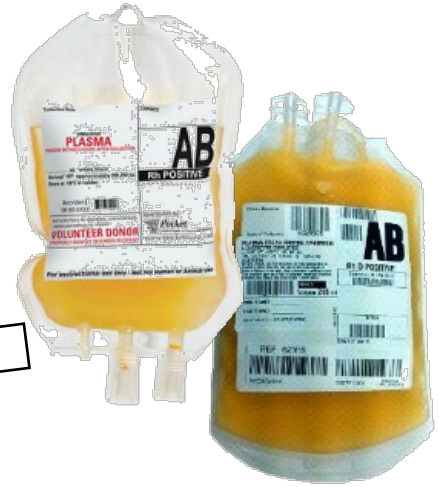
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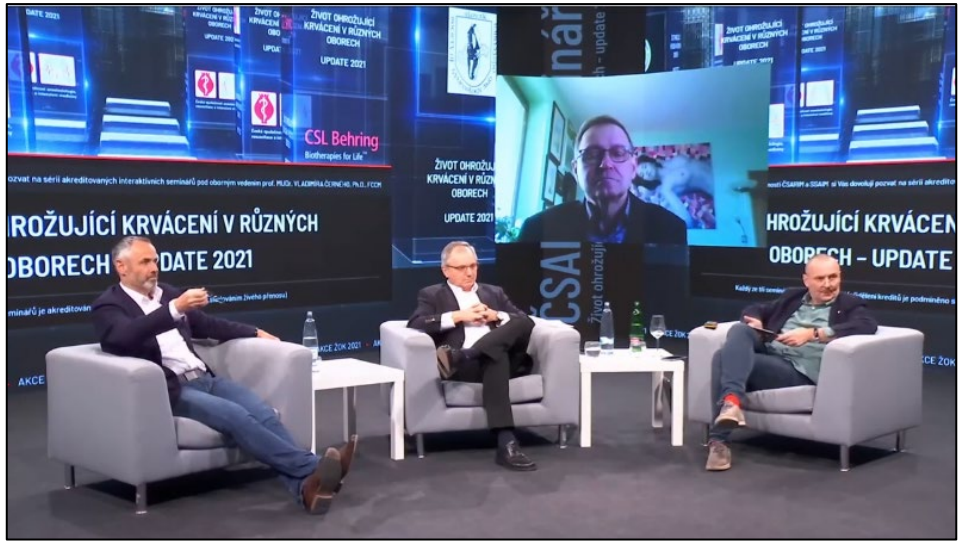
Česká společnost anesteziologie, resuscitace a intenzivní medicíny

Slovenská spoločnosť anestéziológie a intenzívnej medicíny

SEMINÁŘE ŽIVOT OHROŽUJÍCÍ KRVÁCENÍ V RŮZNÝCH OBORECH - UPDATE 2021

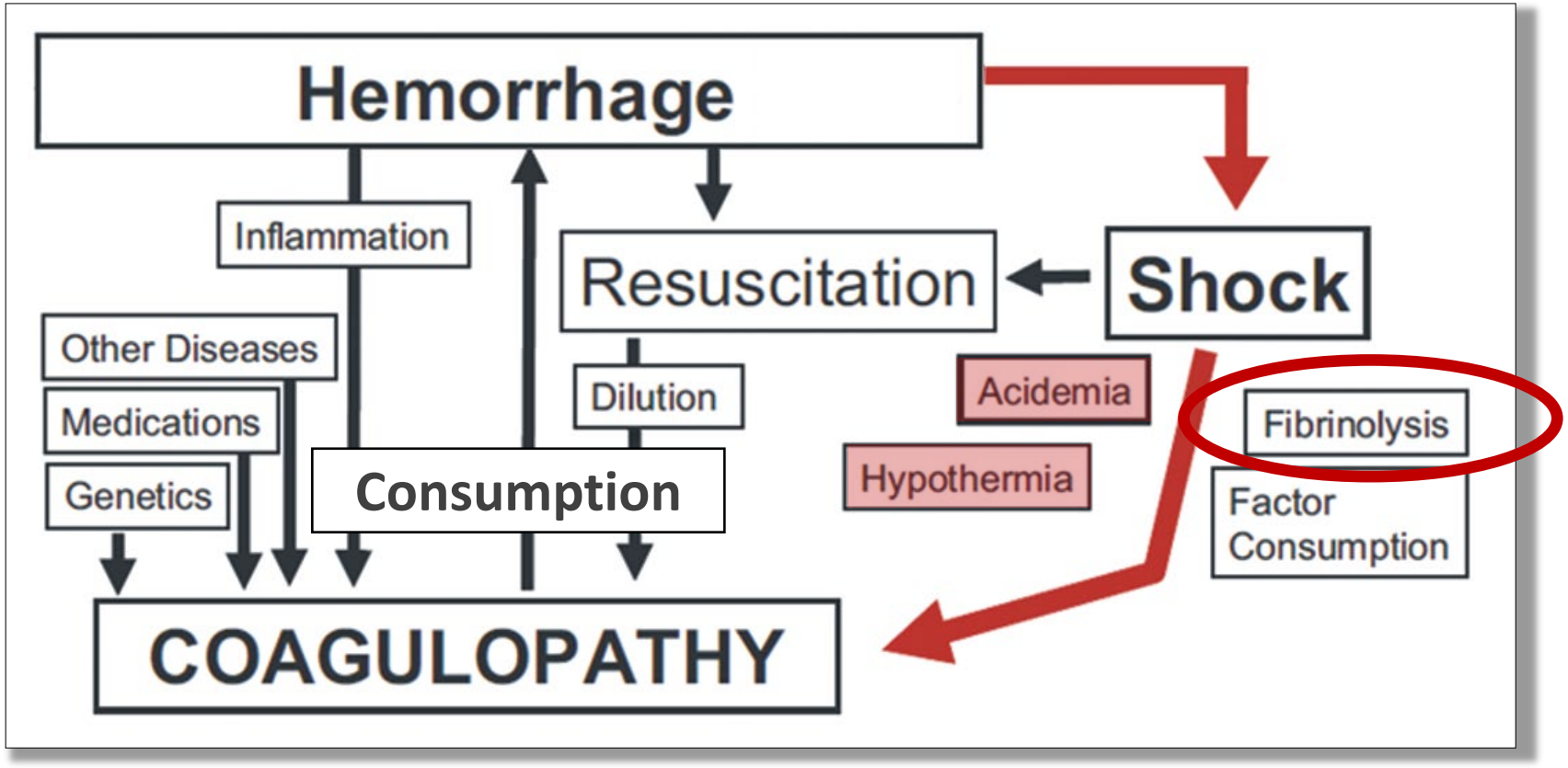
KAŽDÝ ZE TŘÍ SEMINÁŘŮ MÁ JINÝ OBSAH A JE AKREDITOVÁN ČLK



Jaký typ hemokoagulační podpory nejčastěji volíte u rodičky s život ohrožujícím krvácením?

ČERSTVĚ ZMRAŽENOU PLASMU — 30%

FIBRINOGEN — 70%



Adaptováno z Hess et al. J Trauma. 2008;65:748-54

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.

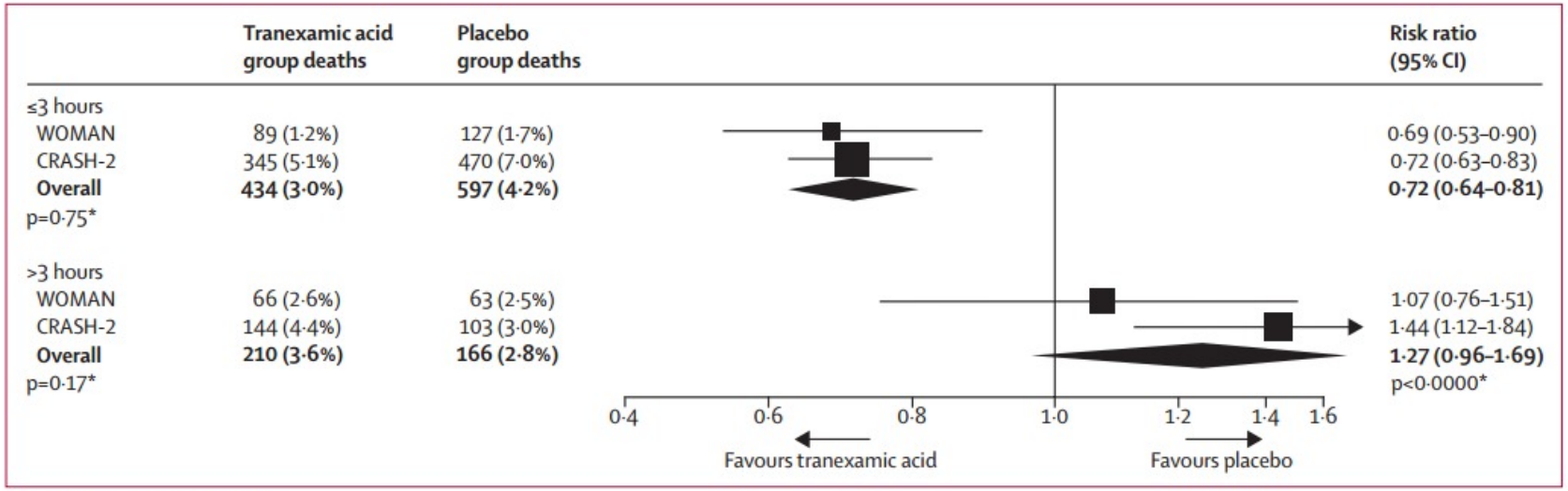


Figure 5: **Time to treatment**
*Heterogeneity p value.

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

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

Injury, Int. J. Care Injured 48 (2017) 1074–1081

Fibrinogen is an independent predictor of mortality in major trauma patients: A five-year statewide cohort study

Zoe K. McQuilten[a,b,*], Erica M. Wood[b], Michael Bailey[a], Peter A. Cameron[c], David J. Cooper[a]

Table 2
Patient outcomes according to fibrinogen level on admission.

Outcome	Less 1 g/L	1–1.5 g/L	1.6–2.0 g/L	2.1–4.0 g/L	Greater than 4 g/L	p-value
Massive transfusion	63 (55.3%)	93 (32.9%)	104 (16.9%)	124 (4.1%)	12 (1.6%)	<0.01
ICU LOS days[a], mean (95% CI)	8 (6, 11)	7.5 (6, 9)	6 (5, 7)	5 (4, 5)	5 (4, 5)	<0.01
Hospital LOS days[a], mean (95% CI)	21 (17, 26)	17 (15, 19)	12 (11, 13)	8 (8, 9)	9 (8, 10)	<0.01
24-h mortality	36 (31.6%)	29 (10.2%)	24 (3.9%)	44 (1.5%)	3 (0.4%)	<0.01
In-hospital mortality	54 (47.4%)	71 (25.1%)	77 (12.5%)	186 (6.2%)	53 (7.2%)	<0.01

ICU – intensive care unit; LOS – length of stay.
[a] Restricted to patients who survived until hospital discharge.

International Journal of Obstetric Anesthesia (2018) **33**, 4–7
0959-289X/$ - see front matter © 2017 Published by Elsevier Ltd.
https://doi.org/10.1016/j.ijoa.2017.08.008

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EDITORIAL

How to replace fibrinogen in postpartum haemorrhage situations? (Hint: Don't use FFP!)

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

1.7. General coagulation management

Fibrinogen concentration of less than 1.5 to 2 g l^{-1} is considered as hypofibrinogenaemia in acquired coagulopathy and is associated with increased bleeding risk. **C**

We recommend treatment of hypofibrinogenaemia in bleeding patients. **1C**

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

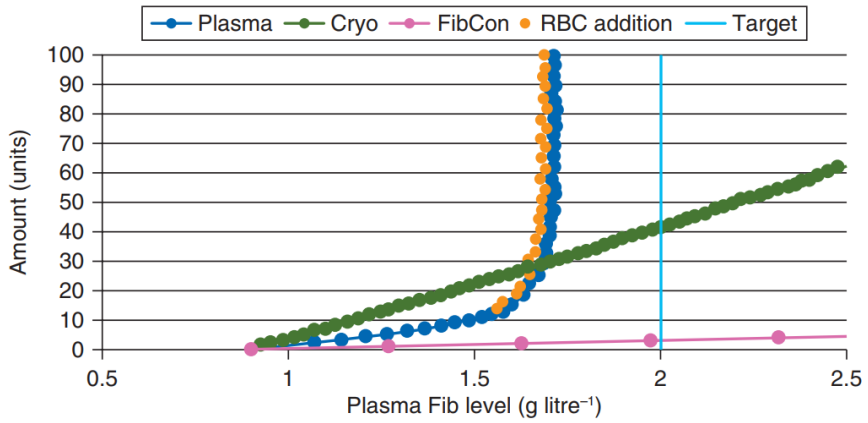
British Journal of Anaesthesia 113 (4): 585–95 (2014)

BJA

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

P. W. Collins[1*], C. Solomon[2,3], K. Sutor[4], D. Crispin[4], G. Hochleitner[5], S. Rizoli[6], H. Schöchl[7,8], M. Schreiber[9] and M. Ranucci[10]

Fib level graph



Submitted: 29 December, 2020 Accepted: 22 January, 2021 Online Published: 09 February, 2021 DOI:10.22514/sv.2021.030

MINIREVIEW

Signa Vitae

Blood management in post-partum haemorrhage, including point of care coagulation tests

Martha Belete[1,†], Edmund Gerrans[1,†], Madhavi Keskar[1,*]

[1]Somerset Foundation Trust, Musgrove Park Hospital, Parkfield Drive, Taunton, TA1 5DA, UK

*Correspondence
madhavi.keskar@so
(Madhavi Keskar)

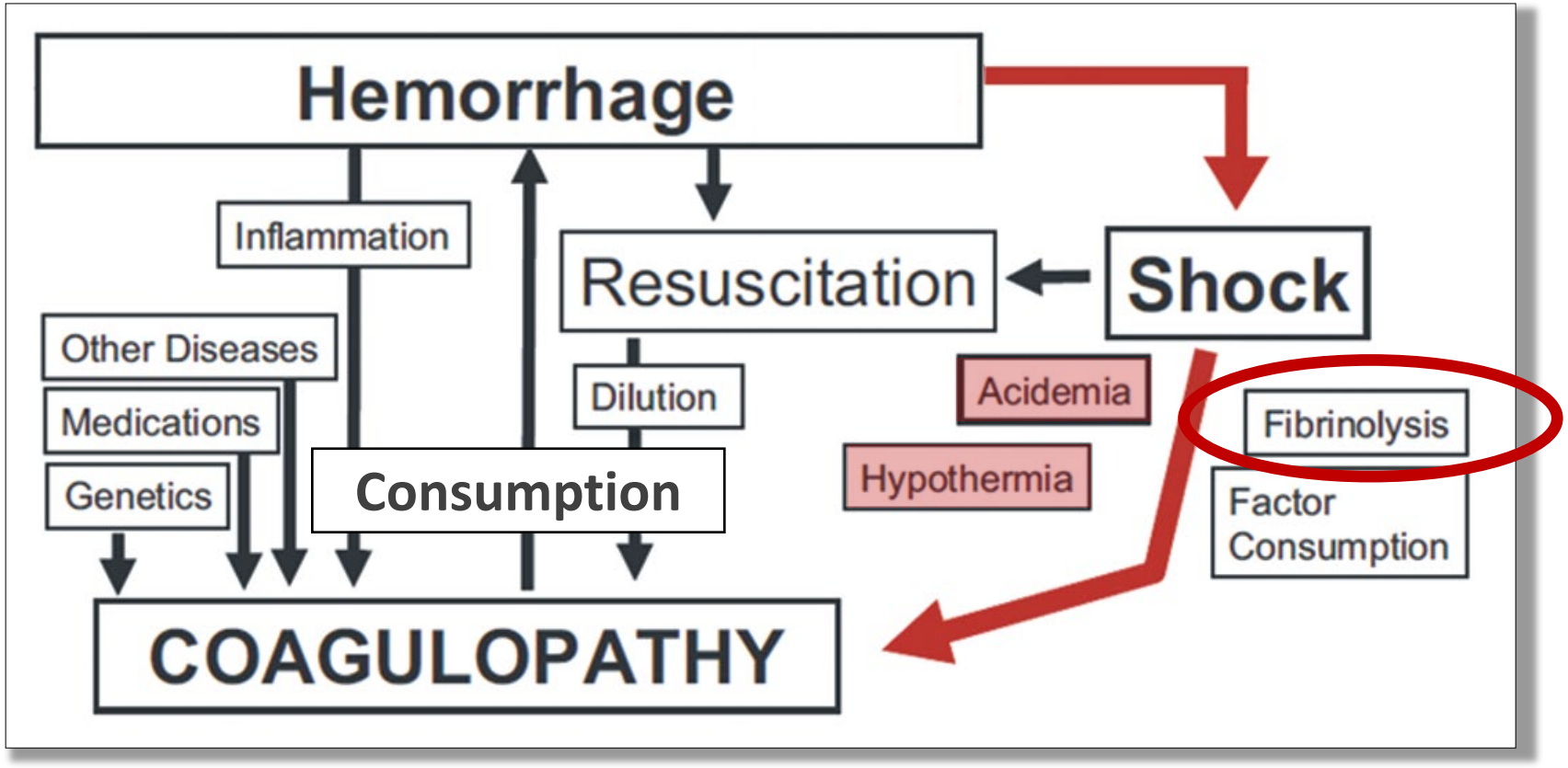
† These authors con

Abstract

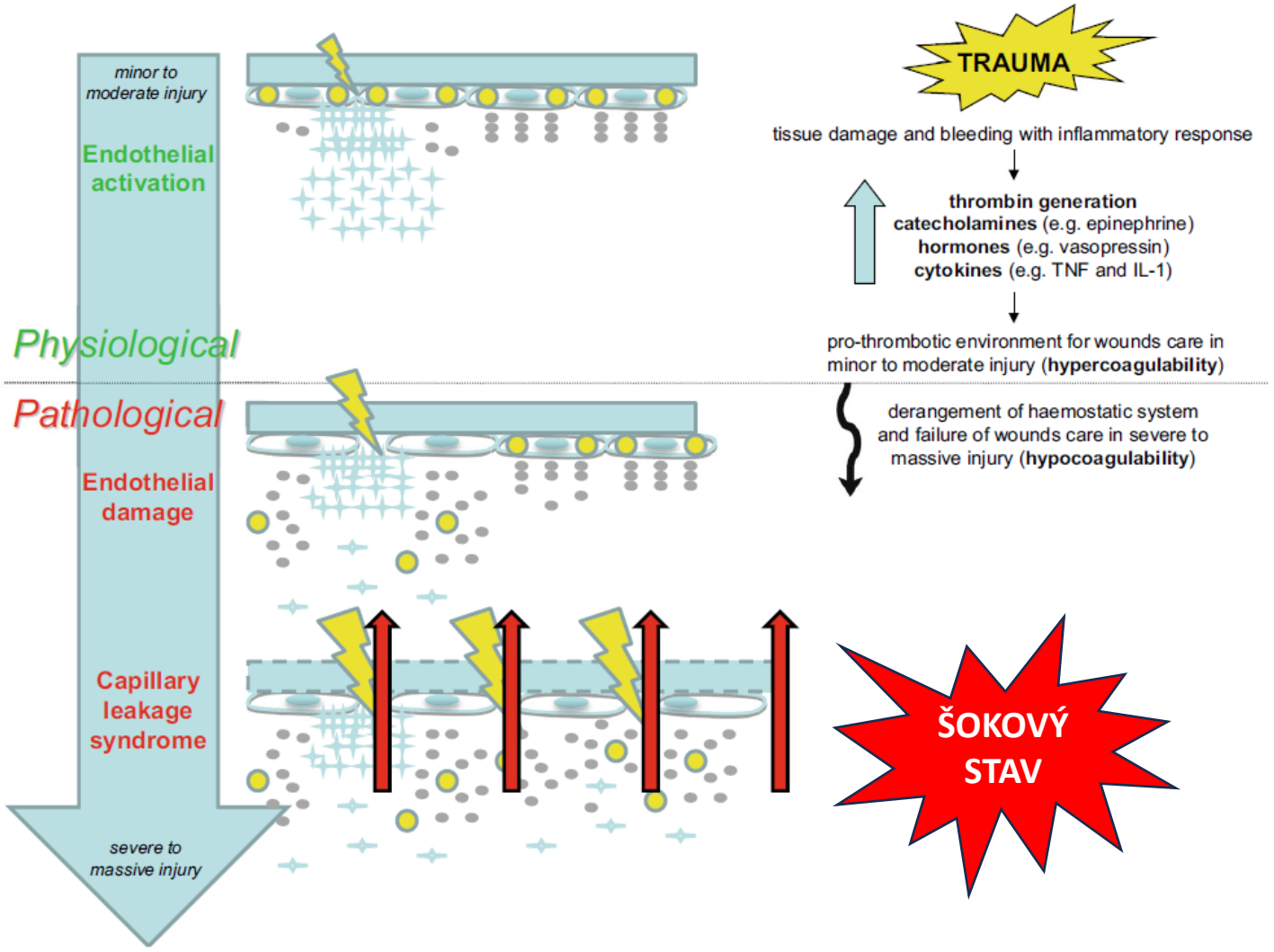
Postpartum haemorrhage (PPH) is the leading global cause of maternal mortality, and an important cause of morbidity and mortality in the UK. Management of PPH requires a patient centred team approach to ensure effective management. Early recognition
rted as soon as
ge. Pregnancy
t state. Blood
xed transfusion
s uncommon in
d transfusion of
ical assessment.
ibrinogen is an
blood products
pidly increasing
n tests such as
EG) allow rapid
ate markers of
d inform blood
e used to safely
fusion rates and
quired to clarify
nt in PPH, with
he use of blood

6.2 Replacing Fibrinogen

Fibrinogen should be replaced either by giving cryoprecipitate or fibrinogen concentrate [1, 55]. Both contain higher concentrations of fibrinogen compared to FFP, which has relatively low concentrations of fibrinogen and can dilute down existing fibrinogen within the circulation [13]. A multicentre double-blinded RCT in primary PPH showed outcomes were not improved when fibrinogen was empirically replaced [59]. 2 pools of cryoprecipitate or 4 g of fibrinogen concentrate should be transfused if FIBTEM A5 7-11 mm or Clauss fibrinogen is < 2 g/L. If FIBTEM A5 < 7 mm then 3 pools of cryoprecipitate or 6 g fibrinogen concentrate should be transfused [55]. Cryoprecipitate requires thawing, which can delay transfusion. Fibrinogen concentrate does not require thawing and so can be more rapidly transfused [13]. If these transfusion triggers are met but bleeding has stopped and there is no clinical concern then fibrinogen replacement can be withheld [40, 55].



Adaptováno z Hess et al. J Trauma. 2008;65:748-54



Giordano S et al. Intern Emerg Med (2017) 12:981–991

Intern Emerg Med (2017) 12:981–991 DOI 10.1007/s11739-017-1674-0

The current understanding of trauma-induced coagulopathy (TIC): a focused review on pathophysiology

Stefano Giordano[1] · Luca Spiezia[1] · Elena Campello[1] · Paolo Simioni[1]
Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, University of Padua, Padua, Italy

Fig. 3 Evolution from progressive endothelial reaction (from physiological activation to pathological damage and capillary leakage) to progressive traumatic damage (from minor to massive injury, indicated with a thunderbolt in the figure). When trauma occurs, tissue damage and bleeding activate the inflammatory response with the generation of greater amounts of thrombin, catecholamines, hormones and cytokines. The aim is to create a pro-thrombotic environment with hypercoagulability capacities that are vital to restore endothelial function after minor-to-moderate injuries. In case of severe-to-massive injuries, a derangement of the haemostatic system takes place resulting in the failure of healing capacities. The final stage is the capillary leakage syndrome with excessive vascular permeability (*red arrow* in the figure) that leads to edema, hypovolemia and hypotension. *DIC* disseminated intravascular coagulation, *ACoTS* acute coagulopathy induced by trauma and shock, *FDPs* fibrinogen degradation products, *TM* thrombomodulin, *EPCR* endothelial protein C receptor, *APC* activated protein C, *EGL* endothelial glycocalyx layer, *Syn1* syndecan-1, *HA* hyaluronic acid, *HS* heparan sulfate, *CS* condroitin sulfate, *WPBs* weibel-palade bodies, *tPA* tissue plasminogen activator, *Ang2* angiopoietin-2, *PAR1* protease activated receptor 1, *TM* thrombomodulin, *APC* activated protein C, *NO* nitric oxide, PGI_2 prostaglandin I_2, *tPA* tissue plasminogen activator. ⟶ directly leads to, ⇢ inhibits, ⇝ indirectly leads to and ⟶ higher/lower levels of

J Trauma Acute Care Surg. 2017 June ; 82(6): S41–S49

Hemorrhagic blood failure: Oxygen debt, coagulopathy and endothelial damage

Nathan J. White, Kevin R. Ward, Shibani Pati, Geir Strandenes and **Andrew P. Cap**

University of Washington Division of Emergency Medicine and Harborview Medical Center

Michigan Center for Integrative Research in Critical Care and University of Michigan Department of Emergency Medicine, Ann Arbor, MI USA

Blood Systems Research Institute and the University of California, San Francisco, CA USA

Norwegian Naval Special Operations Command and Department of Immunology and Transfusion Medicine, Haukeland University Hospital, Bergen, Norway

Coagulation and Blood Research, US Army Institute of Surgical Research, JBSA Fort Sam Houston, TX USA

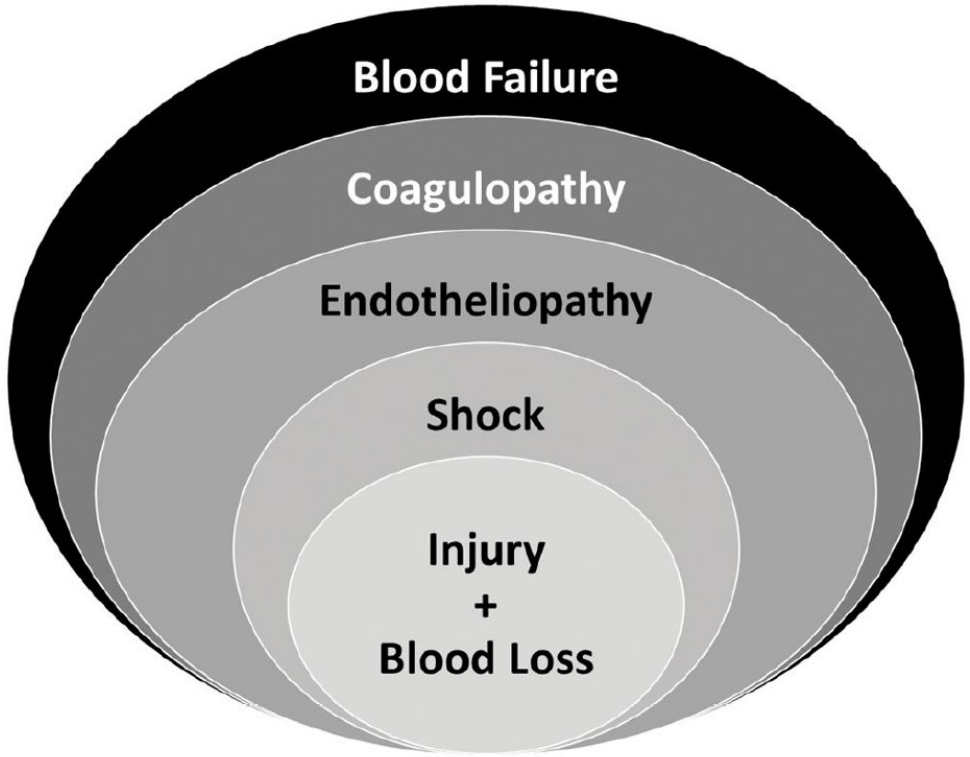


Figure 1.
Schematic representing the components of hemorrhagic blood failure.

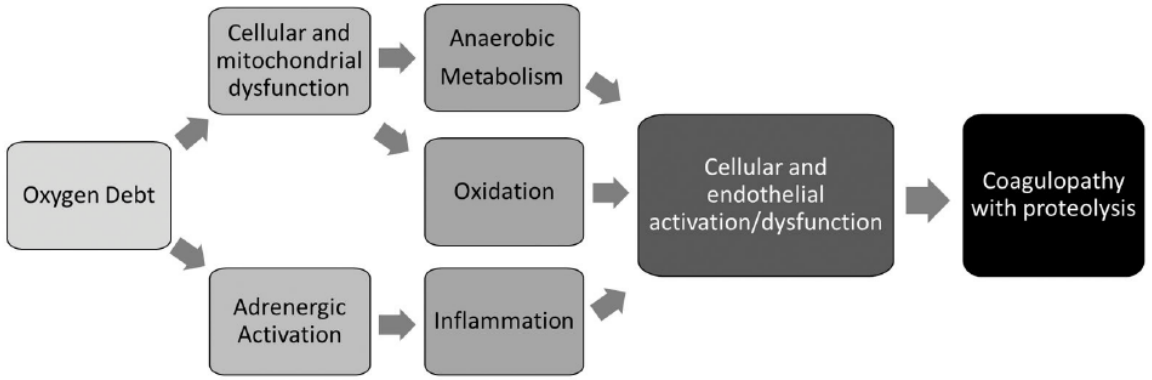


Figure 2.
Schematic of key linkages between oxygen debt, cellular dysfunction, and coagulopathy during hemorrhagic blood failure.

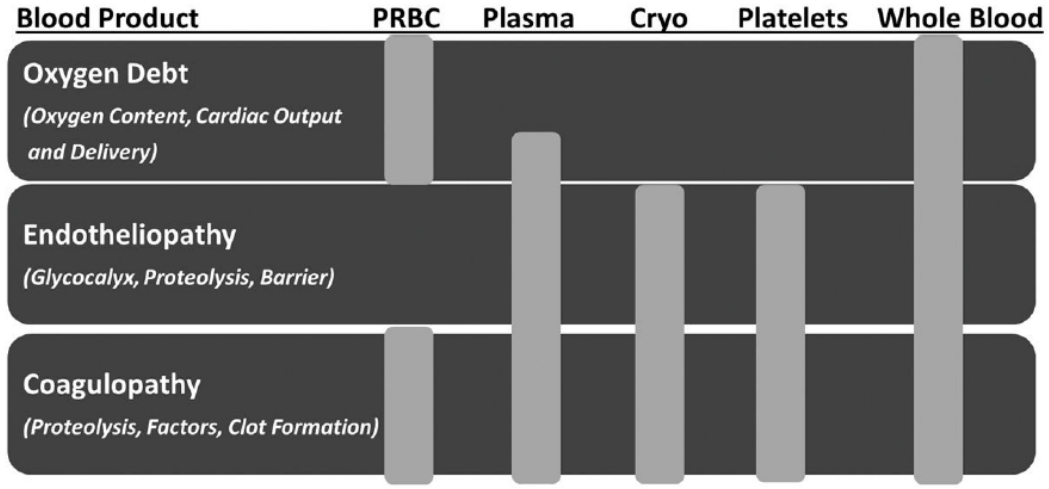
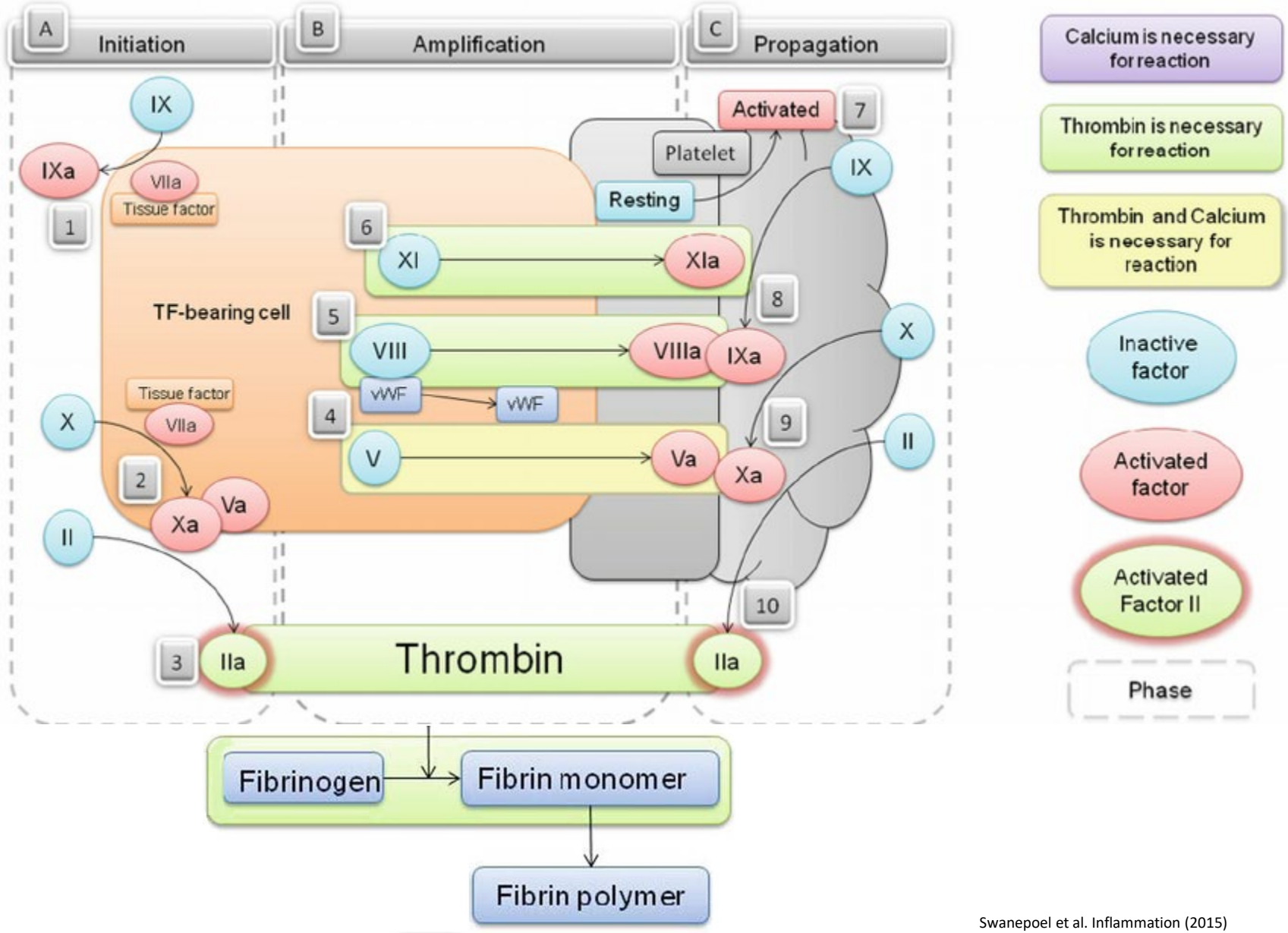
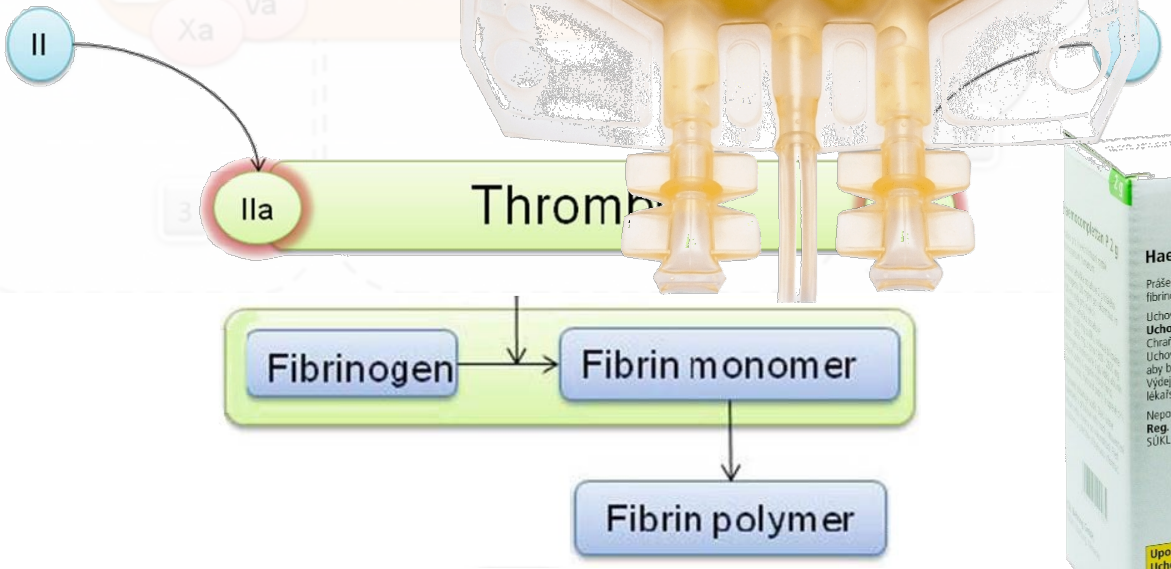


Figure 3.
Schematic summarizing the effects of individual blood products on the three components of hemorrhagic blood failure. PRBC= packed red blood cells, Cryo= cryoprecipitate



Swanepoel et al. Inflammation (2015)

Swanepoel et al. Inflammation (2015)



Swanepoel et al. Inflammation (2015)

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Octaplas® neobsahuje zjistitelné hladiny leukocytárních a granulocytárních protilátek[14]

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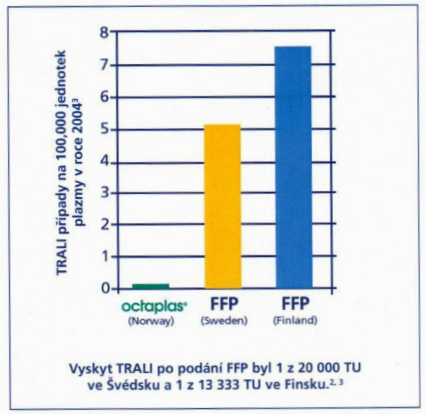
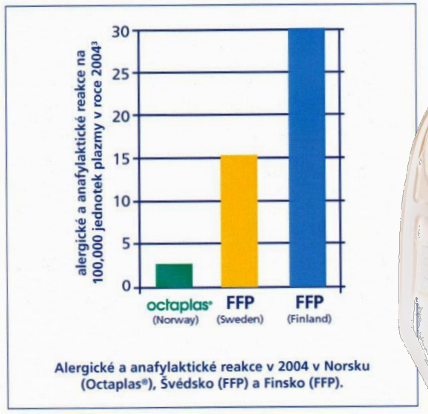
V souvislosti s podáváním přípravku Octaplas nebyl hlášen žádný případ TRALI[15, 16]

U přípravku Octplas bylo pozorováno méně alergických a anafylaktických reakcí nez u FF



Vyskyt TRALI po podání FFP byl 1 z 20 000 TU ve Švédsku a 1 z 13 333 TU ve Finsku.[2, 3]



Alergické a anafylaktické reakce v 2004 v Norsku (Octaplas®), Švédsko (FFP) a Finsko (FFP).

solvent/detergent plazma je farmaceutický produkt
se standardizovaným obsahem koagulačních faktorů,
bez protilátek podílejících se na patogenezi TRALI,
a s velmi vysokou úrovní dekontaminace od infekčních agens

British Journal of Anaesthesia **106** (4): 505–11 (2011)
Advance Access publication 9 February 2011 · doi:10.1093/bja/aer003

BJA

Relative concentrations of haemostatic factors and cytokines in solvent/detergent-treated and fresh-frozen plasma

O. M. Theusinger[1*†], W. Baulig[1†], B. Seifert[4], M. Y. Emmert[3], D. R. Spahn[1] and L. M. Asmis[2]

[1] Institute of Anaesthesiology, [2] Division of Haematology and [3] Clinic of Cardiac and Vascular Surgery, University Hospital Zurich, Zurich, Switzerland
[4] Biostatistics Unit, Institute of Social and Preventive Medicine, University of Zurich, Switzerland

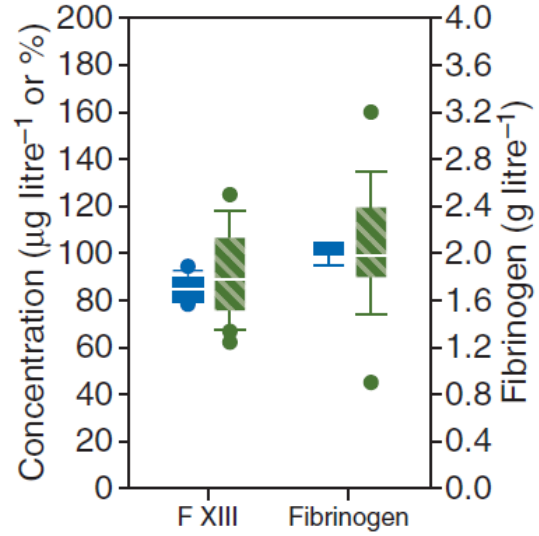
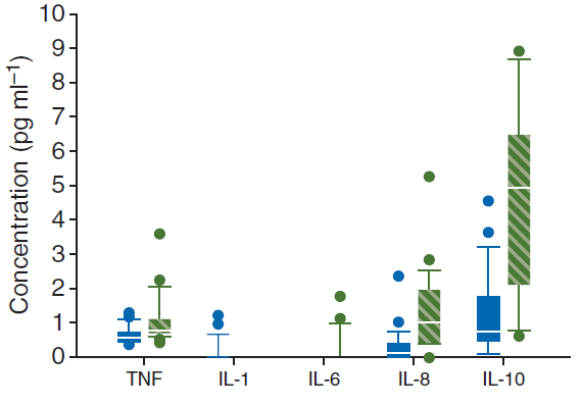


Fig 1 Haemostatic parameters and cytokine levels in SDP (blue bars) and FFP samples (green striped bars).



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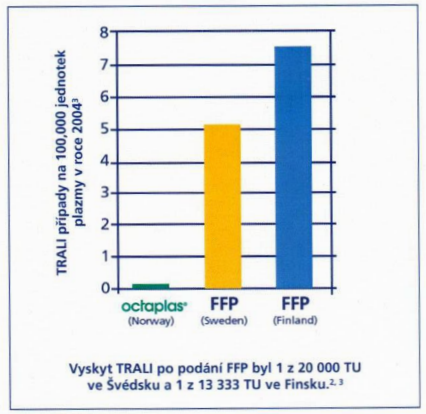

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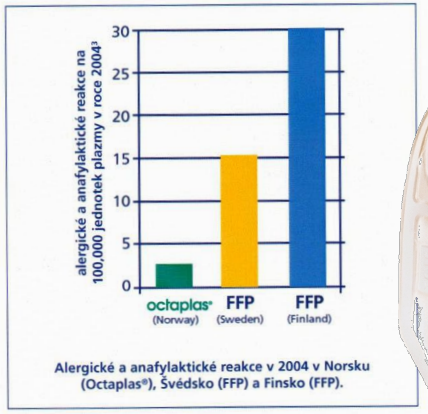

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bez protilátek podílejících se na patogenezi TRALI,
a s velmi vysokou úrovní dekontaminace od infekčních agens

All plasma products are not created equal: Characterizing differences between plasma products

Philip C. Spinella, MD, Elfaridah Frazier, PhD, Heather F. Pidcoke, MD, PhD, Dennis J. Dietzen, PhD, Shibani Pati, MD, PhD, Oleg Gorkun, PhD, James K. Aden, PhD, Philip J. Norris, MD, *and* Andrew P. Cap, MD, PhD, *St. Louis, Missouri*

Sysmex	cells/μL		
	RBC	WBC	Platelets
FFP	100 (0.0–125)*	0.5 (0.0–25.3)	800 (450–1,450)*
SD	0 (0.0–0.0)	0 (0.0–1.3)†¶	0 (0.0–0.0)*

Flow cytometry	cells/μL		
	RBC	WBC	Platelets
FFP	233.5 (103.8–415.8)	0.0 (0.0–9.5)‖	959.0 (784.8–1,514.0)*‖
SD	125.5 (83.0–210.0)	7.0 (3.0–9.8)	700.5 (303.8–782.0)†

Values presented as median with IQR. For all significant comparison, $p \leq 0.05$.

*Significant between FFP versus SDP.


STOP

Anaesthesia 2019, 74, 180–189 doi:10.1111/anae.14495

Fibrinogen concentrate vs. fresh frozen plasma for the management of coagulopathy during thoraco-abdominal aortic aneurysm surgery: a pilot randomised controlled trial

G. A. Morrison,[1] J. Koch,[1] M. Royds,[1] D. McGee,[2] R. T. A. Chalmers,[3] J. Anderson[4] and A. F. Nimmo[1]

1 Consultant, Department of Anaesthesia, 3 Consultant, Department of Vascular Surgery, 4 Consultant, Department of Haematology, Royal Infirmary of Edinburgh, Scotland, UK

Summary

Major vascular surgery is frequently associated with significant blood loss and coagulopathy. Existing evidence suggests hypofibrinogenaemia develops earlier than other haemostatic deficiencies during major blood loss. The purpose of this study was to assess whether the use of an infusion of fibrinogen concentrate to prevent and treat hypofibrinogenaemia during surgery resulted in satisfactory haemostasis, removing or reducing the need for blood component transfusion. Twenty patients undergoing elective extent-4 thoraco-abdominal aortic aneurysm repair were randomly allocated to receive either fresh frozen plasma or fibrinogen concentrate to treat hypofibrinogenaemia during surgery. Coagulation was assessed during and after surgery by point-of-care and laboratory testing, respectively, and treatment was guided by pre-defined transfusion triggers. Despite blood losses of up to 11,800 ml in the patients who received the fibrinogen concentrate, none required fresh frozen plasma during surgery, and only two required platelet transfusions. The median (IQR [range]) allogeneic blood component administration during surgery and in the first 24 h was 0 (0–0 [0–2]) units in patients allocated to fresh frozen plasma vs. 4.5 (3–11 [0–19]) units in patients allocated to fibrinogen concentrate (p = 0.011). All patients in both groups were assessed as having adequate haemostasis at the end of surgery. Mean (SD) postoperative fibrinogen concentrations were similar in patients allocated to fresh frozen plasma and fibrinogen concentrate (1.6 (0.3) g.l^{-1} vs. 1.6 (0.2) g.l^{-1}; p = 0.36) but the mean (SD) international normalised ratio and activated partial thromboplastin time ratio were lower in patients allocated to fresh frozen plasma (1.1 (0.1) vs. 1.8 (0.3); p < 0.0001 and 1.1 (0.2) vs. 1.7 (0.5); p = 0.032, respectively). Fibrinogen concentrate may be used as an alternative to fresh frozen plasma in the treatment of coagulopathy during thoraco-abdominal aortic aneurysm repair.

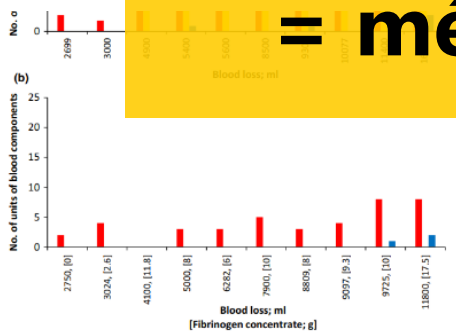

Figure 2 Blood component administration (red = packed red cells, yellow = fresh frozen plasma, blue = platelets) during surgery for each patient randomly allocated to receive either fresh frozen plasma (FFP) (a) or fibrinogen concentrate (b) during thoraco-abdominal aortic aneurysm surgery. Blood loss and fibrinogen concentrate administration during surgery is also shown.

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

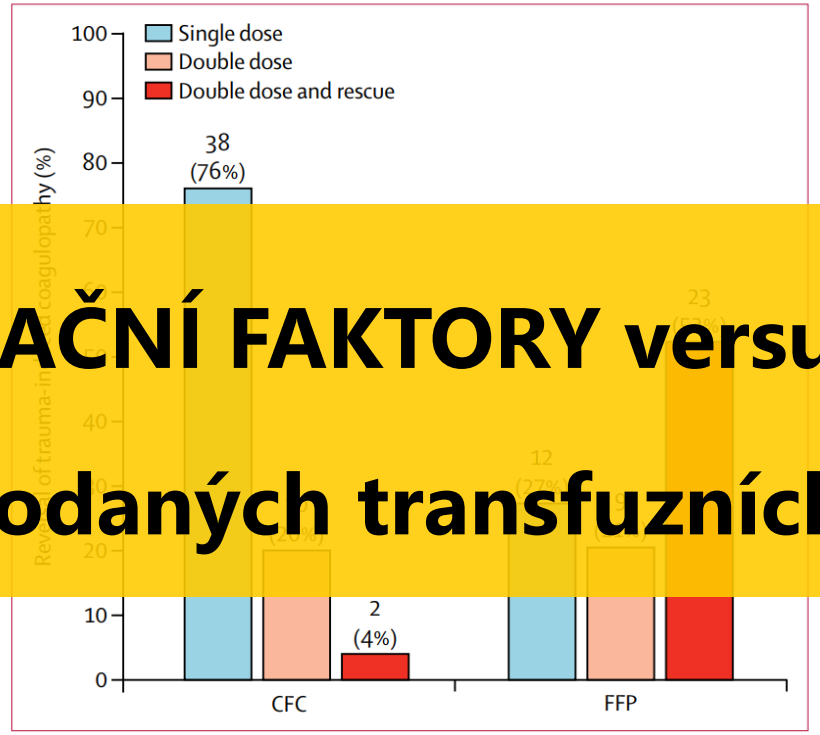

Figure 3: **Percentage of patients with reversal of coagulopathy after either single-dose or double-dose study drug administration during the first therapy loop, and percentage of patients needing double-dose and rescue medication during the first 24 h in the intention-to-treat population** CFC=coagulation factor concentrates. FFP=fresh frozen plasma.

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	7.00 ± 1.93	>0.05
PT%	58.5 ± 16.6	59.5 ± 19.8	>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

e treatment, and 0 units of red blood

ercentage; RCC, red cell ntrate; F, fresh frozen plasma alone.

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NÁZEV	**PLAZMA** **(P)**
DEFINICE	Plazma z plné krve se získá zpracováním 1 TU plné krve odebrané jednomu dárci do 63 ml antikoagulačního roztoku CPD. Při centrifugaci se uzavřeným způsobem plazma oddělí a rychle zmrazí. Při zpracování přejde do plazmy 95 % původního roztoku CPD, který obsahuje: kys. citronová 0, g, hydrogenfosfát sodný 0,139 g, dextroza 1,606 g Zmrazená plazma se ponechává v karanténě 6 ke klinickému použití musí být dárce opětně pře (s negativními výsledky). Ke snížení rizika TRALI je na plazma od dárců s malou pravděpodobností přítor m (muži, ženy bez anamnézy těhotenství). Před podáním se plazma rozmrazuje v lázni o te **na vyšší teplotu, plazma by se znehodnotila !)**
VLASTNOSTI	Objem jedné jednotky plazmy je 260 ml ± 40 ml Kontaminace trombocyty méně než 50 x 10^9/ TU TU; erytrocyty méně než 6 x 10^9/ TU Zachovány jsou labilní koagulační faktory (FVIII alespoň 70% výchozí hladiny).

JAMA Surgery | Original Investigation

Association of Perioperative Red Blood Cell Transfusions With Venous Thromboembolism in a North American Registry

Ruchika Goel, MD, MPH; Eshan U. Patel, MPH; Melissa M. Cushing, MD; Steven M. Frank, MD; Paul M. Ness, MD; Clifford M. Takemoto, MD; Ljiljana V. Vasovic, MD; Sujit Sheth, MD; Marianne E. Nellis, MD; Beth Shaz, MD; Aaron A. R. Tobian, MD, PhD

Table 4. Subgroup Analysis by Surgical Subspecialty of the Association Between Any Perioperative RBC Transfusion and the Development of Postoperative VTE[a]

Surgical Subspecialty[b]	Total No. of Patients	No. of Patients Receiving a Transfusion	No. (%) of Patients Who Developed VTE		OR (95% CI)[c]	Adjusted OR (95% CI)
			No Transfusion	Transfusion		
General surgery	360 397	16 931	2242 (0.7)	778 (4.6)	7.3 (6.7-8.0)	2.3 (2.1-2.5)
Neurosurgery	37 442	1900	401 (1.1)	97 (5.1)	4.7 (3.8-5.9)	2.4 (1.8-3.1)
Cardiothoracic surgery	13 113	2764	123 (1.2)	75 (2.7)	2.3 (1.7-3.1)	1.8 (1.2-2.5)
Orthopedic surgery	153 320	12 641	1142 (0.8)	280 (2.2)	2.8 (2.4-3.2)	1.7 (1.5-2.0)
Vascular surgery	49 582	7197	274 (0.7)	162 (2.3)	3.5 (2.9-4.3)	2.5 (2.0-3.2)
Gynecological surgery	55 339	2933	188 (0.4)	92 (3.1)	9.0 (7.0-11.6)	2.9 (2.1-4.0)[d]
Urological surgery	39 632	2388	230 (0.6)	101 (4.2)	7.1 (5.6-9.0)	2.9 (2.2-3.9)[d]

Asociace mezi perioperační TRF a výskytem VTE v prvních 30 dnech po operaci !

Transfusion Clinique et Biologique 24 (2017) 277–284

State of art

The storage lesions: From past to future

Les lésions de stockage : entre peurs rétrospectives et perspectives

J.-D. Tissot[a,b,*], M. Bardyn[a], G. Sonego[a], M. Abonnenc[a], M. Prudent[a,b]

[a] *Transfusion interrégionale CRS, Laboratoire de Recherche sur les Produits Sanguins, 2, route de la Corniche, CH-1066 Epalinges, Switzerland*
[b] *Faculté de biologie et de médecine, université de Lausanne, Lausanne, Switzerland*

Available online 30 June 2017

Abstract

Red blood cell (RBC) concentrates are s
at 22 °C with continuous agitation for up tc
Storage induces cellular lesion and alters eitl
prove reversible, while other changes are i
blood component quality and thus the transf
both RBCs and PCs. Uncertainty is not con
older blood products; however, no clear si
understanding of the occurrence of storage
advancement of blood transfusion processes
in charge of planning and controlling clini
principles, but also on clinical evidences.

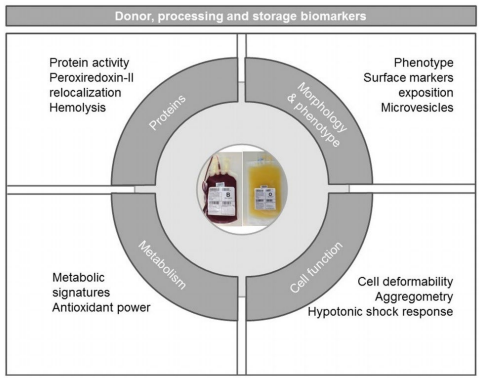

Fig. 2. Key parameters of the storage lesions: a virtuous circle to be considered.

Thrombosis Research 165 (2018) 54–60

Contents lists available at ScienceDirect

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Full Length Article

Postpartum blood transfusion and hemorrhage as independent risk factors for venous thromboembolism

L. Thurn[a], A. Wikman[b], P.G. Lindqvist[c,*]

[a] *Department of Obstetrics*
[b] *Department of Clinical Im*
[c] *Department of Obstetrics*

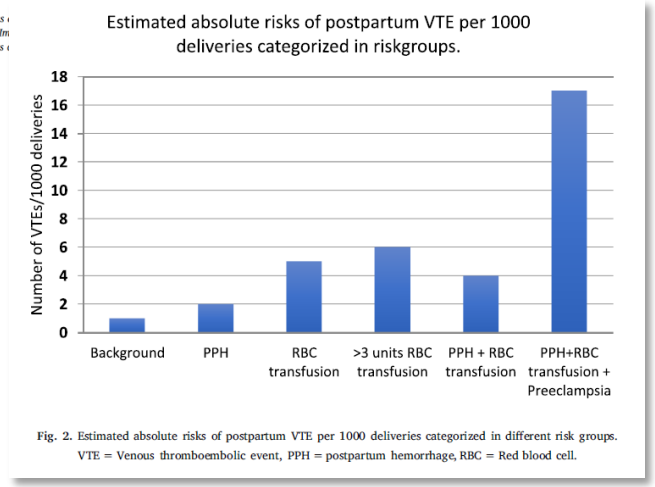


Fig. 2. Estimated absolute risks of postpartum VTE per 1000 deliveries categorized in different risk groups. VTE = Venous thromboembolic event, PPH = postpartum hemorrhage, RBC = Red blood cell.

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? (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.

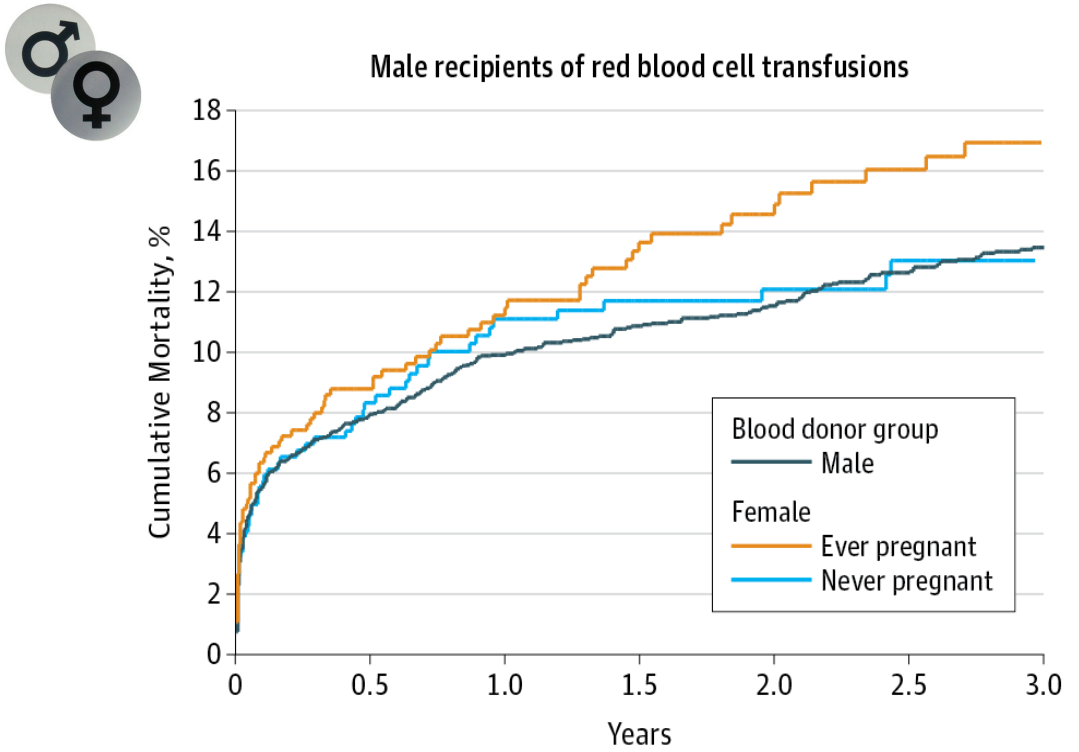
Madjdpour et al. Crit Care Med 2006; 34:S102–S108

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

Camila Caram-Deelder, MSc[1,2]; Aukje L. Kreuger, MD[1,2]; Dorothea Evers, MD[1,3]; et al » Author Affiliations

JAMA. 2017;318(15):1471-1478. doi:10.1001/jama.2017.14825



No. at risk by donor group							
Male	6189	2408	2102	1833	1624	1421	1236
Female							
Ever pregnant	1190	438	367	305	245	197	163
Never pregnant	1084	393	331	279	225	177	146

Prothrombin complex concentrate (PCC)

4F-PCC = koncentrát faktorů II, VII, IX a X + protein C a S

Anesthesiology 2015; 122:923–31

Prothrombin Complex Concentrates in Trauma and Perioperative Bleeding

Oliver Grottke, M.D., Ph.D., Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M.

		Coagulation Factors (IU/ml)				Anticoagulant Proteins (IU/ml)				
Product	Availability	Factor II	Factor VII	Factor IX	Factor X	Protein C	Protein S	Antithrombin	Heparin (IU/ml)	Volume per Vial (ml)*
Bebulin VH (Baxter Healthcare Corporation, USA)	United States	24–38	<5	24–38	24–38	N/A	N/A	N/A	<0.15†	20 ml
Profilnine SD (Grifols, USA)	United States	1.5†	0.35†	100‡	1†	N/A	N/A	N/A	None	5 ml (500 IU); 10 ml (1,000 & 1,500 IU)
Prothromplex TIM 3 (Baxter, USA)	Europe	25	N/A	25	25	N/A	N/A	N/A	3.75	N/A
Uman Complex DI (Kedrion, Italy)	Italy	25	N/A	25	20	N/A	N/A	N/A	N/A	20 ml
Beriplex P/N, Confidex, or Kcentra (CSL Behring, Germany)	Europe, Canada, United States	20–48	10–25	20–31	22–60	15–45	12–38	0.2–1.5	0.4–2.0	10 ml (250 IU); 20 ml (500 IU); 40 ml (1,000 IU)
Cofact/PPSB SD (Sanquin/CAF, The Netherlands)	Europe	≥15	≥5	≥20	≥15	N/A	N/A	N/A	N/A	10 ml (250 IU); 20 ml (500 IU)
Kaskadil (LFB, France)	France	40	25	25	40	N/A	N/A	N/A	N/A	10 ml (250 IU); 20 ml (500 IU)
Octaplex (Octapharma, Austria)	Europe, Canada	14–38	9–24	25	18–30	13–31	12–32	N/A	5–12.5	20 ml
PPSB-human SD/Nano (Octapharma)	Germany	25–55	7.5–20	24–37.5	25–55	20–50	5–25	0.5–3.0	0.5–6.0	10 ml (300 IU); 20 ml (600 IU)
Prothromplex Total/S-TIM 4 (Baxter, Austria)	Europe	30	25	30	30	>20	N/A	0.75–1.5	<15	20 ml
FEIBA NF (Baxter, USA)	United States, Europe	1.3§	0.9§‖	1.4§	1.1§	1.1§	N/A	N/A	None	20 ml (500 IU)

N/A = not available, which indicates that the presence or level of this factor was not provided by the manufacturer.

* Volume after reconstitution; † Unit: IU/IU factor IX; ‡ Unit: IU per dose; § Unit: U/U; ‖ Mainly in activated form.

Table 3
INR levels, transfusion rates, and hospital length of stay

	PCC (n = 20)	FFP (n = 20)
INR1	13.20 (4.45-21.0)	9.97 (2.96-21) ($P = .076$)
INR2	1.53 (1.14-2.30)	4.50 (2.18-12.2) (***P = .000***)
INR3	1.52 (1.09-2.13)	2.41 (1.19-5.0) (***P = .000***)
RBC transfusion (U)	3.15 (0–6)	4.30 (1-9) ($P = .058$)
Length of stay in ED (d)	1.62 (0.5-3)	3.46 (2-13) (***P = .000***)
Length of stay at hospital (d)	5.60 (2-14)	7.36 (2–40) ($P = .583$)

Plt, Platelet; INR1, INR level at admission; INR2, INR level at the second hour after admission; INR3, INR level at the sixth hour after admission; RBC, red blood cell.

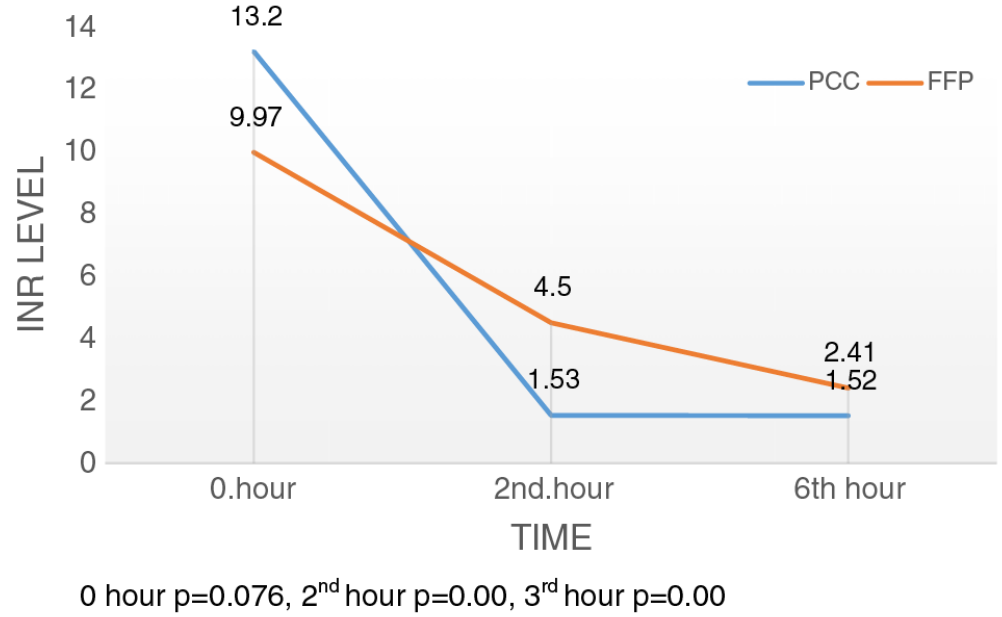


Fig. 3. Time dependent change of mean INR levels.

M.A. Karaca et al. / American Journal of Emergency Medicine 32 (2014) 660–664

Lancet Neurol 2016; 15: 566–73

Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial

Thorsten Steiner, Sven Poli*, Martin Griebe, Johannes Hüsing, Jacek Hajda, Anja Freiberger, Martin Bendszus, Julian Bösel, Hanne Christensen, Christian Dohmen, Michael Hennerici, Jennifer Kollmer, Henning Stetefeld, Katja E Wartenberg, Christian Weimar, Werner Hacke, Roland Veltkamp*

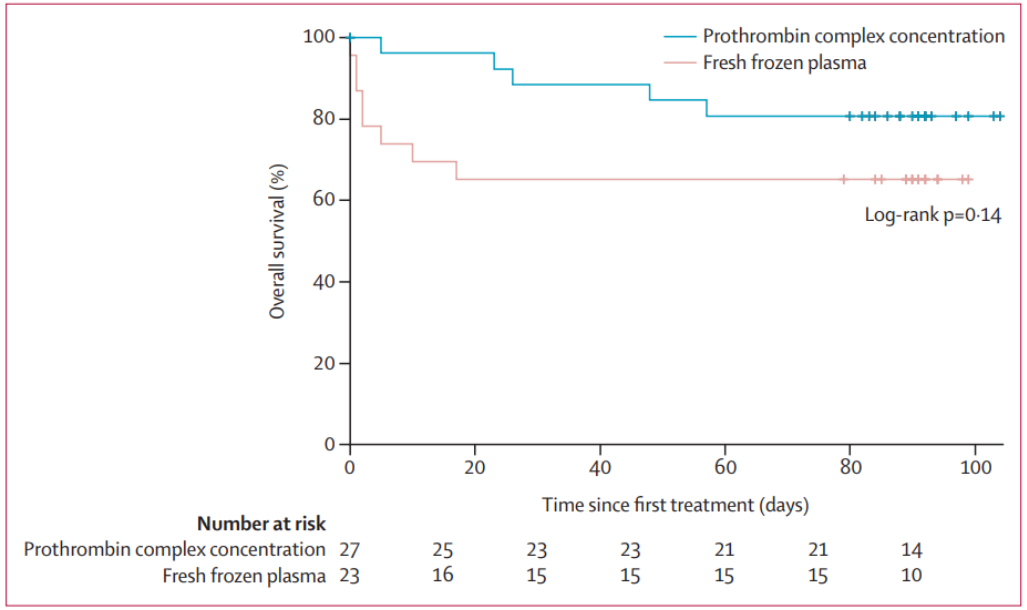


Figure 3: **Kaplan-Meier survival curve** Crosses represent censored patients.

Dávkovací režimy dle výše dávky inhibitoru FXa a doby uplynuté od poslední dávky

Inhibitor FXa	Poslední dávka
Apixaban	≤ 5 mg
	> 5 mg
Rivaroxaban	≤ 10 mg
	> 10 mg

Není-li známa velikost poslední dávky antikoagulancia nebo časový interval mezi poslední dávkou a epizodou krvácení, doporučení pro dávkování není k dispozici.[1]

1.1 CHARAKTERISTIKA ŽIVOT OHROŽUJÍCÍHO KRVÁCENÍ

- ztráta určitého objemu krve za časovou jednotku, např.:
  - ztráta celého objemu krve v průběhu 24 hodin (u dospělého člověka ekvivalent cca 10 transfuzních jednotek erytrocytů) nebo
  - ztráta 50 % objemu krve během 3 hodin nebo
  - pokračující krevní ztráta přesahující objem 150 ml/min,
- krevní ztráta v lokalizaci vedoucí k ohrožení životních funkcí (např. krvácení do CNS),
- přítomnost klinických/laboratorních známek tkáňové hypoperfuze v průběhu krvácení.

American Journal of Emergency Medicine 55 (2022) 38–44

Andexanet alfa versus four-factor prothrombin complex concentrate for the reversal of apixaban- or rivaroxaban-associated intracranial hemorrhages

Haithuy Pham, PharmD [a,*], Whitney Gibson Medford, PharmD [c,f], Spencer Horst, PharmD [b], Melissa Levesque, PharmD [c], David Ragoonanan, PharmD [c], Christine Price, PharmD [d], Harold Colbassani, MD [d],

[a] Memorial Regional Hospital, 3501 Johnson Street, Hollywood, FL 33021, United States of America
[b] St. Anthony's Hospital, 1200 7th Ave N, St. Petersburg, FL 33705, United States of America
[c] Tampa General Hospital, 1 Tampa General Cir, Tampa, FL 33606, United States of America
[d] Morton Plant Hospital, 300 Pinellas St, Clearwater, FL 33756, United States of America

A B S T R A C T

Methods: A retrospective chart review was conducted to assess patients admitted to a multi-center healthcare system and a stand-alone teaching hospital in central Florida from June 2016 to December 2020. Patients included in the study were at least 18 years of age, taking apixaban or rivaroxaban prior to admission, had radiographical evidence of an intracranial hemorrhage, and received either AA or 4F-PCC as a reversal agent. The primary outcome analyzed was the level of excellent hemostasis achieved, based on a standardized rating system for effective hemostasis defined by the International Society of Thrombosis and Hemostasis (ISTH), after administration of AA or 4F-PCC. Secondary outcomes analyzed included changes in the initial hemorrhage volume as reported on c
bolic events, rate of inpa

Results: A total of 109 pa
group (56.9%). There we
and secondary outcomes
after reversal administra
istration ($p = 1$, p adjust
There was no statistically
baseline to 12–24 h afte
0.601) in the AA and 4F-
6 [9.7%], $p = 1$, adjusted
[34.0%] vs. 13 [21.0%], p
the total cost of reversal

Conclusions: No statistica
the two agents with the
recommend AA over 4F-
rivaroxaban.

5. Conclusions

No significant difference was found in efficacy or safety between AA and 4F-PCC when used for ICH. There is insufficient evidence to recommend one reversal agent over the other for patients with ICHs associated with the use of apixaban or rivaroxaban. Further studies with a larger patient population to assess whether there is truly a difference between AA and 4F-PCC in hemostatic efficacy are needed.

Table 4
Secondary outcomes.

Outcome	Andexanet alfa (N = 47)	4F-PCC (N = 62)	Difference with 95% CI	p
% Change in hemorrhage volume from baseline to 12–24 h after reversal treatment	0 [−0.17–0.24)	0 [−0.021–0.29]	0 (−0.058–0.00)	0.439
Thromboembolism event	4 (8.5)	6 (9.7)	−1.2 (−12.0–9.7)	1
Myocardial infarction	1 (2.1)	0 (0.0)	2.1 (−2.0–6.3)	0.431
Stroke	0 (0.0)	0 (0.0)	0 (*–*)	1
Deep vein thrombosis	3 (6.4)	5 (8.1)	−1.7 (−11.4–8.1)	1
Pulmonary embolism	0 (0.0)	1 (1.6)	−1.6(−4.7–1.5)	1
Inpatient mortality	16 (34.0)	13 (21.0)	13.1(−3.8–30.0)	0.134
Total cost of reversal treatment ($)	$23,602 [$23,602–$23,602]	$6692 [$5950–$7649]	$16,910 ($16,082–$17,022)	0.000

Nominal data presented as n (%) and continuous data as median [IQR].
* p-value when adjusted for age, ICH score, regional mass effect, and midline shift.

Costa *et al. Critical Care* (2022) 26:180
https://doi.org/10.1186/s13054-022-04043-8

Critical Care

Andexanet alfa versus four-factor prothrombin complex concentrate for the reversal of apixaban- or rivaroxaban-associated intracranial hemorrhage: a propensity score-overlap weighted analysis

Olivia S. Costa[1,2], Stuart J. Connolly[3,4], Mukul Sharma[3,4], Jan Beyer-Westendorf[5], Mary J. Christoph[6], Belinda Lovelace[6] and Craig I. Coleman[1,2*]

Abstract

Background: Andexanet alfa is approved (FDA "accelerated approval"; EMA "conditional approval") as the first specific reversal agent for factor Xa (FXa) inhibitor-associated uncontrolled or life-threatening bleeding. Four-factor prothrombin complex concentrates (4F-PCC) are commonly used as an off-label, non-specific, factor replacement approach to manage FXa inhibitor-associated life-threatening bleeding. We evaluated the effectiveness and safety of andexanet alfa versus 4F-PCC for management of apixaban- or rivaroxaban-associated intracranial hemorrhage (ICH).

Methods: This two-cohort comparison study included andexanet alfa patients enrolled at US hospitals from 4/2015 to 3/2020 in the prospective, single-arm ANNEXA-4 study and a synthetic control arm of 4F-PCC patients admitted within a US healthcare system from 12/2016 to 8/2020. Adults with radiographically confirmed ICH who took their last dose of apixaban or rivaroxaban < 24 h prior to the bleed were included. Patients with a Glasgow Coma Scale (GCS) score < 7, hematoma volume > 60 mL, or planned surgery within 12 h were excluded. Outcomes were hemostatic effectiveness from index to repeat scan, mortality within 30 days, and thrombotic events within five days. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated using propensity score-overlap weighted logistic regression.

Results: The study included 107 andexanet alfa (96.6% low dose) and 95 4F-PCC patients (79.3% receiving a 25 unit/kg dose). After propensity score-overlap weighting, mean age was 79 years, GCS was 14, time from initial scan to reversal initiation was 2.3 h, and time from reversal to repeat scan was 12.2 h in both arms. Atrial fibrillation was present in 86% of patients. Most ICHs were single compartment (78%), trauma-related (61%), and involved the intracerebral and/or intraventricular space(s) (53%). ICH size was ≥ 10 mL in volume (intracerebral and/or ventricular) or ≥ 10 mm in thickness (subdural or subarachnoid) in 22% of patients and infratentorial in 15%. Andexanet alfa was associated with greater odds of achieving hemostatic effectiveness (85.8% vs. 68.1%; OR 2.73; 95% CI 1.16–6.42) and decreased odds of mortality (7.9% vs. 19.6%; OR 0.36; 95% CI 0.13–0.98) versus 4F-PCC. Two thrombotic events occurred with andexanet alfa and none with 4F-PCC.

Conclusions: In this indirect comparison of patients with an apixaban- or rivaroxaban-associated ICH, andexanet alfa was associated with better hemostatic effectiveness and improved survival compared to 4F-PCC.

Hemostatic effectiveness	Weighted incidence, % (95% CI) AA (N=107)	4F-PCC (N=95)	OR (95% CI)
Overall cohort analysis	85.8 (77.7; 91.8)	68.1 (57.7; 77.3)	2.73 (1.16; 6.42)
Sensitivity analysis adjudicating missing scans	85.0 (76.9; 91.2)	72.2 (62.1; 80.2)	2.19 (0.91; 5.25)
Intracerebral and/or intraventricular subgroup (N=47 AA, 37 4F-PCC)	78.2 (69.1; 85.6)	67.7 (57.4; 76.9)	1.71 (0.36; 8.11)

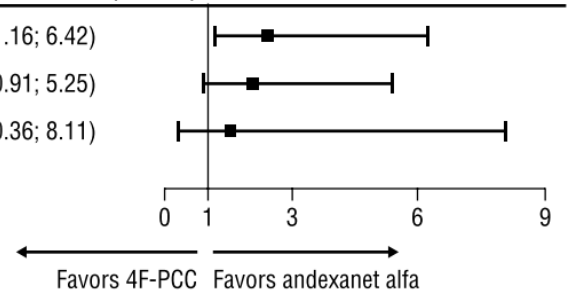


Fig. 2 Odds of hemostatic effectiveness after propensity score-overlap weighting for andexanet alfa versus 4F-PCC (referent). AA = andexanet alfa, CI = confidence interval, 4F-PCC = four-factor prothrombin complex concentrate, OR = odds ratio

DOAC

CEREBROVASKULÁRNÍ MANUÁL

Mírné krvácení

- odložit nebo vynechat následující dávku
- zhodnotit konkomintantní medikaci (interakce), ověřit indikaci antikoagulace a správnost dávky

Středně těžké krvácení

- ev. ošetření zdroje, lokální opatření ke stavění krvácení
- vysadit DOAC
- zvážit antidotum / substituční léčbu
- zajistit dostatek tekutin, zvýšit diurézu (hlavně dabigatran je vylučován močí)
- aktivní uhlí (< 2 h od užití DOAC)
- podat destičky, pokud Tr < 60-80 x 10^9 /L ev. krevní transfúze
- zvážit jako adjuvans u koagulopatie/trombocytopatie
  - ***EXACYL*** (tranexamová kyselina) 1g i.v. á 6h
  - ***OCTOSTIM*** (desmopresin acetát) 0.3 ug/kg ve 100ml FR iv. inf. během 15-30 minut (max 20 ug)

Závažné, život ohrožující krvácení

- vše výše uvedené +
- antidotum
  - ***PRAXBIND*** (dabigatran) → ***viz zde***
  - ***ONDEXXYA*** rivaroxaban, apixaban, edoxaban) → ***viz zde***
- pokud není antidotum dostupné, pak substituční léčba / hemodialýza (dabigatran)
  - ***PCC (Prothromplex)*** 50 IU/kg
- hemofiltrace přes aktivní uhlí
- i po podání antidota se může znovu obnovit signifikantní efekt DOAC a vést k rekurenci krvácení (více po podání andexanetu alfa, minimálně po podání idarucizumabu) ⇒ nutno pokračovat v klinickém i laboratorním monitorování pacienta

https://www.manual-cmp.cz/neutralizace-antikoagulacniho-ucinku/#1628172802986-2356bdc0-80b81628172816750e73e-14c616317655530741631765616084

Dávkovací režimy dle výše dávky inhibitoru FXa a doby uplynuté od poslední dávky

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Není-li známa velikost poslední dávky antikoagulancia nebo časový interval mezi poslední dávkou a epizodou krvácení, doporučení pro dávkování není k dispozici.[1]

VFN PRAHA

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Metodický pokyn | MP-ULP-21 | strana 2 z 3 | verze 1

POUŽÍTÍ SPECIFICKÉHO ANTIDOTA PŘI ZÁVAŽNÉM KRVÁCENÍ

1 Účel a oblast platnosti dokumentu

1. Metodický pokyn upravuje postup a pravidla použití nákladného léčivého přípravku, specifického antidota **Ondexxya**.
2. Dokument je závazný pro zdravotnické pracovníky VFN, kteří navrhují a předepisují podání léčivého přípravku.

2 Pojmy a zkratky

SPC souhrn údajů o léčivém přípravku

3 Odpovědnosti a pravomoci

Odpovědnosti a pravomoci ošetřujících lékařů a primářů pracoviště jsou uvedeny v kapitole 4.

4 Postup (popis činností)

1. Indikace k podání specifického antidota **Ondexxya** je život ohrožující nebo nekontrolované krvácení u dospělých pacientů léčených antikoagulancii – přímo působícím inhibitorem faktoru Xa (FXa); **apixaban** (Eliquis) a **rivaroxaban** (Xarelto).
2. Indikaci podání léčivého přípravku navrhuje **primář** pracoviště, jeho **zástupce** nebo **vedoucí lékař služby** a každá indikace podléhá schválení **supervizora intenzivní péče**, který schválení zaznamená do hlášení supervizora.
3. Po schválení supervizorem intenzivní péče vydá pověřený pracovník KARIM žádajícímu pracovišti léčivý přípravek. Do následujícího pracovního dne pověřený pracovník KARIM objedná do zásoby další balení v Nemocniční lékárně VFN.
4. **Ondexxya 200 mg prášek pro infuzní roztok** obsahuje v jednom balení 4 nebo 5 lahviček, ředí a dávkuje se dle SPC. Léčivý přípravek se podává intravenózně.
5. Po podání léčiva je ošetřující lékař povinen předat písemnou žádost ke schválení revizním lékařem na Ekonomický úsek – Oddělení vyúčtování zdravotní péče(zadanky.pojistovny@vfn.cz), žádost obsahuje:
   a. vyplněný tiskopis VZP-21: **„Žádanka o schválení (povolení)"** (v NIS MEDEA je označena jako **„Žádost o zvýšení úhrady"**),
   b. **lékařská zpráva** se zdůvodněním podání,
   c. **zálohová faktura** za léčivo, která je součástí balení léčiva.
6. Oddělení vyúčtování zdravotní péče vše zaeviduje odešle do následujícího pracovního dne datovou schránkou na pojišťovnu ke schválení revizním lékařem.
7. Po schválení pojišťovnou Oddělení metodické podpory a vyúčtování zdravotní péče - dokumentarista kliniky léčivo vykáže v hospitalizačním dokladu (kód 0238451). Při výkazu pojišťovně musí být v NIS MEDEA

Brede *et al. Critical Care* (2022) 26:57 https://doi.org/10.1186/s13054-022-03942-0

COMMENT Open Access

Resuscitative endovascular balloon occlusion of the aorta: the postpartum haemorrhage perspective

Jostein Rødseth Brede[1,2,3,4*], Edmund Søvik[5] and Marius Rehn[2,6,7]

Keywords: REBOA, Postpartum haemorrhage, PPH, Aortic occlusion

Not only in trauma centres, but also in hospitals with obstetric departments, REBOA should be considered an emergency procedure to be immediately available 24/7 by physicians trained in ultrasound-guided and fluoroscopy-free Seldinger technique. Local considerations will decide whether the REBOA is placed by an emergency physician, anaesthesiologist, obstetricians, interventional radiologist or the general surgeon.

Conclusions

REBOA carries more indications than trauma and should be increasingly considered and evaluated in management of PPH. REBOA may not only save a life, it might also save a uterus.

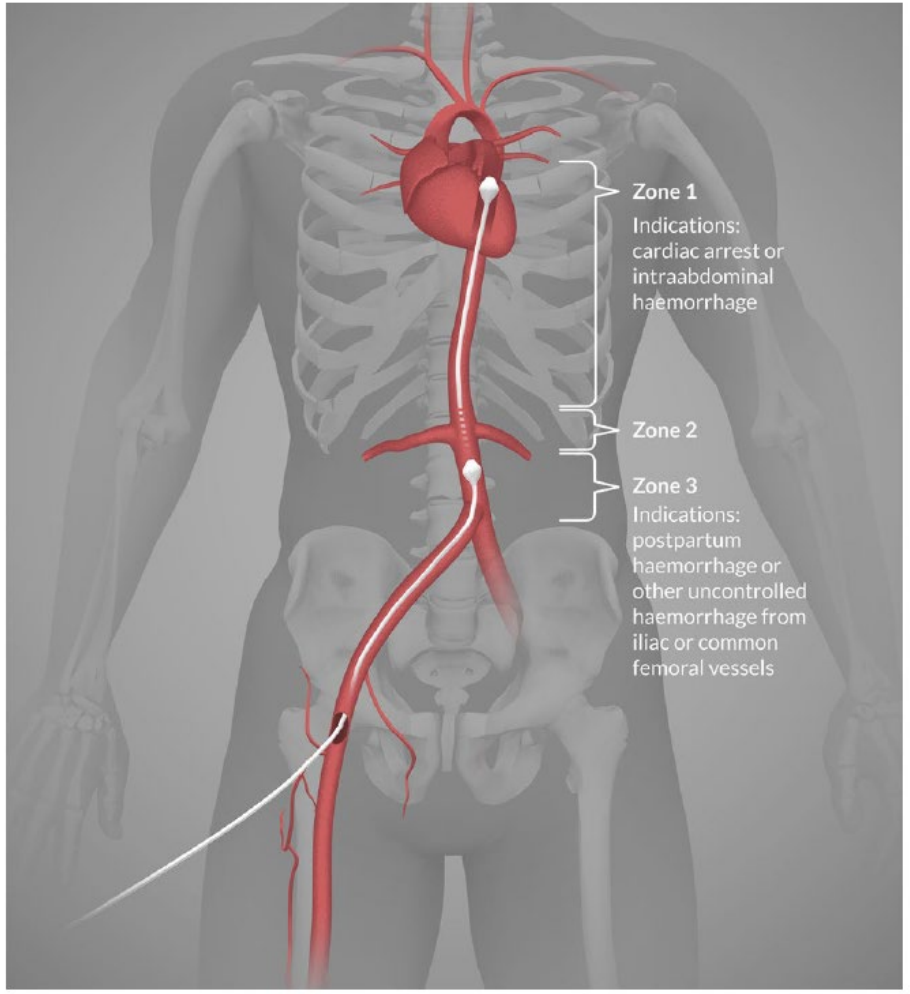

Fig. 1 Aortic zones and indications for occlusion

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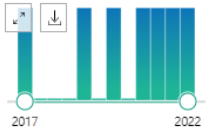

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Resuscitative endovascular balloon occlusion of the aorta: the postpartum haemorrhage perspective.

Brede JR, Søvik E, Rehn M.

Crit Care. 2022 Mar 11;26(1):57. doi: 10.1186/s13054-022-03942-0.

PMID: 35277189 Free PMC article. No abstract available.

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Needs assessment of resuscitative endovascular balloon occlusion of the aorta (**REBOA**) in patients with major haemorrhage: a cross-sectional study.

Godø BN, Brede JR, Krüger AJ.

Emerg Med J. 2021 May 26:emermed-2020-210808. doi: 10.1136/emermed-2020-210808. Online ahead of print.

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Successful management of uncontrolled postpartum hemorrhage due to morbidly adherent placenta with Resuscitative endovascular balloon occlusion of the aorta during emergency cesarean section - A case report.

Ji SM, Cho C, Choi G, Song J, Kwon MA, Park JH, Kim S.

Anesth Pain Med (Seoul). 2020 Jul 31;15(3):314-318. doi: 10.17085/apm.19051.

PMID: 33329830 Free PMC article.

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Management of post-pancreatectomy haemorrhage using resuscitative endovascular balloon occlusion of the aorta.

Singh G, Nahm CB, Jamieson NB, Chua TC, Wong S, Thoo C, Mittal A, Gill AJ, Samra JS.

Langenbecks Arch Surg. 2019 Mar;404(2):253-255. doi: 10.1007/s00423-019-01759-0. Epub 2019 Feb 13.

PMID: 30758668

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Fluoroscopy-free Resuscitative Endovascular Balloon Occlusion of the Aorta (**REBOA**) for controlling life threatening postpartum hemorrhage.

Stensaeth KH, Sovik E, Haig IN, Skomedal E, Jorgensen A.

PLoS One. 2017 Mar 29;12(3):e0174520. doi: 10.1371/journal.pone.0174520. eCollection 2017.

PMID: 28355242 Free PMC article.

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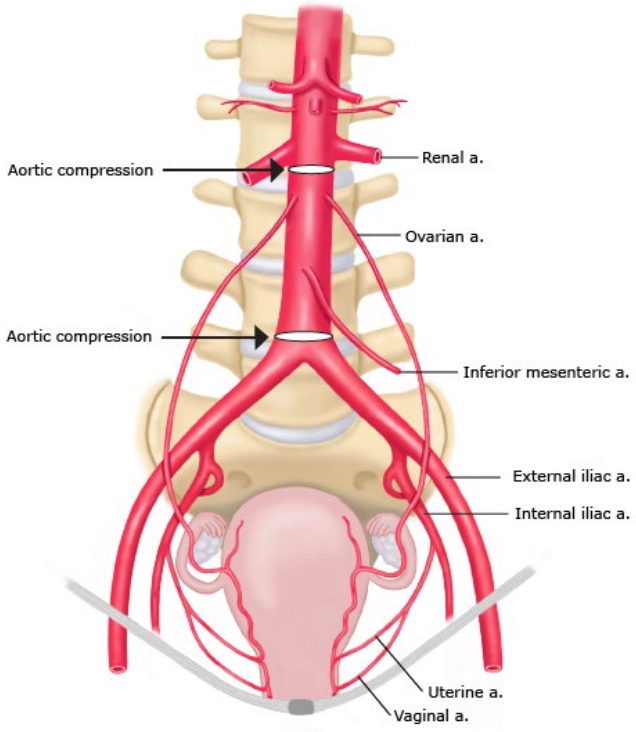

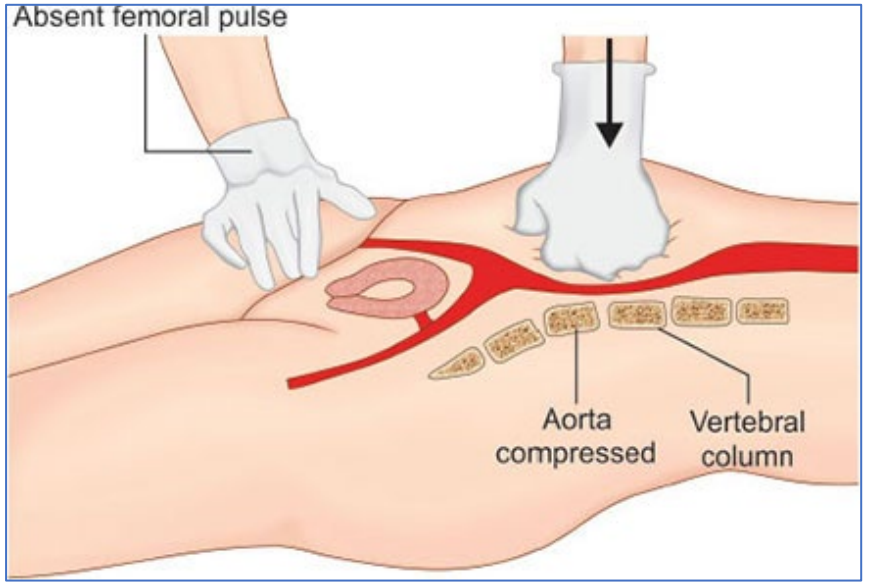

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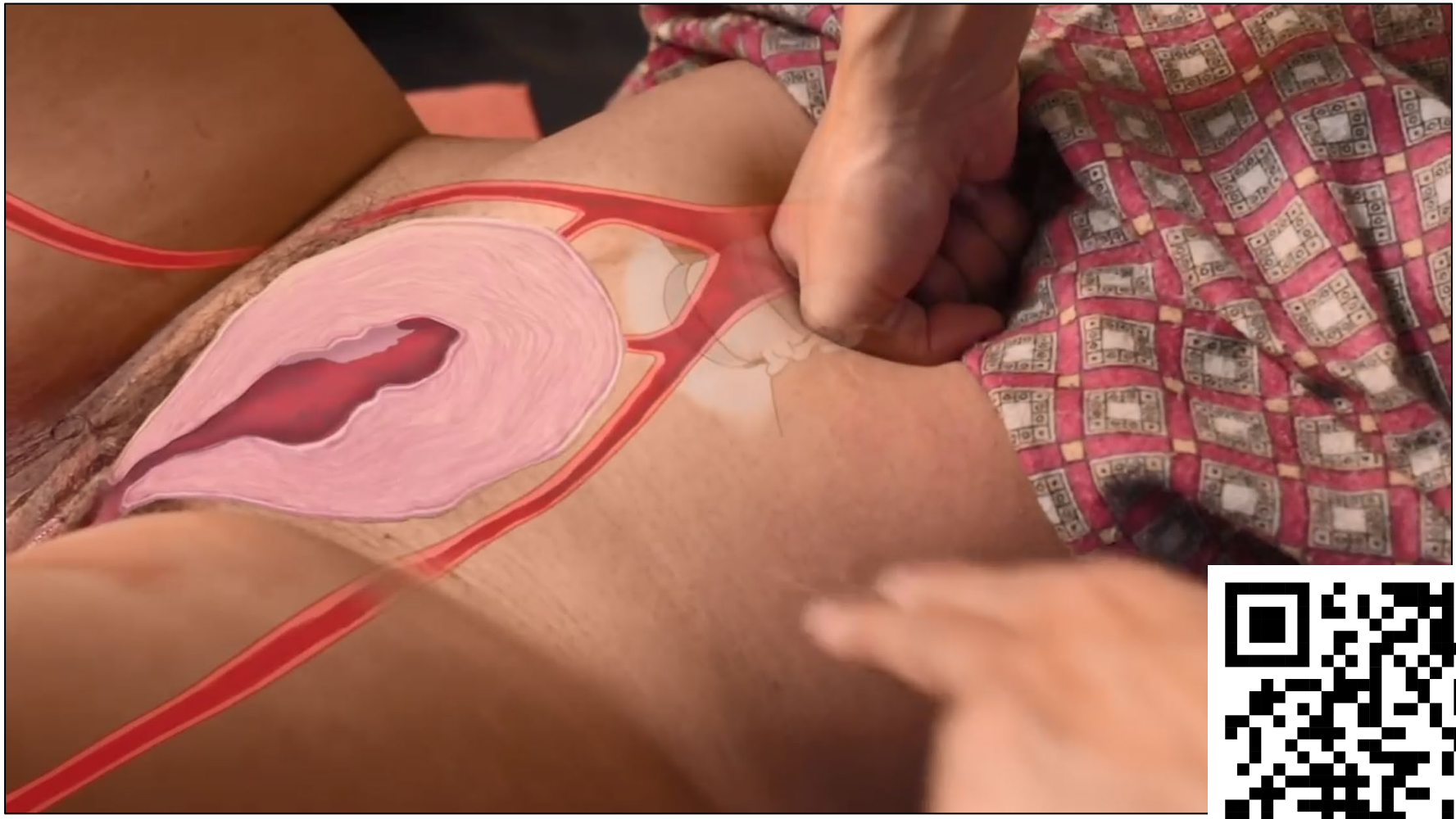

jan.blaha@vfn.cz