JAN BLÁHA

KLINIKA ANESTEZIOLOGIE, RESUSCITACE
A INTENZIVNÍ MEDICÍNY

1. LÉKAŘSKÁ FAKULTA
Univerzita Karlova

VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

jan.blaha@vfn.cz

PLAZMA FIBRINOGEN

update 2022

PubMed.gov

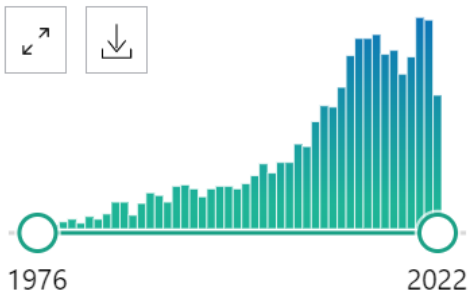
FFP heamorrhage | Search

All (2,268)

Free Full Text (631)

Review (235)

RESULTS BY YEAR



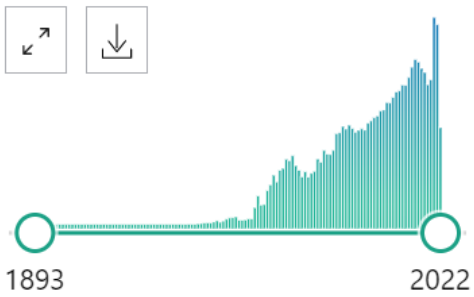
fibrinogen heamorrhage | Search

All (49,903)

Free Full Text (13,196)

Review (3,762)

RESULTS BY YEAR



FFP fibrinogen heamorrhage | Search

All (340)

Free Full Text (85)

Review (36)

RESULTS BY YEAR

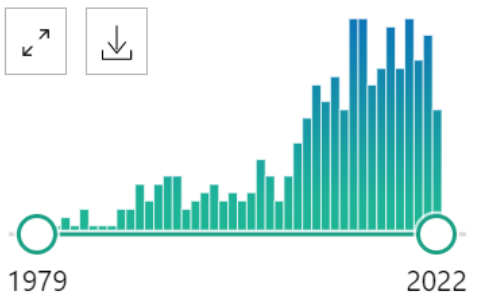


FIGURE 75.—Medical care on Omaha Beach, June 1944. Note the absence of a litter.

Wounded soldier on Okinawa being administered blood plasma

Private Roy W. Humphrey of Toledo, Ohio is being given blood plasma after he was wounded by shrapnel in Sicily on 8/9/43

Vietnam, 1968

The original photo, taken in Vietnam in 1967. CREDIT:COURTESY OF THE AUSTRALIAN WAR MEMORIAL

The fighting in Hue City, Vietnam, mid-February 1968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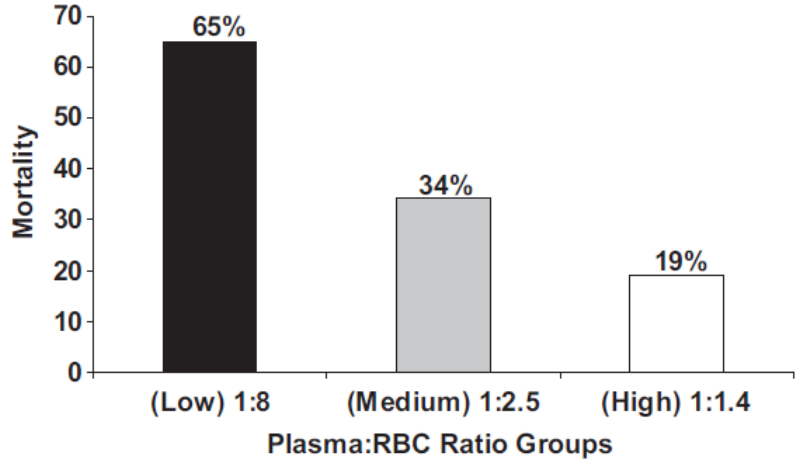


Fig. 1. *Percentage mortality associated with low, medium, and high plasma to RBC ratios transfused at admission. Ratios are median ratios per group and include units of fresh whole blood counted both as plasma and RBCs.*

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

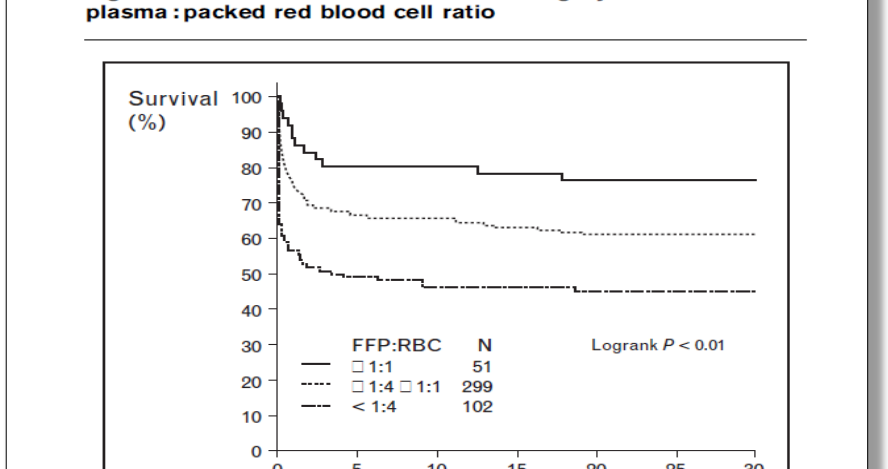


Figure 1 Survival curves for each category of fresh frozen plasma : packed red blood cell ratio

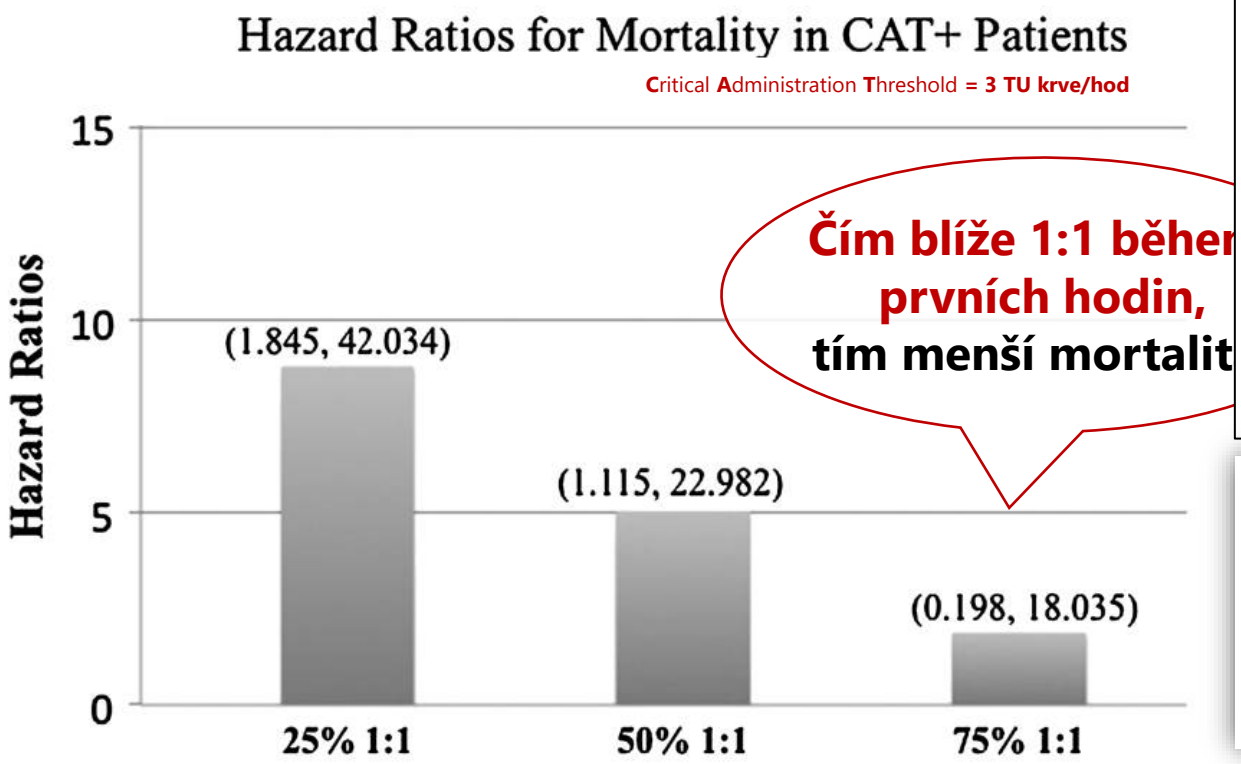
The lowest mortality was observed in the category of patients who received a ratio of fresh frozen plasma : packed red blood cells (FFP : PRBCs) equal to or greater than 1 : 1. Most of the separation of the survival curves occurred immediately after the injury. Data from [16].

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



Čím blíže 1:1 během prvních hodin, tím menší mortalit

Transfusion Medicine Reviews 32 (2018) 6–15

Optimal Dose, Timing and Ratio of Blood Products in Massive Transfusion: Results from a Systematic Review

Zoe K. McQuilten [a,b,*], Gemma Crighton [a], Susan Brunskill [c], Jessica K. Morison [a], Tania H. Richter [a], Neil Waters [a], Michael F. Murphy [c], Erica M. Wood [a]

[a] *Transfusion Research Unit, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*
[b] *Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*
[c] *Systematic Reviews Initiative, NHS Blood and Transplant/Oxford University Hospitals NHS Trust, Oxford, United Kingdom*

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Hemorrhage
Fresh frozen plasma
Cryoprecipitate
Platelet transfusion
Trauma

ABSTRACT

Optimal dose, timing and ratio to red blood cells (RBC) of blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) to reduce morbidity and mortality in critically bleeding patients requiring massive transfusion is unknown. We performed a systematic review for randomized controlled trials (RCT) in MEDLINE, *The Cochrane Library*, Embase, CINAHL, PubMed the Transfusion Evidence Library and using multiple clinical trials registries to 21 February 2017. Sixteen RCTs were identified: six completed (five in adult trauma patients, one pediatric burn patients) and ten ongoing trials. Of the completed trials: three were feasibility trials, comparing a FFP, platelets and RBC ratio of 1:1:1 to laboratory-guided transfusion practice [n = 69], early cryoprecipitate compared to standard practice [n = 41], and early fibrinogen concentrate compared to placebo [n = 45]; one trial compared the effect of FFP, platelets and RBC ratio of 1:1:1 with 1:1:2 on 24-hour and 30-day mortality [n = 680]; one compared whole blood to blood component therapy on 24-hour blood use [n = 107]; one compared a FFP to RBC ratio of 1:1 with 1:4 [n = 16]. Data from two trials were pooled in a meta-analysis for 28-day mortality because the transfusion ratios achieved were similar. Results from these two trials suggest higher transfusion ratios were associated with transfusion of more FFP and platelets without evidence of significant difference with respect to mortality or morbidity. On the limited evidence available, there is insufficient basis to recommend a 1:1:1 over a 1:1:2 ratio or standard care for adult patients with critical bleeding requiring massive transfusion.

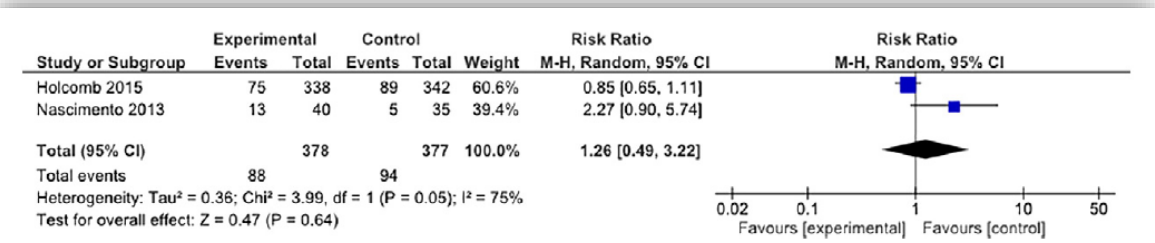


Fig. 2. Forrest plot for 28-day mortality.

FIBRINOGEN OF THE BLOOD AS INFLUENCED BY THE LIVER NECROSIS OF CHLOROFORM POISONING.[1]

By G. H. WHIPPLE, M.D., and S. H. HURWITZ.

(*From the Hunterian Laboratory of Experimental Pathology, Johns Hopkins Medical School, Baltimore.*)

During the course of some experiments on chloroform poisoning in dogs, it was noted that operations upon many of these animals resulted fatally because of uncontrollable hemorrhage. At autopsy the abdominal cavity was frequently full of fluid blood and, in cases of extreme poisoning, even the blood vessels and heart contained fluid blood and no clots. The present series of experiments was undertaken with the hope of clearing up this feature of chloroform poisoning, but, as the work progressed, it seemed to throw some light on interesting problems connected with blood coagulation and liver function. These experiments seem to indicate clearly that fibrinogen is formed by the liver or that its formation is quite dependent upon the functional activity of that organ.

It will be seen that fibrinogen in the blood can be made to decrease or almost to vanish at will through the production of liver necrosis by chloroform anesthesia. Also, the drop of fibrinogen is found to parallel closely the extent of liver necrosis and, in severe poisoning where the liver shows extensive necrosis, the fibrinogen may be practically absent. In this latter condition, which is not unlike hemophilia, the animal bleeds steadily from large or small cuts. Moreover, the fibrinogen reappears in the blood as the liver begins to repair the injury to its lobules and keeps pace with the repair of the liver cells. The repair is very rapid and may be complete in five or six days. Finally, at the end of the reparatory activity of the liver, we may find an excess of fibrinogen in the blood, an over-production corresponding to Weigert's law of tissue injury and repair (Chart I).

[1] Received for publication, August 10, 1910.

BLOOD COAGULATION IN OBSTETRIC EMERGENCIES

In pregnancy a haemostatic defect may develop from disturbances of blood coagulation. This haemorrhagic state, arising in some obstetrical emergencies, has been recognized for many years but has recently received renewed attention, and is the subject of two papers in this week's *Journal*. The coagulation abnormality is most commonly s
antepartum haemo
(p. 290) and Dr.
(p. 287) point out,
embolism, in assoc
foetus in an Rh-immunized mother, in missed abortion, and in hydatidiform mole. The exact nature of this clotting defect is not clearly understood, but two changes have been accepted as features of the condition—deficiency of fibrinogen and an active fibrinolytic system. Some believe that the depletion of fibrinogen is due to excessive utilization as a consequence of intravascular clotting or of the formation of retroplacental clot or of fibrin deposit
it is a result
in the blood
genolysis.

[1] Barry, A. P., Fe
1955, **2**, 12.
[2] *Surg. Gynec. Obs*
[3] *J. Obstet. Gynec.*
[4] *Amer. J. Obstet.*
[5] *Renal Cortical Ne*
1952, Oxford.

Patients who have had a concealed accidental haemorrhage, a death *in utero*, am
or premature separation of the placenta are prone to severe haemorrhage associated with a defect of blood coagulation (Weiner *et al.*, 1950; Reid *et al.*, 1953). This is thought to be due to a reduction in the fibrinogen level of the blood (Dieckmann, 1936), and while theories about the causation of the defect are various (Weiner *et al.*, 1950; Albrechtsen *et al.*, 1955; Ratnoff *et al.*, 1955), the response to fibrinogen therapy has now been proved by experience (Weiner *et al.*, 1950; Reid *et al.*, 1953; Barnett and Cussen, 1954; Scott, 1955).

...příčina je v deficitu fibrinogenu a aktivním fybrinolytickém systému

... prokazatelné zlepšení po podání fibrinogenu

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

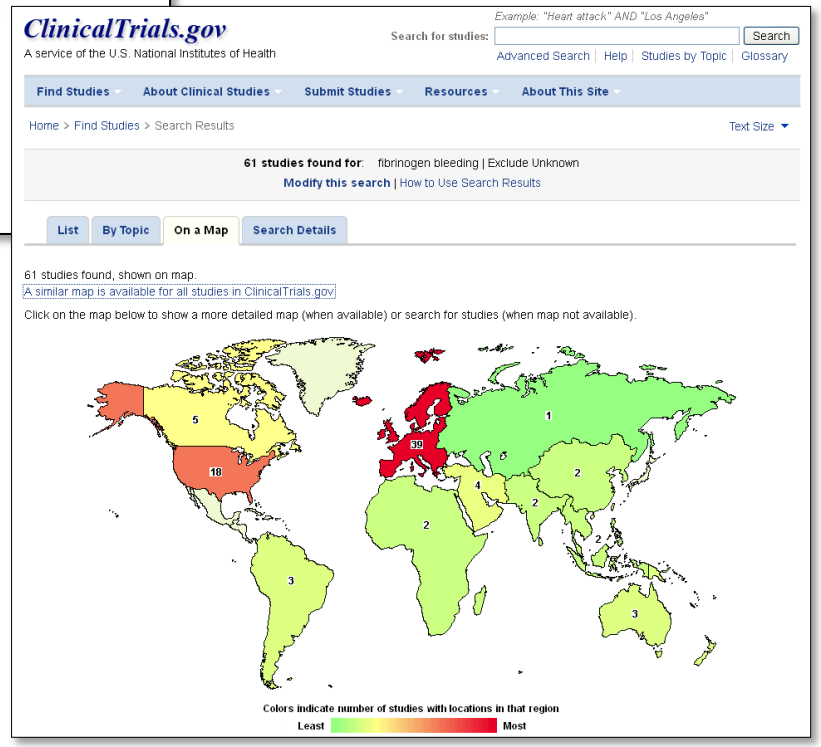
Product Name	Availability[a]	Date of First Approval
Haemocomplettan® P[b]		
Argentina		August 2012
Austria		June 1994
Brazil		March 1963 (March 2008[c])
Bulgaria		January 2009
Czech Republic		March 1993
Germany		March 1966 (March 2005[c])
Hungary		June 1998
Iran		January 2010
Kuwait		October 2003
Lebanon		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.

Perioperative Coagulation Management:

Out With the Old (Plasma)

and In With the New (Fibrinogen)?



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 be improved.

75% úmrtí na krvácení je pravděpodobně preventabilní

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:

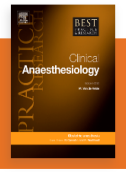
1. Clinical shock, sometimes out of proportion to blood loss or hypotension.
2. Disseminated deposition of fibrin.
3. An *in vivo* defibrination of the blood with a decrease or absence of fibrinogen, sometimes resulting in incoagulable blood.
4. Ischemia of the renal cortex, leading to varying degrees of necrosis.
5. Activation of a fibrinolysin in the plasma.

nutné okamžité doplnění fibrinogenu

3. Therapy of Systemic Disease

Treatment of systemic disease must include prompt replacement of fibrinogen, if indicated, and ample quantities of fresh whole blood. Bank blood is of less value in restoring fibrinogen levels and may actually lower them. A minimum of 4 gm. of fibrinogen is usually recommended, but as much as three times this amount may be needed to restore normal hemostasis.

Frequent determinations or estimations of plasma fibrinogen will enable the physician to determine the actual amount needed. Fibrinogen should be administered until a stable clot will form.



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Impact Factor

Best Practice & Research Clinical Anaesthesiology

Epidemiology and Definition of PPH Worldwide

--Manuscript Draft--

Manuscript Number:	
Article Type:	Issue 36.2
Keywords:	Postpartum/peripartum hemorrhage; definition of PPH; epidemiology of PPH; risk and causes of PPH
Corresponding Author:	Jan Bláha, MD, PhD, MHA, LLM Charles University, First Faculty of Medicine Praha2, Česká republika CZECH REPUBLIC
First Author:	Jan Bláha, MD, PhD, MHA, LLM
Order of Authors:	Jan Bláha, MD, PhD, MHA, LLM
Abstract:	Postpartum/peripartum hemorrhage (PPH) is an obstetric emergency complicating 1–10% of all deliveries and is a leading cause of maternal mortality and morbidity worldwide. However, the incidence of PPH differs widely according to the definition and criteria used, the way of measuring postpartum blood loss, and the population being studied with the highest numbers in developing countries. Despite all the significant progress in health care, the incidence of PPH is arising due to an incomplete implementation of guidelines, resulting in treatment delays and suboptimal care. A consensus clinical definition of PPH is needed to enable awareness, early recognition, and initiation of appropriate intensive treatment. Unfortunately, the most used definition of PPH based on blood loss ≥ 500 ml after delivery suffers from inaccuracies in blood loss quantification and is not clinically relevant in most cases, as the amount of blood loss does not fully reflect the severity of bleeding.

Although in low-and-middle-income countries, there has been an impressive reduction in obstetric hemorrhage and associated deaths in the last years as services and medical care improve, in high-income regions, despite all the significant progress in health care, the problem seems to be worsening, and incidence of PPH is on the rise in many of these countries[101, 102]. In the United States, ate of PPH (defined as blood loss >1000 ml) requiri tely 8 to 40 per 10 000 deliveries [103]. An increas , 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 inade treating PPH are believed to directly affect complications such as coagulopathy, and r orted to be caused by misinterpretation of the ex e to recognize hidden bleeding, and failure to escalate care to more senior colleagues [116-118].

Zpoždění léčby až u 90% případů krvácení (PPH)

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

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

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

John B. Holcomb, MD, FACS

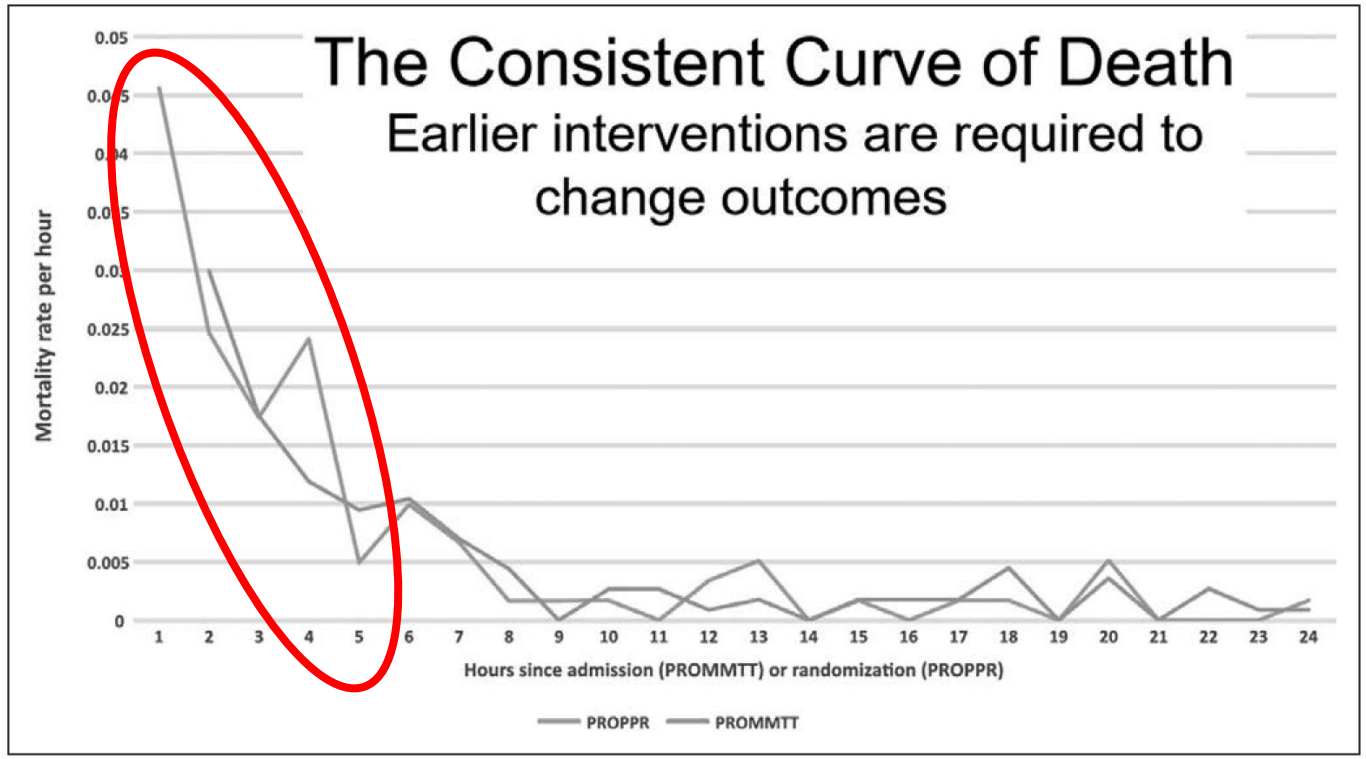


Figure 2. After admission, PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) and Pragmatic Randomized Optimal Platelet and Plasma Ratio (PROPPR) patients die early and at a very reproducible rate, $n = 1{,}925$. Modified from Fox et al (22).

35

minutes

8

minutes

International Journal of Obstetric Anesthesia 50 (2022) 103547

Short Report

Comparison of haematological indices and transfusion management in severe and massive postpartum haemorrhage: analysis of a two-year national prospective observational study

S.F. Bell [a,*], R.E. Collis [a], P.W. Collins [b]

[a] Department of Anaesthetics, Intensive Care and Pain Medicine, Cardiff and Vale University Health Board, Cardiff, UK
[b] Institute of Infection and Immunity, School of Medicine, Cardiff University, Cardiff, UK

Keywords:
Abruption
Coagulopathy
Fibrinogen
Postpartum haemorrhage

A B S T R A C T

Introduction: This two-year prospective cohort study compared the management of women experiencing severe or massive postpartum haemorrhage (PPH) to explore the impact of targeted blood product administration on reducing PPH progression (from >1500 mL to ≥2500 mL blood loss). During the study, viscoelastic haemostatic assays (VHA) guided blood product transfusion.

Methods: All women experiencing blood loss after PPH >1000 mL were included in a national database. Haematological indices, transfusion and PPH aetiology were analysed in severe (>1500 mL blood loss or transfusion of any blood product) and massive PPH (≥2500 mL blood loss or transfusion ≥5 units red blood cells).

Results: Of the 61 094 maternities in Wales (2017 to 2018), 2111 had severe and 349 massive PPH. Red blood cells were transfused to 42.5% severe and 80.6% massive PPH cases. Hypofibrinogenaemia (fibrinogen <2 g/L and/or Fibtem A5 <12 mm) was the most frequent coagulation abnormality, occurring in 5.4% severe and 17.0% massive PPH, with blood coagulation products (fresh frozen plasma, platelets, cryoprecipitate and/or fibrinogen concentrate) administered to 3.6% and 22.9%. Women with hypofibrinogenaemia received targeted fibrinogen replacement in 97.8% severe and 93.6% massive PPH. The only aetiology with similar rates of hypofibrinogenaemia in severe and massive PPH was abruption (40.0% and 36.8%).

Conclusion: Hypofibrinogenaemia was less frequent in severe PPH, although coagulopathy was observed across a range of PPH aetiologies, highlighting the importance of coagulation testing for all. Cases of abruption in severe and massive PPH had similar rates of hypofibrinogenaemia. Early VHA-guided fibrinogen replacement may reduce PPH progression in abruption and requires further evaluation.

Table 2
Haemostatic impairment and blood product transfusion for women with severe (>1500 mL blood loss or transfusion of any blood product) and massive (≥2500 mL blood loss or transfusion ≥5 units red blood cells) postpartum haemorrhage

	Severe PPH, n (%)	Massive PPH, n (%)	*P*-value
Haemostatic impairment			
Hypofibrinogenaemia (fibrinogen <2 g/L and/or Fibtem A5 <12 mm, with the lowest value of either result used)	89/1652 (5.4)	56/328 (17.0)	<0.001
Thrombocytopaenia (platelet count $<75 \times 10^9$/L)	25/1893 (1.3)	17/334 (5.1)	<0.001
aPTT >1.5 × reference range (>48 s)	3/1440 (0.2)	9/293 (3.0)	<0.001
PT >1.5 × reference range (>16.5 s)	7/1440 (0.5)	10/293 (3.4)	<0.001
Blood product transfusion			
RBC	887/2095 (42.3)	279/346 (80.6)	<0.001
Fibrinogen concentrate and or cryoprecipitate	49/2098 (2.3)	53/346 (15.3)	<0.001
Platelets	18/2098 (0.9)	15/345 (4.3)	0.01
FFP	28/2098 (1.3)	43/346 (12.4)	<0.001

Values are n, %.

Thrombosis Research Volume 116, Issue 4, 2005, Pages 345-356
https://doi.org/10.1016/j.thromres.2004.12.009

Regular Article

A new global assay of coagulation and fibrinolysis

Neil A. Goldenberg [a, b], William E. Hathaway [a, b], Linda Jacobson [b], Marilyn J. Manco-Johnson [a, b]

Abstract

Introduction: Global clotting assays may reflect an individual's net hemostatic balance and could contribute to prothrombotic and hemorrhagic risk assessment. In this research, a global assay that measures both coagulation and fibrinolytic capacities was developed and investigated.
Materials and methods: In the Clot Formation and Lysis (CloFAL) assay, a buffered reactant solution containing trace amounts of calcium, tissue factor, and tissue-type plasminogen activator is added to plasma samples on a 96-well microplate in an automated, thermoregulated (37 °C) spectrophotometer. Clot formation and lysis are monitored as continuous changes in absorbance over the course of 3 h. Measurements include maximum amplitude (MA), times to maximum absorbance (T_1) and completion of the first phase of decline in absorbance (T_2), and area under the curve (AUC), from which a coagulation index (CI) and various fibrinolytic indices (FI) may be calculated.
Results and conclusions: MA, T_1, and CI were principally influenced by fibrinogen and procoagulant factors. FI was found to be altered by inhibiting activation of plasminogen or thrombin activatable fibrinolytic inhibitor. Median CI was significantly decreased, while FI was markedly increased, in term neonates as compared to healthy adults (CI: 58% vs. 115%, FI: 210% vs. 90%; $P<0.001$ for each). By contrast, median CI was notably increased, and FI decreased, in healthy pregnant women when compared to adults (CI: 239% vs. 115%, FI: 59% vs. 90%; $P<0.001$ for each). The CloFAL global assay is analytically sensitive to several key components in the coagulation and fibrinolytic systems, as well as to physiologic alterations in hemostasis.

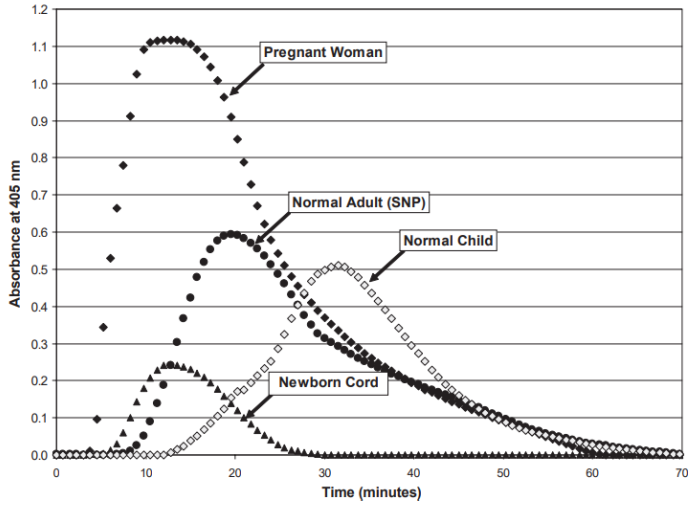


Figure 2 Representative CloFAL curves from a healthy adult and child, newborn infant, and pregnant woman. SNP=standard normal pooled adult plasma.

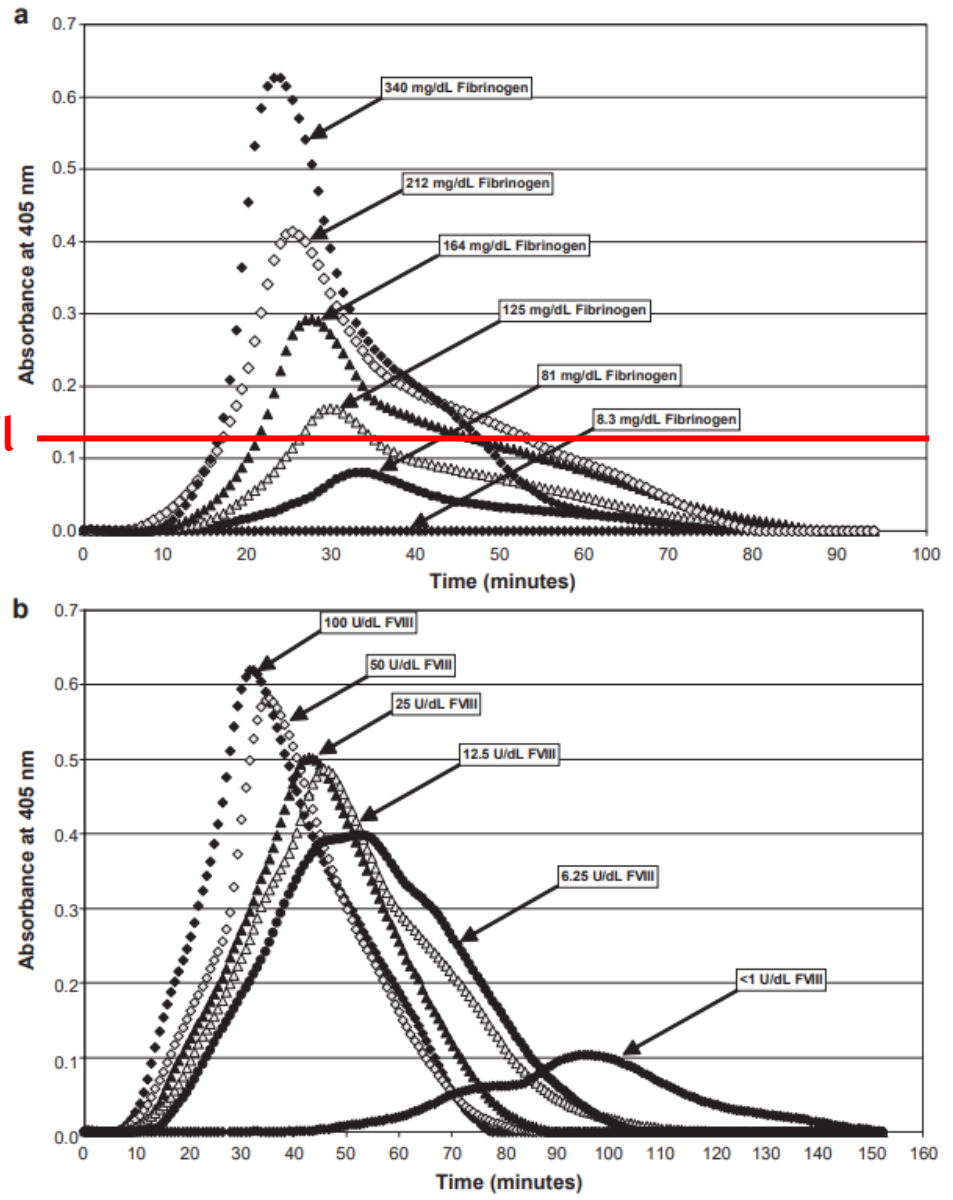


Figure 3 Influence of (a) fibrinogen concentration and (b) factor VIII activity upon the CloFAL curve.

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.

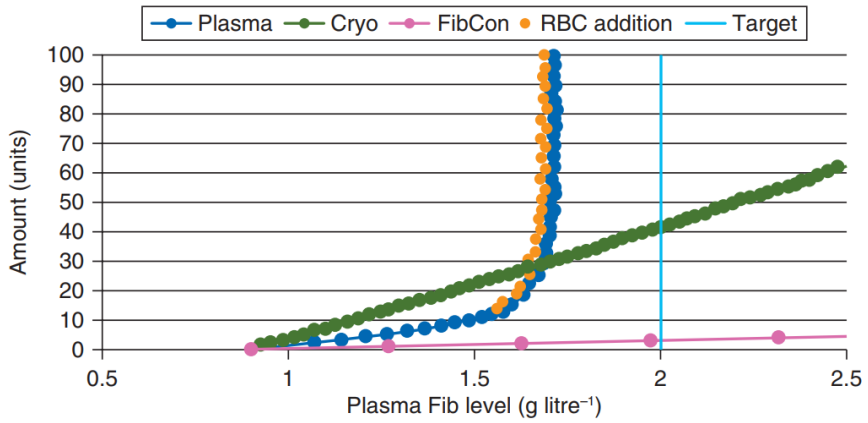
British Journal of Anaesthesia 113 (4): 585–95 (2014)

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



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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
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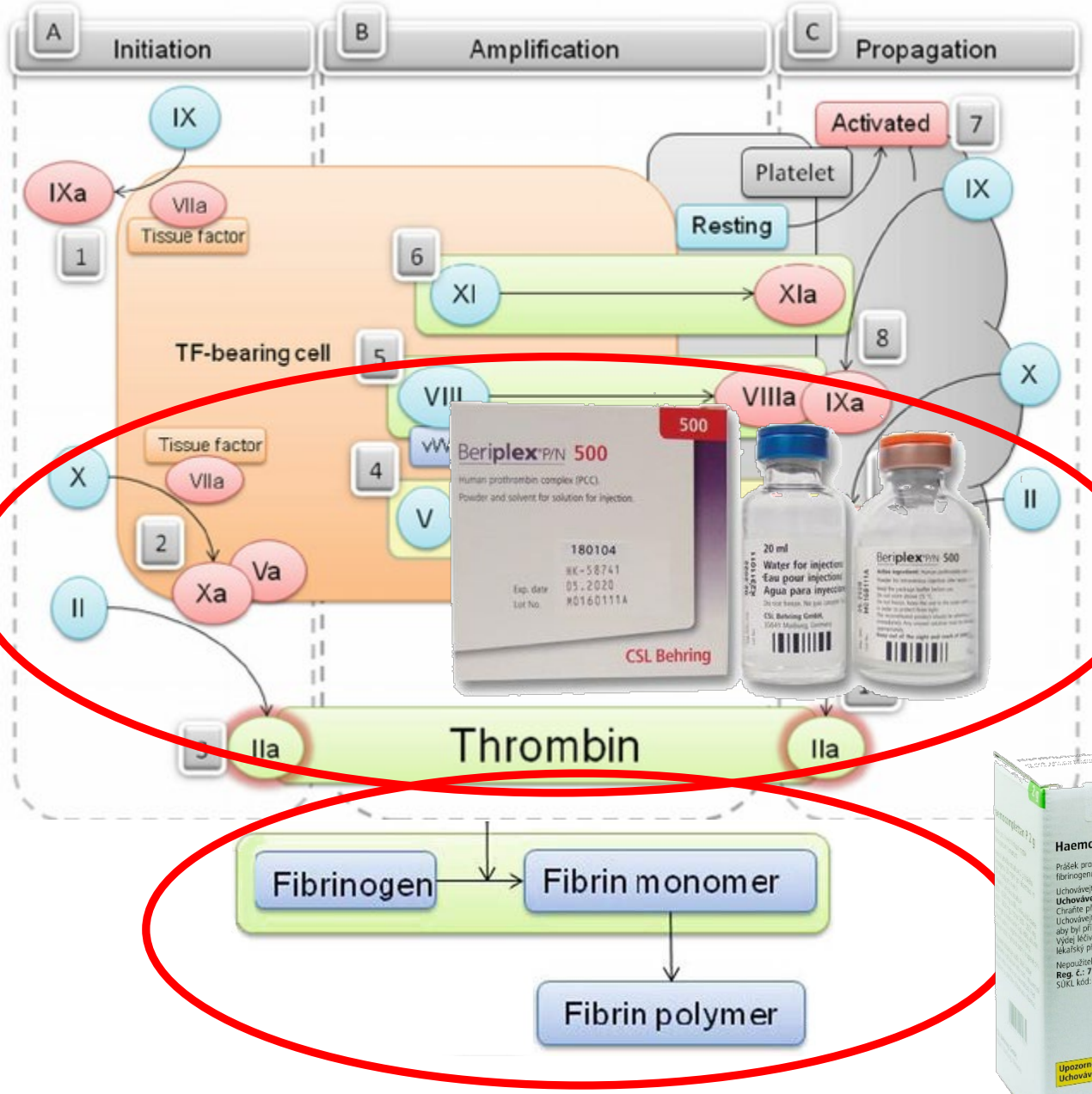
xed transfusion
s uncommon in
d transfusion of
ical assessment.
ibrinogen is an
blood products
pidly increasing
n tests such as
EG) allow rapid
ate markers of
nd inform blood
e used to safely
fusion rates and
quired to clarify
nt in PPH, with
he use of blood

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].


A
Initiation
B
Amplification
C
Propagation
IX
IXa
VIIa
Tissue factor
1
TF-bearing cell
6
XI
XIa
Activated
7
Platelet
Resting
IX
8
X
5
VIII
VIIIa
IXa
Tissue factor
VIIa
X
4
V
2
Xa
Va
II
IIa
Thrombin
IIa
Fibrinogen
Fibrin monomer
Fibrin polymer
Calcium is necessary for reaction
Thrombin is necessary for reaction
Thrombin and Calcium is necessary for reaction
Inactive factor
Beriplex P/N 500
CSL Behring
FXIII Concentrate (Human)
Corifact
CSL Behring
Haemocomplettan P 2 g
Phase

015)

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 postoperatively was 22.5 (14–28 [2–41]) units in patients allocated to fresh frozen plasma vs. 4.5 (3–11[0–17]) in patients allocated to fibrinogen concentrate (p = 0.011). All patients in both groups were assessed by the surgeon to have satisfactory 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.

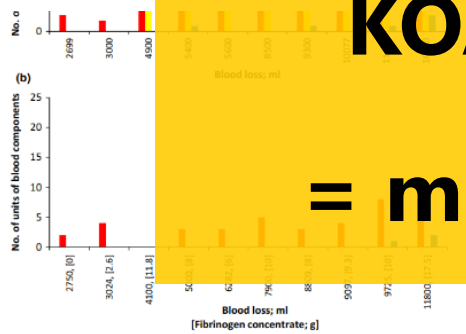


Figure 2 Blood component administration (red = packed red cells, yellow = fresh frozen plasma, blue = platelets) during surgery for each patient randomly allocated to receive either fresh frozen plasma (FFP) (a) or fibrinogen concentrate (b) during thoraco-abdominal aortic aneurysm surgery. Blood loss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

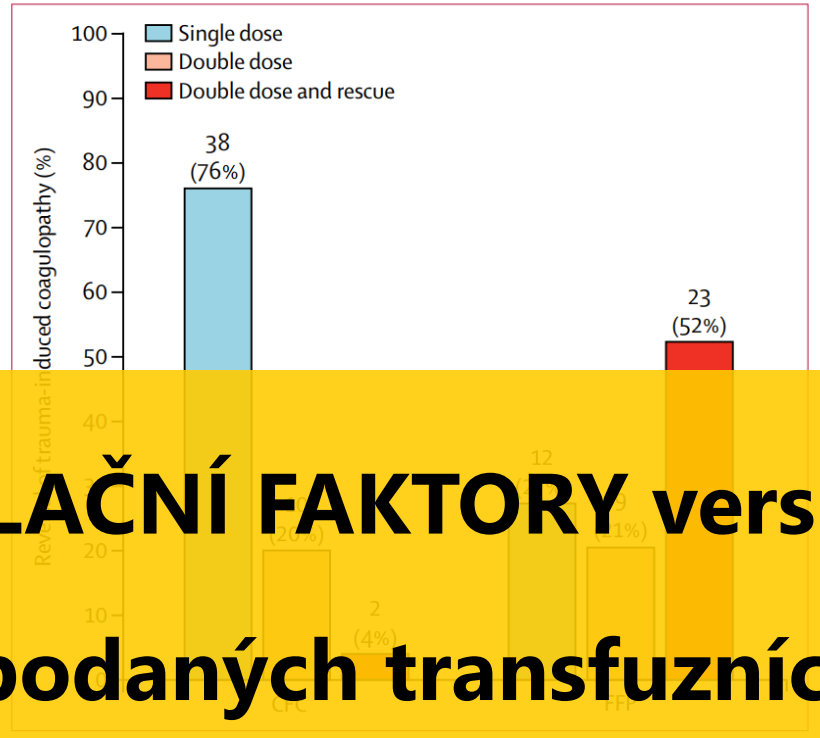


Figure 3: Percentage of patients with reversal of coagulopathy after either single-dose or double-dose study drug administration during the first therapy loop, and percentage of patients needing double-dose and rescue medication during the first 24 h in the intention-to-treat population
CFC=coagulation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

OPEN

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

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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

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.

KOAGULAČNÍ FAKTORY versus PLASMA

= méně podaných transfuzních přípravků!

Effect of a factor-based coagulation management on blood product use after major burn injury: A retrospective cohort study

Sebastian D. Sahli [a,1], Nadine Pedrazzi [b,1], Julia Braun [c], Donat R. Spahn [a], Alexander Kaserer [a,2], Jan A. Plock [d,e,*,2]

[a] Institute of Anesthesiology, University and University Hospital Zurich, Zurich, Switzerland
[b] Department of Plastic and Hand Surgery, Lausanne University Hospital, Lausanne, Switzerland
[d] Department of Plastic Surgery and Hand Surgery, Burn Center, University Hospital Zurich,
[e] Department of Plastic Surgery and Hand Surgery, Cantonal Hospital Aarau, Aarau, Switzerland

ABSTRACT

Background: Transfusion of allogenic blood products was shown to be associated with more adverse events and a higher mortality in severely burned patients. This study investigated the impact of a goal-directed and factor-based coagulation algorithm on blood product use and clinical outcomes in severely burned patients.

Methods: This retrospective cohort study included adult patients admitted to the burn center of the University Hospital Zurich with major burn injuries compromising 20–80% of total body surface area. We compared two 3-year periods, one before the introduction of a goal-directed coagulation and transfusion algorithm (period 1: 2009–2011) and one after (period 2: 2016–2018). We applied linear and logistic regression models adjusted for confounders.

Results: We analyzed 36 patients (27.8% female) versus 42 patients (14.3% female) in period 1 and 2, respectively. Comorbidities and burn types were comparable between both collectives. Treatment according to the coagulation algorithm resulted in an overall reduction of 33 units of red blood cells (95% CI −52.8 to −12.9, $p = 0.002$), 9 units fresh frozen plasma (95% CI −14.7 to −2.6, $p = 0.006$) and 1.4g fibrinogen (95% CI −2.2 to −0.5, $p = 0.001$) per patient. We observed less infections (61.8% vs. 41.5%, $p = 0.11$) and a reduced mortality (38.9% vs. 26.8%, $p = 0.33$) during the algorithm treated period, although not significant.

Table 2 – Differences in the number of patients receiving allogeneic blood products and coagulation factors between the periods during the length of hospital stay.

	Period 1 [n = 36]	Period 2 [n = 42]	Odds ratio [95% CI]	*p*-value
Allogenic transfusions				
Red blood cells	26 (72.2%)	23 (54.8%)	0.47 [0.18 to 1.19]	0.11
Fresh frozen plasma	14 (38.9%)	4 (9.5%)	0.17 [0.04 to 0.53]	<0.01
Platelet concentrate	2 (5.6%)	2 (4.8%)	0.85 [0.10 to 7.39]	0.87
Coagulation factors				
4-factor PCC	4 (11.1%)	2 (4.8%)	0.40 [0.05 to 2.18]	0.31
Coagulation factor XIII	17 (47.2%)	17 (40.5%)	0.76 [0.31 to 1.87]	0.55
Fibrinogen	11 (30.6%)	4 (9.5%)	0.24 [0.06 to 0.79]	0.03

Data reported as number and percentage (%). Period 1 refers to the patient cohort before the introduction and Period 2 to the cohort treated according to the coagulation algorithm.
Abbreviation: 4-factor PCC, 4-factor prothrombin complex concentrate.

Table 3 – Adjusted models for the comparison of transfused allogeneic blood products and administered coagulation factors between the periods.

	Coefficient	95% confidence interval	*p*-value
Allogenic transfusions			
Red blood cells (units)	−33	−52.8 to −12.9	0.002
Fresh frozen plasma (units)	−9	−14.7 to −2.6	0.006
Platelet concentrate (units)	0	−0.7 to 0.2	0.300
Coagulation factors			
4-factor PCC (IU)	−61	−141.9 to 19.7	0.140
Coagulation factor XIII (IU)	−1211	−2443.7 to 20.9	0.054
Fibrinogen (g)	−1.4	−2.2 to −0.5	0.001

The coefficients represent the difference for the patients treated according to the coagulation algorithm (period 2) in comparison with patients treated before (period 1). The models are adjusted for age, sex, the Abbreviated Burn Severity Index (ABSI) and Charlson Comorbidity Index.
Abbreviation: 4-factor PCC, 4-factor prothrombin complex concentrate.

BURNS 47 (2021) 1486–1494

Effect of a factor-based coagulation management on blood product use after major burn injury: A retrospective cohort study

Sebastian D. Sahli [a,1], *Nadine Pedrazzi* [b,1], *Julia Braun* [c], *Donat R. Spahn* [a], *Alexander Kaserer* [a,2], *Jan A. Plock* [d,e,*,2]

[a] *Institute of Anesthesiology, University and University Hospital Zurich, Zurich, Switzerland*
[b] *Department of Plastic and Hand Surgery, Lausanne University Hospital, Lausanne, Switzerland*
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[e] *Department of Plastic Surgery and Hand Surgery, Cantonal Hospital Aarau, Aarau, Switzerland*

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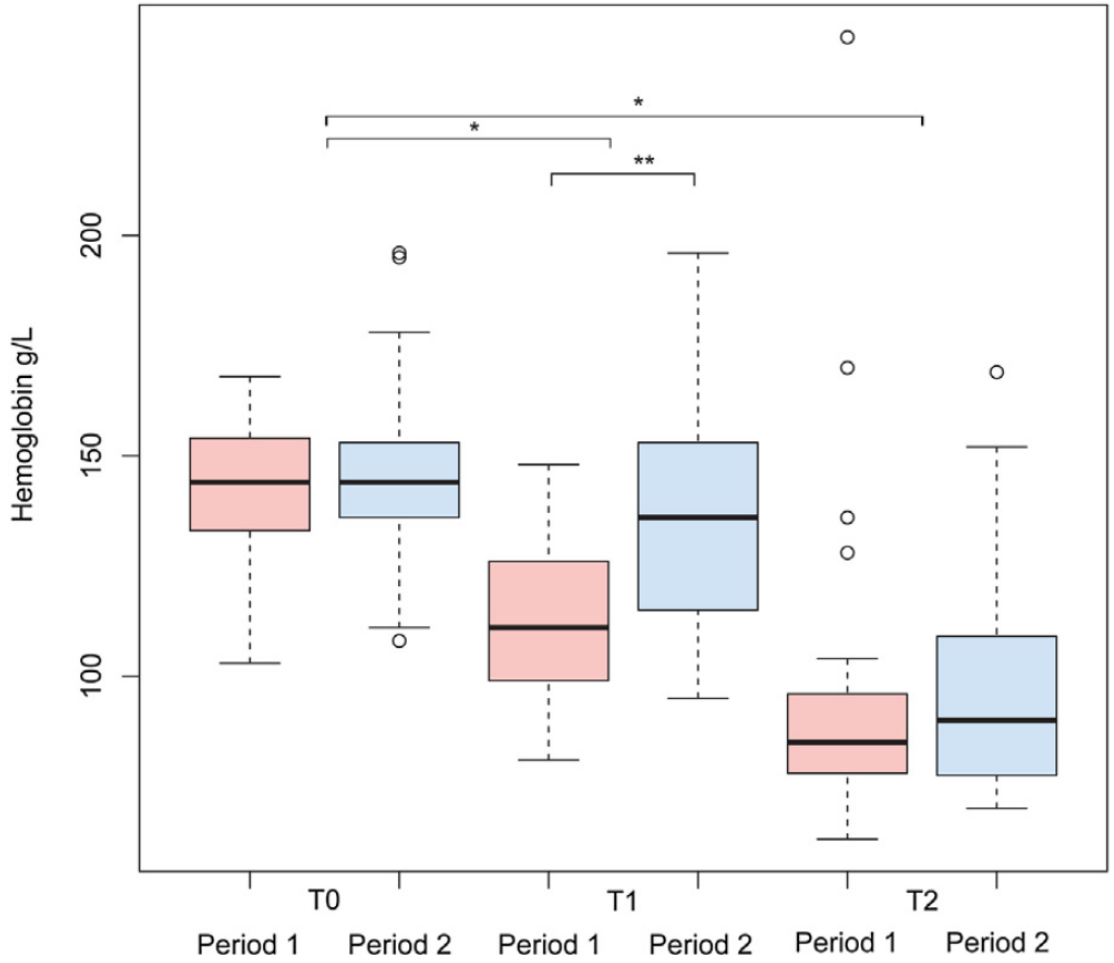

Fig. 3 – Boxplots for hemoglobin levels over time.
Comparing the patient cohort treated before (Period 1 = red) and with the coagulation algorithm (Period 2 = blue) between the course of different values over three time points T0 (baseline at admission), T1 (before the first surgical intervention), and T2 (discharge from ICU).
***Mixed linear models for a difference of T0 and T1, T0 and T2 ($p < 0.0001$, each), overall difference between period 1 and period 2 ($p = 0.02$). ** Unadjusted comparison at T1 between period 1 and period 2 ($p = 0.0005$); unadjusted comparison at T0 and T2 n.s. Level of significance 0.05.**

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-Related Acute Lung Injury

Report of a Clinical Look-Back Investigation

Patricia M. Kopko, MD
Carol S. Marshall, MD
Malcolm R. MacKenzie, MD
Paul V. Holland, MD
Mark A. Popovsky, MD

Context Transfusion-related acute lung injury (TRALI) is a syndrome that includes dyspnea, hypotension, bilateral pulmonary edema, and fever. TRALI is the third leading cause of transfusion-related mortality, but it is probably underdiagnosed and underreported.

Objective To determine if blood products from a frequent plasma donor, whose blood product was implicated in a fatal case of TRALI, caused symptoms of TRALI in other recipients of her plasma.

Design, Setting, and Participants Retrospective chart review (conducted from

JAMA. 2002;287:1

The Incidence of Transfusion-Related Acute Lung Injury at a Large, Urban Tertiary Medical Center: A Decade's Experience

David E. Meyer, MD, MS,* Jacob W. Reynolds, MD,* Rhonda Hobbs, MT (ASCP),†
Yu Bai, MD, PhD,‡ Beth Hartwell, MD,§ Matthew J. Pommerening, MD,* Erin E. Fox, PhD,‖
Charles E. Wade, PhD,*‖ John B. Holcomb, MD,*‖ and Bryan A. Cotton, MD, MPH*‖

BACKGROUND: While transfusion-related acute lung injury (TRALI) remains the primary cause of transfusion-related fatalities (37%), recent reports estimate the incidence of TRALI at 0.008% per unit of plasma transfused and 0.004% per all products transfused. Because blood banks have moved toward male-predominant plasma, TRALI appears, anecdotally, to have been reduced to an extremely rare event. The purpose of this study was to estimate the current incidence of TRALI at a large, urban center known for its early and aggressive use of plasma in the setting of trauma, hemorrhagic shock, and massive transfusion.
METHODS: The Blood Bank Registry of our hospital was queried for all transfused patients admitted from September 2002 through March 2013. The blood bank collected and investigated all cases of clinical acute lung injury meeting the consensus definition for TRALI, as well as potential cases for which the donor product was recalled for having a high reactivity level of human leukocyte antigen antibodies (ie, the antibodies that could cause TRALI). Clinical reactions were reviewed in conjunction with independent serological testing and classified by transfusion medicine physicians as being "probable TRALI" or of "unrelated etiology." The total number of units transfused at our facility during this time period was also obtained, allowing the incidence of TRALI to be estimated. Cases were analyzed based on demographics, outcome, blood types, observed symptoms and their duration, and type of product transfused.
RESULTS: Seven cases were identified at our center for the indicated time period, with only 3 of these occurring in trauma. A total of 714,757 units of blood products were transfused between September 2002 and March 2013. The incidence of TRALI was estimated to be 1 case per 100,000 units of product for the entire study period. A broad range of patients was affected. Consistent with previous descriptions, an acute duration of symptoms (average, 1.4 days) was observed and usually resolved with supportive care. Reactions were observed predominantly in plasma products, both type specific and nontype specific.
CONCLUSIONS: This study demonstrates that while TRALI still occurs, clinically meaningful cases are rare. Moreover, TRALI rates remain low despite the increasingly aggressive use of plasma and platelets in the trauma setting.

(Anesth Analg 2018;127:444–9)

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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)
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vCJD	First two cases (4,5)	?
Immunological reactions		
Hemolytic transfusion reactions		
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Alloimmunization	1:1,600 (10)	?
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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.

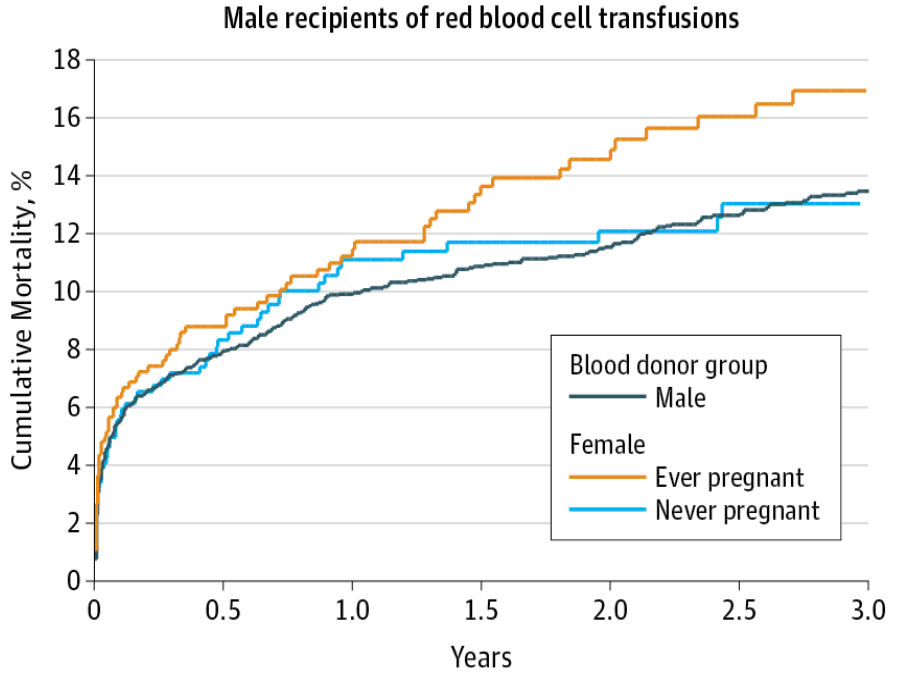
Madjdpour et al. Crit Care Med 2006; 34:S102–S108

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

MINI REVIEW article
Front. Med., 04 December 2017 | https://doi.org/10.3389/fmed.2017.00219

Pathogen Inactivation of Cellular Blood Products—An Additional Safety Layer in Transfusion Medicine

Axel Seltsam*

German Red Cross Blood Service NSTOB, Institute Springe, Springe, Germany

INTERCEPT Blood System for Platelets and Plasma

The INTERCEPT Blood System for platelets and plasma is manufactured by Cerus Corporation (Concord, CA, USA). The mechanism of action of this PI technology is based on the properties of amotosalen HCl (S-59), a photoactive compound which penetrates cellular and nuclear membranes and binds to the double-stranded regions of DNA and RNA. When activated by low-energy UVA light (320–400 nm), amatosalen cross-links nucleic acids and thus irreversibly blocks the replication of DNA and RNA (11). After illumination, residual amotosalen and its photoproducts must be removed during an incubation step lasting up to 16 h. The amatosalen/UVA procedure is not suitable for RBCs because of UVA light absorption by hemoglobin.

MIRASOL PRT System for Platelets and Plasma

The MIRASOL system was developed by TerumoBCT (Lakewood, CO, USA). This photodynamic procedure employs riboflavin (vitamin B2) and broad spectrum UV light (mainly UVA und UVB, 285–365 nm). On exposure to UVA and UVB light, riboflavin associates with nucleic acids and mediates oxygen-independent electron transfer, causing irreversible damage to the nucleic acids (12). Because naturally occurring vitamin B2 and its photodegradation products are non-toxic and non-mutagenic, they do not need to be removed prior to transfusion. In addition to plasma and platelets, protocols for extension of the MIRASOL system to whole blood are now in development.

THERAFLEX System for Platelets

THERAFLEX UV-Platelets is a novel UVC-based PI technology that works without photoactive substances. It is the product of a joint venture between Macopharma (Mouvaux, France) and the German Red Cross Blood Service NSTOB in Springe, Germany. Shortwave UVC light (254 nm) directly interacts with nucleic acids to form pyrimidine dimers that block the elongation of nucleic acid transcripts (13). UVC irradiation mainly affects the nucleic acids of pathogens and leukocytes and does not impair plasma and platelet quality. As no photoactive substances are involved, UVC treatment is just as simple but faster (takes less than 1 min) than gamma irradiation, and can easily be integrated into the manufacturing processes at blood banks (Figure 1). The THERAFLEX system was originally developed for platelets but is also suitable for plasma and RBC units.

	Technology			
	INTERCEPT blood system	**MIRASOL PRT system**	**THERAFLEX UV-Platelets**	**S-303 system**
Mechanism of action	UVA plus amotosalen (alkylating agent)	UV plus riboflavin (vitamin B2 = photosensitizer)	UVC alone	Alkylating agent
Blood products	Plasma and platelets	Plasma and platelets (in development for whole blood)	Plasma and platelets (in development for RBCs)	RBCs
Status	Approved in some countries	Approved in some countries	In clinical development	In clinical development

UV, ultraviolet light; UVA, wavelength A; UVC, wavelength C; RBC, red blood cell.

British Journal of Anaesthesia **106** (4): 505–11 (2011)
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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

Background. Indications, efficacy, and safety of plasma products are highly debated. We compared the concentrations of haemostatic proteins and cytokines in solvent/detergent-treated plasma (SDP) and fresh-frozen plasma (FFP).

Methods. Concentrations of the following parameters were measured in 25 SDP and FFP samples: fibrinogen (FBG), factor (F) II, F V, F VII, F VIII, F IX, F X, F XIII, von Willebrand factor (vWF), D-Dimers, ADAMTS-13 protease, tumour necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, IL-8, and IL-10.

Results. Mean FBG concentrations in SDP and FFP were similar, but in FFP, the range was larger than in SDP ($P<0.01$). Mean F II, F VII, F VIII, F IX, and F XIII levels did not differ significantly. Higher concentrations of F V ($P<0.01$), F X ($P<0.05$), vWF ($P<0.01$), and ADAMTS-13 ($P<0.01$) were found in FFP. With the exception of F VIII and F IX, the range of concentrations for all of these factors was smaller ($P<0.05$) in SDP than in FFP. Concentrations of TNF-α, IL-8, and IL-10 (all $P<0.01$) were higher in FFP than in SDP, again with a higher variability and thus larger ranges ($P<0.01$).

Conclusions. Coagulation factor content is similar for SDP and FFP, with notable exceptions of less F V, vWF, and ADAMTS-13 in SDP. Cytokine concentrations (TNFα, IL-8, and IL-10) were significantly higher in FFP. The clinical relevance of these findings needs to be established in outcome studies.

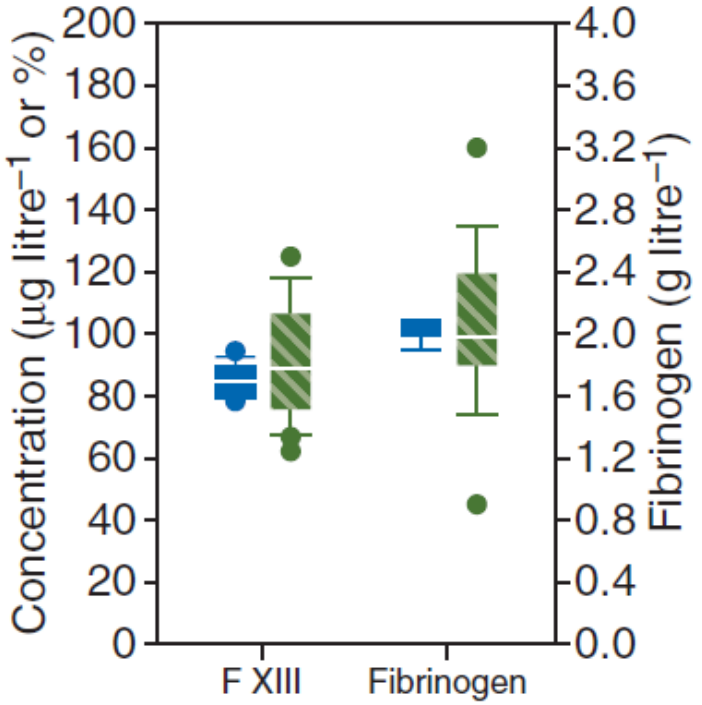
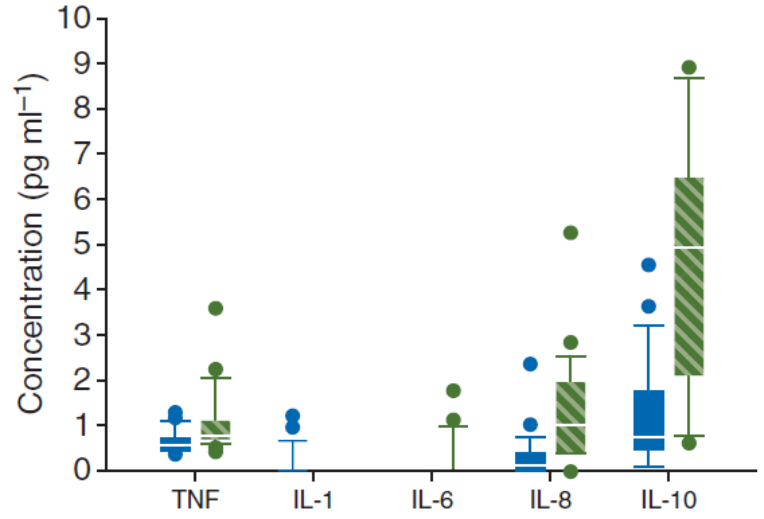


Fig 1 Haemostatic parameters and cytokine levels in SDP (blue bars) and FFP samples (green striped bars).



TRANSFUSION 2020;60;54–61

Solvent detergent treated pooled plasma and reduction of allergic transfusion reactions

Andrea M. McGonigle,[1] *Eshan U. Patel*,[2] *Kevin M. Waters*,[3] *Alison R. Moliterno*,[4] *Sandra K. Thoman*,[2] *Sonja O. Vozniak*,[2] *Paul M. Ness*,[2] *Karen E. King*,[2,†] *Aaron A. R. Tobian*,[2,‡] *and Parvez M. Lokhandwala*[2,‡]

BACKGROUND: Thrombotic thrombocytopenic purpura (TTP) patients have increased risk for allergic transfusion reactions (ATR) due to the number of plasma products they require. This study evaluated the efficacy of solvent detergent treated plasma (S/D treated plasma) to reduce ATRs.

STUDY DESIGN AND METHODS: All TTP patients who presented from April 2014 to February 2015 and experienced a moderate–severe ATR to untreated plasma with TPE were switched to S/D treated plasma (Octaplas) for their remaining procedures and included in the study. Patient records were retrospectively reviewed.

RESULTS: The overall ATR rate per procedure
.0% (95% CI = 15.4%-59.2%) with
o 1.4% ([1/73] 95% CI = 0.0%-7.4%)
asma. The moderate–severe ATR rate
.0% ([4/20] 95% CI = 5.7%-43.7%)
ma to 0.0% ([0/73] 95% CI = 0.0%-
ated plasma. The overall ATR rate per
sed from 2.6% (95%CI = 1.0%-5.1%)
ma to 0.1% (95% CI = 0.0%-0.4%)
asma. No patients experienced VTE
reated plasma. Four patients
vents while receiving S/D treated
s who experienced a VTE had
ors for VTE.
S/D plasma has promise as an
reduce the risk of ATRs in TTP
high risk of ATR in TTP patients,
D plasma instead of untreated plasma
atients may be warranted, especially
history of moderate to severe ATR.
dies are needed to confirm these

TABLE 3. Overall allergic transfusion reaction (ATR) rate per procedure and per plasma un

Patient	Untreated plasma: No. overall ATR	No. moderate–severe ATR	No. procedures	No. units	ATR per procedure rate (%)	ATR per unit rate (%)	No. overall ATR
Patient 1	4	1	10	147	40.0	2.7	1
Patient 2	1	1	1	7	100.0	14.3	0
Patient 3	1	1	6	80	16.7	1.3	0
Patient 4	1	1	3	40	33.3	2.5	0
Patient 5*	–	–	–	–	–	–	0
Patient 6*	–	–	–	–	–	–	0
Overall†	7	4	20	274	35.0	2.6	1

* S/D Patients #5 and #6 received all of their TPE with untreated plasma at the OSH; the exact number of TPE proce
† Overall values only include Patients #1-4, in whom data on plasma transfusion and occurrence of ATRs was availal
ATR = allergic transfusion reaction; No. = number; mL = milliliter.

TABLE 1. Allergic symptoms with untreated plasma versus S/D treated plasma

	Symptoms with untreated plasma	Symptoms with S/D treated plasma
Patient 1	Itching, hives, oropharyngeal edema (multiple episodes); SOB	Itching, eyelid swelling (1 episode)
Patient 2	Respiratory distress, threatened intubation	None
Patient 3	Acute onset of rapid, dry cough	None
Patient 4	Chest tightness, itching	None
Patient 5	Hives, chest tightness, SOB prior to transfer*	None
Patient 6	Hives, chest tightness, SOB prior to transfer*	None

* Per patients' report.
SOB = shortness of breath.

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https://doi.org/10.1007/s11239-018-1789-9

Individual differences of plasma proteins and factors in fresh frozen plasma from Chinese regional blood donors

Abstract
Currently, single fresh frozen plasma (FFP) for clinical use is derived from individual blood donors. The objective of this study is to investigate the differences in single FFP units to make related strategies for improving FFP transfusion efficacy. 120 units of single FFP were selected randomly from Chinese PLA Clinical Blood Transfusion Center in Beijing, China. Single FFP samples were thawed in 37 °C water bath and were assessed immediately for total protein (TP), albumin (Alb), fibrinogen (Fg), factor V (FV), factor VIII (FVIII), antithrombin-III (AT-III) and protein C (PC). Multiple comparisons were employed to analysis the differences. The quality levels of 120 single FFP units showed wider ranges and presented normal distribution. Fg, FV and PC showed larger fluctuation range but TP, Alb, FVIII and AT-III showed smaller. The mean level of TP was 56.07 g/L and FVIII was 0.62 IU/mL. There were no significant differences to genders in single FFP units. FFP from younger people with 18–30 years old showed a trend towards reduced activity of coagulation factors, especially FV and FVIII. TP and Alb levels in FFP with type O were significantly higher than that in non-O type, but FVIII, AT-III and PC levels were lower in type O than that in non-O type. In a word, the whole quality of single FFP units from Chinese regional donors was acceptable, except FVIII. There were great differences of plasma proteins and factors in single FFP units, age and ABO blood type were main influence factors.

analýza složení plazmy

Parameters	n	M ± SD	Range
Fg (g/L)	120	2.21 ± 0.47	1.32–3.96
FV (IU/mL)	120	0.83 ± 0.15	0.48–1.39
FVIII (IU/mL)	120	0.62 ± 0.18	0.33–1.36
AT-III (IU/mL)	120	1.26 ± 0.14	0.84–1.61
PC (IU/mL)	120	1.05 ± 0.22	0.51–1.77

Table 1 Quality range of plasma factors in 120 single FFP units

rozdíly dle ABO skupin

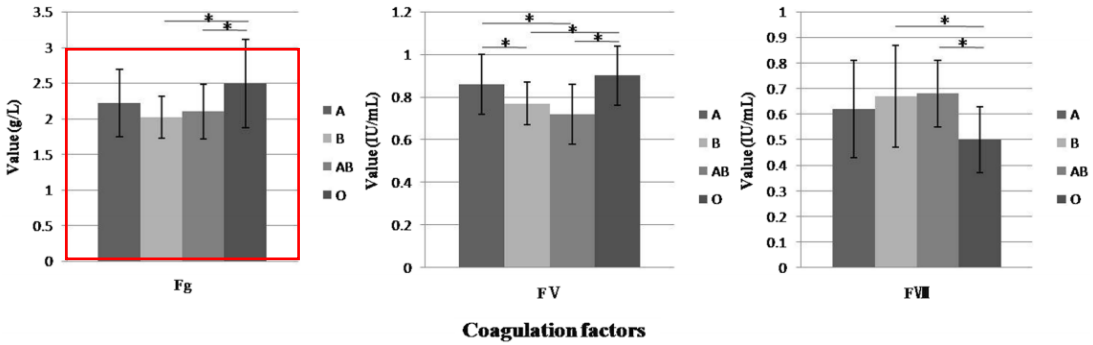


Fig. 4 Blood type differences of plasma proteins and factors in 120 single FFP units. *$P < 0.05$

rozdíly jednotlivců

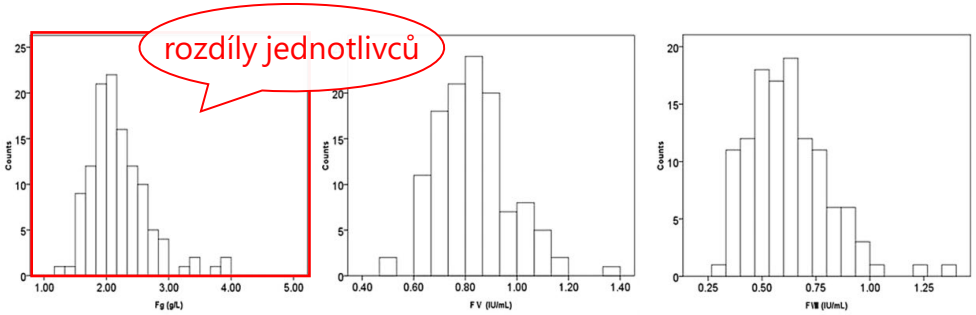


Fig. 1 Frequency distribution of plasma proteins and factors in 120 single FFP units

National Comparative Audit of Blood Transfusion

2018 Audit of the Management of Major Haemorrhage

Figure 5. Boxplot of issued, transfused and wasted RBC units by cause of haemorrhage

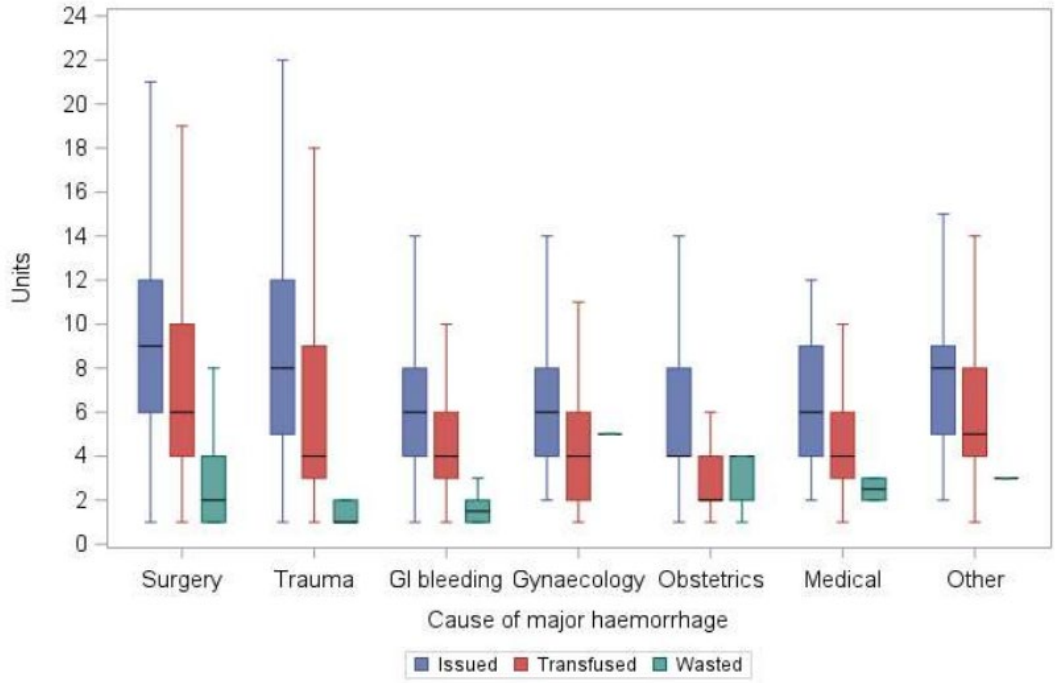
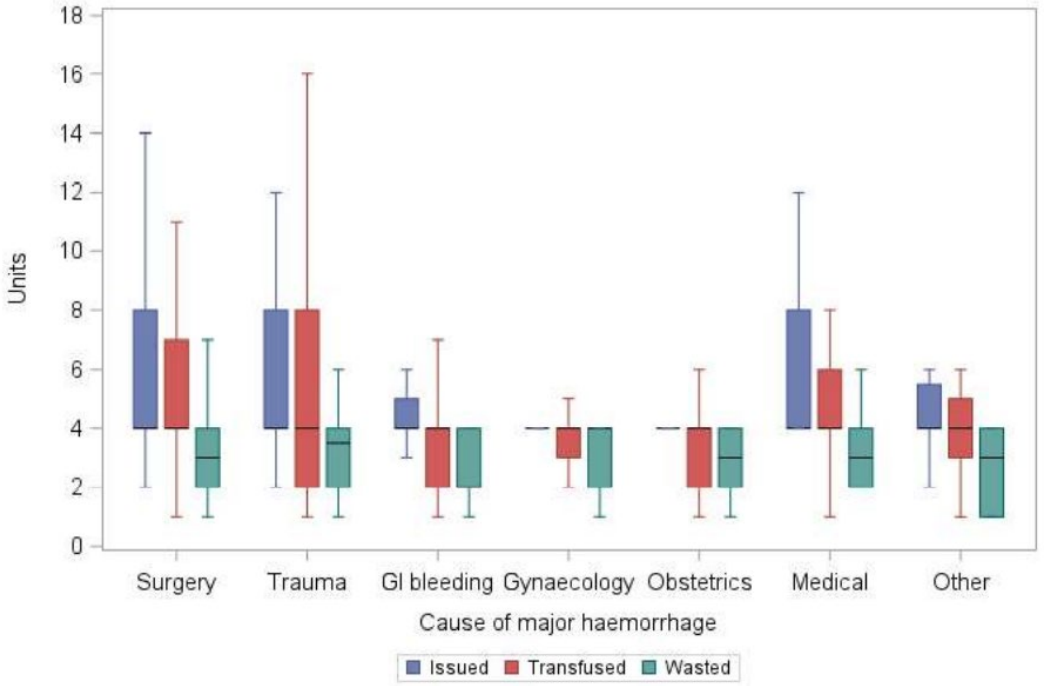
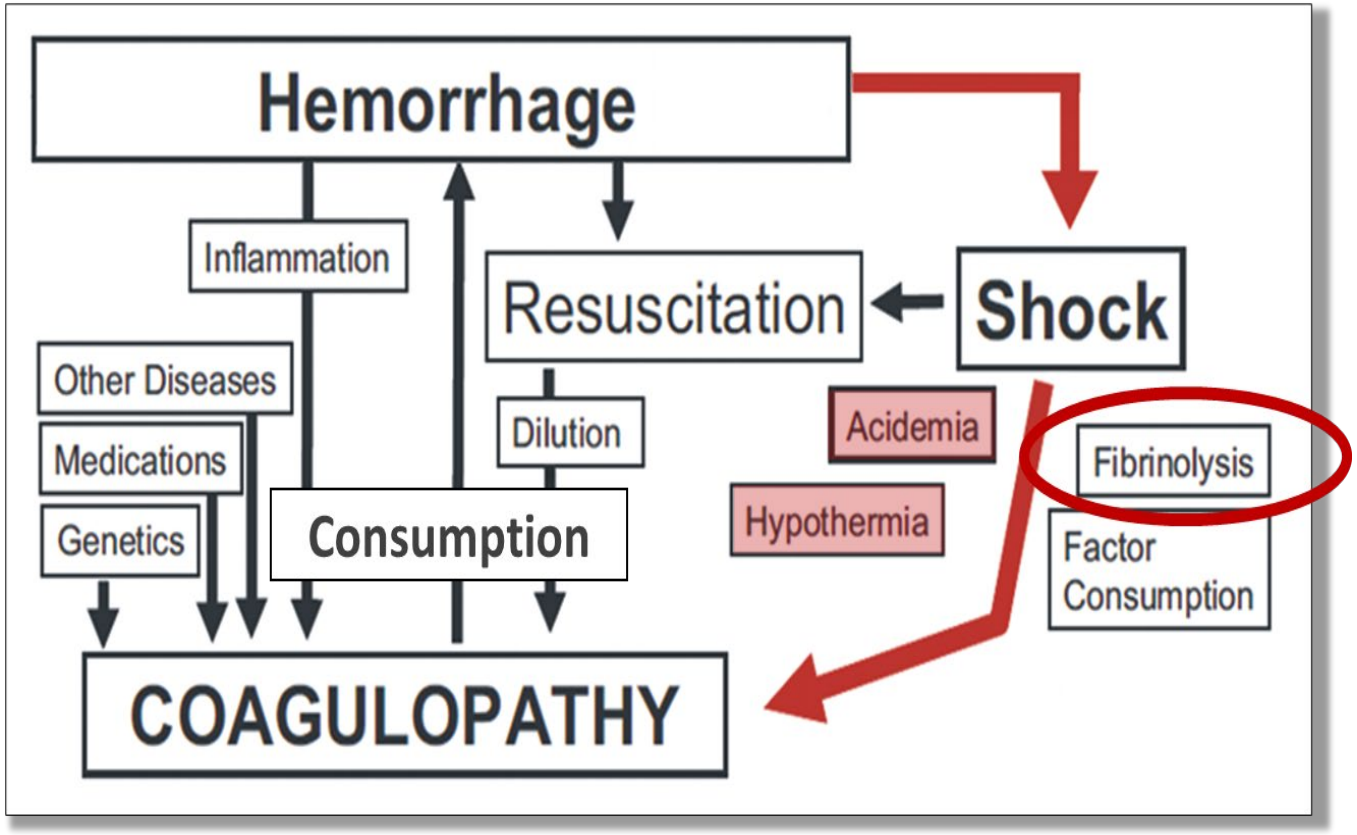
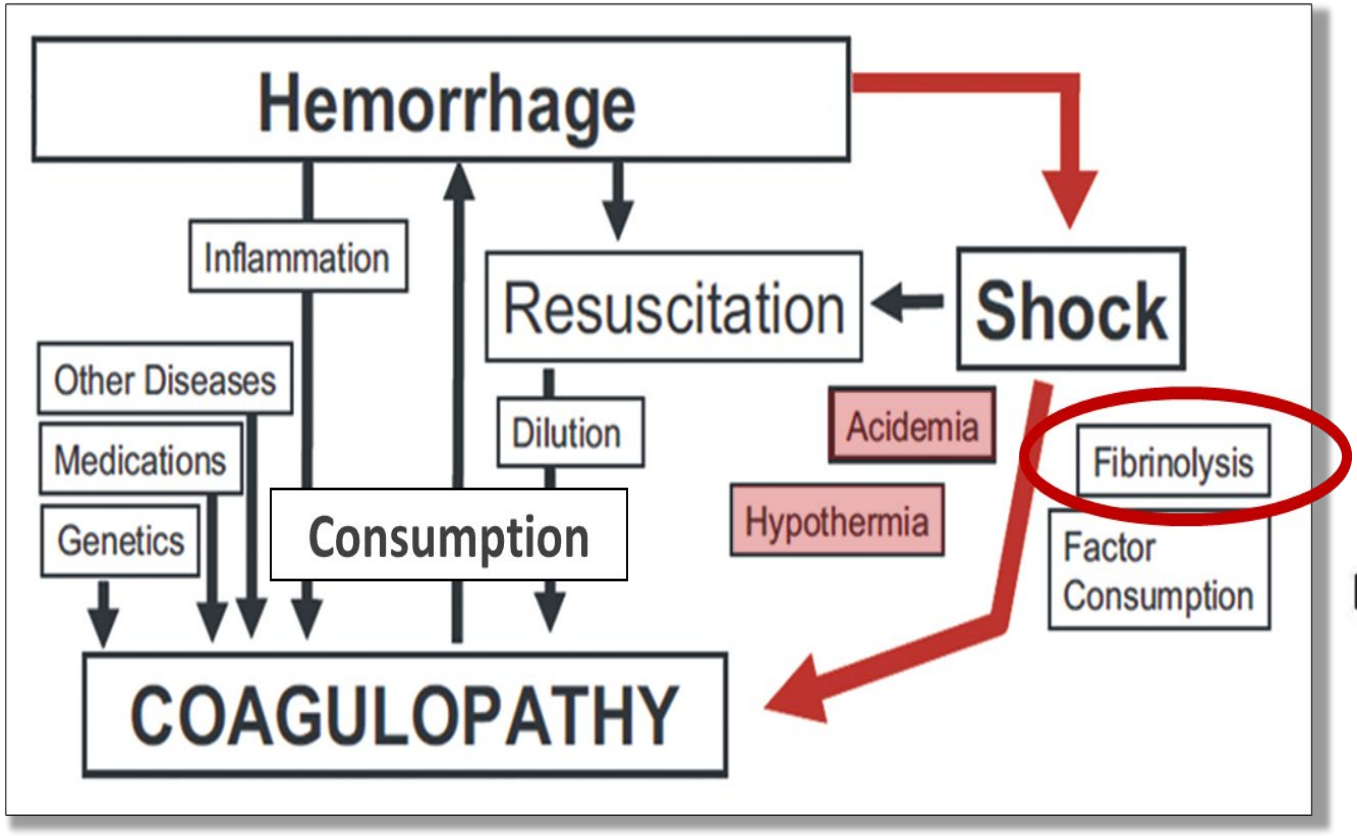


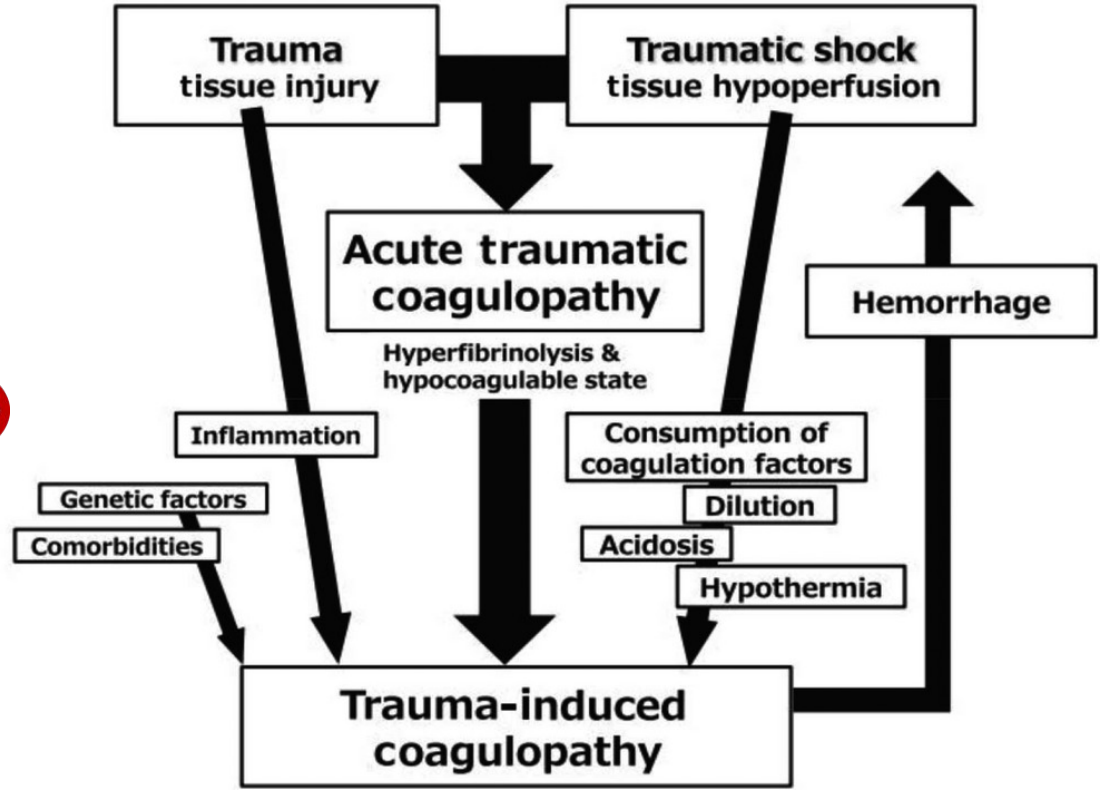
Figure 6. Boxplot of issued, transfused and wasted FFP units by cause of haemorrhage





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



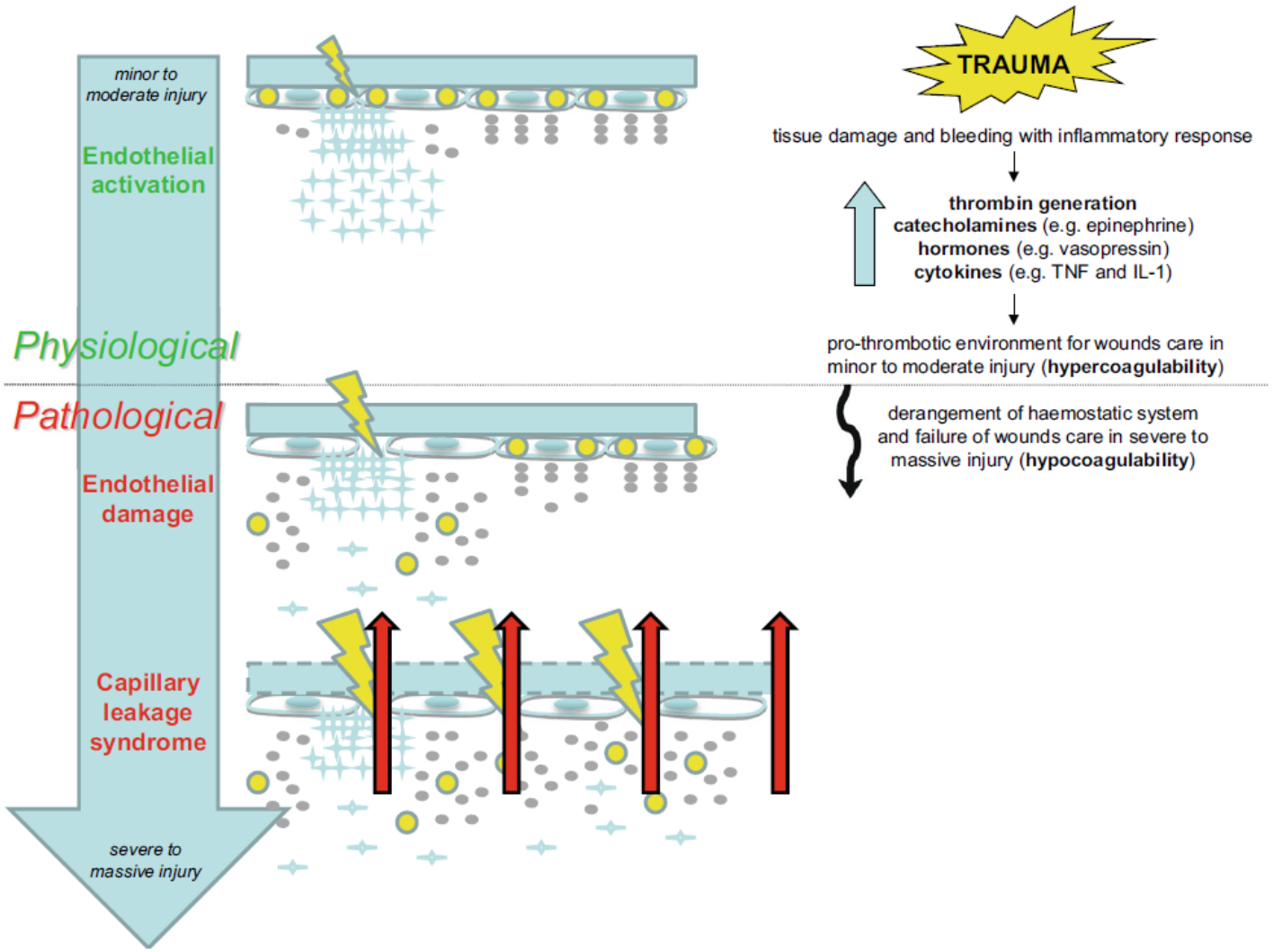


Adaptováno z Hess et al. J Trauma. 2008;65:748-54

Fig. 1. Pathophysiologic response timeline and the trauma-induced coagulopathy dynamic.

Vernon, T et al.. Acute Med Surg 2019, 6: 215-222.

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

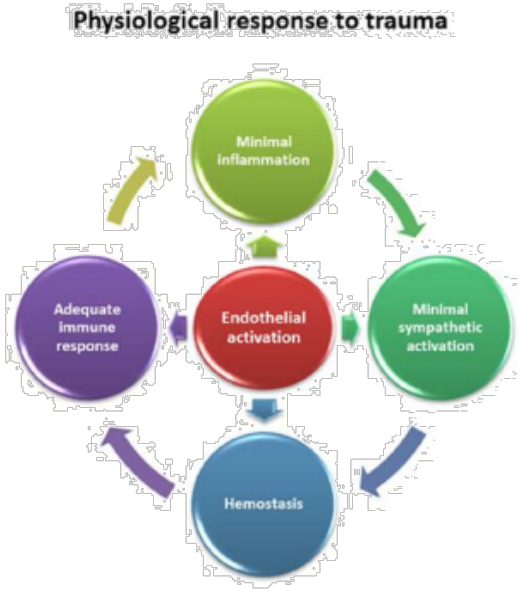
The current understanding of trauma-induced coagulopathy (TIC): a focused review on pathophysiology

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

Pathophysiological Response to Trauma-Induced Coagulopathy: A Comprehensive Review

Patricia Duque,* Lidia Mora,† Jerrold H. Levy,‡ and Herbert Schöchl,§‖



Hypercoagulability can occur after severe tissue injury, that is likely related to tissue factor exposure and impaired endothelial release of tissue plasminogen activator (tPA). In contrast, when shock and hypoperfusion occur, activation of the protein C pathway and endothelial tPA release induce a shift from a procoagulant to a hypocoagulable and hyperfibrinolytic state with a high risk of bleeding. Both thrombotic and bleeding phenotypes are associated with increased mortality and are influenced by the extent and severity of tissue injury and degree of hemorrhagic shock. Response to trauma is a complex, dynamic process in which risk can shift from bleeding to thrombosis depending on the injury pattern, hemostatic treatment, individual responses, genetic predisposition, and comorbidities. Based on this body of knowledge, we will review and consider future directions for the management of severely injured trauma patients. (Anesth Analg 2020;130:654–64)

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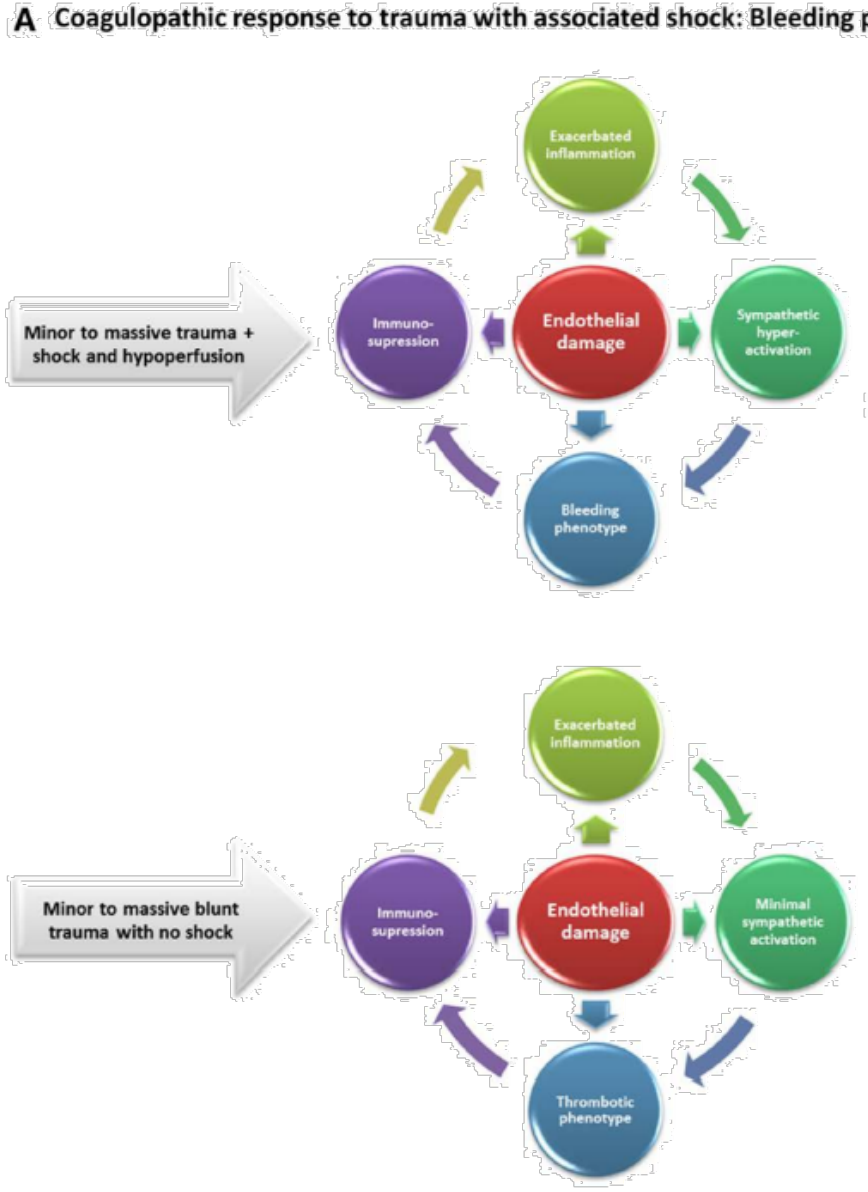


Figure 2. Coagulopathic response to trauma. Novel concepts. A, Coagulopathic response to trauma with associated shock: bleeding phenotype. Shock and hypoperfusion in patients with severe trauma can induce hypocoagulability and hyperfibrinolysis that might lead to life-threatening bleeding. B, Coagulopathic response to trauma without associated shock: thrombotic phenotype. Severe tissue injury is shortly followed by a hypercoagulable state probably related to tissue factor exposure and impaired endothelial release of tissue plasminogen activator.

Duque et al. Anesth Analg 2020;130:654–64

Therapeutic approach

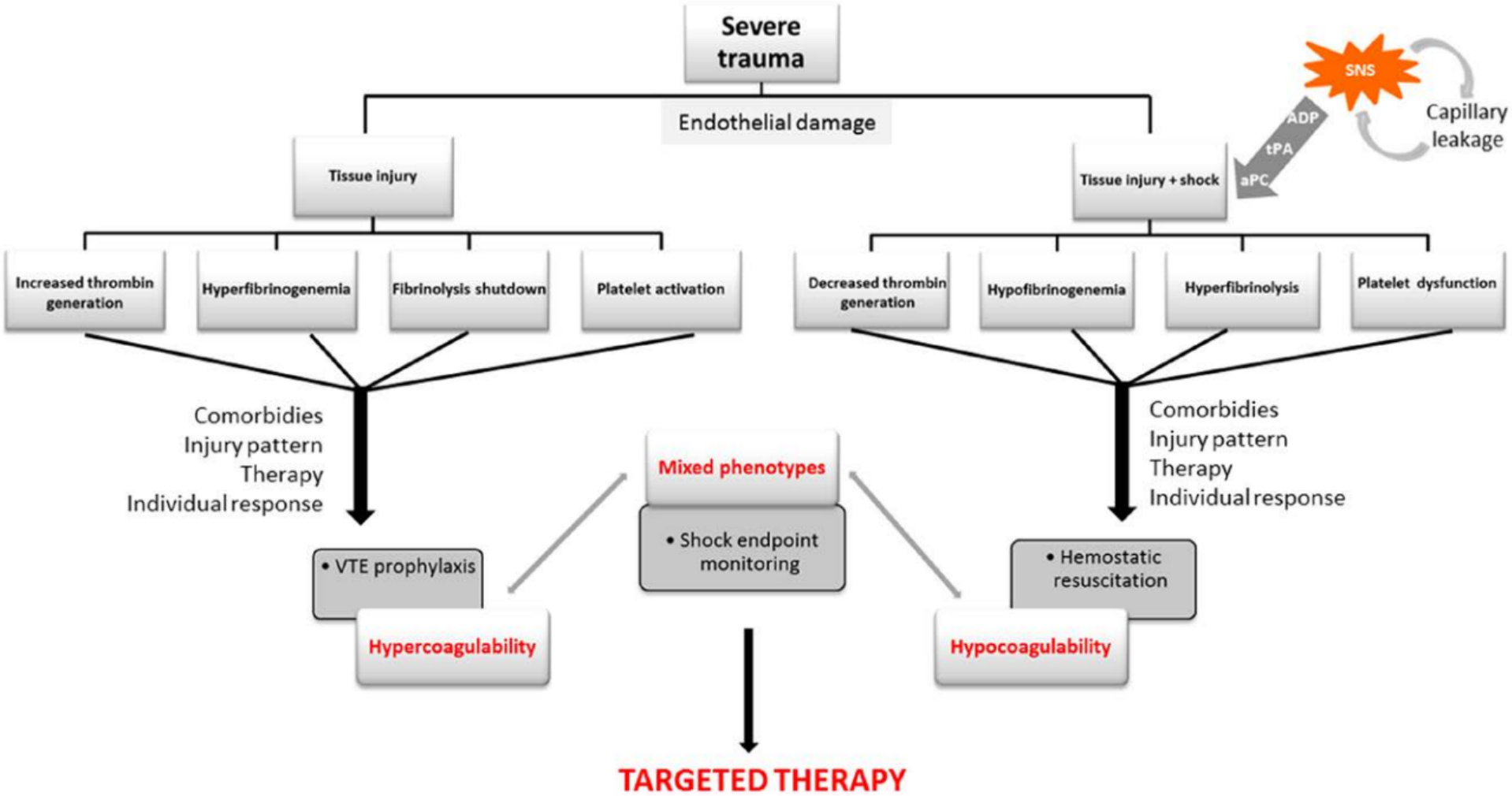


Figure 3. Therapeutic approach. Patients presenting with severe tissue injury without shock are at high risk of thrombosis and every effort should be made to prevent this serious condition. However, shock and hypoperfusion in patients with severe trauma can induce hypocoagulability and hyperfibrinolysis. This state is associated with very high mortality and needs to be treated urgently with early hemostatic goal-directed resuscitation. Response to trauma is a complex, dynamic process in which risk can shift from bleeding to thrombosis depending on the injury pattern, treatment administered, individual responses, and comorbidities.

Duque et al. Anesth Analg 2020;130:654–64

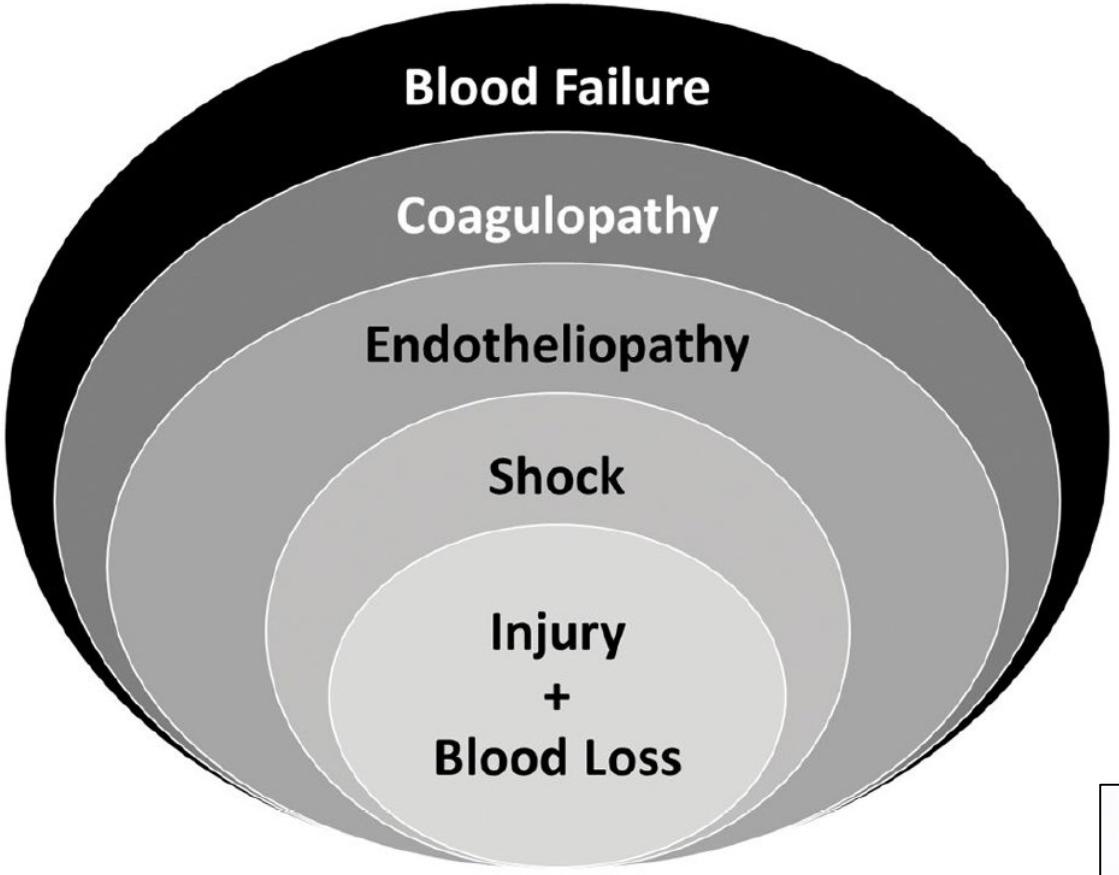


Figure 1.
Schematic representing the components of hemorrhagic blood failure.

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**

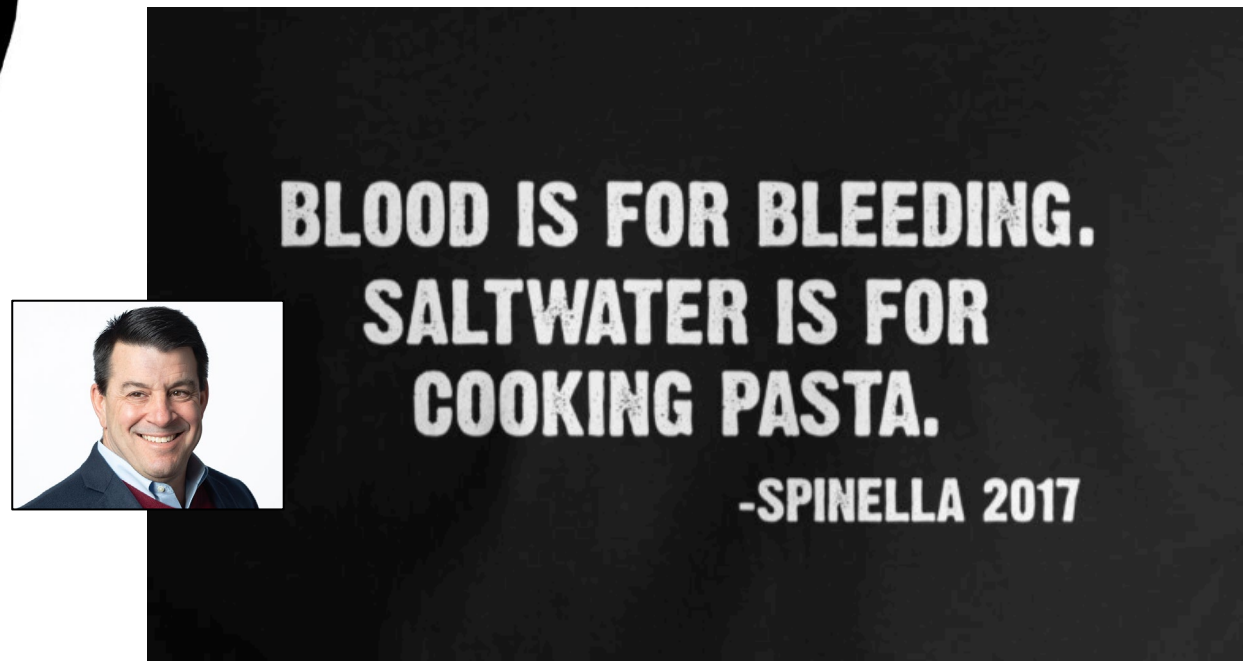
University of Washington Division of Emergency Medicine and Harborview Medical Center

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



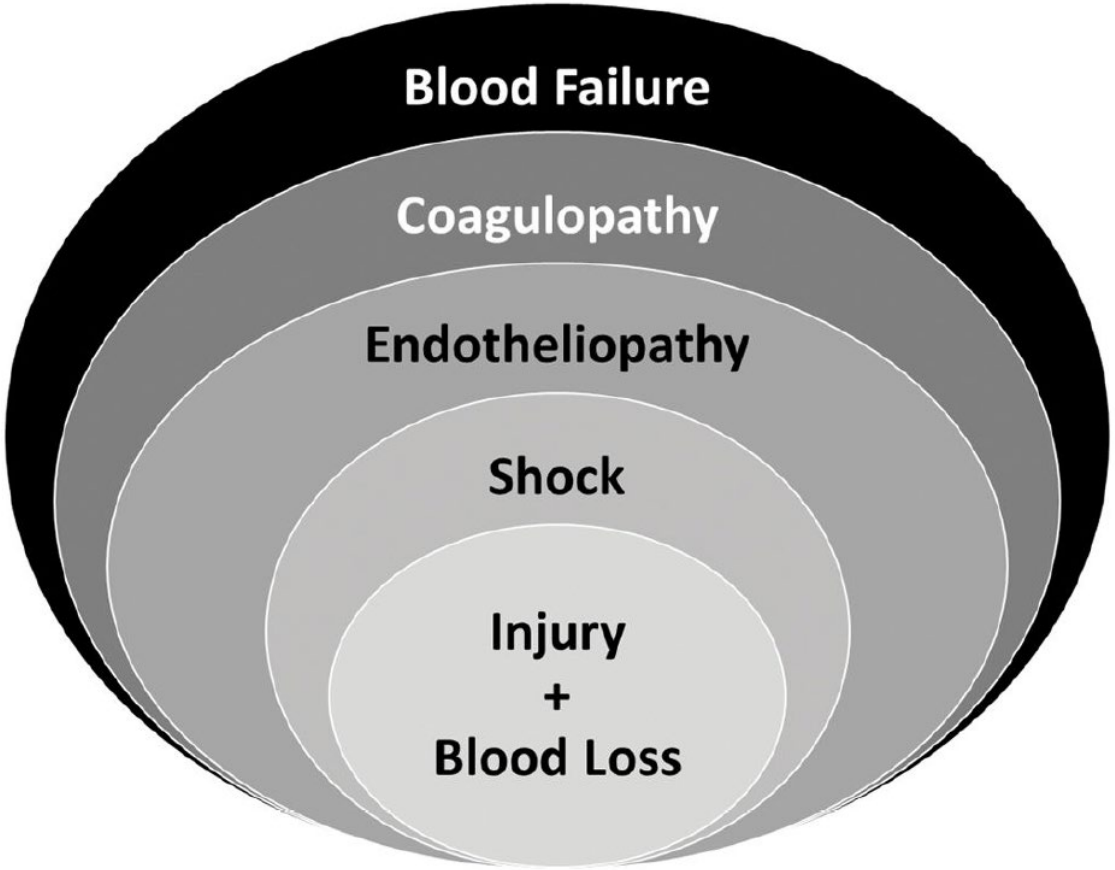


Figure 1.
Schematic representing the components of hemorrhagic blood failure.

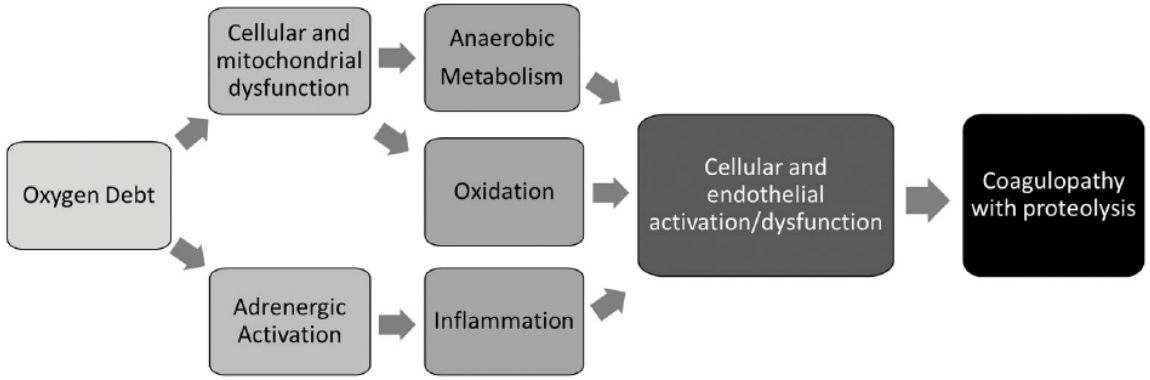


Figure 2.
Schematic of key linkages between oxygen debt, cellular dysfunction, and coagulopathy during hemorrhagic blood failure.

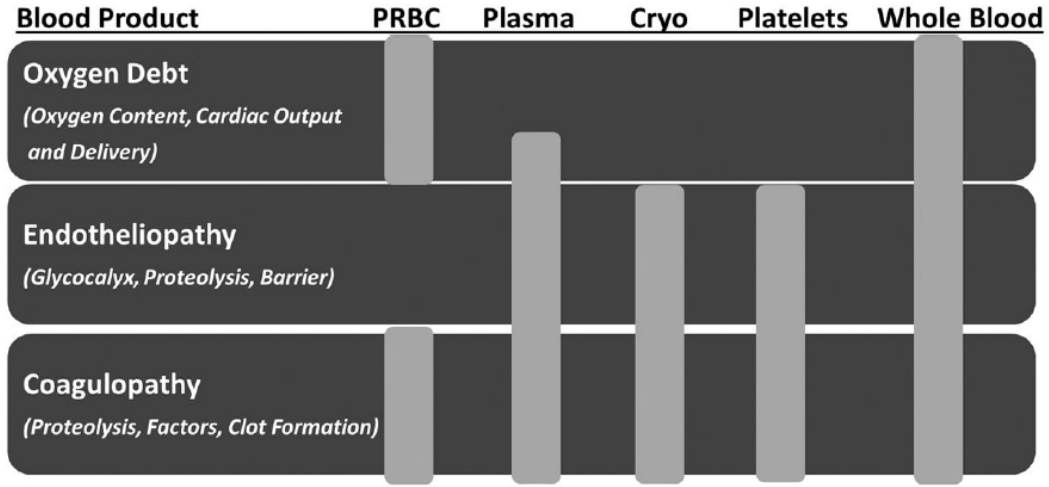


Figure 3.
Schematic summarizing the effects of individual blood products on the three components of hemorrhagic blood failure. PRBC= packed red blood cells, Cryo= cryoprecipitate

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

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Prognostic value of preoperative plasma fibrinogen levels in resected stage I non-small cell lung cancer

Suguru Mitsui | **Yugo Tanaka** | **Takefumi Doi** | **Daisuke Hokka** | **Yoshimasa Maniwa**

Division of Thoracic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

Background: The number of surgical procedures has increased among patients with early-stage lung cancer. If the poor prognostic factors for stage I non-small cell lung cancer (NSCLC) can be simply validated preoperatively, appropriate treatment will be provided. The current study aimed to evaluate the prognostic value of preoperative plasma fibrinogen levels in patients with resected stage I NSCLC.

Methods: We retrospectively analyzed the clinicopathological information of patients ($n = 149$) who underwent lobectomy for stage I NSCLC between May 2014 and July 2016. Data about peripheral blood analysis, histopathological finding, and follow-up assessment results were collected from the databases. Patients were divided into the low and high fibrinogen groups. Univariate and multivariate analyses were performed to evaluate the predictors of recurrence and survival.

Results: Compared with the low fibrinogen group (<377 mg/dl), the high fibrinogen group (≥377 mg/dl) had a significantly greater number of male participants ($p = 0.04$), smokers ($p < 0.001$), and those with elevated cytokeratin antigen levels ($p = 0.04$), lymphatic invasion ($p = 0.007$), and squamous cell carcinoma ($p < 0.001$). Plasma fibrinogen level was considered a significant independent factor for recurrence and overall survival on both the univariate and multivariate analyses ($p < 0.001$ and $p = 0.010$) and the multivariate analysis alone ($p = 0.020$ and $p < 0.012$).

Conclusion: Preoperative plasma fibrinogen level might be a useful predictor of recurrence and survival in patients with stage I NSCLC. The treatment strategy for patients with high fibrinogen levels could be cautiously considered preoperatively.

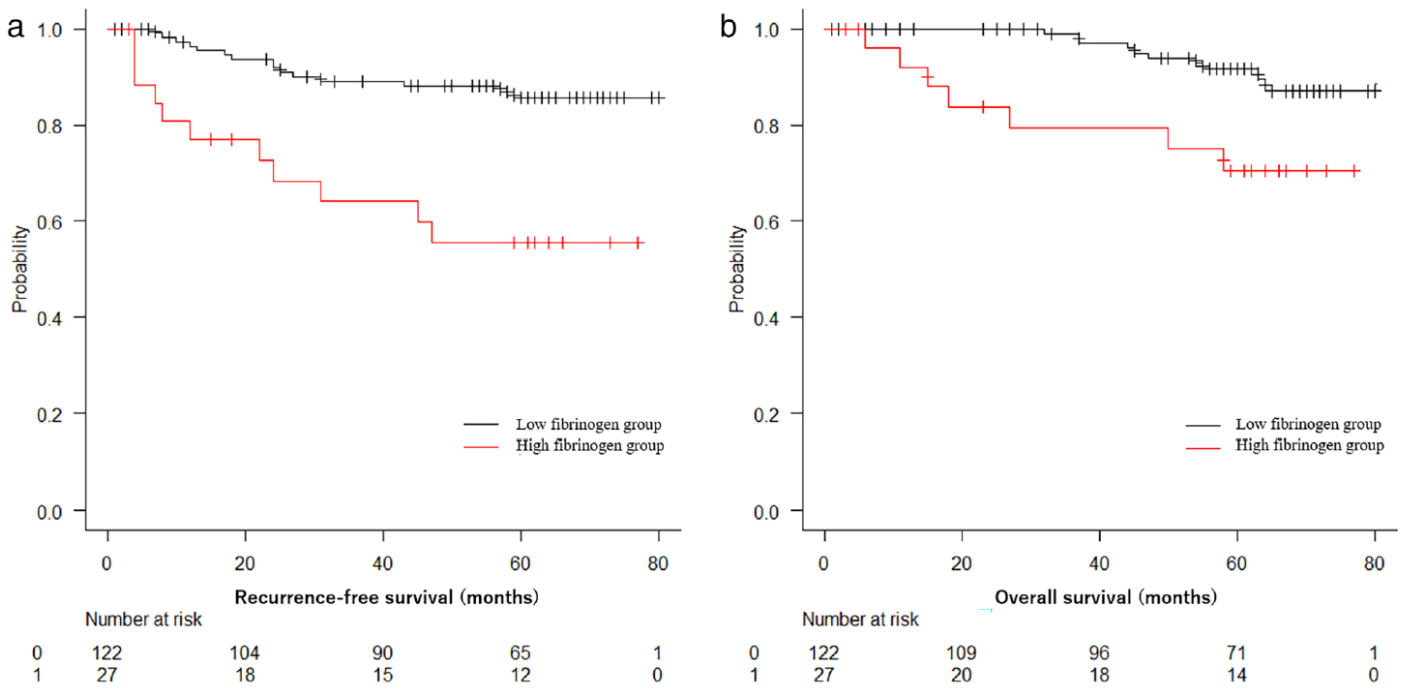


FIGURE 2 (a) Recurrence-free survival curves of the high and low fibrinogen groups. The 5-year recurrence-free survival rates of the high and low fibrinogen groups were 55.6% and 85.7%, respectively. (b) Overall survival curves of the high and low fibrinogen groups. The 5-year overall survival rates were 70.6% in the high fibrinogen group and 91.8% in the low fibrinogen group

Fibrinogenolysis in Venom-Induced Consumption Coagulopathy after *Viperidae* Snakebites: A Pilot Study

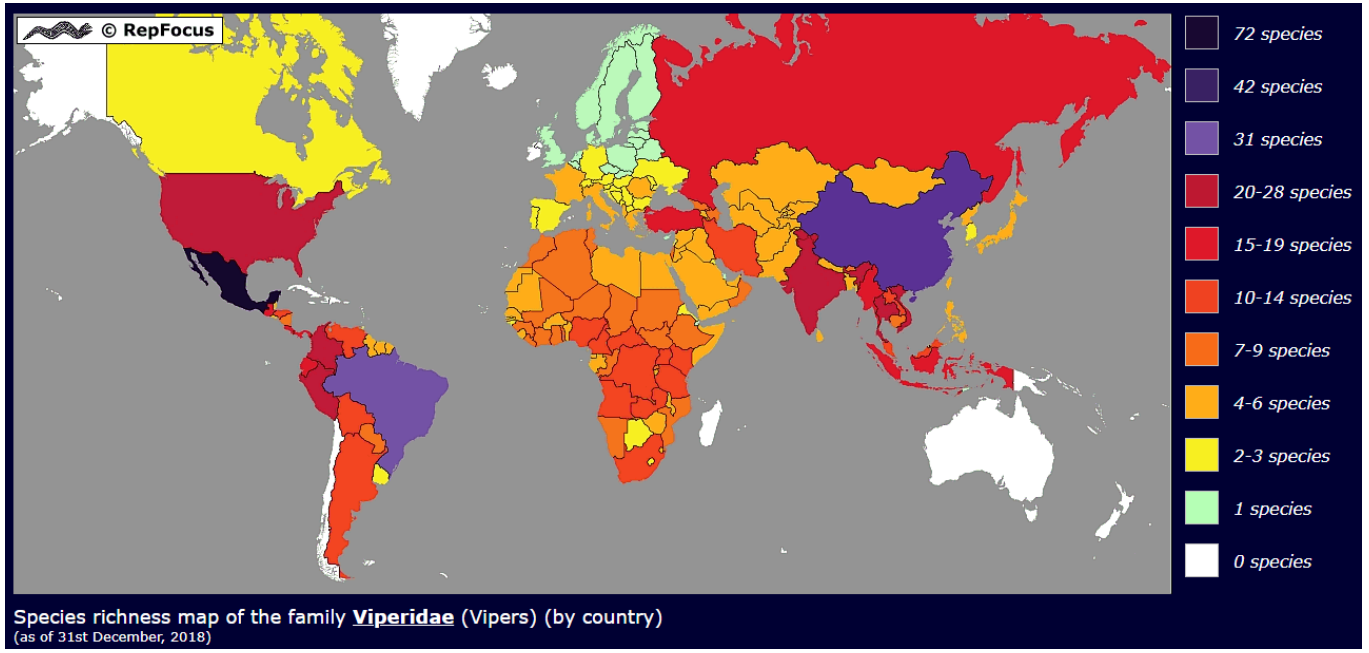
Jiri Valenta [1], Alzbeta Hlavackova [2,*], Zdenek Stach [1], Jana Stikarova [2], Marek Havlicek [2] and Pavel Michalek [1,*]

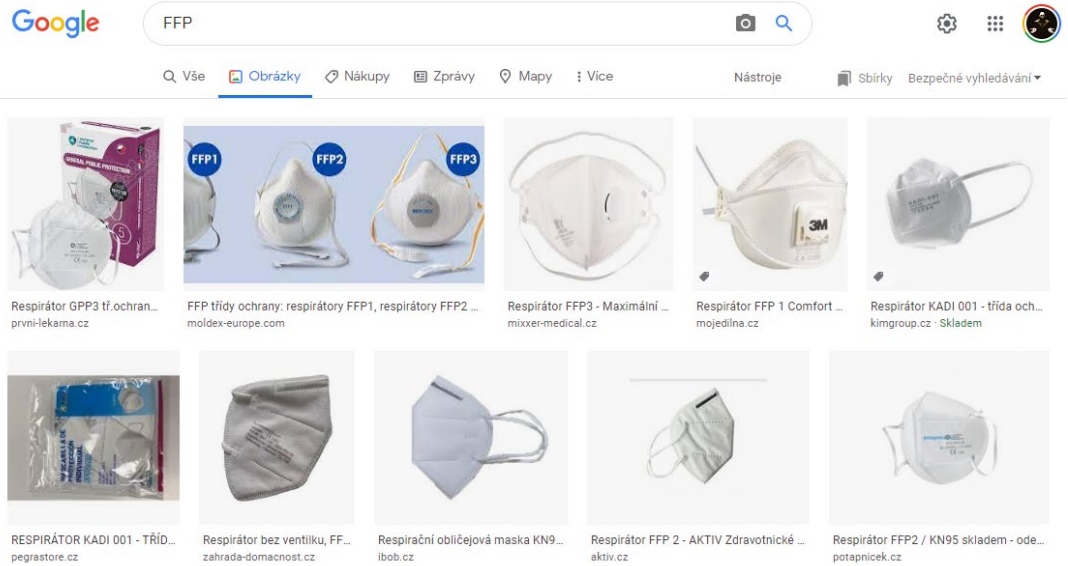
[1] Department of Anaesthesiology and Intensive Medicine, Toxinology Center, First Medical Faculty, Charles University, General University Hospital, Prague, Czech Republic
[2] Department of Biochemistry, Institute of Hematology and Blood Transfusion, Prague, Czech Republic

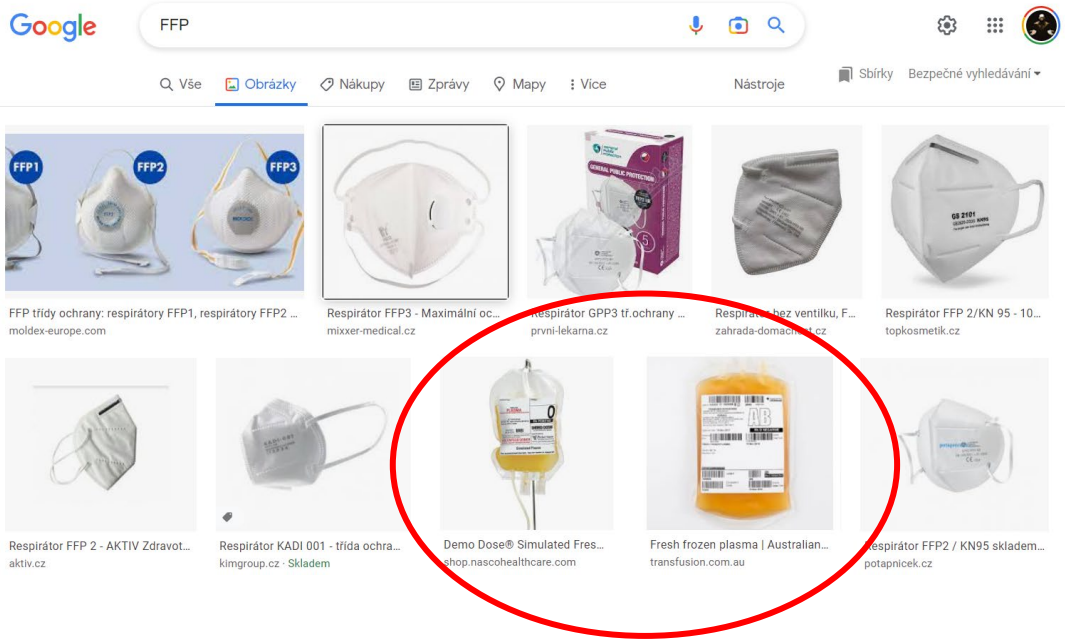
Abstract: Envenomations that are caused by *Viperidae* snakebites are mostly accompanied by venom-induced consumption coagulopathy (VICC) with defibrination. The clinical course of VICC is well described; however, reports about its detailed effects in the hemocoagulation systems of patients are sparse. In this pilot study, we prospectively analyzed the changes in plasma fibrinogen that were caused by the envenomation of six patients by five non-European *Viperidae* snakes. Western blot analysis was employed and fibrinogen fragments were visualized with the use of specific anti-human fibrinogen antibodies. All of the studied subjects experienced hypo- or afibrinogenemia. The western blot analysis demonstrated fibrinogenolysis of the fibrinogen chains in all of the cases. Fibrinogenolysis was considered to be a predominant cause of defibrination in *Crotalus*, *Echis*, and *Macrovipera* envenomation; while, in the cases of VICC that were caused by *Atheris* and *Calloselasma* envenomation, the splitting of the fibrinogen chains was present less significantly.

Atheris nitschei

Hours Since Bite	0.75	3.75	12	18	22	28	36
PT/INR	0.94	1.02	1.13	1.38	1.35	1.31	1.17
APTT (s)	26.1	27.8	27.8	36.8	34.8	33.2	32.8
TT (s)	NA	NA	NA	22.8	19.4	16.8	15.0
AT III (% activity)	105	84	74	81	76	77	81
FBG Claus (g/L)	2.6	1.6	0.3	0.2	0.3	0.3	0.94
D-dimers (μg/L)	210	3110	18,500	5190	2226	1100	691
PLT ($\times 10^9$/L)	186	NA	159	180	172	172	180







jan.blaha@vfn.cz