Platelets: What, how much, for whom, does it matter?

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Disclosure

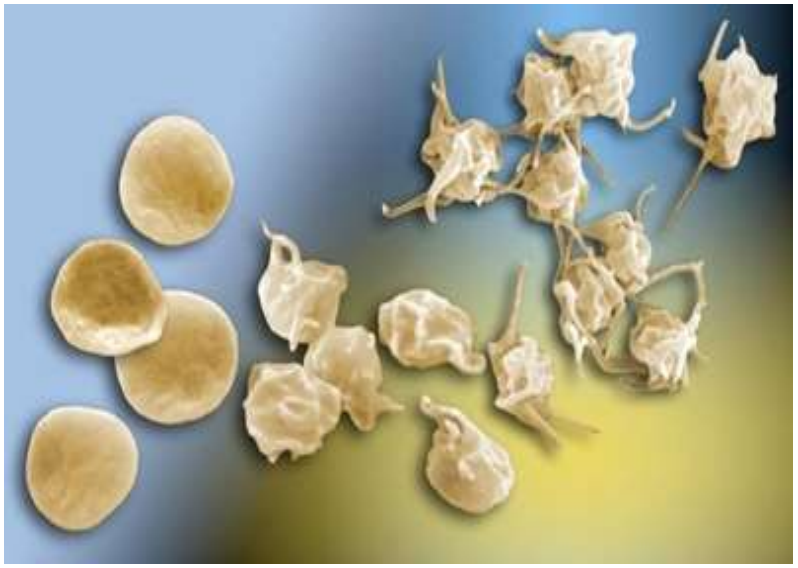
I received in the past travel grants and speaker fees from Bayer, GSK, Novo-Nordisk, Pfizer and Sanofi-Aventis

Co-author of 2013 European Guidelines on management of the trauma bleeding patients – unrestricted grant from CLS Behring and LFB France

Co-author of 2013 ESA Guidelines on management of the severe perioperative bleeding

Platelets

- Anucleate, discoid circulating blood cells
- Derived from bone marrow megakaryocytes
- 1-2 µm diameter
- Mean volume 8 femtoliters (10^{-15}/L)
- Each liter of whole blood has $2\ \mathrm{mL}$ of platelets
- Total body platelet volume is 15 mL
- 1/3 of platelets are in the spleen
- Normal range in blood 150-400 x 10^9/L (150,000-400,000 ml^{-1})
- 10 % are produced daily

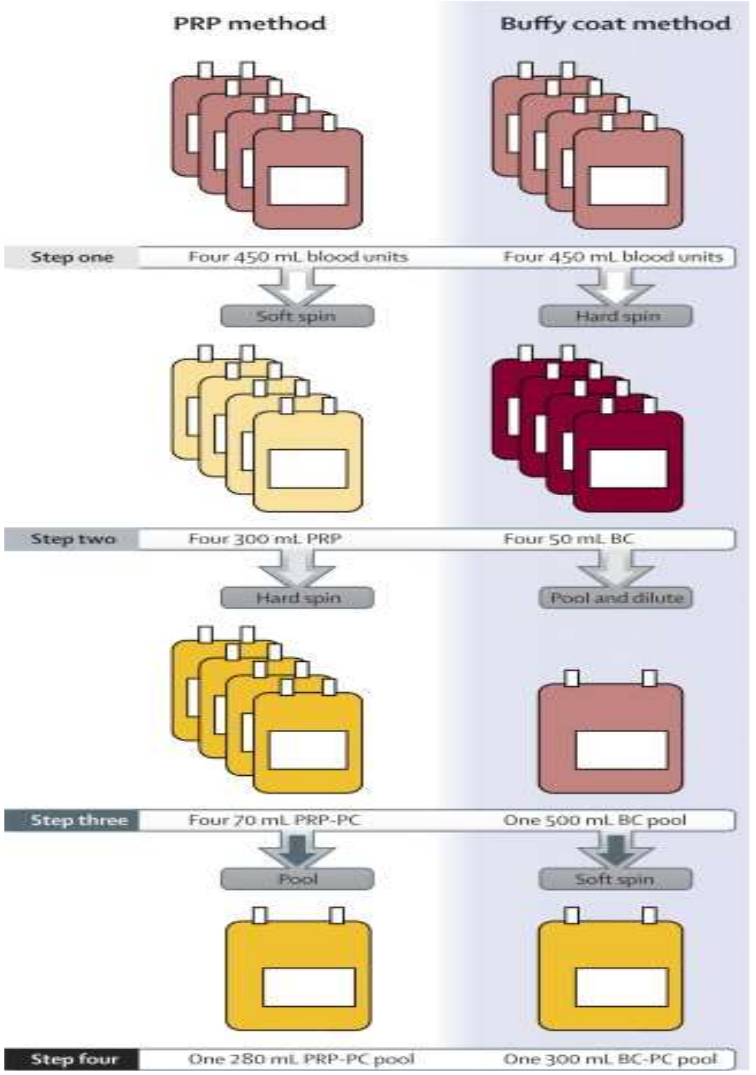


Weber KE et al. Transf Med Rev 2014;84-97

What ?
Platelet products

- Random Donor Platelets (RDP)
  preparation from whole blood using a platelet rich plasma (PRP) or buffy coat (BC) intermediary

- BC RDP contain less plasma/leucocytes
- BC RDP are re-suspended in plasma or platelet additive solutions (PAS)
- 1 RDP unit contains: 1-1.5 x 10^9 platelets/ml
  0.5 x 10^{11} platelets

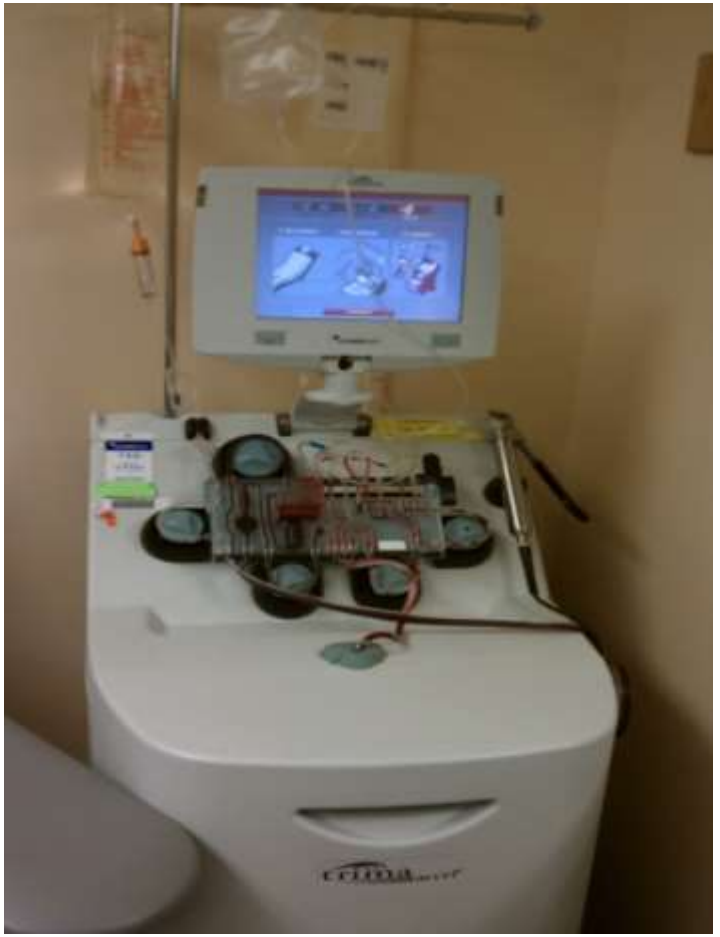


Katus MC et al. Vox Sanguinis 2014:103-113

Stroncek DF & Rebulla P. Lancet 2007:427-438

What ?
Platelet products

- Single Donor Apheresis Platelets (SDAP)
- 1 apheresis unit contains 3 x 10^{11} platelets (> 2.4 x 10^{11})



Holbro A et al. Swiss Med Weekly 2013:13885
Parker RI. Critical Care Med 2014: 675-690

What ?
Platelet products

RDP units
+ availability
- require pooling from 4-6/3-5 donors to obtain an adult dose
- increased donor exposure
- difficult matching
- increased risk of bacterial contamination?

SDAP
+ higher corrected count increments
+ selected donors can provide 2-3 doses within a single collection
- higher cost (equipment, technician labor)
- increased donation time
- increased rate of donor reactions

Same effectiveness in terms of bleeding prevention

Katus MC et al. Vox Sanguinis 2014:1-3-113
Holbro A et al. Swiss Med Weekly 2013:13885

Triulzi DJ et al. Blood 2012:5553-5562

What ?
Storage of platelet products

Stored at 20-24º Celsius

Constantly gently agitated

Shelf life 4-7 days

Infused in 30 mins

Stroncek DF & Rebulla P.
Lancet 2007:427-438

Quality indicators:
Visible swirl score
Morphology
pH
Lactate
Glucose concentration
Extent of shape change
CD62P expression

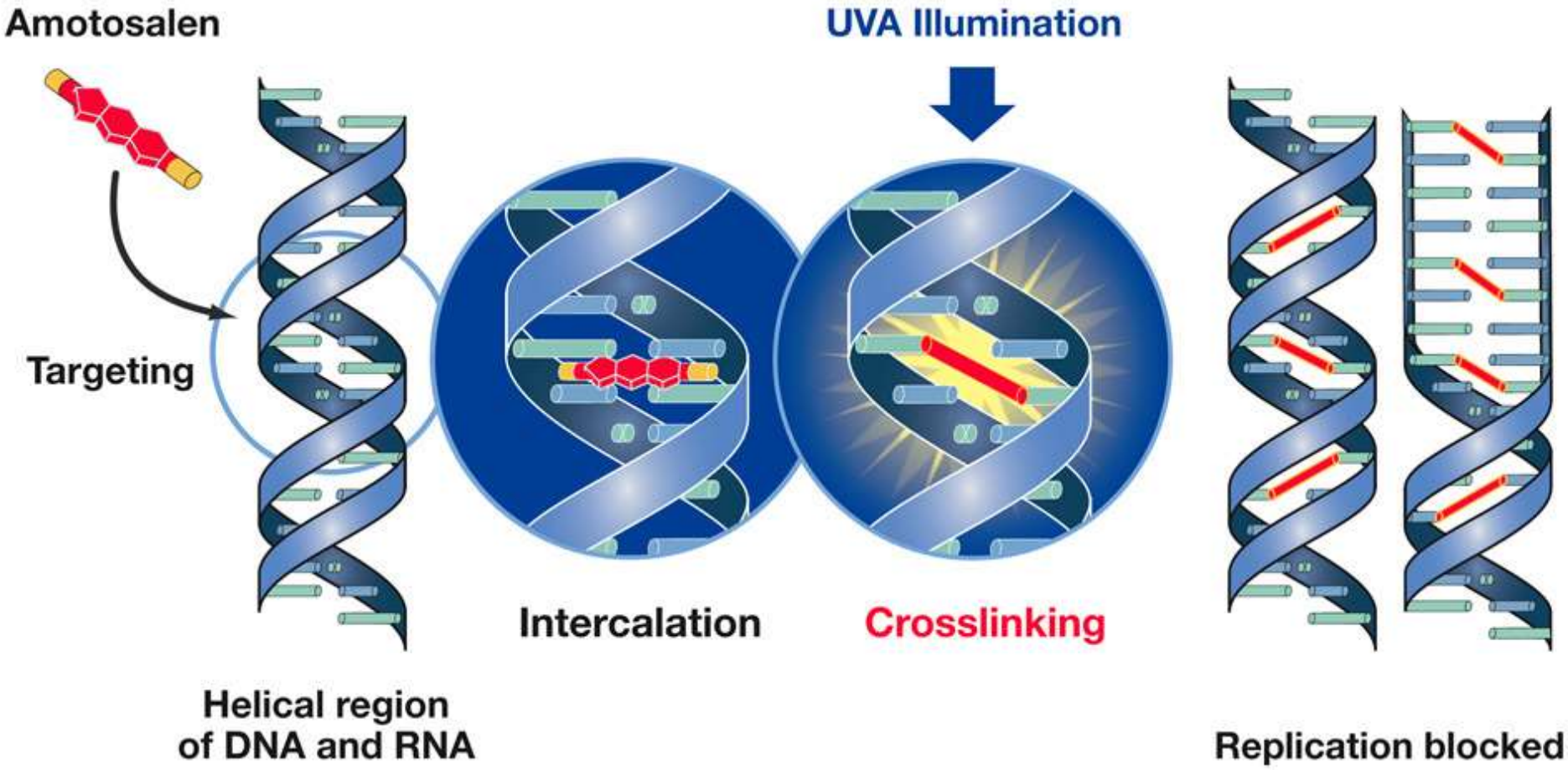
Weber KE et al. Transf Med Rev 2014;84-97

What ?
Bacterial contamination

- Incidence in platelet concentrates
  - 1:5000 culture positive
  - 1:10,000 cause reactions
  - 1:10-25,000 cause sepsis
  - 1:40-75,000 cause mortality
- Organisms involved
  - Gram neg. rods, Gram pos. cocci
- Sources
  - Contaminated equipment, nonsterile procedure
  - Donor skin
  - Donor blood

O'Brien et al. Transfusion 2007:316-325

Pathogen reduction



Holbro A et al. Swiss Med Weekly 2013:13885
Courtesy of Cerus Corporation , CA USA

ESA Guideline
Management of severe perioperative bleeding

We recommend photochemical pathogen inactivation with amotosalen and UVA light for platelets.

1C

Kozek-Langenecker S et al. EJA 2013

What?
Pathogen reduced platelets for the prevention of bleeding

1422 patients included in 10 trials.

- No evidence of a difference in mortality, 'clinically significant' or 'severe bleeding', transfusion reactions or adverse events between pathogen-reduced and standard platelets.
- For a range of laboratory outcomes the results indicated evidence of some benefits for standard platelets over pathogen-reduced platelets.

Butler C et al. Cochrane Database Syst Rev 2013

What ?
Platelet products

Special platelet products

- Male donors only
- “Fresh” platelets
- Leukodepleted
- Cryopreserved
- Washed
- Irradiated

ESA Guideline
Management of severe perioperative bleeding

We recommend that multiparous women be excluded from donating blood for the preparation of FFP and for the suspension of platelets in order to reduce the incidence of TRALI

1C

EJA 2013

What?
TRALI: antibody theory

- White blood cell (WBC) alloimmunization may occur following previous exposure to WBCs through pregnancy or transfusion
  - 332 female plateletpheresis donors
  - 17% had detectable anti-HLA antibody
  - Frequency of HLA antibodies increased with pregnancy:

0 pregnancies:	7.8%
1-2 pregnancies:	14.6%
3 or more:	26.3%

Densmore et al. Transfusion 1999;39:103-6
Triulzi DJ. Anesth Analg 2009;108:770-776

What?
TRALI: incidence

- 1:5,000-1:12,000 units
- 1:260,000 for all components
- FFP-1:22,500-1:66,000 units
- PLTs-0-1:420,000 units
- RBCs-1:82,500-1:2,860,000 units

Bux J & Sachs UJ. Br J Hematol 2007:788
Shaz BH, et al. Blood 2011:1463
Poretti L, et al. Blood Transf 2012:351
Toy P, et al. Blood 2012:1757

French Hemovigilance Network

2007-2008

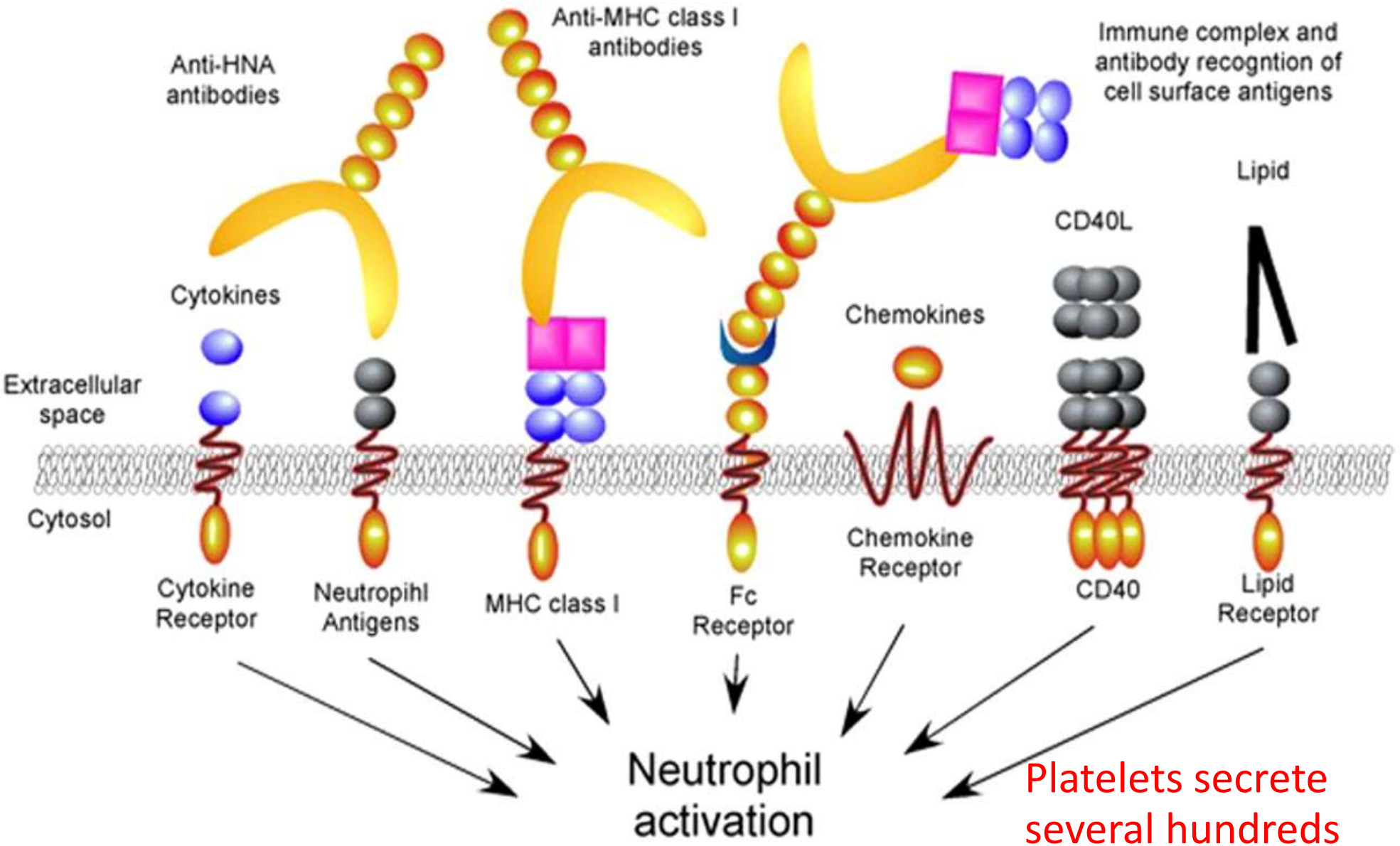
- 1:83,000 all blood products
- 1:31,000 units for FFP and apheresis PLTs
- no cases due to whole blood pooled PLTs

Ozier Y, et al. Transfusion 2011:2102

UK 2012: 11 suspected TRALI; no death

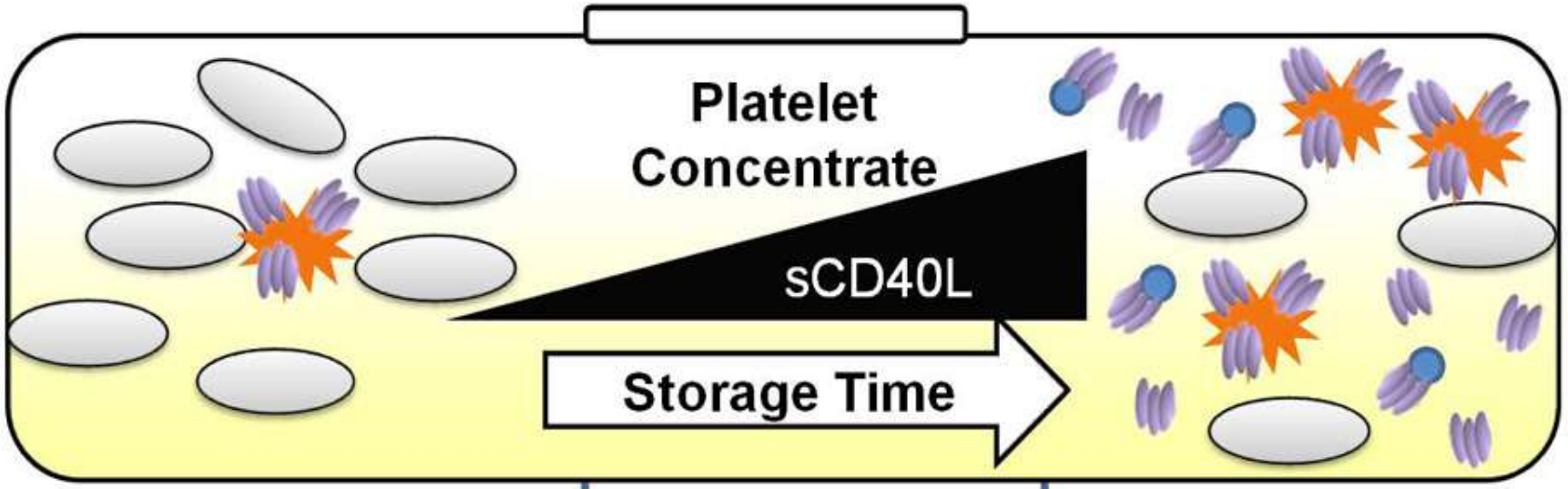
Katus MC et al. Vox Sanguinis 2014:1-3-113

Transfusion-associated neutrophil activation



Shaz B H et al. Blood 2011;117:1463-1471
Nguyen KA et al. Plos One 2014 e97082

Platelets secrete several hundreds biological response modifiers (BRM)

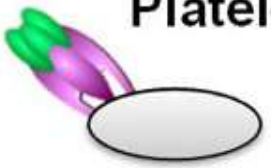


Transfusion

PMN

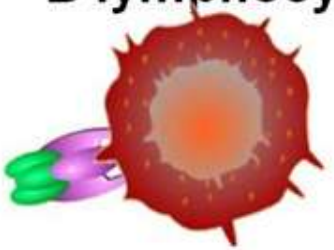
- Superoxide production
- Cytokine release
- Chemokine release
- Adhesion molecule surface expression

Platelet



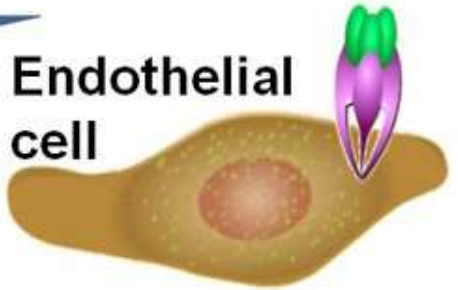
- Cytokine release
- Chemokine release
- Adhesion molecule surface expression
- Prothrombotic mediator release

B lymphocyte



- Antibody production
- Immunoglobulin class switch
- Affinity maturation

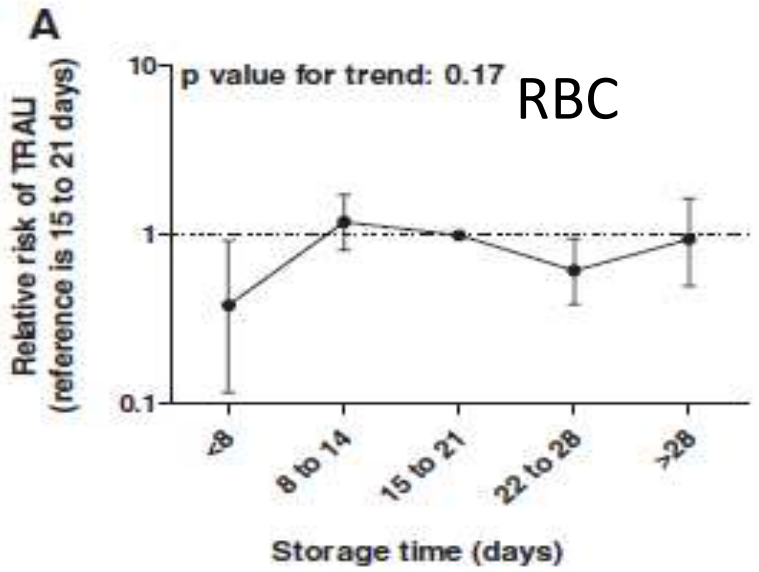
Endothelial cell

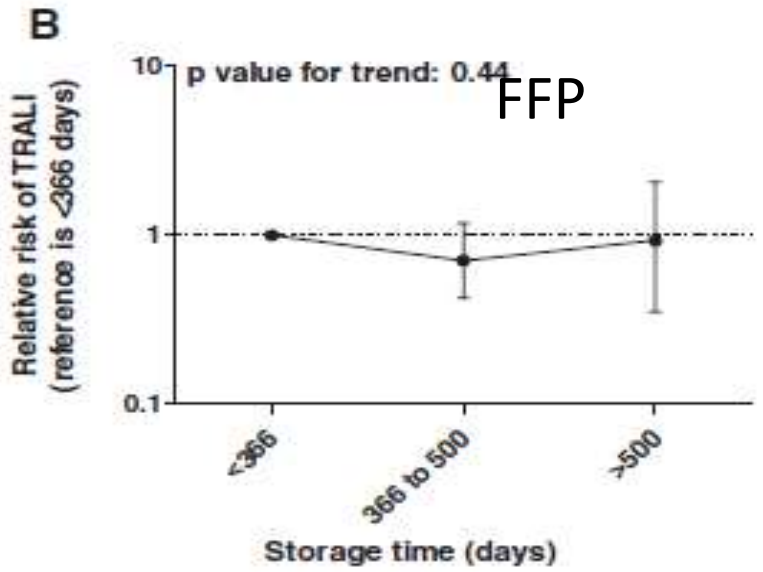


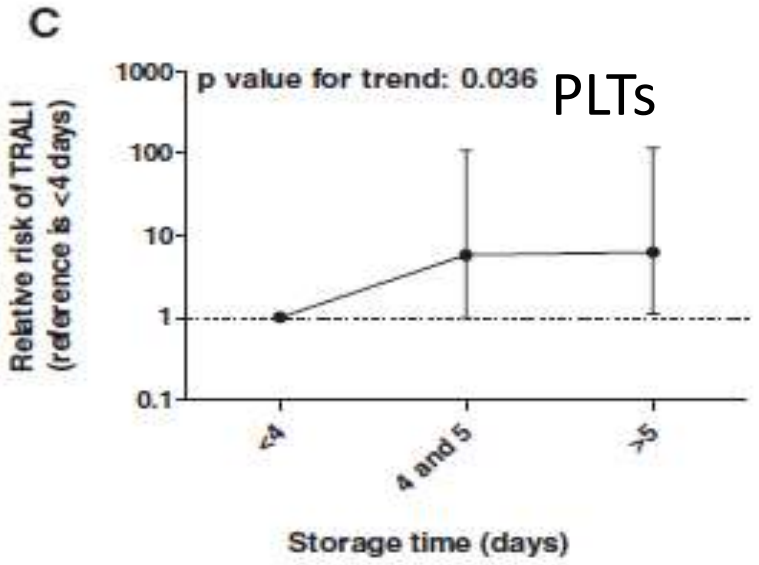
- Cytokine release
- Chemokine release
- Adhesion molecule surface expression
- Increase vascular permeability
- Prothrombotic mediator release

Sahler J et al. Transf Clin Biol 2012:19(3)

What?
TRALI: duration of storage







Middelburg RA et al. Transfusion 2012;52:658

What ?
Leuko-depleted platelets

Residual leucocytes

EU: $< 1 \times 10^6$ per unit in 90% of units

FDA: $< 5 \times 10^6$ per unit in 90% of units

Universal leukoreduction may reduce

- febrile reactions (FNHTR)
- platelet refractoriness due to HLA alloimunisation
- transmission of CMV

Holbro A et al. Swiss Med Weekly 2013:13885
Katus MC et al. Vox Sanguinis 2014:1-3-113

ESA Guideline
Management of severe perioperative bleeding

We recommend that labile blood components used for transfusion are leuko-depleted

1B

Kozek-Langenecker S et al. EJA 2013

How much?
Platelet dose

- Platelet dose (x 10^{11}):

  Target platelet count increment x Blood volume x 1.5/100

- Traditional dose in onco-haematology
  - 0.07 x 10^{11}/kg for stable thrombocytopenic pts
  - 0.15 x 10^{11}/kg for acute platelet consumption

  Higher and lower doses are debated

  1 Random donor platelet unit / 10 kg (6-8 RDPs)

  1 Single Donor Apheresis Platelets (equivalent to 6-8 RDPs)

Weber KE et al. Transf Med Rev 2014;84-97
Holbro A et al. Swiss Med Weekly 2013:13885
Reffai M et al. Thromb Res 2011:287-291

How much?
Platelet dose

Assessment of platelet transfusion efficacy

- Clinical endpoints (bleeding)
- Absolute platelet increment (API): PLT post- PLT pre

  1 dose of platelets should raise patient's counts by 30 $x10^9$/L in 1h
- Corrected count increment (CCI): API x body surface/ PLT dose

  >7.5 at 1h and > 4.5 at 24hrs
- Platelet recovery: API x blood volume/ PLT dose
- > 20% at 1h and > 10% at 24hrs

Holbro A et al. Swiss Med Weekly 2013:13885
Reffai M et al. Thromb Res 2011:287-291

How much?
Factors associated with refractoriness

Product factors

- Dose of platelet
- Storage time
- ABO mismatch
- Re-suspension in additive solutions vs. plasma
- Pathogen reduction
- Irradiation

Patient factors

- Clinical situation: fever, sepsis, splenomegaly, bleeding, DIC, GVHD
- Alloimunization
- Drugs (IVIG, Ampho B, Vancomycin, Heparin, GPIIb/IIIa antagonists)

Holbro A et al. Swiss Med Weekly 2013:13885
Slichter SJ. Am Soc Hematol Educ Program 2007: 172-178

How much?
Strategies to improve response to platelet transfusions

- Treat underlying condition
- Transfuse ABO identical platelets
- Transfuse platelets <48 hrs in storage
- Increase platelet dose
- Select HLA *identical* or *compatible* or *permissive* platelet product

For whom?
Prophylactic transfusion in patients with thrombocytopenia

Hemato-oncological patients

< 10,000 -20,000/ mL (10-20 x 10^9/L)

Increased threshold in uncontrolled hypertension, intracranial mass lesion, recent haemorrhage or surgery, recent gastrointestinal hemorrhage

Lower threshold (5-10 x 10^9/L) is safe in chronic stable thrombocytopenia

Most of platelet transfusion do not conform guidelines

Prophylactic or no-prophylactic platelet transfusion was controversial in hemato-oncology

Recent studies support prophylactic platelet transfusion at 10 x 10^9/L

Lieberman L et al. Blood 2014; 1146-1151

Holbro A et al. Swiss Med Weekly 2013:13885

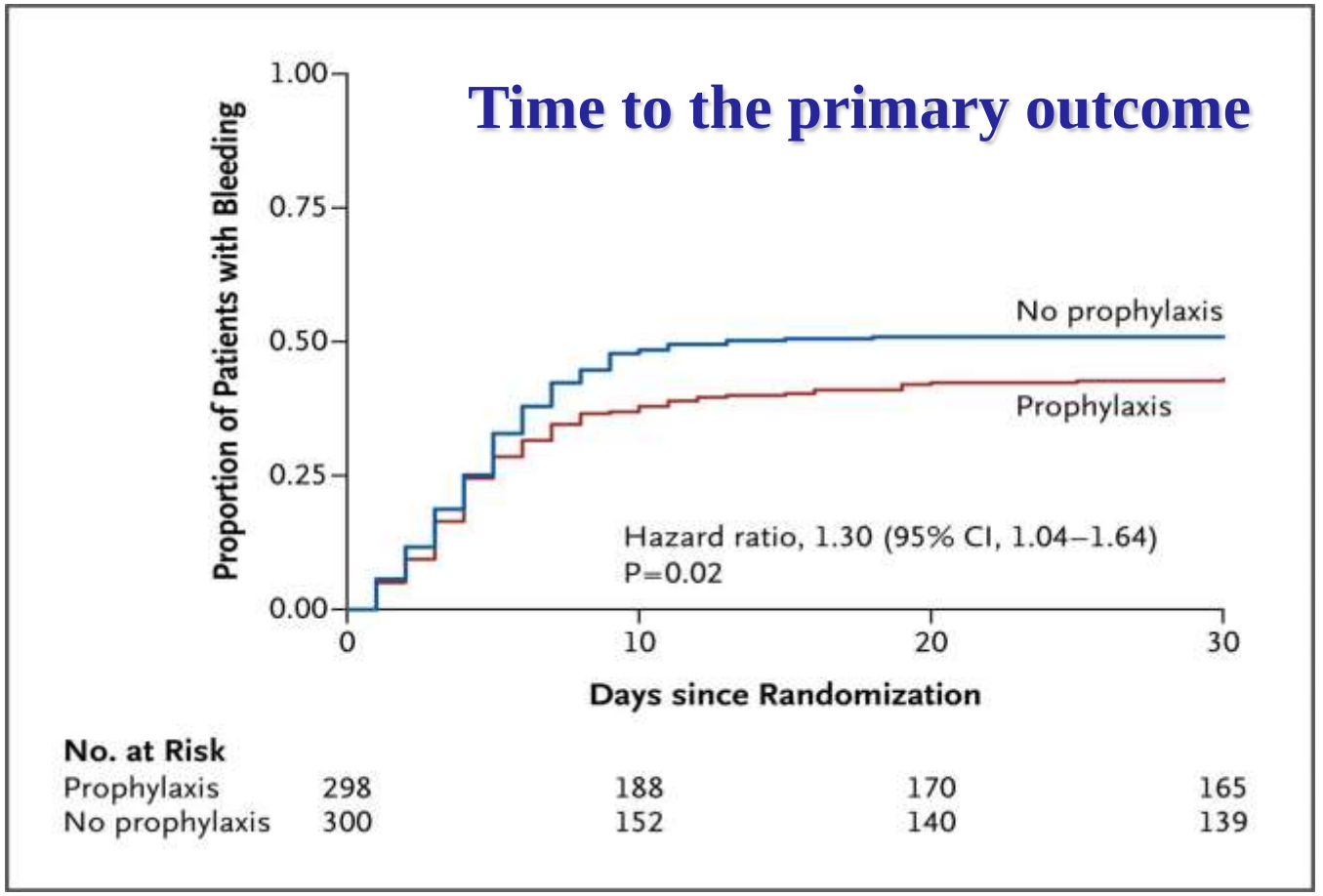
Estcourt L et al. Cochrane Database Syst Rev 2012

Weber KE et al. Transf Med Rev 2014;84-97

Parker RI. Critical Care Med 2014: 675-690

For whom?

Prophylactic transfusion in patients with thrombocytopenia



Stanworth SJ et al. N Engl J Med 2013;368:1771-1780

For whom?
Prophylactic transfusion in patients with thrombocytopenia

Periprocedural

$< 50 \times 10^9/L$ prior to invasive procedures (central venous catheter placement, bronchoscopy, endoscopy, solid organ biopsy)

$< 100 \times 10^9/L$ CNS/eye/spinal procedures

Weber KE et al. Transf Med Rev 2014;84-97
Holbro A et al. Swiss Med Weekly 2013:13885
Parker RI. Critical Care Med 2014: 675-690
Estcourt L et al. Cochrane Database Syst Rev 2012

Is 50 x10^9/L a too high threshold?

No severe bleedings occurred in more than 600 central venous catheter insertions in patients with hematologic malignancies.

Moderate bleedings may occur at any PLT counts.
The risk of non severe bleeding was increased only in patients with PLT counts below 20 x 10^9/L , but not with PLT counts between 20 x 10^9/L and 49 x 10^9/L .

Thus, only patients with PLT counts below 20 x 10^9/L should receive preprocedural PLT transfusions.

Strict adherence to this transfusion policy could save approximately 40% of all PLT transfusions before CVC insertions.

Zeidler K et al. Transfusion 2011:2269-2276

For whom?
Therapeutic transfusion

Platelet transfusions for active bleeding are much more common on surgical and cardiology services

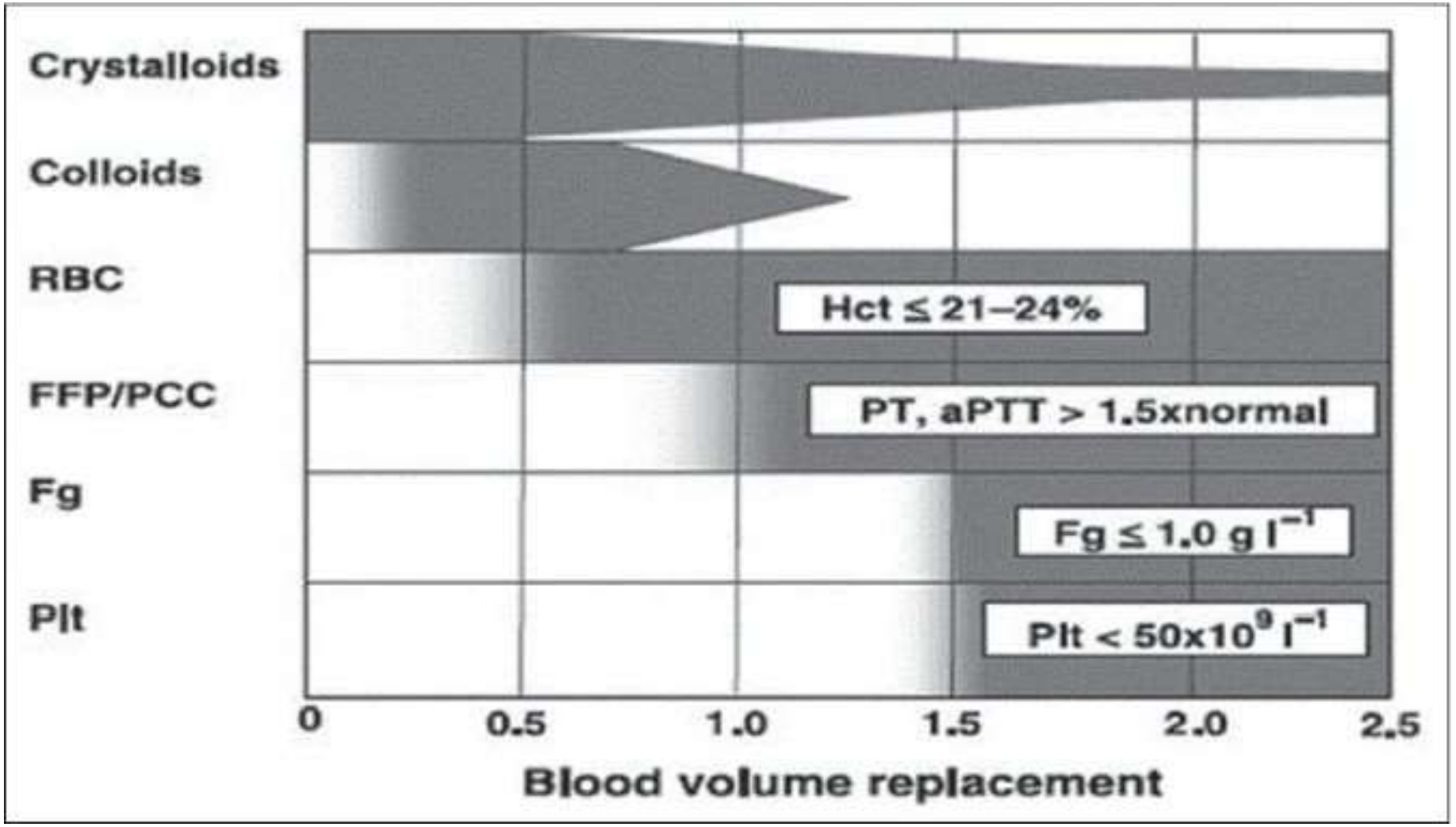
Stop bleeding in patients with

- thrombocytopenia $< 50 \times 10^9/L$
- drug induced platelet dysfunctions
- trauma and massive transfusion

Weber KE et al. Transf Med Rev 2014;84-97
Lieberman L et al. Blood 2014; 1146-1151
Holbro A et al. Swiss Med Weekly 2013:13885

For whom?

Traditional way of replacement therapy in severe bleeding



Spahn D R & Rossaint R. Br. J. Anaesth. 2005;95:130-139

Hemostatic Factors and Replacement of Major Blood Loss with Plasma-Poor Red Cell Concentrates

Seppo T. Hiippala, MD, Gunnar J. Myllylä, MD, and Elina M. Vahtera, PhD

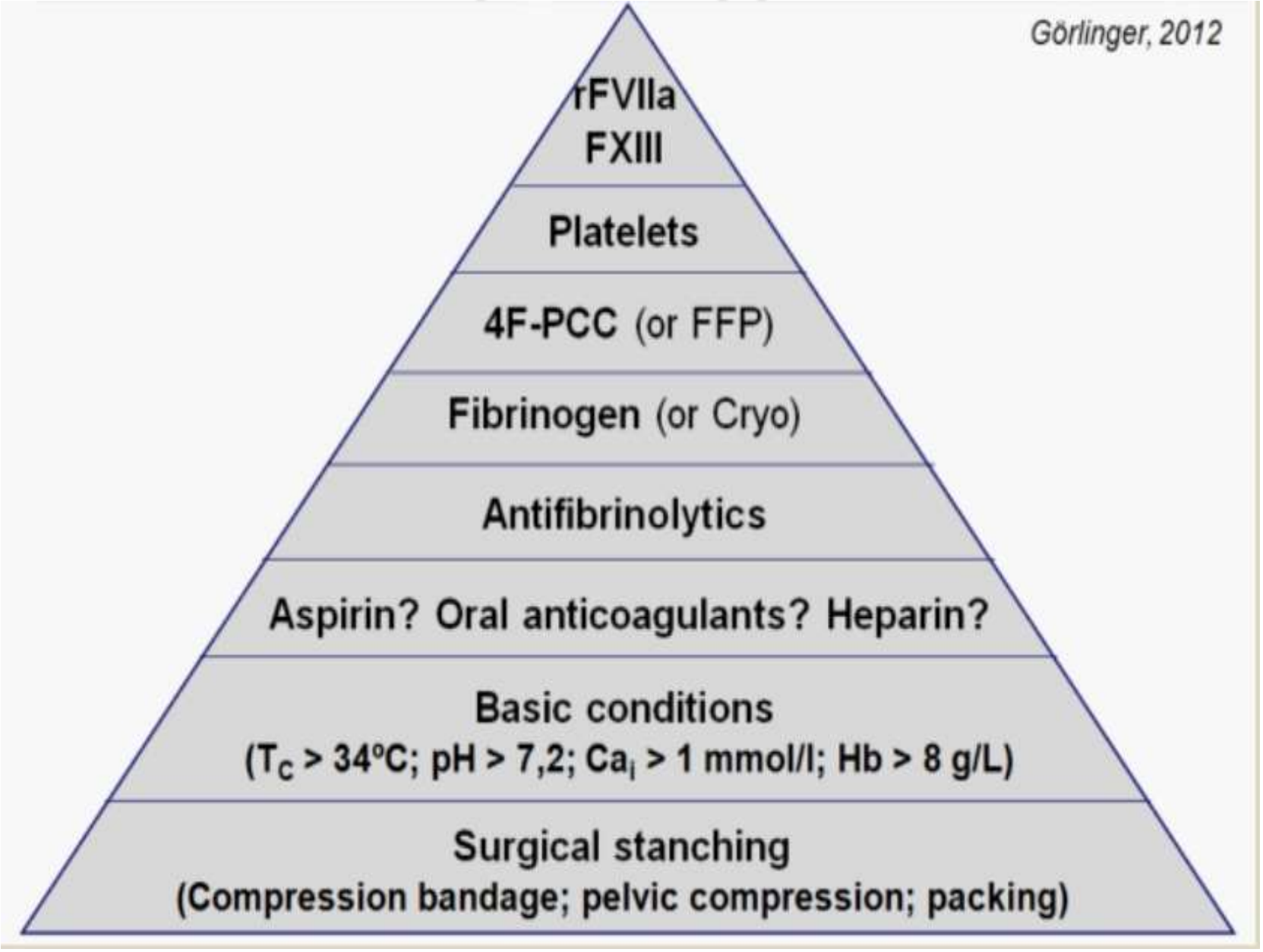
Department of Anesthesiology, Helsinki University Central Hospital, and Finnish Red Cross Blood Transfusion Service, Helsinki, Finland

Anesth Analg 1995;81:360-5

Critical level of hemostatic factors and the inversely predicted corresponding blood loss (95% confidence interval) as percent of calculated blood volume

Hemostatic factor	**Critical level**	**Blood loss (%)**
Platelets	50 x 10^3 / mm^3	230 (169-294)
Fibrinogen	1.0 g / L	142 (117-169)
Prothrombin	20	201 (160-244)
Factor V	25	229 (167-300)
Factor VII	20	236 (198-277)

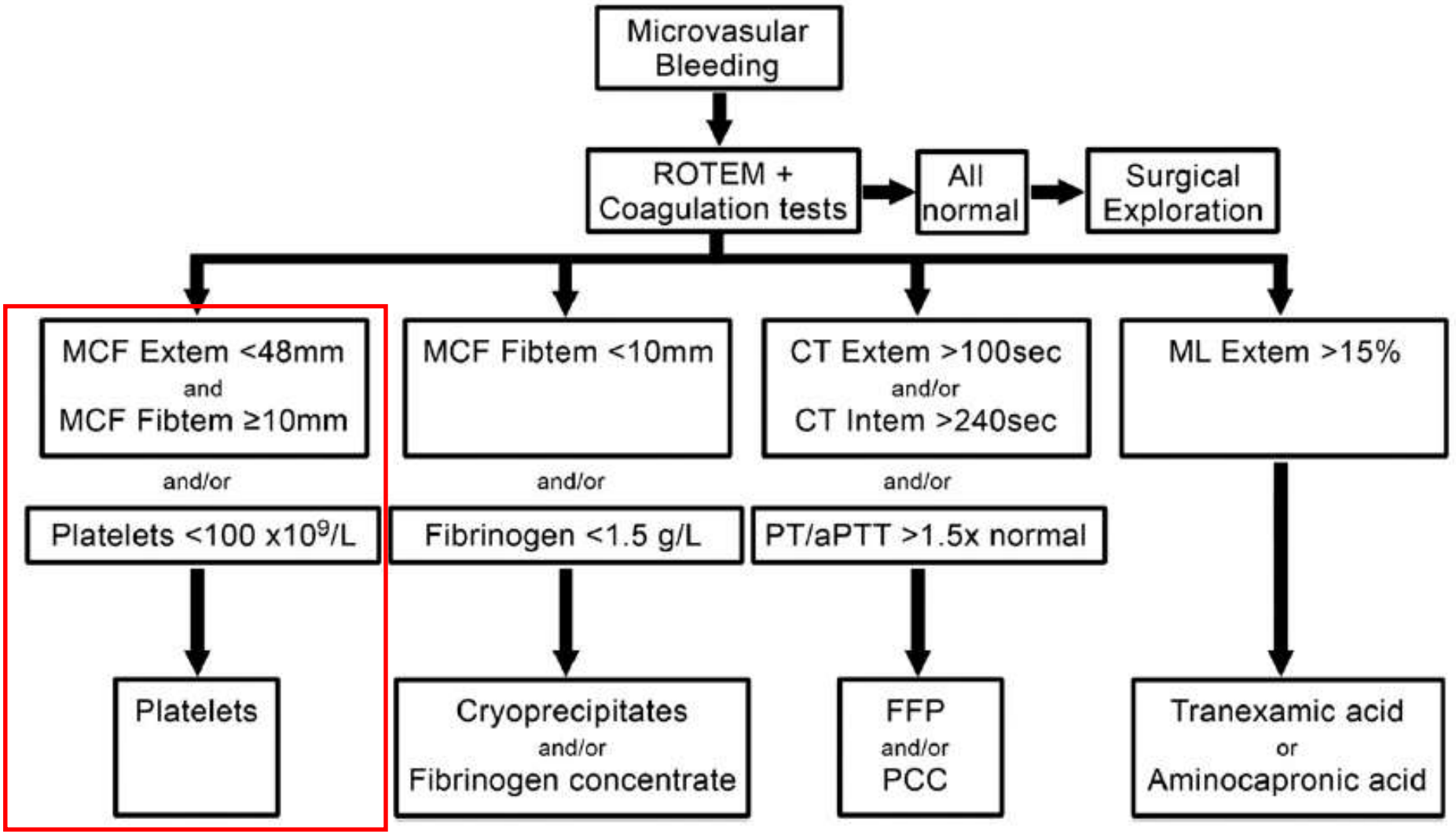
For whom?
Therapeutic approach



Principles and Practice of Thromboelastography in Clinical Coagulation Management and Transfusion Practice

Daniel Bolliger, Manfred D. Seeberger, and Kenichi A. Tanaka

Transfusion Medicine Reviews, Vol 26, No 1 (January), 2012: pp 1-13



Algorithm in bleeding patients based on conventional coagulation and ROTEM parameters.

For whom?
Thrombocytopenia in ICU

Platelet count < 150 x 10^9/L

Incidence: 8.3-67.6% on admission in ICU
13-44% acquired during ICU stay in adults

Causes: infection, inflammation, coagulation factor consumption

Treatment: 9-30% receive platelet transfusion

Associated with bleeding
Independent predictor of mortality
Lack of evidence for benefit from platelet transfusion

Hui P et al Chest 2011:271-278
Lauzier F et al Intensive Care Med 2013:2135-2143
Roberts I et al. Blood Rev 2008:173-186

For whom?
Platelet transfusion for thrombocytopenia in ICU

Platelet count increment
- sustained correction rarely achieved
- median increase 15x 10^9/L

Bleeding
- no report on bleeding avoidance with platelet transfusion

Mortality
- Insufficient evidence

For critically ill adults with severe thrombocytopenia and no evidence of bleeding there is insufficient evidence to make a recommendation for or against platelet transfusion

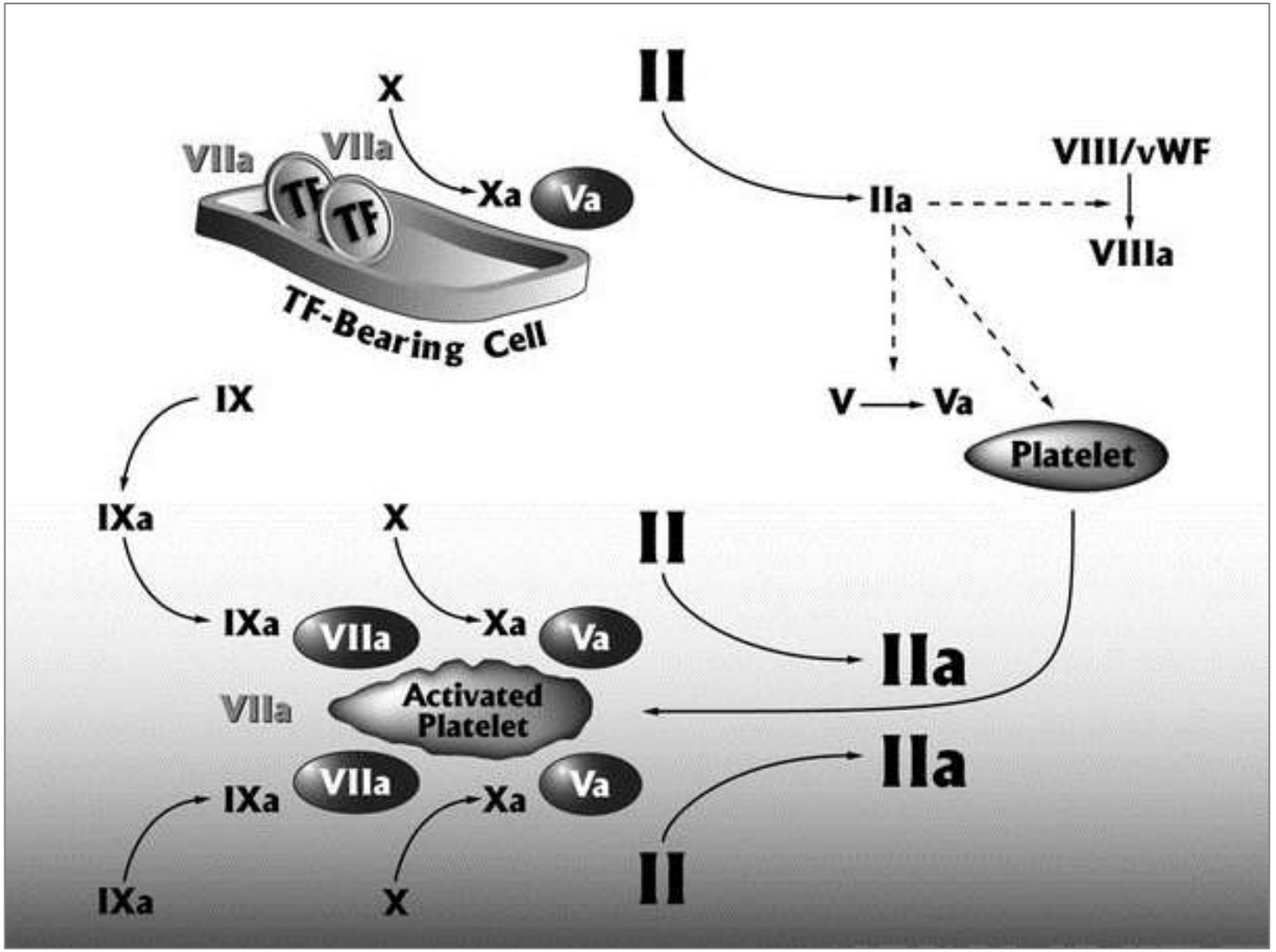
Lieberman L et al. Blood 2014; 1146-1151

For whom?
Platelet transfusion indications in sepsis

In patients with severe sepsis, we suggest that platelets be administered prophylactically when counts are ≤ 10,000/mm^3 (10 × 10^9/L) in the absence of apparent bleeding, as well when counts are ≤ 20,000/mm^3 (20 × 10^9/L) if the patient has a significant risk of bleeding.
Higher platelet counts (≥ 50,000/mm^3 [50 × 10^9/L]) are advised for active bleeding, surgery, or invasive procedures (grade 2D).

Dellinger P et al. Intensive Care Med 2013; 165-228

Does it matter?
The "cell based model" of coagulation



Kashuk JL et al. Annals of Surgery 2010; 251(4):604-614

Does it matter?
Efficacy of platelet transfusion

Table 1. Results of the Analyses Performed Before and After Platelet Transfusions

	Before Transfusion	After Transfusion
Hb (g/L)	91 (88–101)	88.5 (83–94)
PT (INR)	1.2 (0.9–1.4)	1.2 (0.9–1.3)
aPTT (s)	35.5 (27–54)	37 (27–61)
Platelet count ($\times 10^9$/L)	31.5 (20–44)	43.5 (38–71)*
Clotting time (s)	103.5 (81–215)	108.5 (51–158)
Clot formation time (s)	181.5 (108–347)	123 (89–233)*
Maximum clot firmness (mm)	42 (38–50)	51.5 (45–56)*
G (dynes/cm^2)	3623 (2353–6111)	5319 (3333–7500)*

PT = prothrombin time; aPTT = activated partial thromboplastin time; Hb = hemoglobin.
* $P = 0.005$, when compared with before transfusion.

Flisberg P et al. Anaesth Analg 2009: 1430-1432

Liver International ISSN 1478-3223

CIRRHOSIS AND LIVER FAILURE

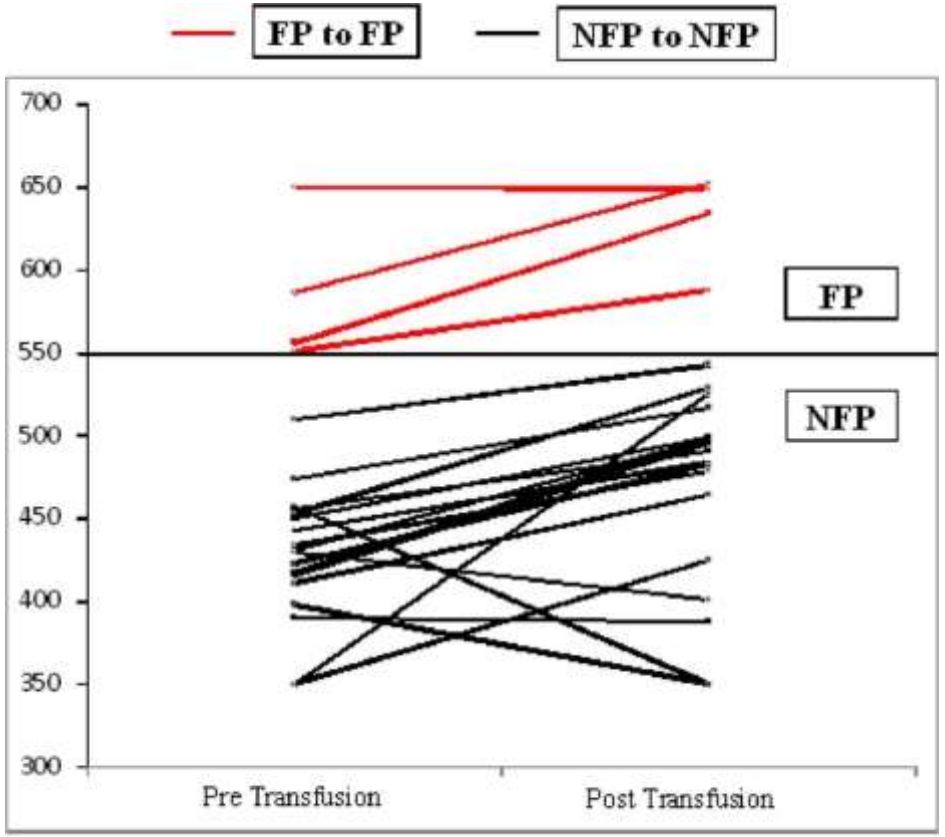
Global hemostasis tests in patients with cirrhosis before and after prophylactic platelet transfusion

Armando Tripodi[1,5], Massimo Primignani[2,5], Veena Chantarangkul[1,5], Laura Lemma[1,5], Manol Jovani[2,5], Paolo Rebulla[3,5] and Pier M. Mannucci[4,5]

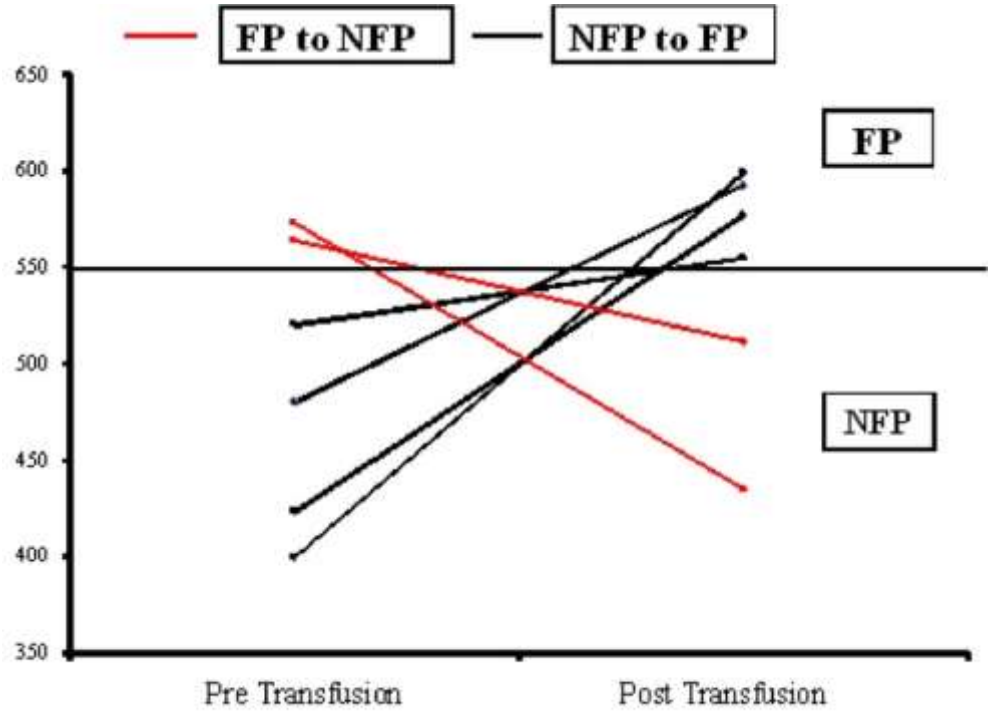
26 Patients with variceal ligations
Thrombocytopenia < 50,000/ml
1 adult standard dose
Results:
Slightly increase in platelet count
Thrombin generation marginally improved
Vascolelastic tests improved statistically but not clinically significant

Does it matter?

Platelet function assay before and after platelet transfusion platelet



FP – Functional Platelet, NFP – Nonfunctional Platelet

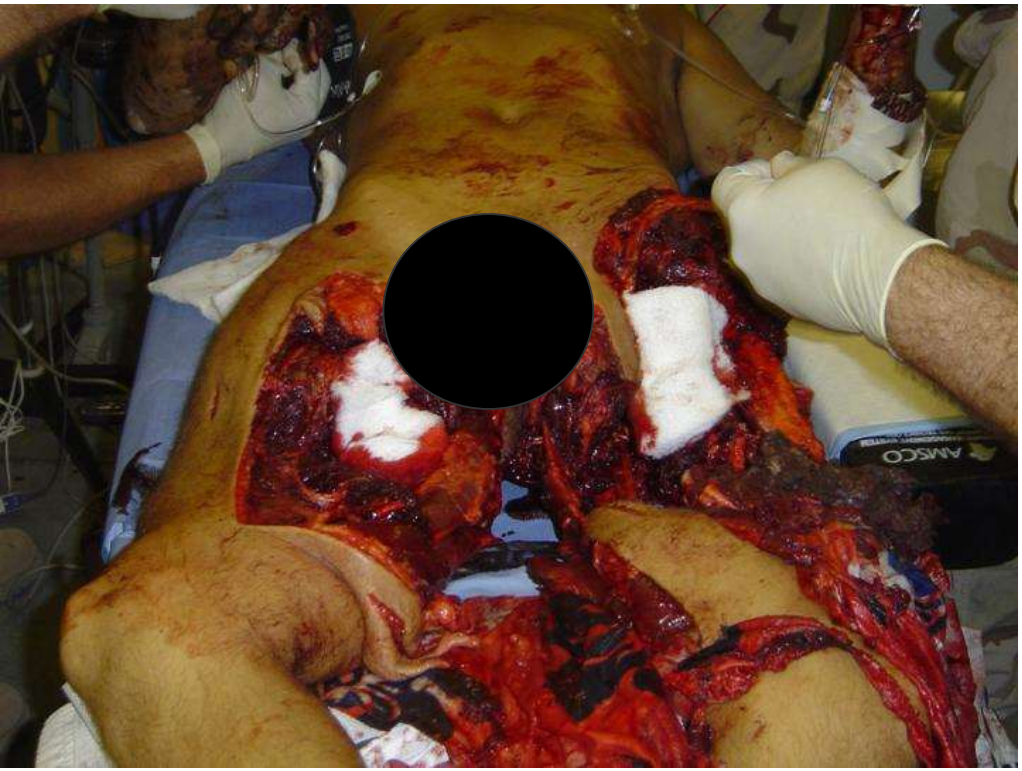


FP – Functional Platelet, NFP – Nonfunctional Platelet

Joseph, B et al Journal of Trauma and Acute Care Surgery. 2013;75(6):990-994

Does it matter?
Trauma

How would you transfuse (resuscitate) this type of casualty?

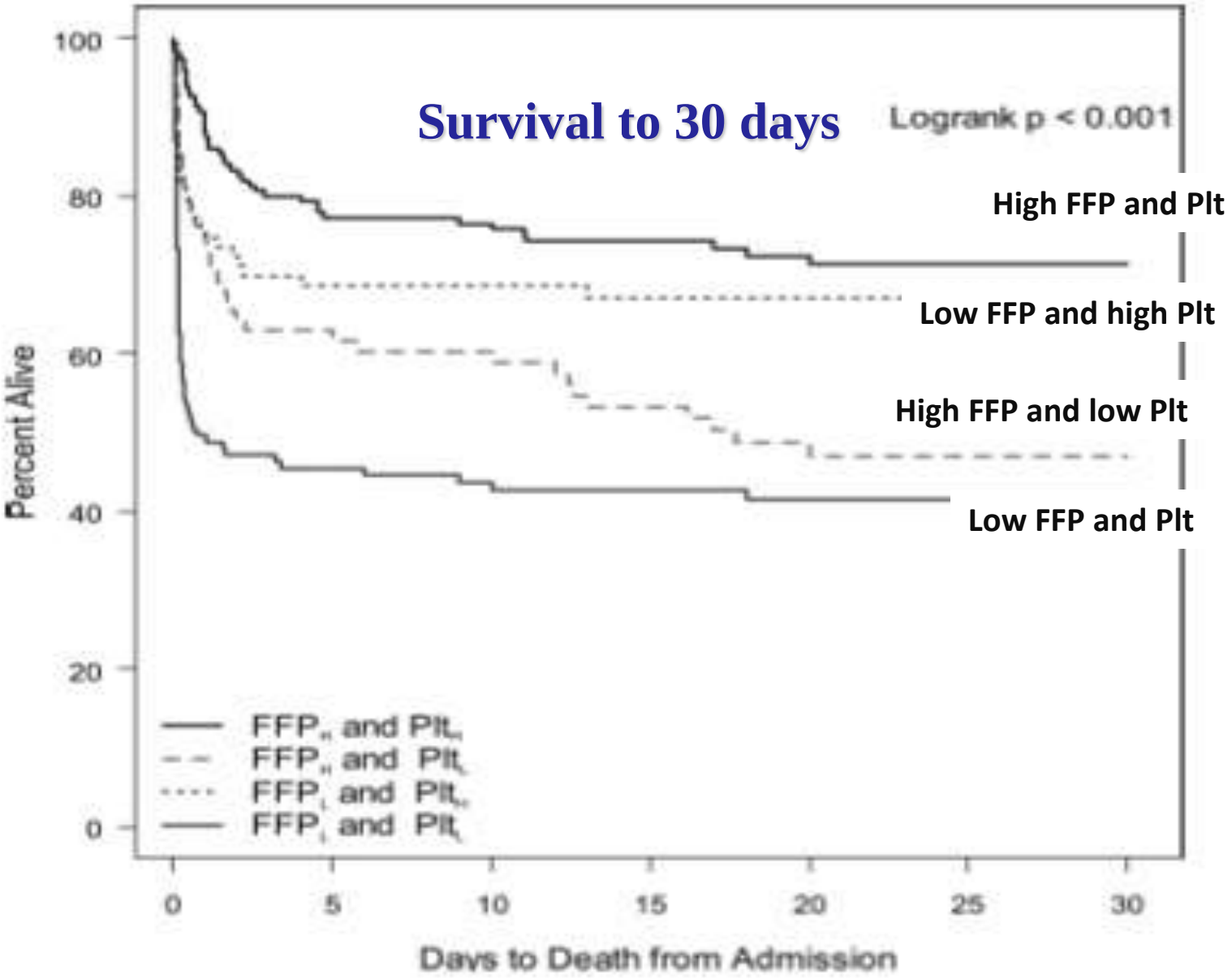


War as a laboratory for trauma research

Current US Army Policy

- Transfuse to a ratio of 1:1:1 of FFP:RBC:PLT for those patients presenting with
  - **severe life threatening trauma/hemorrhage**
  - **at risk for massive transfusion**
- Use of fresh whole blood is authorized for patients with life-threatening injuries (at discretion of MD)

More plasma & platelets, better outcome…



Holcomb JB, et al. Ann Surg. 2008;248:4477-458

Increased Platelet:RBC Ratios Are Associated With Improved Survival After Massive Transfusion

John B. Holcomb, MD, FACS, Lee A. Zarzabal, MS, Joel E. Michalek, PhD, Rosemary A. Kozar, MD, PhD, Phillip C. Spinella, MD, FCCM, Jeremy G. Perkins, MD, Nena Matijevic, PhD, Jing-Fei Dong, MD, PhD, Shibani Pati, MD, PhD, Charles E. Wade, PhD, and the Trauma Outcomes Group

J Trauma. 2011;71: S318–S328

TABLE 7. Propensity Score Adjusted Multivariate Cox Regressions: Variables Associated With 24-Hour and 30-Day Mortality Comparison to Reference (High)

	24-Hour Survival		30-Day Survival	
Variable	**RR (95% CI)**	***p****	**RR (95% CI)**	***p****
Platelet:RBC ratio Grp (low vs high)	2.81 (1.36–5.8)	0.005	1.77 (1.16–2.68)	0.007
Platelet:RBC ratio Grp (med vs high)	3.13 (1.52–6.45)	0.002	1.75 (1.15–2.65)	0.008
ISS	1.03 (1.02–1.05)	<0.001	1.04 (1.03–1.05)	<0.001
Admission deficit	0.91 (0.87–0.95)	<0.001	0.95 (0.92–0.97)	<0.001
FFP:RBC ratio	0.15 (0.06–0.42)	<0.001	0.49 (0.28–0.86)	0.01

* p from χ^2 test.

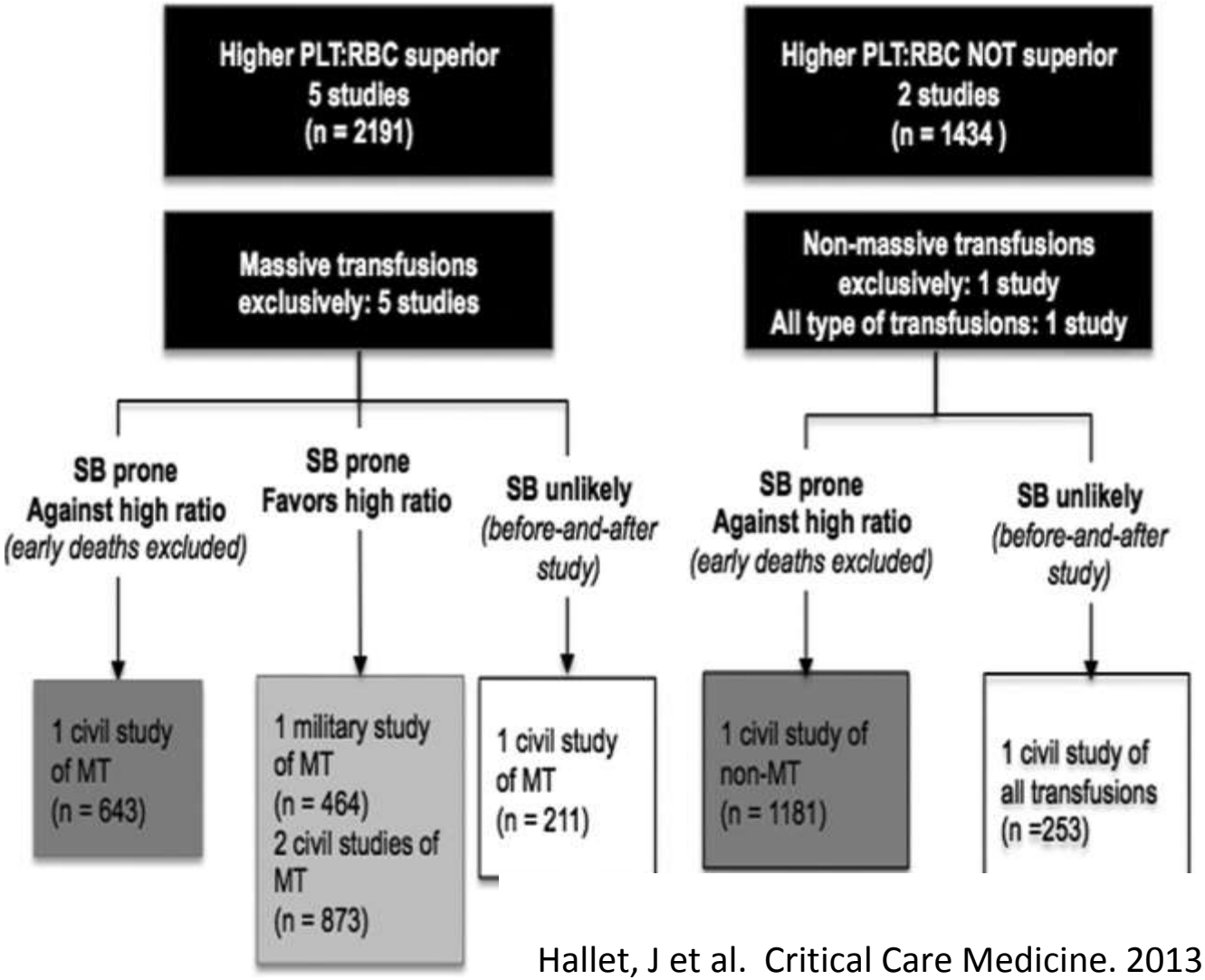
Survivorship bias

"As component blood products are not administered uniformly and simultaneously in civilian clinical practice, and many deaths occur early, it is possible that the survival advantage observed among those receiving a higher FFP:PRBC ratio may simply reflect the fact that they lived long enough to receive the higher ratio of products."

Snyder et al, J Trauma 66:358-364, 2009

Does it matter?
Trauma patients

Summary of mortality outcomes according to survival bias



Hallet, J et al. Critical Care Medicine. 2013 41(12):2800-2811

Does it matter?
Trauma patients

Early coagulopathy in trauma patients: An on-scene and hospital admission study

Bernard Floccard [a,*], Lucia Rugeri [b], Alexandre Faure [a], Marc Saint Denis [a], Eileen Mary Boyle [a], Olivier Peguet [a], Albrice Levrat [a], Christian Guillaume [a], Guillaume Marcotte [a], Alexandre Vulliez [a], Etienne Hautin [a], Jean Stéphane David [a], Claude Négrier [b], Bernard Allaouchiche [a]

Injury 2012: 26–32

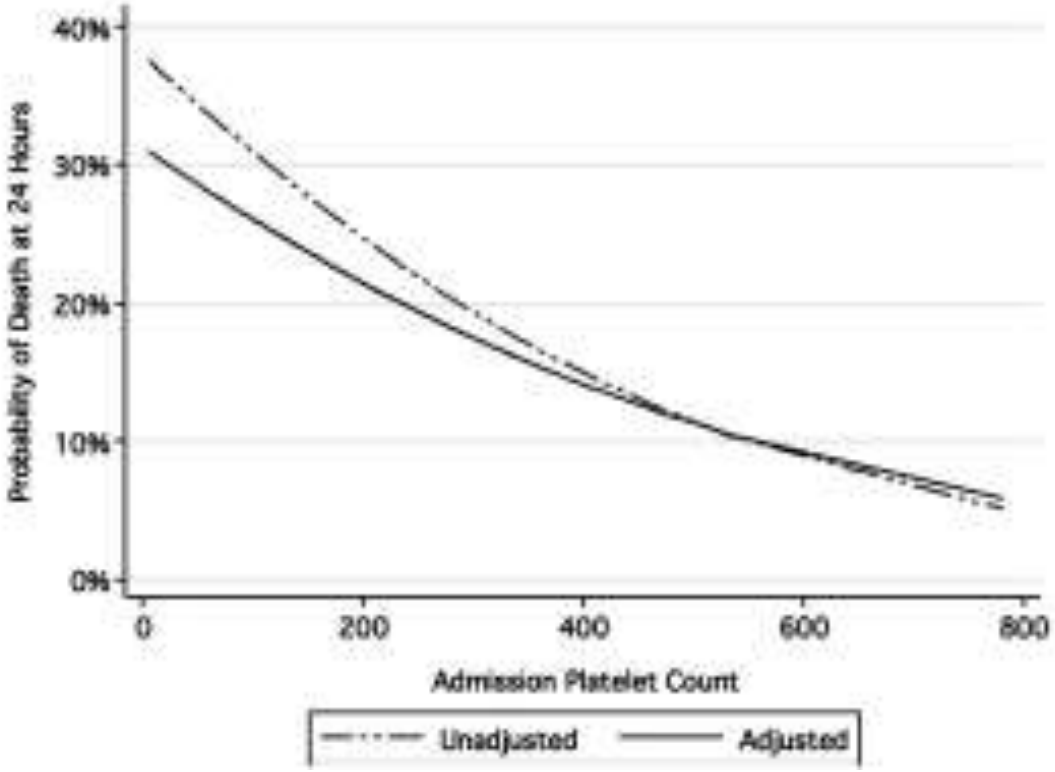
Injury severity score ranges and coagulation parameters on admission.

	0 < ISS < 14 (n = 12)	15 < ISS < 23 (n = 9)	24 < ISS < 39 (n = 16)	40 < ISS ≤ 75 (n = 8)	p
aPTT (s)	26 (25–27)	28 (25–34)	28.5* (27–39)	43† (28–57)	.03
Prothrombin time (s)	14.4 (14–15)	15.5 (14–17)	16* (15–19)	18.7†,‡ (16–30)	.003
INR	1.3 (1.3–1.3)	1.4 (1.3–1.6)	1.5* (1.3–1.9)	1.8†,‡ (1.4–3)	.005
Fibrinogen (g/L)	2.5 (2.2–2.6)	2.4 (1.5–2.8)	1.9*,# (1.4–2.3)	1.2†,‡,# (1.1–1.7)	.001
Factor II (UI/mL)	.8 (.8–1)	.9 (.6–1.1)	.8 (.6–.9)	.6†,‡ (.3–.7)	.04
Factor V (UI/mL)	1 (.9–1.1)	.8 (.6–1)	.7* (.5–.8)	.4†,‡ (.3–.6)	.001
FDP (μg/mL)	20 (4.5–120)	20 (10–20)	80 (15–480)	320†,‡ (120–640)	.008
PC (UI/mL)	.9 (.7–1)	.8 (.6–.9)	.7 (.4–.9)	.4†,‡ (.2–.6)	.01
AT (UI/mL)	.9 (.8–1)	.8 (.6–.9)	.9 (.7–1)	.6†,# (.3–.8)	.02
Platelets (10^9/L)	220 (172–271)	215 (167–301)	254 (199–298)	183 (147–265)	.2
Haemoglobin (g/L)	138 (117–149)	119 (110–140)	133 (96–138)	92†,‡ (79–112)	.04
AIS head	0 (0–.5)	2 (0–3)	2* (0–5)	5† (2–5)	.01
Volume fluid administration (mL)	500 (375–625)	1000 (250–1125)	500 (500–1000)	1250 (875–2125)	.2

A Normal Platelet Count May Not Be Enough: The Impact of Admission Platelet Count on Mortality and Transfusion in Severely Injured Trauma Patients

Lisa M. Brown, MD, MAS, Mariah S. Call, BS, M. Margaret Knudson, MD, Mitchell J. Cohen, MD, and the Trauma Outcomes Group

J Trauma. 2011;71: S337–S342

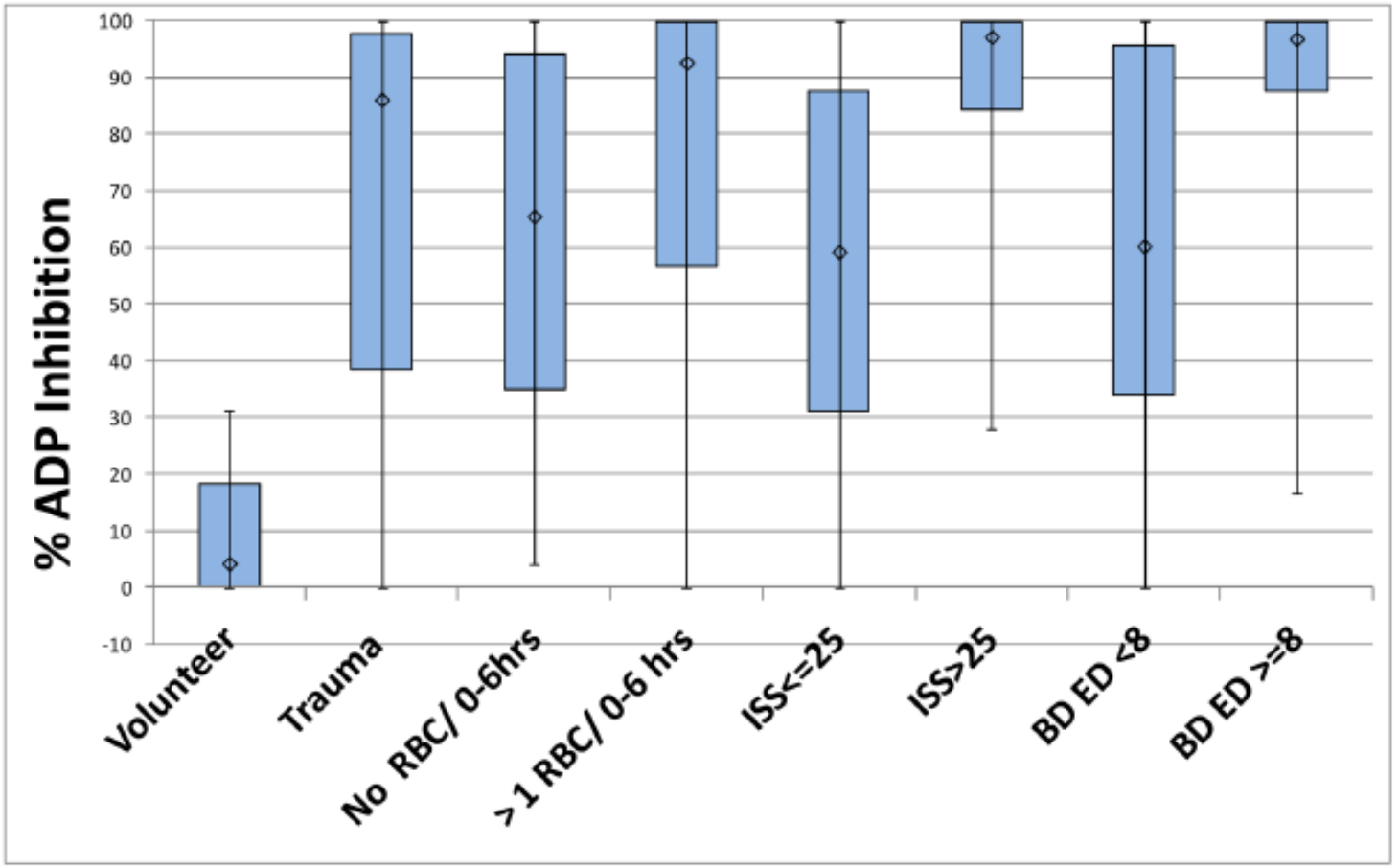


Probability of death at 24 hours by admission platelet count.
Unadjusted logistic regression model includes admission platelet count.

Early Platelet Dysfunction: An Unrecognized Role in the Acute Coagulopathy of Trauma

Max V. Wohlauer, MD[1], Ernest E. Moore, MD, FACS[1,2], Scott Thomas, MD, FACS[3,4], Angela Sauaia, MD, PhD[1], Ed Evans, BA, CCP[4], Jeffrey Harr, MD, MPH[1], Christopher C. Silliman, MD, PhD[6,7], Victoria Ploplis, PhD[3,5], Francis J. Castellino, PhD[3,5], and Mark Walsh, MD.[3,4,5]

J Am Coll Surg 2012:739-746



Does it matter?

Traumatic brain injury

Independent risk factors for death in patients with severe TBI

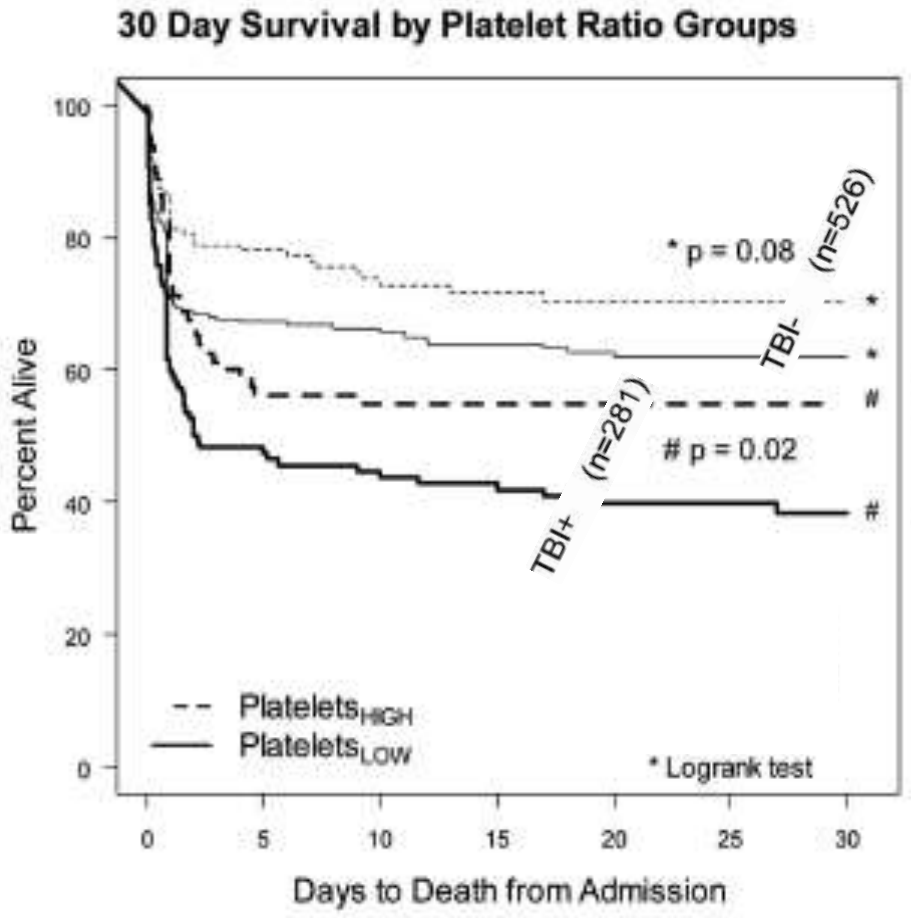
Independent Variables	OR (CI 95%)	*p*
ISS ≥25	10.75 (2.78–41.67)	0.001
AIS head 4 or 5	10.31 (2.36–45.45)	0.002
Platelet <100,000/mm^3 at admission	9.52 (1.26–71.43)	0.029
aPTT ≥36 s at admission	9.09 (2.82–29.41)	<0.001
Age ≥55	5.08 (2.02–12.82)	0.001
GCS score ≤8 at admission	2.59 (1.08–6.21)	0.033
INR ≥1.2 at admission	2.49 (1.08–5.78)	0.033

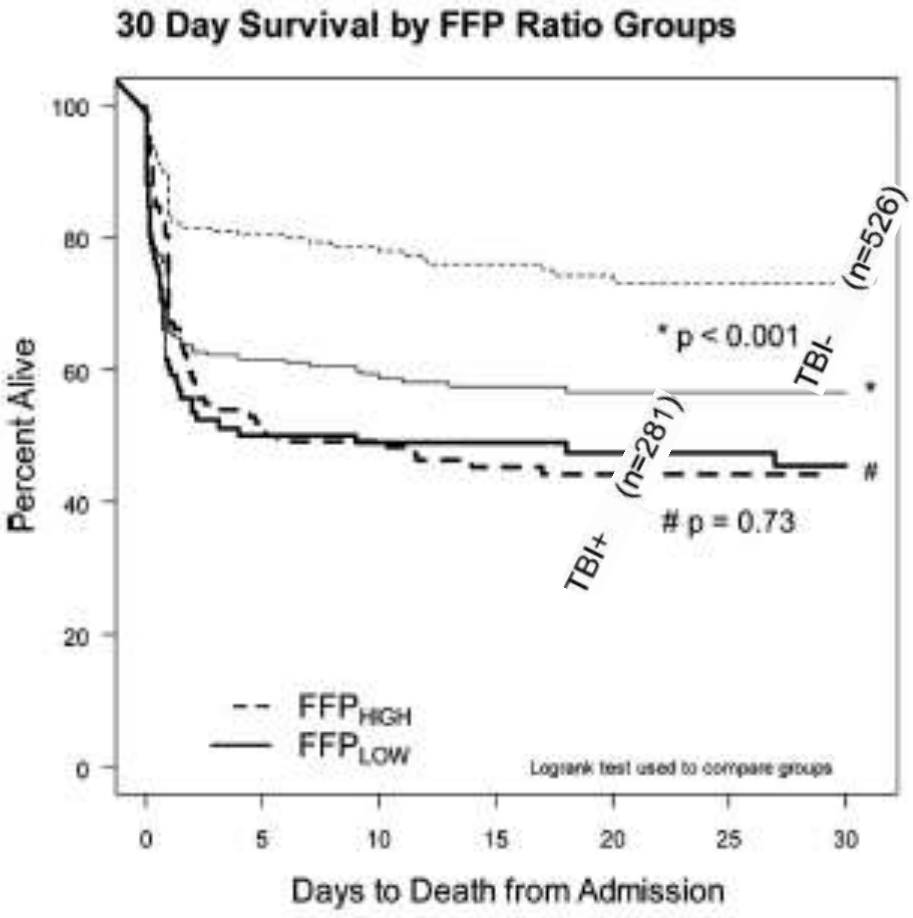
Schnüriger et al. Journal of Trauma and Acute Care Surgery 2010; 68(4):881-885

The Association of Blood Component Use Ratios With the Survival of Massively Transfused Trauma Patients With and Without Severe Brain Injury

Philip C. Spinella, MD, Charles E. Wade, PhD, Lorne H. Blackbourne, MD, Matthew A. Borgman, MD, Lee A. Zarzabal, MS, Fei Du, MS, Jeremy G. Perkins, MD, Marc Maegele, MD, Martin Schreiber, MD, John R. Hess, MD, Kenneth M. Jastrow, III, MD, Ernest A. Gonzalez, MD, John B. Holcomb, MD, Rosemary Kozar, MD, and the Trauma Outcomes Group

(*J Trauma.* 2011;71: S343–S352)





Kaplan-Meier curves for the ≥ 10 units RBC in 24-hour groups

Management of bleeding and coagulopathy following major trauma: An updated European guideline

We recommend that platelets be administered to maintain a platelet count above 50 × 10^9/l.

Grade 1C

We suggest maintenance of a platelet count above 100 × 10^9/l in patients with ongoing bleeding and/or TBI.

Grade 2C

We suggest an initial dose of 4-8 single platelet units or one aphaeresis pack.

Grade 2C

Spahn D et al. Crit Care 2013;17:R76

Doest it matter?
Patients on antiplatelet agents

Aspirin, clopidogrel, prasurgel, ticagrelor, Oh My!

European Society of Anaesthesiology ESA

ESA Guideline
Management of severe perioperative bleeding

For intra- or postoperative bleeding clearly related to aspirin, we suggest that platelet transfusion be considered (dose: 0.7 x 10^{11} [i.e. two standard concentrates] per 7 kg body weight in adults).
2C

We suggest that platelet transfusion be considered (dose: 0.7 x 10^{11} [i.e., two standard concentrates] per 7 kg body weight in adults) in cases of intra- or postoperative bleeding clearly related to clopidogrel or prasugrel
2C

EJA 2013

Normalization of platelet reactivity in clopidogrel-treated subjects

G. VILAHUR,*[1] B. G. CHOI,*†[1] M. U. ZAFAR,* J. F. VILES-GONZALEZ,* D. A. VORCHHEIMER,† V. FUSTER† and J. J. BADIMON*†

Cardiovascular Biology Research Laboratory; and †Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY, USA

Journal of Thrombosis and Haemostasis, 5: 82–90

Table 2 Dose conversion table of % pooled volunteers (V)-platelet rich plasma (PRP) to number of platelet units or pools. The mean platelet count of the 11 subjects participating in the study serves as example (250×10^6 platelets per μL).

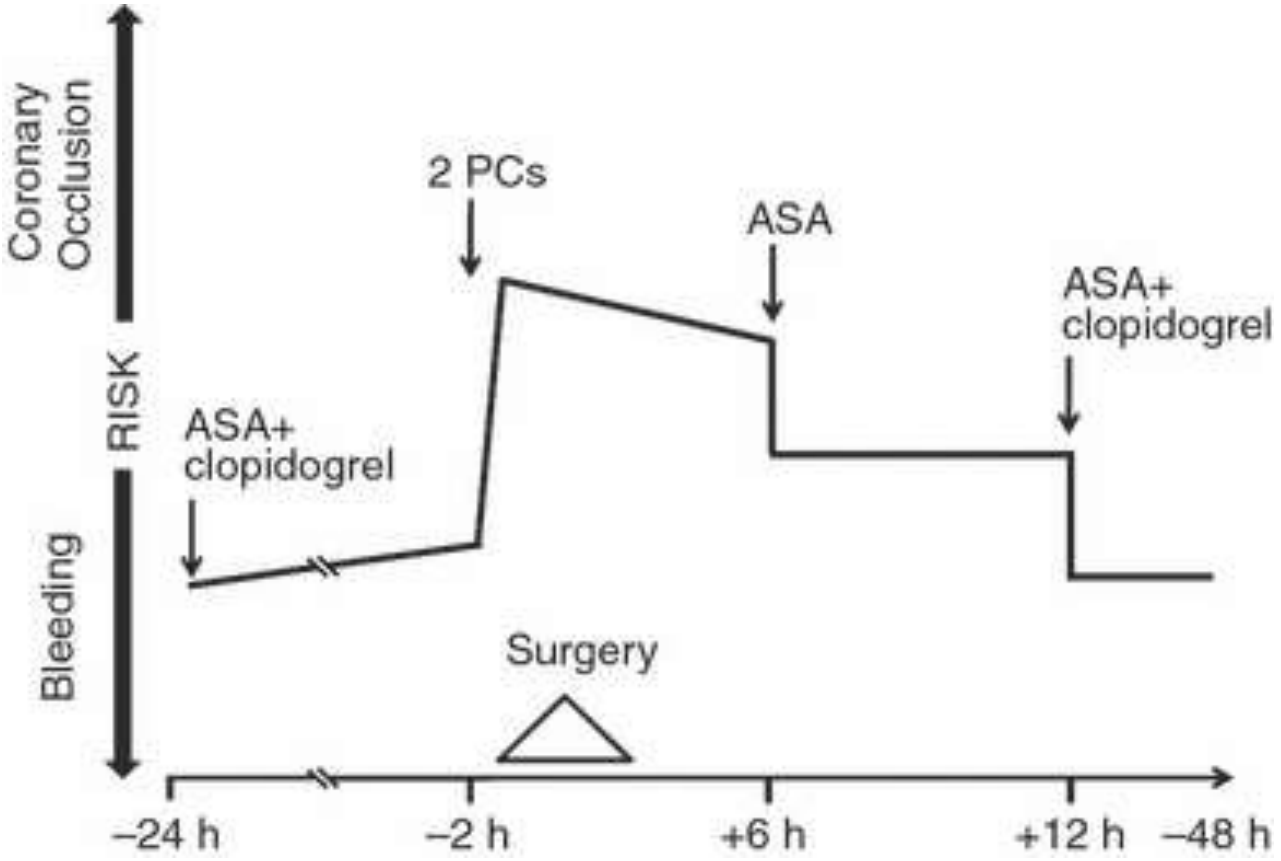
Mean platelet count ($n = 11$): 250×10^6

% Added pooled V-PRP	Platelet units*	Platelet pools†
20	5	1
40	10	2
50	12.5	2–3
60	15	3

*Platelet units: one platelet unit increases platelet count by 10 000 μL.
†Platelet pools: five platelet units = one platelet pool.

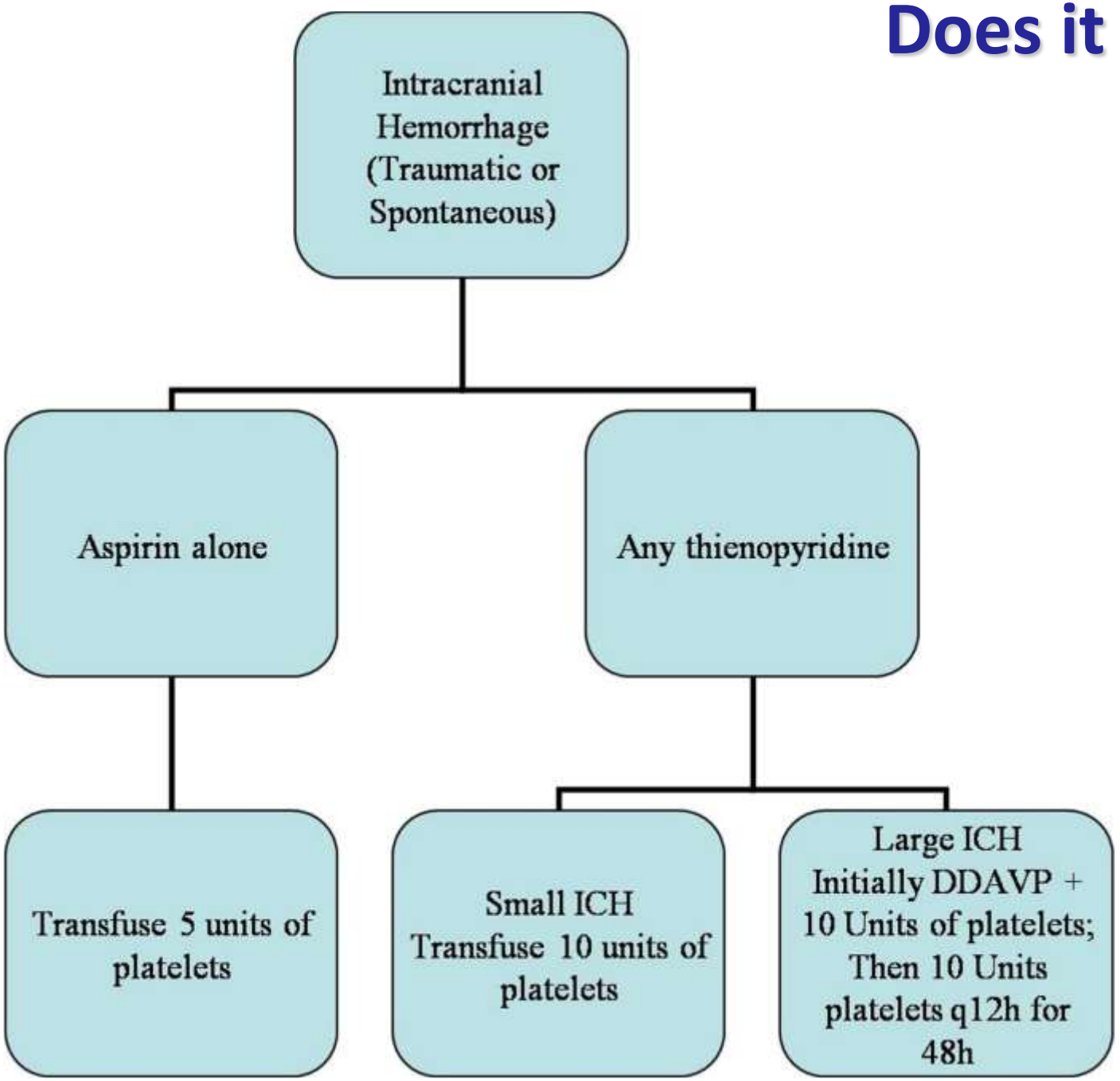
Does it matter?

Platelet transfusion for reversal of dual antiplatelet therapy in patients requiring urgent surgery



Thiele T. Journal of Thrombosis and Haemostasis 2012: 968-971

Does it matter?



World Neurosurgery. 2010;74: 279-285

BMJ open
accessible medical research

A meta-analysis to determine the effect on survival of platelet transfusions in patients with either spontaneous or traumatic antiplatelet medication-associated intracranial haemorrhage

John S Batchelor, Alan Grayson

Key messages

- Six studies were found to be suitable for the meta-analysis (two studies for spontaneous ICH and the remaining four were traumatic intracranial haemorrhage).
- The pooled OR showed no benefit in survival following a platelet transfusion (OR=0.773, 95% CI 0.414 to 1.442).

Utility of platelet transfusion in adult patients with traumatic intracranial hemorrhage and preinjury antiplatelet use: A systematic review

Daniel K. Nishijima, MD, MAS, Shahriar Zehtabchi, MD, Jeanette Berrong, DO, MPH, *and* **Eric Legome, MD,** *Sacramento, California*

J Trauma Acute Care Surg 2012:72

CONCLUSION

Five retrospective registry studies with suboptimal methodologies provide inadequate evidence to support the routine use of platelet transfusion in adult emergency department patients with preinjury antiplatelet use and tICH.

Management of bleeding and coagulopathy following major trauma: An updated European guideline

We suggest the measurement of platelet function in patients treated or suspected of being treated with antiplatelet agents.

Grade 2C

If platelet dysfunction is documented in a patient with continued microvascular bleeding, we suggest treatment with platelet concentrates.

Grade 2C

We suggest administration of platelets in patients with substantial bleeding or intracranial haemorrhage who have been treated with antiplatelet agents.

Grade 2C

Does it matter?
Safety of platelet transfusion

- 1 adverse effect in every 1030 platelet transfusion
- Bacterial contamination 127-1886 per 1, 000 000 cultures
- Febrile non-haemolytic transfusion reactions (FNHTR) 0.09 - 27%
- Allo immunization - 15% of chronic recipients
- Acute haemolytic reactions

  10-40% of platelet transfusions are incompatible
- Transfusion related acute lung injury (TRALI)
- Transfusion associated circulatory overload (TACO)
- Allergic reactions 0.09-21%
- Transfusion –associated graft-versus-host disease (TA-GVHD)

Holbro A et al. Swiss Med Weekly 2013:13885
Katus MC et al. Vox Sanguinis 2014:1-3-113
Adda R et al. ANSM 2012

Does it matter?
Strategies to reduce adverse events

- Use of only ABO-type specific platelets
- Use of plasma compatible platelets (screen the plasma for anti A and anti B antibodies)
- Limitation of quantity of incompatible plasma over time
- Component volume reduction (hyperconcentrated units)
- Resuspension of platelet component in PAS or AB plasma
- Washed platelets resuspended in electrolyte solutions
- Irradiation
- Synthetic analogues
- Alternatives

Katus MC et al. Vox Sanguinis 2014:1-3-113

“The true mystery of the world is in visible, not the invisible”

Oscar Wilde, The portrait of Dorian Grey

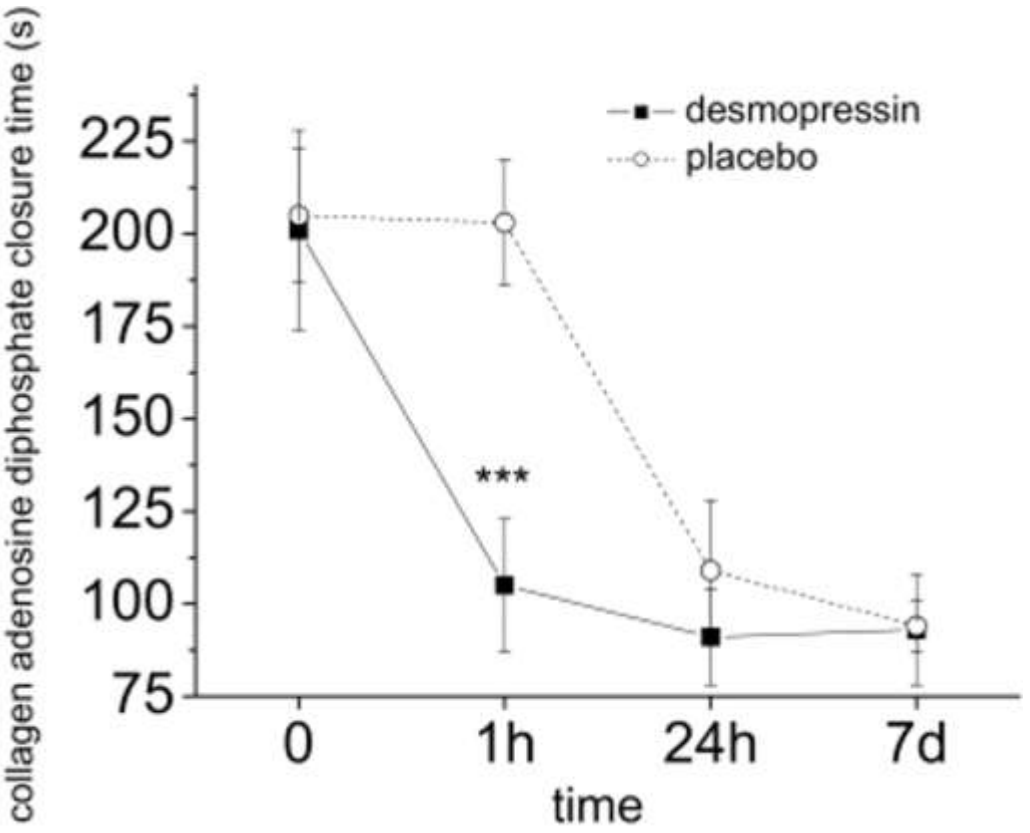
Conclusions

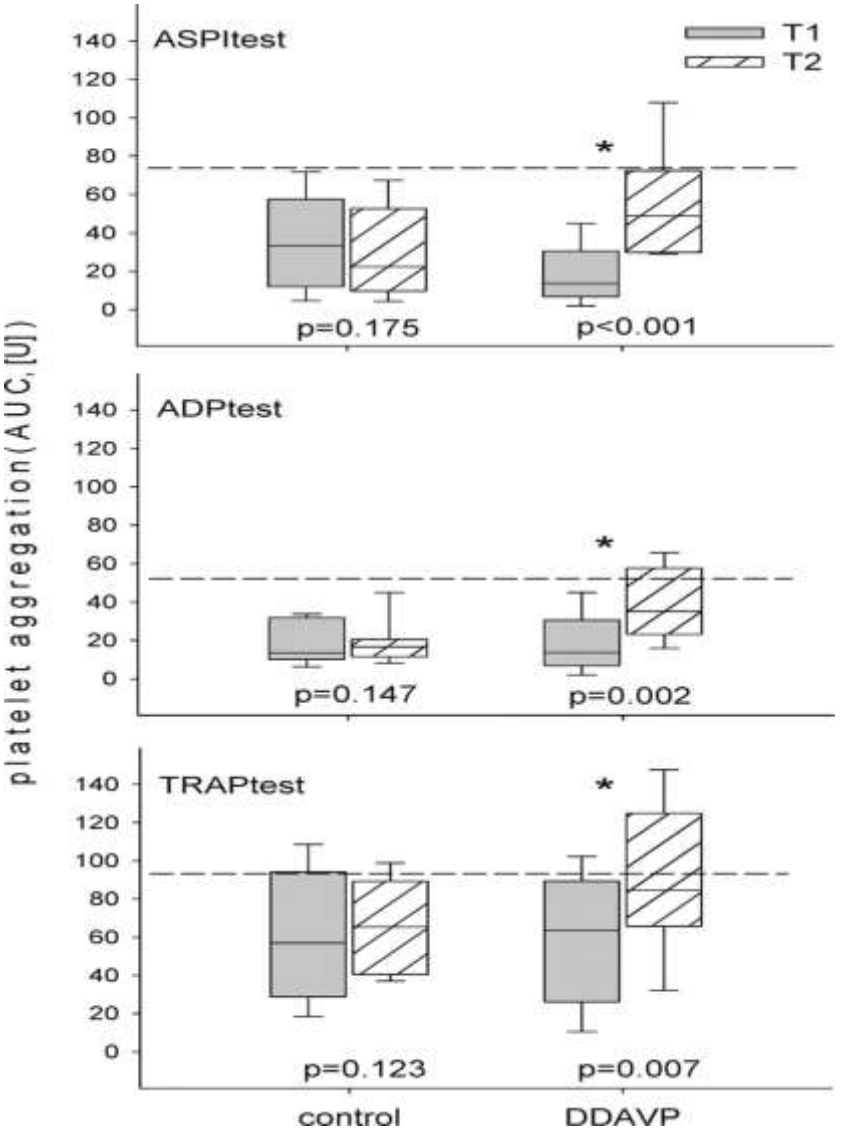
- Maintain platelet count > 100 000 x 10^9/l in ongoing bleeding
- Transfuse platelets if < 50 000 x 10^9/l if there is risk of bleeding
- Up-front platelet transfusion in predefined ratios has inadequate evidences
- Have a local protocol!

Does it matter?
Alternatives?

- **Potential antiplatelet reversal therapies besides platelet transfusion include**
  - **Desmopressin**
  - **Recombinant activated coagulation factor VII (rFVIIa)**
  - **Tranexamic acid**
  - **Fibrinogen**

Desmopressin
Efficacy in primary haemostasis





Weber C F et al. Anesth Analg 2010;110:702-707
Steinlechner B. et al. Ann Thorac Surg 2011;91:1420-1426

Recommendation 30
Desmopressin

We suggest that desmopressin (0.3 µg/kg) be administered in patients treated with platelet-inhibiting drugs or with von Willebrand disease.

Grade 2C

We do not suggest that desmopressin be used routinely in the bleeding trauma patient.

Grade 2C

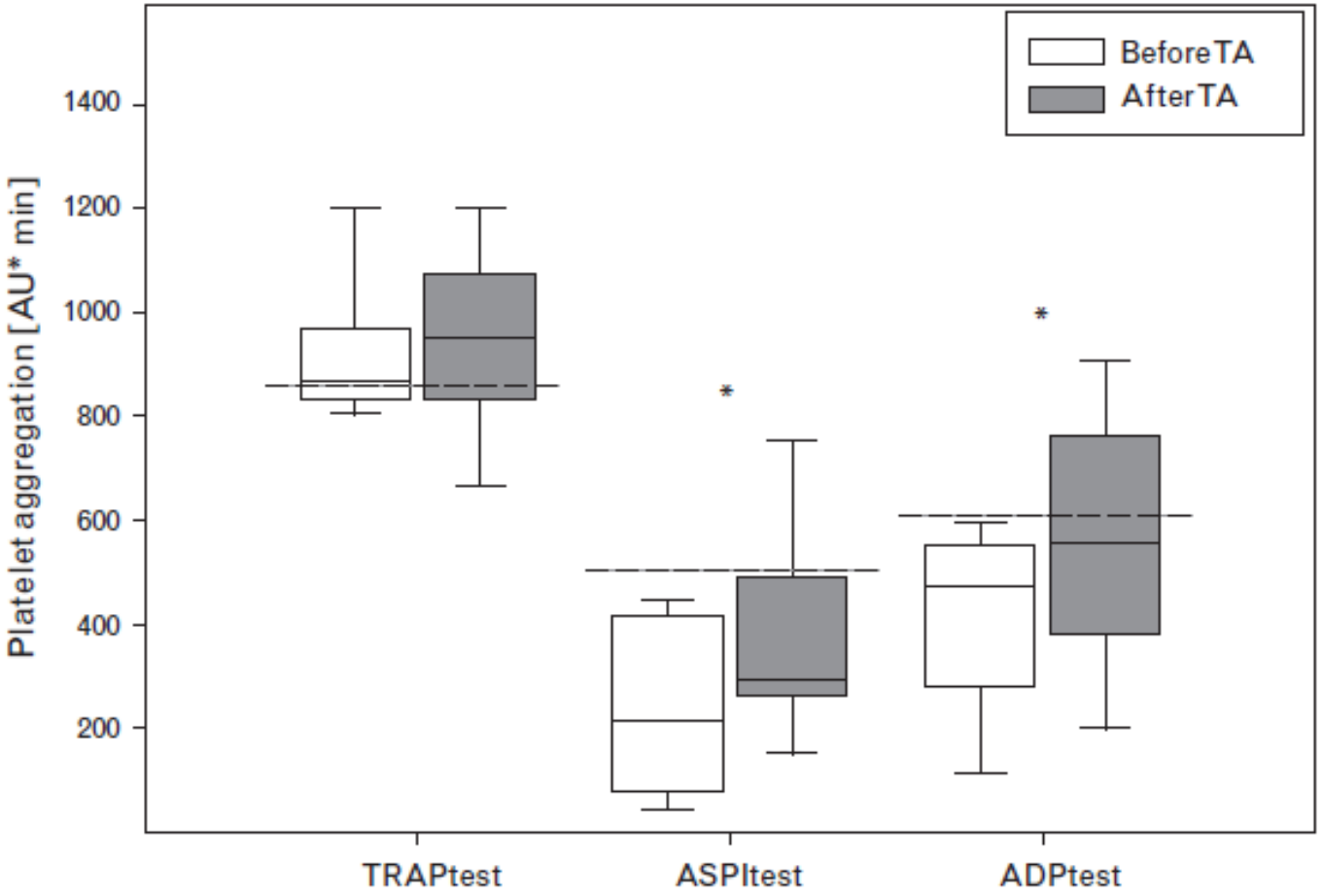
Spahn D et al. Crit Care 2013;17;36

ORIGINAL ARTICLE

Tranexamic acid partially improves platelet function in patients treated with dual antiplatelet therapy

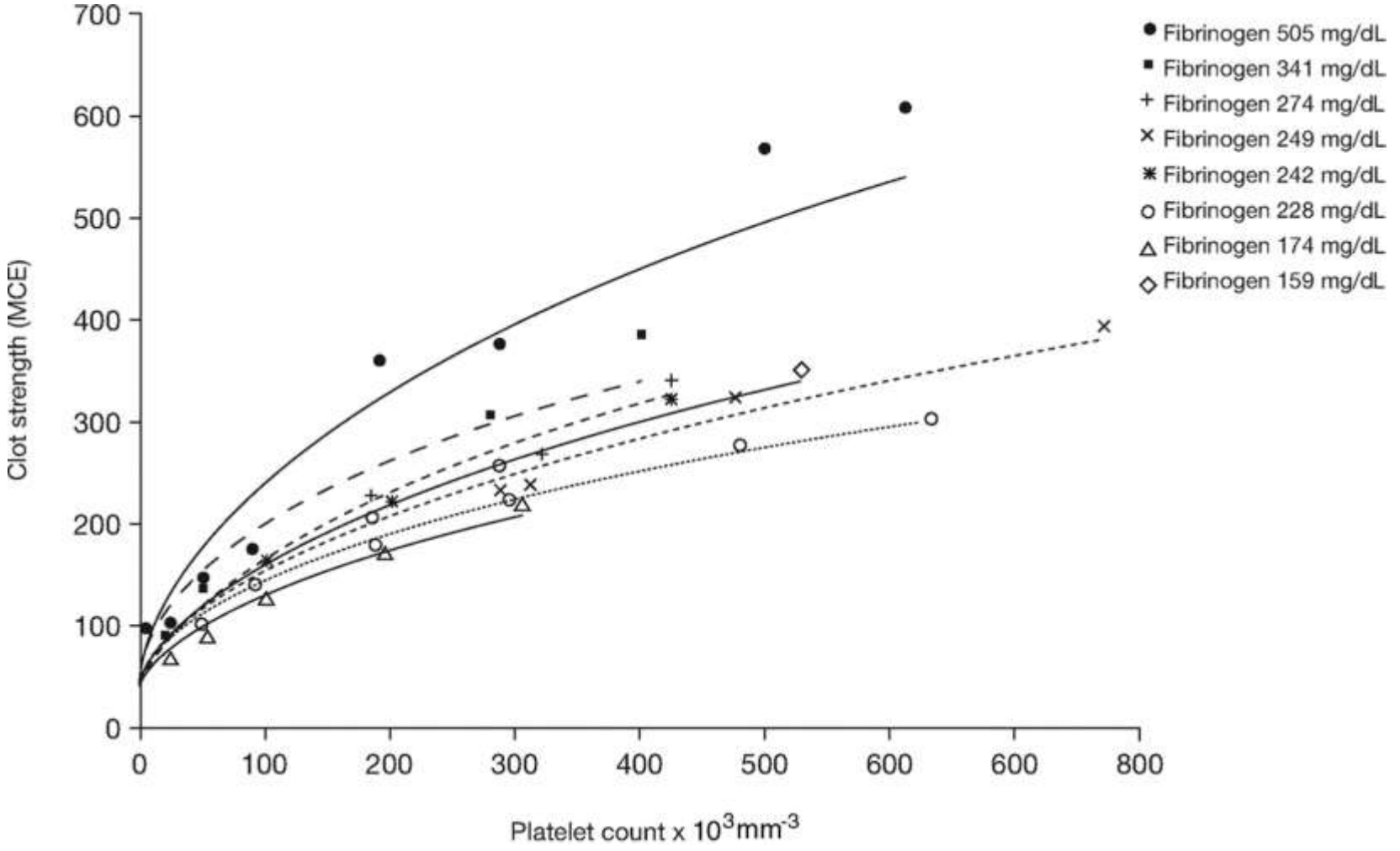
Christian F. Weber, Klaus Görlinger, Christian Byhahn, Anton Moritz, Alexander A. Hanke, Kai Zacharowski and Dirk Meininger

Eur J Anesthesiol 2011:57-62



aspirin & clopidogrel

Effect of platelet count on clot strength in EXTEM. Clot strength is given in maximum clot elasticity (MCE).



Lang T et al. Anesth Analg 2009;108:751-758

World Health Organization

Prescribing blood: a checklist for clinicians

Always ask yourself the following questions before prescribing blood or blood products for a patient

1 What improvement in the patient's clinical condition am I aiming to achieve?

2 Can I minimize blood loss to reduce this patient's need for transfusion?

3 Are there any other treatments I should give before making the decision to transfuse, such as intravenous replacement fluids or oxygen?

4 What are the specific clinical or laboratory indications for transfusion for this patient?

5 What are the risks of transmitting HIV, hepatitis, syphilis or other infectious agents through the blood products that are available for this patient?

6 Do the benefits of transfusion outweigh the risks for this particular patient?

7 What other options are there if no blood is available in time?

8 Will a trained person monitor this patient and respond immediately if any acute transfusion reactions occur?

9 Have I recorded my decision and reasons for transfusion on the patient's chart and the blood request form?

Finally, if in doubt, ask yourself the following question.

10 If this blood was for myself or my child, would I accept the transfusion in these circumstances?