Role trombocytů při ŽOK a co všechno zohledňovat při jejich substituci

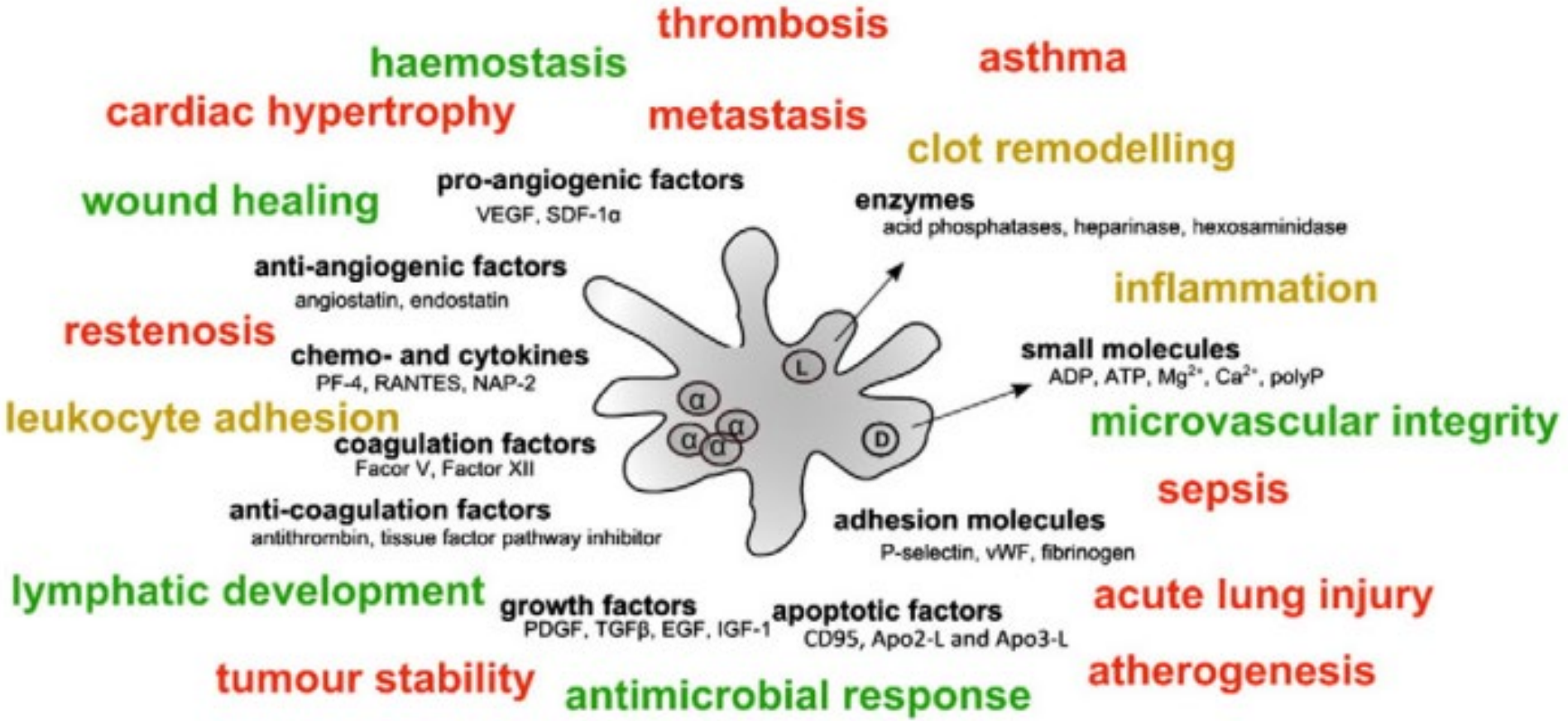
Vaníčková Kateřina

Klinika anesteziologie, resuscitace a intenzivní medicíny LF MU a Fakultní nemocnice Brno

Platelet secretion: From haemostasis to wound healing and beyond

Ewelina M. Golebiewska, Alastair W. Poole

physiological
pathological
combination of factors



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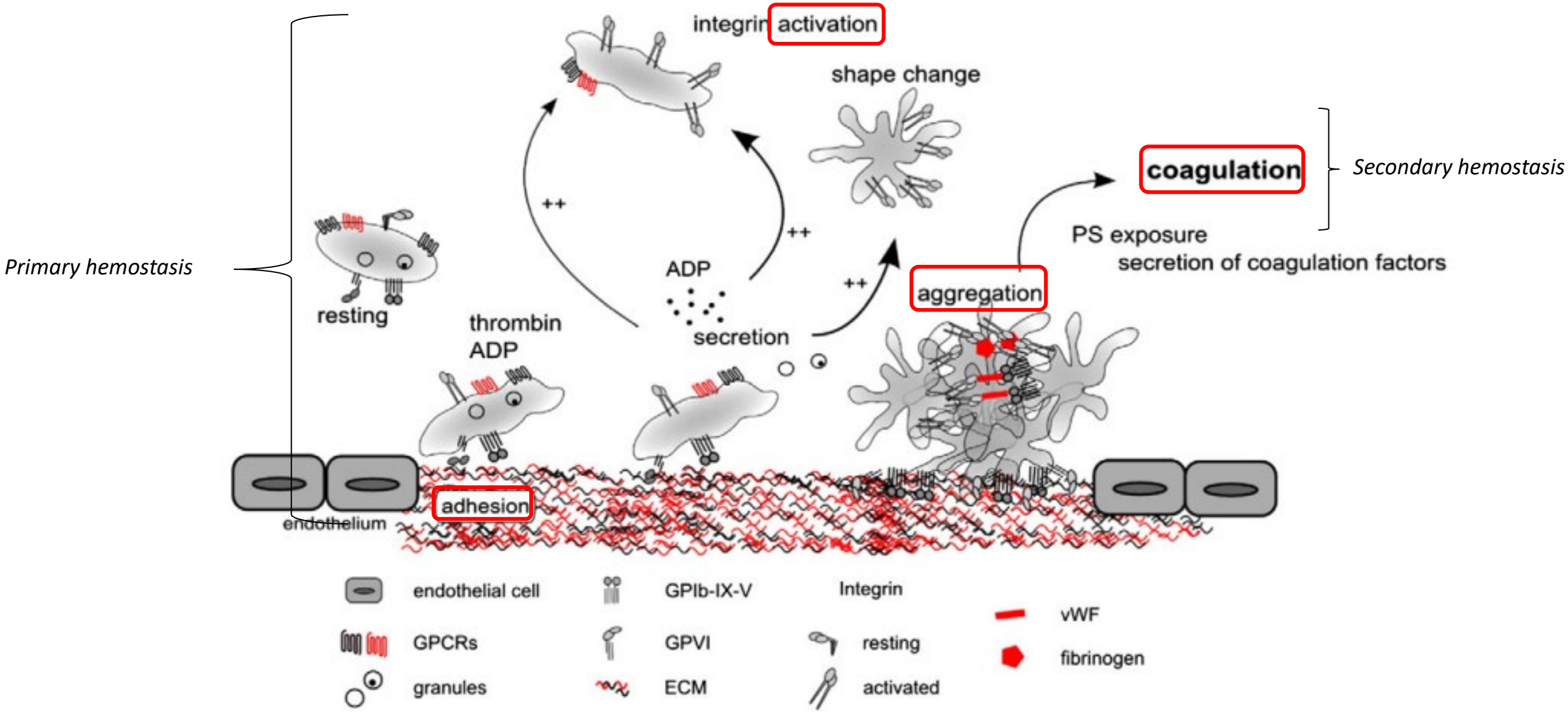
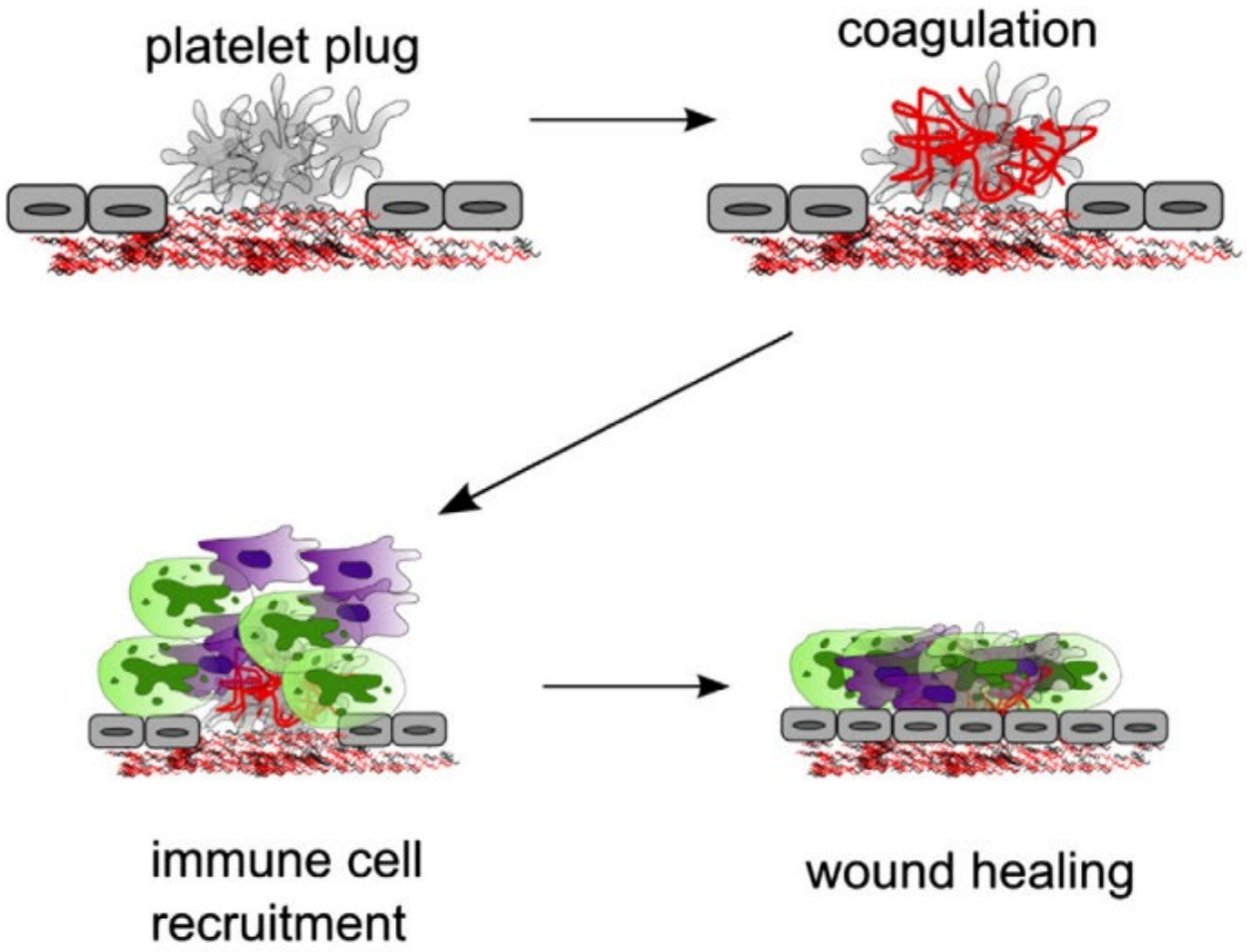
Br J Haematol, Volume: 165, Issue: 2, Pages: 204-216, First published: 30 November 2013, DOI: (10.1111/bjh.12682)



Br J Haematol, Volume: 165, Issue: 2, Pages: 204-216, First published: 30 November 2013, DOI: (10.1111/bjh.12682)



Other roles played by platelet in the body include participation in the inflammation, mitogenesis, wound healing, and antimicrobial host deficiencies.

Br J Haematol, Volume: 165, Issue: 2, Pages: 204-216, First published: 30 November 2013, DOI: (10.1111/bjh.12682)

Research

Original Investigation

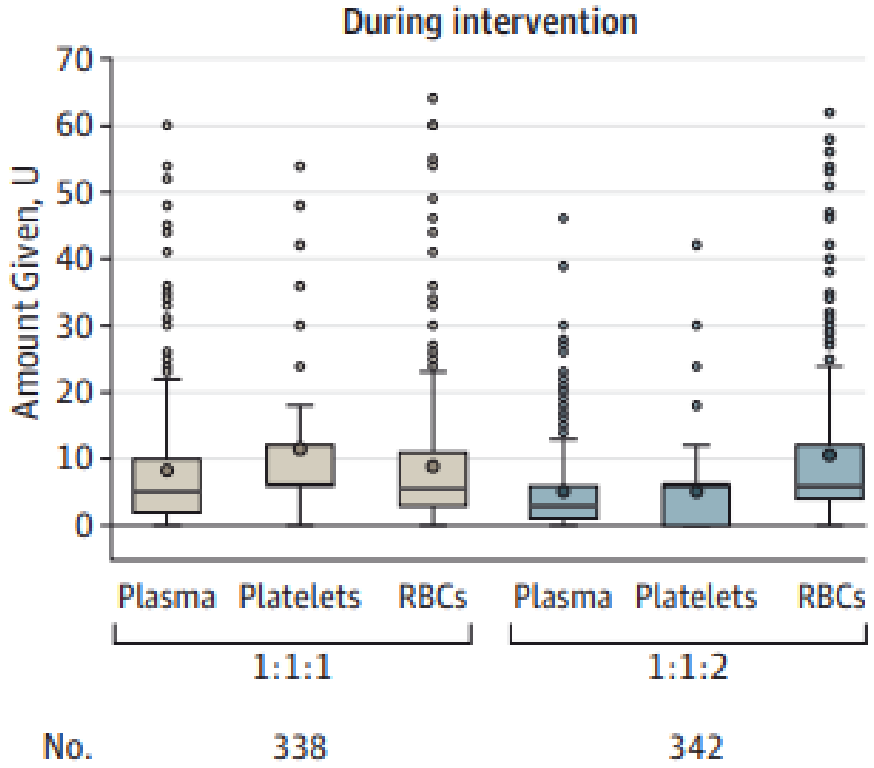
Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma

The PROPPR Randomized Clinical Trial

John B. Holcomb, MD; Barbara C. Tilley, PhD; Sarah Baraniuk, PhD; Erin E. Fox, PhD; Charles E. Wade, PhD; Jeanette M. Podbielski, RN; Deborah J. del Junco, PhD; Karen J. Brasel, MD, MPH; Eileen M. Bulger, MD; Rachael A. Callcut, MD, MSPH; Mitchell Jay Cohen, MD; Bryan A. Cotton, MD, MPH; Timothy C. Fabian, MD; Kenji Inaba, MD; Jeffrey D. Kerby, MD, PhD; Peter Muskat, MD; Terence O'Keeffe, MBChB, MSPH; Sandro Rizoli, MD, PhD; Bryce R. H. Robinson, MD; Thomas M. Scalea, MD; Martin A. Schreiber, MS; Deborah M. Stein, MD; Jordan A. Weinberg, MD; Jeannie L. Callum, MD; John R. Hess, MD, MPH; Nena Matijevic, PhD; Christopher N. Miller, MD; Jean-Francois Pittet, MD; David B. Hoyt, MD; Gail D. Pearson, MD, ScD; Brian Leroux, PhD; Gerald van Belle, PhD; for the PROPPR Study Group

- **PRT in 680 severely injured patients performed in 12 level I trauma centers in the US (initially planned were 580 patients, DSMB increased #)**
- **Blood product ratios: 1:1:1 vs. 1:1:2**
- **Primary outcome: 24h and 30d all cause mortality**
- **Secondary outcomes:**
  - **Time to hemostasis**
  - **Blood product volumes transfused**
  - **Complications**
  - **Incidence of surgical procedures**
  - **Functional status**

Figure 4. Distribution of Blood Product Amounts Within Period up to 24 Hours After Admissio



Conclusions

Among patients with severe trauma and major bleeding, early administration of plasma, platelets, and RBCs in a 1:1:1 ratio compared with a 1:1:2 ratio did not result in significant differences in mortality at 24 hours or at 30 days. However, more patients in the 1:1:1 group achieved hemostasis and fewer experienced death due to exsanguination by 24 hours. Even though there was an increased use of plasma and platelets transfused in the 1:1:1 group, no other safety differences were identified between the 2 groups.

Association Between Ratio of Fresh Frozen Plasma to Red Blood Cells During Massive Transfusion and Survival Among Patients Without Traumatic Injury

Tomaz Mesar, MD[1]; Andreas Larentzakis, MD, PhD[1]; Walter Dzik, MD[2]; et al

Findings In this retrospective study of 865 massive transfusion events in an urban academic hospital, nearly 90% of all massive transfusions were received by patients without trauma, but there was no evidence that a ratio-based transfusion strategy of high fresh frozen plasma to red blood cells ratio improved survival.

Conclusions

At Massachusetts General Hospital, high FFP:RBC transfusion ratios are being used in patients without trauma, who account for nearly 90% of all MT events. Thirty-day survival was not significantly different in patients receiving a high FFP:RBC ratio compared with those receiving a low ratio. Additional studies are necessary to refine MTPs in nontrauma specialties.

Table 4. Blood Product Transfusions and 30-Day Mortality by FFP:RBC Ratio Tertile Excluding Patients With Trauma

Variable	FFP:RBC Ratio			*P* Value[a]
	High (n = 257)	Medium (n = 254)	Low (n = 256)	
Median (IQR) FFP:RBC ratio	1:0.9 (1:0.4-1:1.1)	1:1.4 (1:1.2-1:1.7)	1:3.0 (1:1.7-1:21)	
RBCs transfused, median (IQR), U	16.0 (12.0-24.0)	15.0 (12.0-22.0)	12.0 (11.0-16.0)	<.001
FFP transfused, median (IQR), U	21.0 (15.0-30.0)	12.0 (9.0-18.0)	5.0 (2.0-8.0)	<.001
Cryoprecipitate transfused, median (IQR), U	4.0 (0.0-10.0)	0.0 (0.0-10.0)	0.0 (0.0-5.0)	<.001
Platelets transfused, median (IQR), U	30.0 (18.0-48.0)	18.0 (12.0-36.0)	12.0 (0.0-24.0)	<.001
Mortality rate, No. (%)				
All nontrauma	70 (27)	62 (24)	56 (22)	.16
Cardiac	27 (31)	30 (28)	19 (24)	.39
Liver transplant	10 (14)	2 (8)	4 (27)	.25
General	17 (52)	7 (28)	5 (18)	.008
Vascular	4 (14)	8 (26)	8 (42)	.045
Medicine	8 (80)	4 (40)	14 (25)	.002
Orthopedics	3 (43)	5 (25)	2 (7)	.04
Cardiopulmonary transplant, No. (%)	0	5 (23)	1 (17)	.40
Obstetrics/gynecology	0	0	0	NA
Urology	0	0	1 (17)	>.99
Neurosurgery	0	0	0	NA
Burns	NA	1 (50)	2 (50)	NA
Thoracic	1 (50)	0 (0)	0	>.99
Otolaryngology	NA	NA	0	NA

JAMA Surg. 2017;152(6):574-580. doi:10.1001/jamasurg.2017.0098

Platelet-to-red blood cell ratio and mortality in bleeding trauma patients: A systematic review and meta-analysis

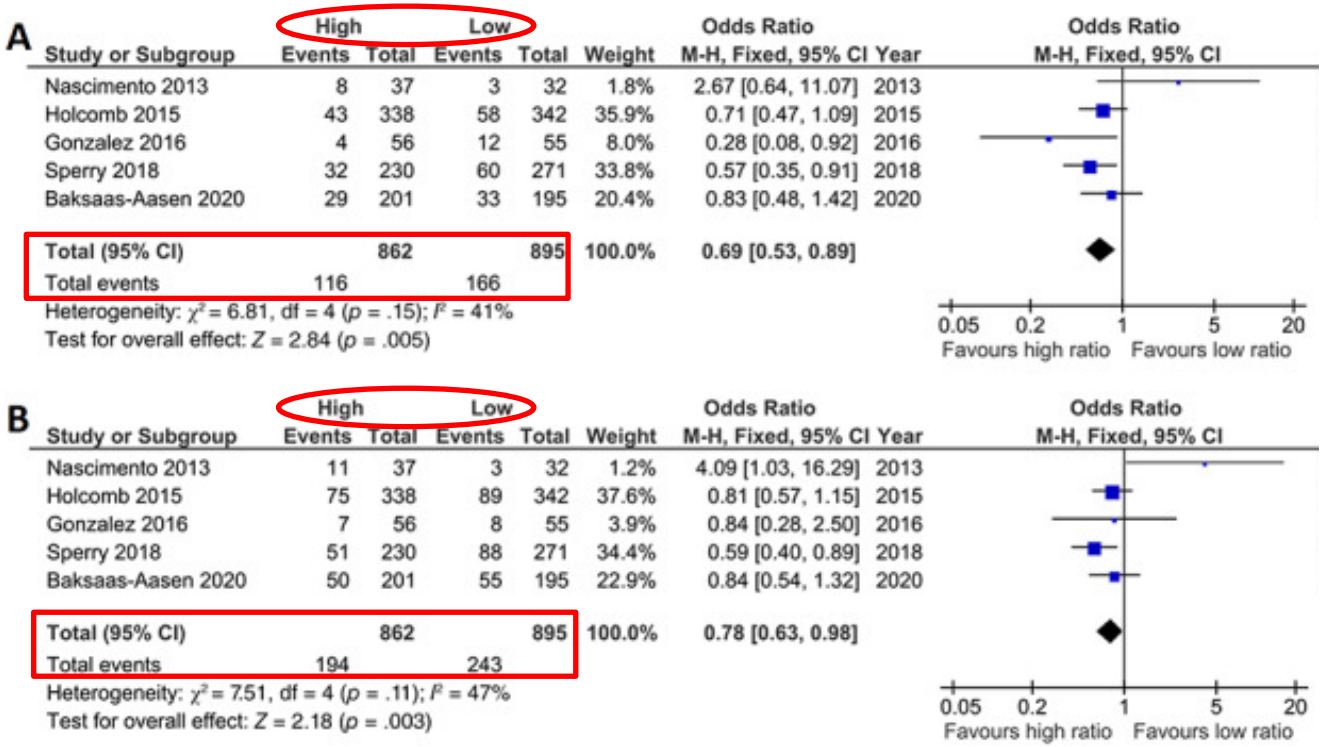
Derek J. B. Kleinveld[1,2] | Rombout B. E. van Amstel[1,2] | Mathijs R. Wirtz[1,2] | Leo M. G. Geeraedts[3] | J. Carel Goslings[4] | Markus W. Hollmann[2,5] | Nicole P. Juffermans[1,2,6]

Methods

Pubmed, Medline, and Embase were screened for randomized controlled trials (RCTs) in bleeding trauma patients (age ≥16 years) receiving platelet transfusion between 1946 until October 2020.

Results

In total five RCTs (n = 1757 patients) were included. A high platelet:RBC compared with a low platelet:RBC ratio significantly improved 24 hour mortality (odds ratio [OR] 0.69 [0.53–0.89]) and 30- day mortality (OR 0.78 [0.63–0.98]).
There was no difference between platelet:RBC ratio groups in thromboembolic events and organ failure.
Correction of coagulopathy was reported in five studies, in which platelet dose had no impact on trauma-induced coagulopathy.



High platelet:RBC ratio improves 24-h and 30-day mortality in randomized controlled trials compared with low platelet:RBC ratio. Meta-analyses of (A) 24-h and (B) 30-day mortality represented in a forest plot. Weighted mean platelet:red blood cell ratio in the high ratio group was 0.85 (SD 0.56) and in the low platelet dose group 0.40 (0.27).

TRANSFUSION First published: 16 July 2021 https://doi.org/10.1111/trf.16455

Indications for therapeutic platelet transfusions

A therapeutic platelet transfusion is transfusion of allogeneic platelets in patients with thrombocytopenia and/or functional platelet abnormalities who have significant bleeding, provided the platelet disorder is likely to be causing or contributing to the bleeding. It is sometimes difficult to make this judgement clinically. It is suggested by the British Society for Haematology (BSH) Guidelines[7] and The National Institute of Health Consensus Conference,[8] that a platelet count of 50×10^9/l or less with active bleeding is an indication for therapeutic transfusion. This advice appears to be based on clinical opinion and a retrospective study by Gaydos et al.[9] This study assessed the likelihood of bleeding in leukaemic patients according to their platelet count. Serious spontaneous haemorrhage due to thrombocytopenia alone is unlikely to occur at platelet counts above $10–20 \times 10^9$/l,[10] the cut-off level will be discussed fully elsewhere at this meeting.

Blood Reviews (1998) **12**, 227–233

Guidelines for the use of platelet transfusions

British Committee for Standards in Haematology, Blood Transfusion Task Force (Chairman P. Kelsey)

Recommendations (grade C, level IV)

- Here is consensus that the platelet count should not beallowed to fall below 50·109⁄l in patients with acutebleeding *(BCSH, 1988; Consensus Conference on PlateletTransfusion, 1998; Stainsbyet al,2000).*
- A higher target level of 100·109⁄l has been recom-mended for those with multiple trauma or centralnervous system injury

(Development Task Force ofthe College of American Pathologists, 1994; Horsey,1997).

British Journal of Haematology,2003,122, 10–23

Alterations in platelet behavior after major trauma: adaptive or maladaptive?

Paul Vulliamy, Lucy Z. Kornblith, Matthew E. Kutcher, Mitchell J. Cohen, Karim Brohi, Matthew D. Neal,

Platelet behavior after major injury

Despite well-mapped roles in normal hemostasis, TIC-induced changes in platelet behavior are an active area of investigation . Platelets undergo a number of behavioral changes after major trauma and hemorrhage , both quantitative and qualitative

In about half of patients with TIC, platelets are dysfunctional in their adhesion and aggregation capabilities. Tis platelet dysfunction, known as "platelet exhaustion", is not revealed by the platelet count, which is often normal. Exhaustion has been attributed to platelet overactivation from TF, von Willebrand factor, and DAMPs .
Platelet dysfunction impairs haemostasis even if the blood levels of coagulation factors are maintained within the normal rang.

Platelets. 2021 April 03; 32(3): 295–304. doi:10.1080/09537104.2020.1718633.

ORIGINAL RESEARCH article

Hypothermia-Associated Coagulopathy: A Comparison of Viscoelastic Monitoring, Platelet Function, and Real Time Live Confocal Microscopy at Low Blood Temperatures, an *in vitro* Experimental Study

Bernd Wallner[1,2,3], Bettina Schenk[2], Martin Hermann[2], Peter Paal[4], Markus Falk[3], Giacomo Strapazzon[3], Wenjun Z. Martini[5], Hermann Brugger[3] and Dietmar Fries[2]*

Trauma-related hypothermia has notable effects on the coagulation system and is an independent risk factor for increased morbidity and mortality in trauma patients
Trauma-induced hypothermia with a core temperature <32°C has been associated with 50–100% mortality. In mild hypothermia (35–32°C), bleeding results primarily from a defect in platelet adhesion,
and at 30 C is approximately a 50% reduction in platelet activation.

Front. Physiol., 14 July 2020 Sec. Environmental, Aviation and Space Physiology
https://doi.org/10.3389/fphys.2020.0084

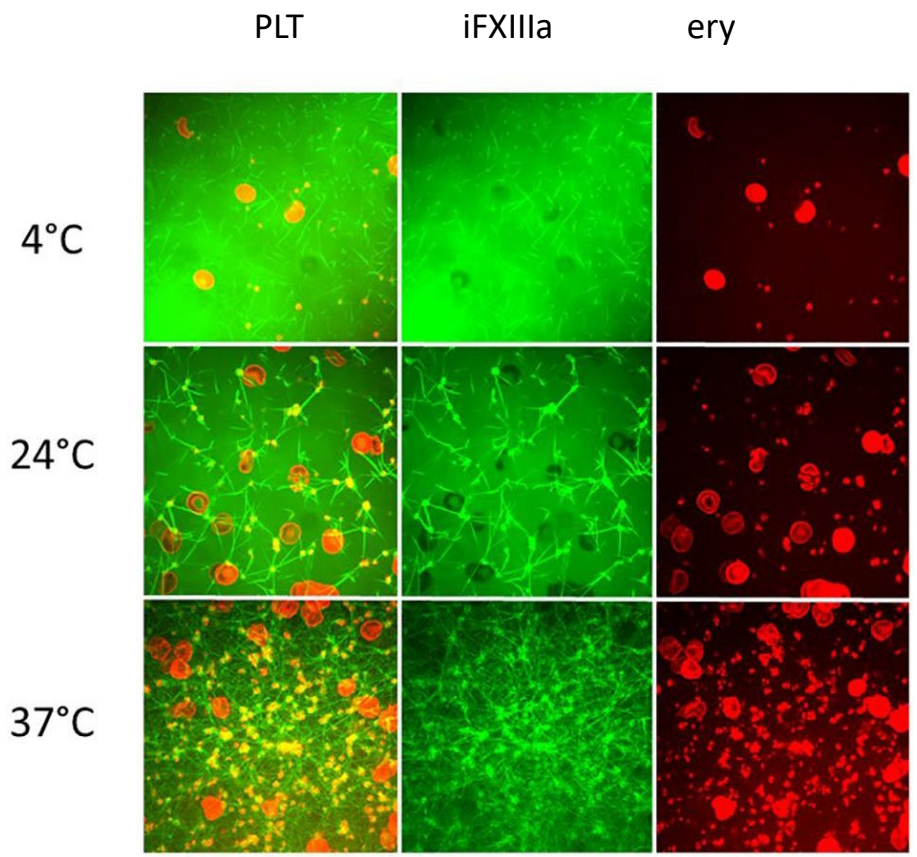


FIGURE 4.
Influence of temperature on coagulation and platelet function visualized with Real Time Live Confocal Imaging visualize the fibrin network (green, iFXIIIa), platelet aggregates (yellow due to WGA and iFXIIIa overlay), and erythrocytes (red, WGA) at 4°C (first row), 24°C (middle row), and 37°C (bottom row).

Role of Platelet Transfusion in the Reversal of Anti-Platelet Therapy

Srikanth Nagalla [a], Ravi Sarode [a,b,*]

[a] Division of Hematology/Oncology, UT Southwestern Medical Center, Dallas, TX
[b] Division of Transfusion Medicine and Hemostasis, UT Southwestern Medical Center, Dallas, TX

Table 3
Studies with clinical endpoints where platelet transfusions were used to reverse the effect of APAs

Year of Publication	Reference	Study type	Summary	Results
2016	Baharoglu et al [24]	Multicenter Phase 3 RCT	The study population involved 190 adult patients with non-traumatic supratentorial intracranial hemorrhage (ICH) who presented within 6 hours of symptom onset, on APAs (71% ASA, 19% ASA plus dipyridamole, 7% P2Y12 receptor antagonists alone or a DAPT in combination with aspirin) for a minimum of 7 days prior to presentation and a Glasgow coma scale ≥8.	The patients in the platelet transfusion group had worse primary outcomes of death and dependence based on the modified Rankin Scale at 3 months compared to the group that did not receive platelet transfusions.
2017	Zakko et al [25]	Single center retrospective cohort study	204 patients with gastrointestinal bleeding (GIB) on APAs (aspirin, clopidogrel and DAPT) were compared to 204 matched controls	Platelet transfusions did not decrease the rebleeding rate and was associated with a higher mortality.
2012	Li et al [27]	Single center, randomized, double-blind, randomized controlled trial	The efficacy of platelet transfusions was studied in 780 patients on ASA who presented with acute hypertensive basal ganglia hemorrhage and underwent an emergent craniotomy for hematoma removal. The patients were divided into five groups with one of the groups not receiving aspirin at the time of enrollment (no platelet transfusions in this group). Among the patients receiving aspirin, the patients were defined as aspirin sensitive, resistant or semi-responsive using light transmittance aggregometry immediately upon admission to the hospital. The aspirin resistant/semi-responsive group did not receive platelet transfusions. The aspirin sensitive group was divided into a no transfusion group, one dose of platelets transfused group and 2 doses of platelets transfused group.	The primary outcome of postoperative hemorrhage and secondary outcome of mortality rate in the platelet transfusion groups were similar to the group of patients not on aspirin and better than the group of patients who were aspirin sensitive and did not receive platelets, suggesting some benefit from transfusion.

RCT- randomized controlled trial; APAs-Anti-platelet agents; ASA-aspirin; DAPT-dual anti-platelet therapy;

https://doi.org/10.1016/j.tmrv.2019.01.002

The effect of platelet transfusion in patients with traumatic brain injury and concomitant antiplatelet use: a systematic review and meta-analysis

Sophie Thorn[1], *Helge Güting*[2], *Tim Mathes*[2], *Nadine Schäfer*[2], *and Marc Maegele*[2,3]

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, (95% CI)
Downey 2009	29	166	27	162	18.1%	1.05 (0.65-1.69)
Fortuna 2008	20	66	16	100	16.3%	1.89 (1.06-3.38)
Guillotte 2018	3	19	1	61	3.1%	9.63 (1.06-87.26)
Holzmacher 2018	2	23	1	43	2.8%	3.74 (0.36-39.07)
Ivascu 2008	11	40	9	69	12.8%	2.11 (0.96-4.65)
Jehan 2019	5	64	25	179	11.0%	0.56 (0.22-1.40)
Lee 2017	4	38	5	49	7.6%	1.03 (0.30-3.58)
Lindblad 2018	9	45	10	46	12.6%	0.92 (0.41-2.05)
Ohm 2005	10	24	11	66	13.9%	2.50 (1.22-5.12)
Washington 2011	2	44	0	64	1.8%	7.25 (0.36-147.36)
Total (95% CI)		**529**		**839**	**100.0%**	**1.50 (0.93-2.42)**
Prediction interval						**(0.49-4.58)**

Heterogeneity: $Tau^2 = 0.1897$; $Chi^2 = 15.87$, df = 9 (p = 0.07); $I^2 = 43\%$

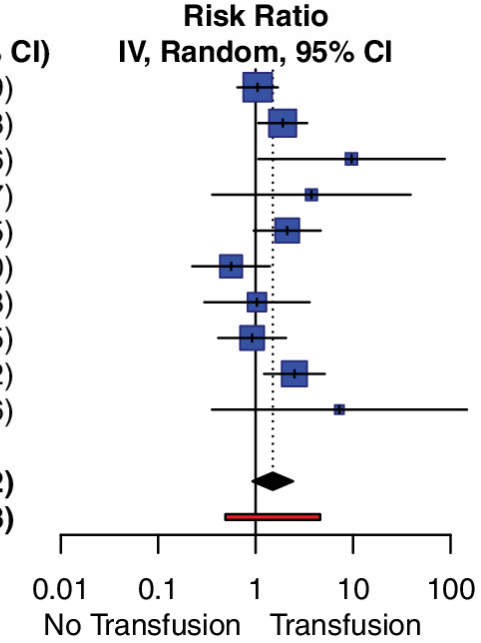


Figure **2** shows a forest plot demonstrating the comparison and meta-analysis of included studies. The pooled RR indicated a higher mortality with the use of platelet transfusion (RR, 1.50; 95% CI, 0.93-2.42; I^2, 43%; prediction interval, 0.49-4.58).

TRANSFUSION 2019;59;3536–3544 doi:10.1111/trf.15526

GUIDELINES

Transfusion strategies in bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine

Alexander P. J. Vlaar[1*], Joanna C. Dionne[2,3,4,21], Sanne de Bruin[1], Marije Wijnberge[1,5], S. Jorinde Raasveld[1], Frank E. H. P. van Baarle[1], Massimo Antonelli[6,7], Cecile Aubron[8], Jacques Duranteau[9], Nicole P. Juffermans[10,11], Jens Meier[12], Gavin J. Murphy[13], Riccardo Abbasciano[13], Marcella C. A. Müller[1], Marcus Lance[14], Nathan D. Nielsen[15], Herbert Schöchl[16,17], Beverley J. Hunt[18], Maurizio Cecconi[19,20] and Simon Oczkowski[2,3,4]

Recommendation
We **suggest** using a restrictive platelet transfusion strategy (no transfusion) in patients with intracranial hemorrhage (spontaneous or traumatic intracerebral hemorrhage) who are on antiplatelet therapy (*Conditional recommendation, moderate certainty evidence*).
We make **no recommendation** for the use of a restrictive (no transfusion) vs liberal platelet transfusion strategy in critically ill patients with non-massive bleeding who are on antiplatelet therapy (*No recommendation, very low certainty of evidence*).

Implementation issues

Given the lack of evidence, decisions about transfusing platelets in patients on antiplatelet agents need to be based upon individual considerations, including the severity and location of bleeding, consideration of risks of transfusion, and availability of blood products. Enthusiasm for platelet transfusion should be tempered given the lack of benefit in ICH, in which even small difference in hemorrhage volumes would be expected to have an impact upon patient outcome; the benefit in other populations is likely to be even less certain.

Intensive Care Med (2021) 47:1368–1392
https://doi.org/10.1007/s00134-021-06531-x

Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2021

RECOMMENDATION

ESGE does not recommend routine platelet transfusion for patients with acute NVUGIH who are taking antiplatelet agents.

Strong recommendation, low quality evidence.

There is no high quality evidence supporting the benefit of routine platelet transfusion in patients who have acute UGIH while taking antiplatelet agents

Role for DDAVP?

RESEARCH Open Access

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

Donat R. Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Jacques Duranteau[7], Daniela Filipescu[8], Beverley J. Hunt[9], Radko Komadina[10], Marc Maegele[11], Giuseppe Nardi[12], Louis Riddez[13], Charles-Marc Samama[14], Jean-Louis Vincent[15] and Rolf Rossaint[16*]

Antiplatelet agents
Recommendation 36

We suggest that the administration of **desmopressin** (0.3 µg/kg) be considered in patients treated with platelet-inhibiting drugs or von Willebrand disease. (Grade 2C)

Spahn et al. Critical Care (2019) 23:98 https://doi.org/10.1186/s13054-019-2347-3

REVIEW ARTICLE

Effect of Desmopressin on Platelet Dysfunction During Antiplatelet Therapy: A Systematic Review

Lise Kjær Andersen[1], Anne-Mette Hvas[1*] and Christine Lodberg Hvas[2]

Abstract Background and Objective: An increasing number of patients receive antiplatelet therapy. Patients exposed to surgery while receiving platelet inhibitors hold an increased bleeding risk. Especially in neurosurgery and neurocritical care patients, bleeding and hematoma expansion are feared complications as even minor bleedings may be hazard- ous. The objective of this systematic review was to investigate the efect of desmopressin (1-deamino-8-d-arginine vasopressin, DDAVP) on platelet function during antiplatelet therapy in patients undergoing non-cardiac surgery, patients who experience spontaneous or traumatic hemorrhage, healthy individuals and in animals**.**

Methods: Studies were identifed through a systematic literature search in PubMed and EMBASE on August 19, 2019, with an update on May 2, 2020, and from reference lists of the included studies. Data on clinical and biochemical efect of DDAVP were extracted from included studies for a qualitative data synthesis.

Results: In total, 22 studies were included: 18 human studies and four animal studies. Overall, DDAVP improved bleeding time and increased platelet aggregation in patients undergoing non-cardiac surgery, patients sufering intracerebral or subarachnoid hemorrhage while receiving antiplatelet therapy as well as in healthy individuals and animals exposed to antiplatelet therapy. Observational data indicate that DDAVP may mitigate hematoma expansion in patients with intracerebral hemorrhage or traumatic brain injury.

Conclusions: The present data hold biochemical evidence that DDAVP improves platelet function during antiplatelet therapy in humans and animals. The need for randomized trials is evident in order to evaluate the potential clinical efect of DDAVP in management of patients with spontaneous or traumatic hemorrhage, or undergoing neurosurgery, while receiving antiplatelet therapy

Neurocrit Care (2021) 34:1026–1046 https://doi.org/10.1007/s12028-020-01055-6

ORIGINAL WORK

The Role of Desmopressin on Hematoma Expansion in Patients with Mild Traumatic Brain Injury Prescribed Pre-injury Antiplatelet Medications

Jeffrey F. Barletta[1*], Diana Abdul-Rahman[2], Scott T. Hall[3], Alicia J. Mangram[4], James K. Dzandu[4], Jennifer A. Frontera[5] and Victor Zach[2,6]

Variable	DDAVP (n = 158)	No DDAVP (n = 44)	p value
Hematoma expansion (> 20% of baseline or new hematoma)	22 (14%)	13 (30%)	0.015
Expansion from baseline*			
Percent	185% (75–580)	221% (72–400)	0.832
Volume (ml)	22 (3.2–32.2) *n = 18	4.7 (2.7–17.2) *n = 12	0.236
Hematoma expansion (> 33% of baseline or new hematoma)	19 (12%)	13 (30%)	0.005
Thrombosis	4 (2.5%) Arterial, n = 2 Venous, n = 2	2 (4.5%) Arterial, n = 2	0.613
Length of stay (days)	6.6 (3.3–7.3)	5 (2.7–7.6)	0.689
Glasgow comas score at discharge	15 (14–15)	15 (14–15)	0.660
Disposition			
Home or rehab	96 (61%)	30 (68%)	0.369
Death or hospice	20 (13%)	6 (14%)	0.864
Death	5 (3.2%)	4 (9.1%)	0.106

DDAVP desmopressin

Abstract

Background/Objective:

Desmopressin (DDAVP) has been suggested for antiplatelet medication reversal in patients with traumatic brain injury (TBI) but there are limited data describing its efect on clinical outcomes. The purpose of this study was to evaluate the efect of DDAVP on hematoma expansion and thrombosis in patients with TBI who were prescribed pre-injury antiplatelet medications.

Results: Of 202 patients included in analysis, 158 (78%) received DDAVP. The incidence of hematoma expansion was 14% and 30% for patients who did and did not receive DDAVP, respectively (p=0.015). After controlling for age, injury severity score, multi-compartmental hemorrhage, and receipt of pre-injury high-dose aspirin (>81 mg), ADP-receptor inhibitors, oral anticoagulants, prothrombin complex concentrates or platelets in a multivariate analysis, the association between DDAVP and hematoma expansion remained signifcant (adjusted OR 0.259 [95% CI 0.103–0.646], p=0.004). Throm- botic events were similar between the two groups (DDAVP, 2.5%, no DDAVP, 4.5%; p=0.613)

Conclusions: DDAVP was associated with a lower incidence of hematoma expansion in patients with mild TBI who were prescribed pre-injury antiplatelet medications. These results justify a randomized controlled trial to further evalu- ate the role of DDAVP for this indication.

Neurocrit Care (2020) 33:405–413 https://doi.org/10.1007/s12028-019-00899-x

Summary….

- platelet transfusion is the primary therapy for patients with thrombocytopenia or platelet dysfunction
- always keep in mind that with every transfusion, there is an additional potential risk to the patient
- specific platelet transfusion triggers and goals vary with the clinical circumstances

“I’m concerned about his platelets.”

CartoonStock.com