ACCADEMIA di FORMAZIONE

SIMTI

Attualità nella gestione della terapia piastrinica

Il supporto trasfusionale piastrinico nel paziente oncoematologico: aggiornamento dei livelli di evidenza

Ursula La Rocca
Centro Nazionale Sangue

La sottoscritta La Rocca Ursula, in qualità di Relatrice
dichiara che nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatrice di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

Il supporto trasfusionale piastrinico

Le PLTS rappresentano il **secondo emocomponente più comunemente trasfuso** (Kaufmann et al. 2015)

In USA, **oltre 2 milioni di trasfusioni di PLTS e 300.000 nel Regno Unito per anno** a **costi considerevoli**, con difficoltà in termini di **approvvigionamento**.

La più frequente indicazione resta la **prevenzione ed il trattamento del sanguinamento nei pazienti ematologici ed oncologici**.

Per anni, la scelta terapeutica trasfusionale guidata da thresholds, nonostante l'**effetto** delle diverse **soglie trasfusionali** non abbia mostrato **validità.**

In 2023, 7,774 units of blood components were transfused per day. Compared to the previous year, there was a slight decrease (-0.10%) (Table 6).

Table 6. Transfused units of blood components (2022-2023)

Blood component	2022	2023	Δ%
Red Blood Cells	**2,393,798**	**2,392,289**	-0.06
Red Blood Cells from whole blood	*2,383,058*	*2,384,659*	-0.07
Red Blood Cells by apheresis	*10,740*	*7,630*	-28.96
Platelets from single donors	934	113	-87.90
Platelets Pools	193,041	201,316	4.29
Platelets by apheresis	47,305	47,292	-0.13
Plasma	**205,552**	**196,795**	-4.26
Recovered Plasma	*68,893*	*67,762*	-1.64
Source Plasma	*24,141*	*23,615*	-2.18
Source Plasma from multiple apheresis	*4,873*	*3,900*	-19.97
Plasma pooled and treated for virus inactivation	*107,645*	*101,518*	-5.69
Total	**2,840,630**	**2,837,805**	-0.10

Table 12. Transfused patients (2022-2023)

Patients* transfused with:	2022	2023	Δ%
Whole Blood^	32	23	-28.13
Red Blood Cells	604,761	603,125	-0.27
Plasma	46,426	43,415	-6.49
Platelets	54,512	55,431	1.69
Other	5,472	5,445	-0.49
Total**	**639,003**	**638,046**	-0.15

* Patients transfused once or more than once during the year under examination were counted only once.

** Patients transfused more than once during the year under examination with blood components of the same type were counted only once; patients transfused with more than one type of blood component were included in the count of each type.

^ Includes reconstituted whole blood.

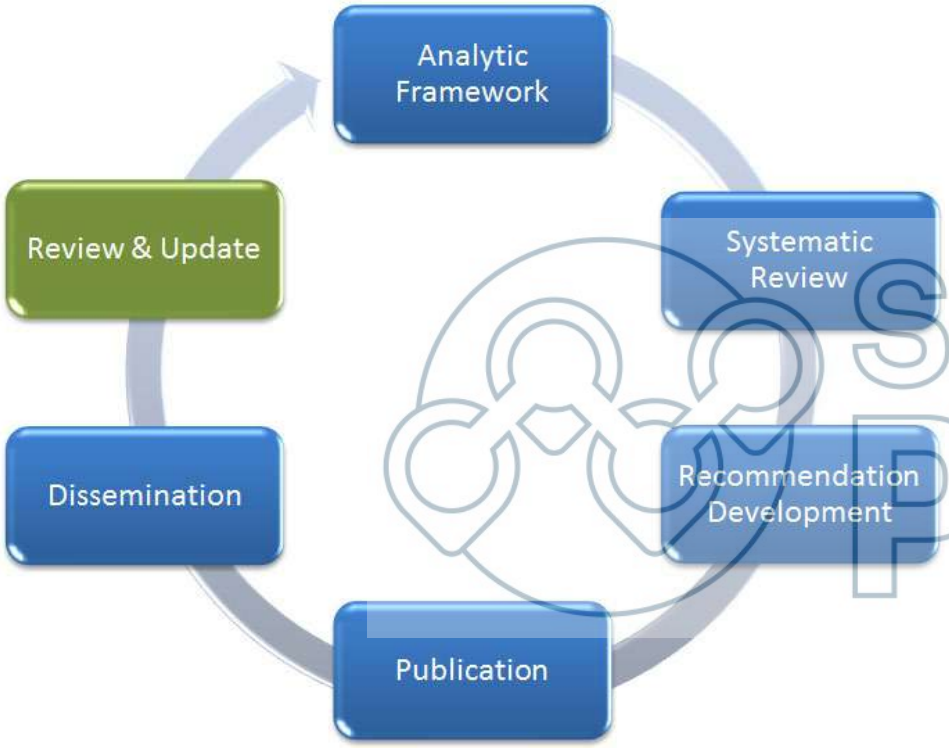
RAPPORTI ISTISAN 24|26

Italian Blood System 2023: activity data, haemovigilance and epidemiological surveillance

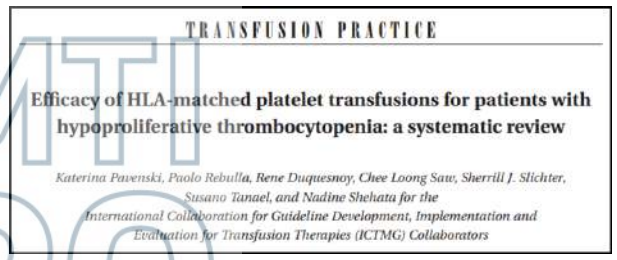
International Collaboration for Tranfusion Medicine Guidelines

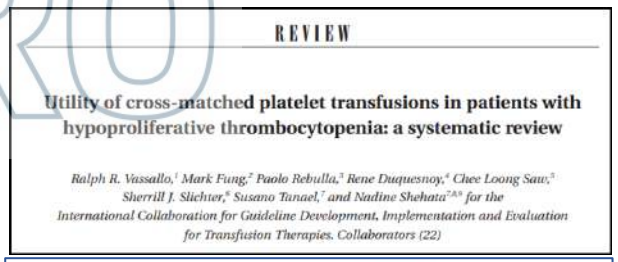
Gruppo di esperti nell'ambito della **medicina trasfusionale nato nel 2011.**
Obiettivo è **creare e promuovere linee guida cliniche basate sull'evidenza**, con il fine di **ottimizzare la pratica della medicina trasfusionale.**
L'ICTMG segue una rigorosa metodologia scientifica, basata su sistemi quali GHRADE, COCHRANE ed AGREE II.

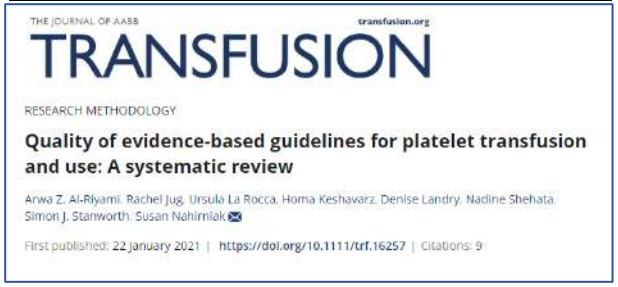
Platelet Transfusion Guideline Development Working Group



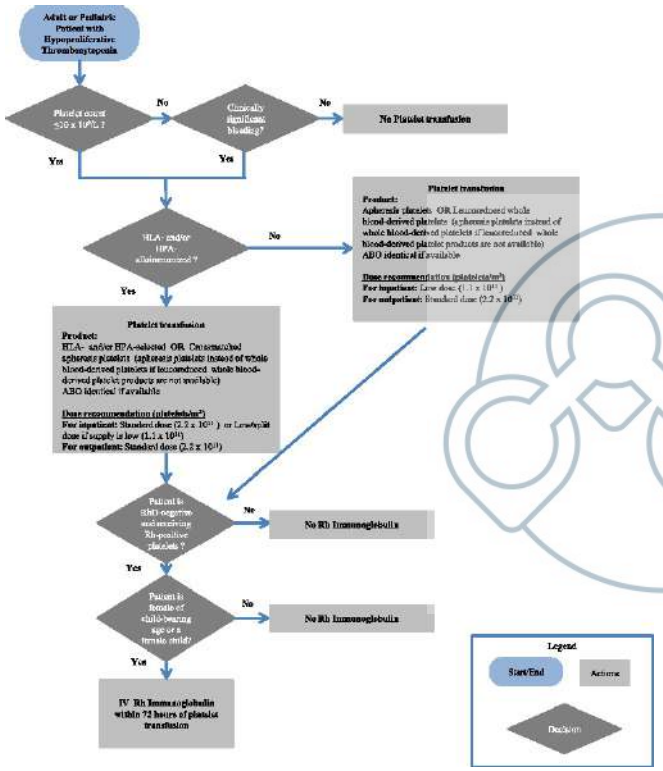

Contents lists available at ScienceDirect
Transfusion Medicine Reviews
journal homepage: www.tmreviews.com
Original Articles
Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia
See Editorial, pages 1–2
Susan Nahirniak [A,*], Sherrill J. Slichter [B], Susano Tanael [C], Paolo Rebulla [D], Katerina Pavenski [E], Ralph Vassallo [F], Mark Fung [R], Rene Duquesnoy [b], Chee-Loong Saw [1], Simon Stanworth [J], Alan Tinmouth [K], Heather Hume [L], Arjuna Ponnampalam [M], Catherine Moltzan [N], Brian Berry [O], Nadine Shehata [P], for the International Collaboration for Transfusion Medicine Guidelines (ICTMG)


TRANSFUSION PRACTICE
Efficacy of HLA-matched platelet transfusions for patients with hypoproliferative thrombocytopenia: a systematic review
Katerina Pavenski, Paolo Rebulla, Rene Duquesnoy, Chee Loong Saw, Sherrill J. Slichter, Susano Tanael, and Nadine Shehata for the International Collaboration for Guideline Development, Implementation and Evaluation for Transfusion Therapies (ICTMG) Collaborators


REVIEW
Utility of cross-matched platelet transfusions in patients with hypoproliferative thrombocytopenia: a systematic review
Ralph R. Vassallo,[1] Mark Fung,[2] Paolo Rebulla,[3] Rene Duquesnoy,[4] Chee Loong Saw,[5] Sherrill J. Slichter,[6] Susano Tanael,[7] and Nadine Shehata[7,8,9] for the International Collaboration for Guideline Development, Implementation and Evaluation for Transfusion Therapies. Collaborators (22)


THE JOURNAL OF AABB
transfusion.org
TRANSFUSION
RESEARCH METHODOLOGY
Quality of evidence-based guidelines for platelet transfusion and use: A systematic review
Arwa Z. Al-Riyami, Rachel Jug, Ursula La Rocca, Homa Keshavarz, Denise Landry, Nadine Shehata, Simon J. Stanworth, Susan Nahirniak
First published: 22 January 2021 | https://doi.org/10.1111/trf.16257 | Citations: 9

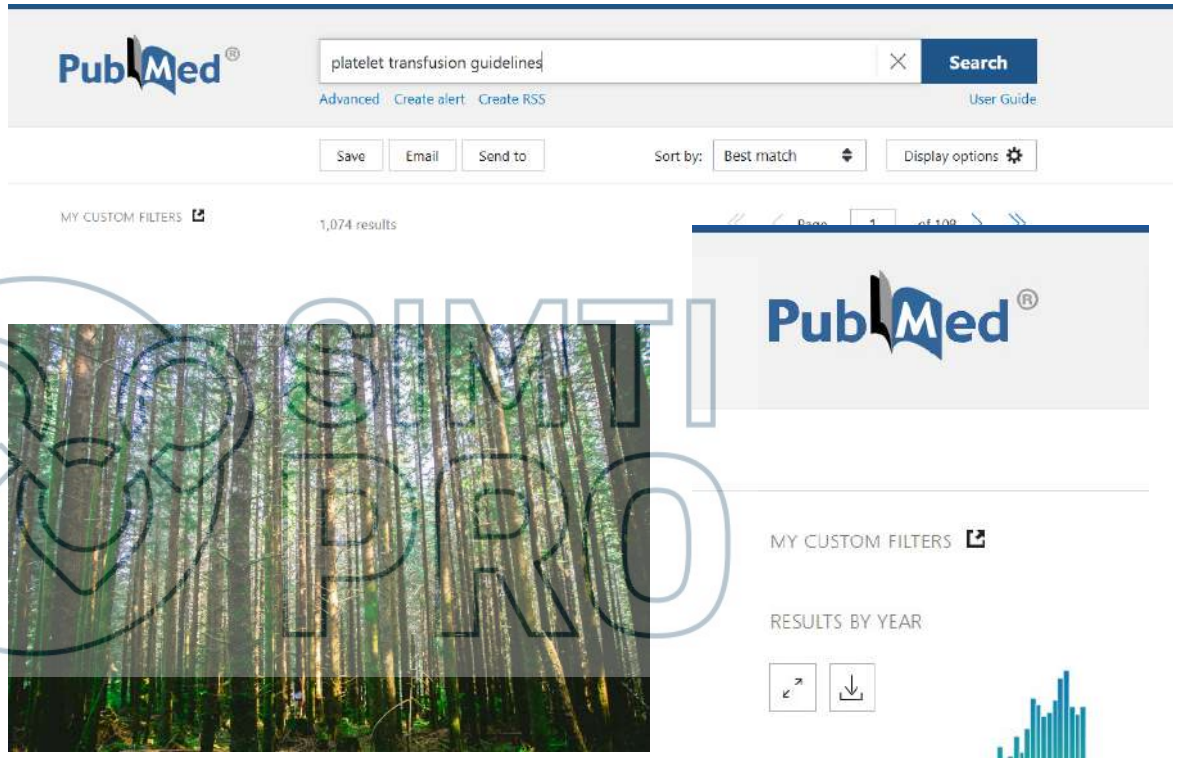
Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia



Nahirniak et al. 2015

- Prophylactic platelet transfusion for PLTS ≤ 10 × 10^9/L is the optimal approach to decrease the risk of hemorrhage for patients requiring chemotherapy or undergoing allogeneic or autologous transplantation.
- A low dose of platelets ($1.41\times10^{11}/m^2$) is as effective as higher dose of platelets but requires more frequent transfusions suggesting that low-dose platelets may be used in hospitalized patients. For outpatients, a median dose ($2.4\times10^{11}/m^2$) may be more cost-effective to prevent clinic visits only to receive a transfusion.
- In terms of platelet products, whole blood–derived platelet concentrates can be used interchangeably with apheresis platelets, and ABO-compatible platelet should be given to improve platelet increments and decrease the rate of refractoriness to platelet transfusion.
- For RhD-negative F children/women of child-bearing potential who have received RhD-positive PLTS, Rh immunoglobulin should probably be given to prevent immunization to the RhD antigen.
- Providing platelet support for the alloimmunized refractory patients with ABOmatched and HLA-selected or crossmatched ≤products is of some benefit, yet the degree of benefit needs to be assessed in the era of leukoreduction.

Il supporto trasfusionale piastrinico



Guideline Appraisal
AGREE II tool

ORIGINAL RESEARCH

TRANSFUSION

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami[1] | Rachel Jug[2,8] | Ursula La Rocca[3,4] | Homa Keshavarz[5] | Denise Landry[5] | Nadine Shehata[6,7,8] | Simon J. Stanworth[9,10,11] | Susan Nahirniak[12,13]

- Qualità molto variabile; molte LG non basate solide evidenze.
- La qualità delle linee guida per la pratica clinica deve essere valutata prima dell'implementazione.

i) Rating Scale

All AGREE II items are rated on the following 7-point scale:

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Domain	Scope (items)
1. Scope & purpose	Aim, including target population (1-3)
2. Stakeholder involvement	Development & representation by appropriate stakeholders (4-6)
3. Rigour of development	Methodology for data gathering, synthesis, recommendation formulation & updating (7-14)
4. Clarity of presentation	Language & formatting (15-17)
5. Applicability	Guideline implementation, uptake, and resource implications (18-21)
6. Editorial independence	Unbiased recommendations (22-23)

Global rating items:
+ overall rating of the quality of the guideline
+ whether the assessor would recommend the guideline for use

Al-Riyami AZ, Jug R, La Rocca U, Keshavarz H, et al. Transfusion 2021; 61: 948-958.

ORIGINAL RESEARCH

TRANSFUSION

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami[1] | Rachel Jug[2,8] | Ursula La Rocca[3,4] | Homa Keshavarz[5] | Denise Landry[5] | Nadine Shehata[6,7,8] | Simon J. Stanworth[9,10,11] | Susan Nahirniak[12,13]

Five guidelines addressed PLT transfusion for hypoproliferative thrombocytopenia.

- Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia if additional risk factors for bleeding exist; PLT threshold

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*
Estcourt, 2017[23]	BSCH	Reversible marrow failure, recovery anticipated • Consider increasing the threshold for prophylactic PLT transfusion to between 10×10^9–20×10^9/L in patients judged to have additional risk factors for bleeding. Individual review is required. *(2C)* Chronic marrow failure, recovery is not anticipated • Manage patients with chronic bleeding of WHO Grade 2 or above individually, according to the severity of their symptoms and signs. Consider a strategy of prophylaxis (eg, twice a week). *(2C)*

- Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia; PLT dose

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*
Estcourt, 2017[23]	BSCH	Reversible marrow failure, recovery anticipated • Consider increasing the threshold for prophylactic PLT transfusion to between 10×10^9–20×10^9/L in patients judged to have additional risk factors for bleeding. Individual review is required. *(2C)* Chronic marrow failure, recovery is not anticipated • Manage patients with chronic bleeding of WHO Grade 2 or above individually, according to the severity of their symptoms and signs. Consider a strategy of prophylaxis (eg, twice a week). *(2C)*
Schiffer, 2017[22]	ASCO	• Prophylactic PLT transfusion should be administered to patients with thrombocytopenia resulting from impaired marrow function to reduce the risk of hemorrhage when the PLT count falls below a predefined threshold level. This threshold level for transfusion

- **Incongruenze per la profilassi** in presenza di **ulteriori fattori di rischio come sanguinamento e sepsi**.
- **Due LG** raccomandavano **una soglia più elevata**, compresa tra **10×10^9/L e 20×10^9/L,** e **20×10^9/L;**
- Una LG raccomandava di trasfondere **in caso di conta piastrinica superiore a 10×10^9/L.**
- Una LG raccomandava che la **soglia per la trasfusione dovesse variare in base alla diagnosi del paziente, alle condizioni cliniche e alla modalità di trattamento, suggerendo la trasfusione anche per soglie superiori a 10×10^9/L.**
- Una LG non specificava **una soglia specifica** in questi contesti.

Guideline Appraisal AGREE II tool

ORIGINAL RESEARCH

TRANSFUSION

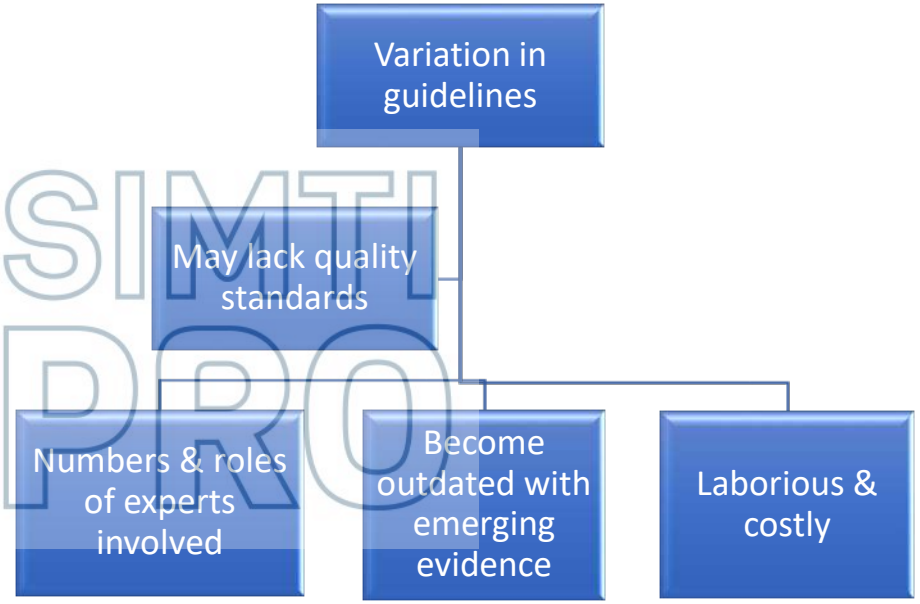
Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami[1] | Rachel Jug[2,8] | Ursula La Rocca[3,4] | Homa Keshavarz[5] | Denise Landry[5] | Nadine Shehata[6,7,8] | Simon J. Stanworth[9,10,11] | Susan Nahirniak[12,13]

Background: Guidelines for platelet (PLT) transfusion are an important source of information for clinicians. Although guidelines intend to increase consistency and quality of care, variation in methodology and recommendations may exist that could impact the value of a guideline. We aimed to determine the quality of existing PLT transfusion guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument and to describe the inconsistencies in recommendations.

Study design and methods: A systematic search was undertaken for evidence-based guidelines from January 1, 2013, to January 25, 2019. Citations were reviewed in duplicate for inclusion and descriptive data extracted. Four physicians appraised the guideline using the AGREE II instrument and the scaled score for each item evaluated was calculated. The protocol was registered in PROSPERO.

Results: Of 6744 citations, 6740 records were screened. Seven of 28 full-text studies met the inclusion criteria. The median scaled score (and the interquartile range of the scaled score) for the following items were as follows: **scope and purpose, 94% (8%); stakeholder involvement, 63% (18%); rigor of development, 83% (14%); clarity of presentation, 94% (6%); applicability, 58% (20%);** and **editorial independence, 77% (4%).** Overall quality ranged from 4 to 7 (7 is the maximum score). **Inconsistent recommendations were on prophylactic PLT transfusion in hypoproliferative thrombocytopenia in the presence of risk factors and**

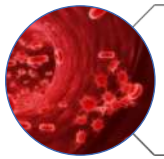


Le **incongruenze** tra le **linee guida** e la **qualità variabile** evidenziano aree da affrontare nelle future LG.
Tra esse, rientrano il **coinvolgimento degli stakeholder** e l'**applicabilità**.

Al-Riyami AZ, Jug R, La Rocca U, Transfusion 2021; 61: 948-958.

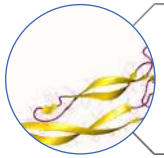
Il supporto trasfusionale piastrinico

Quali sono i **fattori essenziali da considerare** nel valutare la **trasfusione di piastrine in ambito oncoematologico?**



TROMBOCITOPENIA E RISCHIO DI EMORRAGIA

TRASFUSIONE PIASTRINICA IN PROFILASSI/TRATTAMENTO ?



THRESHOLDS TRASFUSIONALI ?

SICUREZZA TRASFUSIONALE

STRATEGIE TRASFUSIONALI LIBERALI E RESTRITTIVE ED EFFICACIA CLINICA (outcomes: sanguinamento e mortalità)

Il supporto trasfusionale piastrinico: background

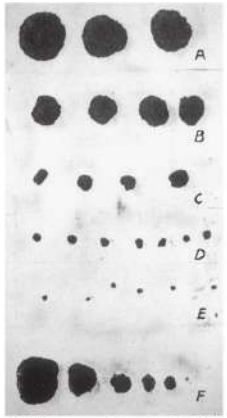


Figure 5. Bleeding time results from patient described by Duke[10] in 1910. The series from rows A to D are blots from the ear wound made when the patient's platelet count was 3000 platelets/μL. The blots in series A were taken immediately after the ear was pricked, series B began at 20 minutes, series C began at 40 minutes, series D began at 60 minutes, and series E began at 80 minutes. The bleeding time was 90 minutes. In row F are the blots obtained after transfusion (platelet count, 110,000 platelets/μL), demonstrating a bleeding time of 3 minutes. (From Duke,[10] with permission.)

THE RELATION OF BLOOD PLATELETS TO HEMORRHAGIC DISEASE

DESCRIPTION OF A METHOD FOR DETERMINING THE BLEEDING TIME AND COAGULATION TIME AND REPORT OF THREE CASES OF HEMORRHAGIC DISEASE RELIEVED BY TRANSFUSION *

From the Hunterian Laboratory of Experimental Pathology, Johns Hopkins University

W. W. DUKE, M.D.
KANSAS CITY, MO.

It is my purpose in this paper to report three cases and experiments which furnish additional evidence to show that the blood platelets play a part in stopping hemorrhage, and that one type of hemorrhagic disease may be attributed to an extreme reduction in the number of platelets. The cases possibly explain the relief which sometimes follows transfusion in hemorrhagic disease. It is my purpose also to describe a method for studying hemorrhage called the bleeding time, and to describe briefly a simple method for determining the coagulation time.

In the cases there was marked hemorrhagic diathesis, a normal coagulation time, and almost an absence of platelets. Transfusion was performed in each case. After transfusion there was a marked increase in the number of platelets and remarkable relief of hemorrhage. When the platelet counts returned to their previous low level, hemorrhages returned. Later in the course of the disease in two of the cases, the platelet count rose spontaneously and this rise also was followed by relief of

JAMA October 1910

Editorials

Blood Platelets and Platelet Transfusions

The application of quantitative biological and biochemical methods to the study of the blood platelets has led to revolutionary developments in our understanding of these elusive structures.[1] Until recently platelets were often regarded as non-cellular in nature, although it has long been known that they are of cellular origin. Tocantins[2] in his important review in 1938 expressed the thought which was then current: "It is preferable to think of the platelet not as a cellular element but as a transition between the microscopically amorphous elements of the blood (proteins, fats, etc.) and definitely cellular constituents such as erythrocytes or leukocytes." The platelet has been looked upon as a fragile envelope containing a group of mysterious and unidentified substances involved in the coagulation of blood. Now, however, there is an accumulation of evidence which clearly demonstrates that platelets are indeed living cellular structures, non-nucleated to be sure, but comparable to the red cells in many of their biochemical activities. Containing many of the enzymes and constituents of other cells, platelets have an intrinsic metabolism upon which their biological functions are largely dependent. Survival of platelets in the circulation appears to be associated with persistence of this metabolic activity. Metabolically inert platelets, like nonviable red cells, are rapidly removed from the circulating blood. Hemostatic effectiveness of platelets is achieved, only when these cells are present in the circulating blood in adequate number.

Riduzione del rischio emorragico con la trasfusione piastrinica riportata per la prima volta in uno studio di caso su un **giovane con epistassi** potenzialmente letale nel 1910.

W.W. Duke, JAMA 1910

Trasfusione piastrinica, aumento della conta piastrinica, riduzione del rischio di sanguinamento.

C.L. Conley, Arch Intern Med 1961

Il supporto trasfusionale piastrinico

- È essenziale promuovere un uso appropriato della trasfusione piastrinica basato su raccomandazioni evidence-based.

- Negli ultimi anni, valutazione di strategie trasfusionali restrittive vs liberali, in considerazione del numero di indicazioni/domande, oltre che di evidenze sicurezza ed efficacia.

- Assenza di evidenze che mostrino superiorità delle strategie trasfusionali liberali nel ridurre mortalità o emorragia nei contesti clinici valutati.

- Dati ed evidenze variano a seconda del contesto clinico. La mancanza di evidenze a favore di strategie trasfusionali liberali comporta l'opportunità di politiche restrittive, per ridurre l'esposizione alla trasfusione piastrinica, laddove non necessaria. Ciò è sostenuto anche dall'evidenza di un numero maggiore di eventi avversi emersi in RCT selezionati nei bracci di trattamento liberali rispetto a quelli restrittivi.