I concentrati piastrinici: come sono seguite le linee guida?

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Negli ospedali la più frequente indicazione alla trasfusione piastrinica è la prevenzione del sanguinamento nei pazienti ematologici ed oncologici

Nel 2009 sono state effettuate circa 3 milioni di trasfusioni piastriniche in Europa e negli USA (Sweeney JP, AABB 2013) con un enorme impegno di risorse

In realtà nei pazienti che hanno effettuato terapia mieloablativa il rischio di sanguinamento severo ed emorragia fatale è molto basso (< 1%)

ma…..il sanguinamento è un evento profondamente

"stressante"

per il paziente, le famiglie e i medici curanti, e richiede spesso interventi che provocano disagio al paziente stesso

Terapia trasfusionale con piastrine nel paziente oncoematologico: quale trigger?

	Recommendations
British Committee for Standards in Haematology,[59] 1992	10×10^9/L*
College of American Pathologists,[60] 1994	5×10^9/L*
Consensus Conference, Royal College of Physicians, Edinburgh,[61] 1998	10×10^9/L*
American Society of Clinical Oncology,[62] 2001	10×10^9/L*
British Committee for Standards in Haematology,[63] 2001	10×10^9/L*
Italian Society of Transfusion Medicine and Imunohaematology,[64] 2009	10×10^9/L*

*Consider raised threshold for patients with additional risk factors for bleeding.

Table 4: **Medical society clinical practice guidelines for trigger for prophylactic platelet transfusions**

Principali linee guida sulla trasfusione piastrinica: valore soglia

Terapia trasfusionale con piastrine nel paziente oncoematologico

BCSH (British Commettee for Standard in Haematology) , 2003

Valore soglia per la trasfusione: conta piastrinica **≤ 5.000 /µL** in assenza di febbre >38 C o emorragia, anche minore.

In presenza di fattori di rischio per il sanguinamento la maggior parte delle raccomandazioni alzano il trigger a 20.000 Plts/ µL

Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study

Hannes Wandt, Kerstin Schaefer-Eckart, Knut Wendelin, Bettina Pilz, Martin Wilhelm, Markus Thalheimer, Ulrich Mahlknecht, Anthony Ho, Markus Schaich, Michael Kramer, Martin Kaufmann, Lothar Leimer, Rainer Schwerdtfeger, Roland Conradi, Gottfried Dölken, Anne Klenner, Mathias Hänel, Regina Herbst, Christian Junghanss, Gerhard Ehninger, for the Study Alliance Leukemia

Summary

Background Routine prophylactic platelet transfusion is the standard of care for patients with severe thrombocytopenia. Lancet 2012; 380: 1309–16

396 pazienti randomizzati

Valutati: 391

201 ABMT **190 CHT (AML)**

Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study

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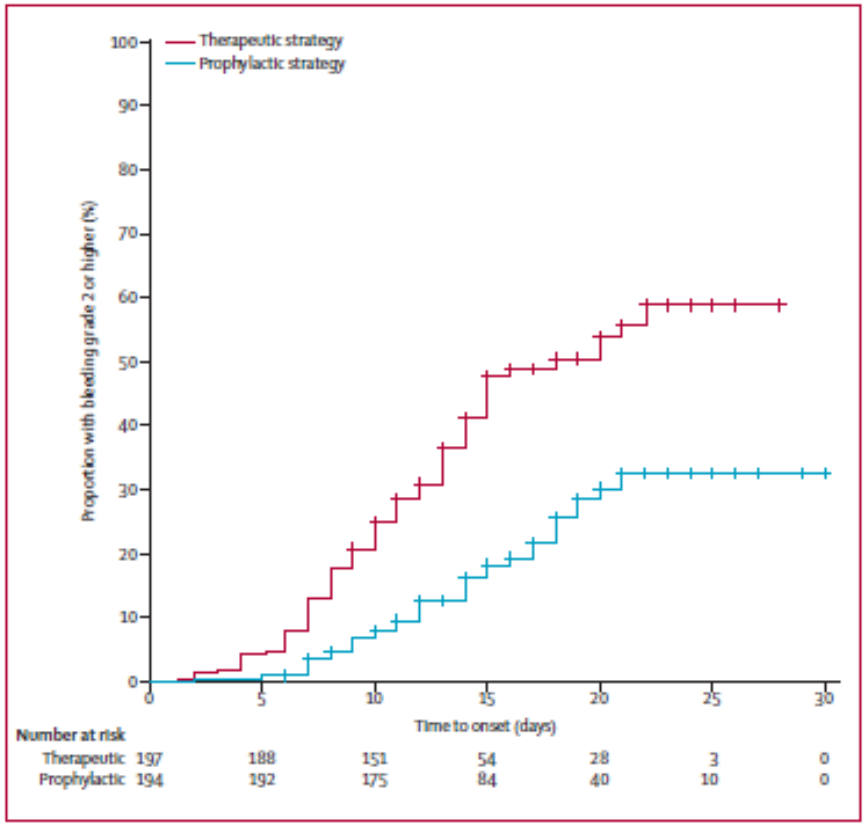

Figure 2: Time to onset of bleeding of grade 2 or higher in all patients

Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study

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Summary

Background Routine prophylactic platelet transfusion is the standard of care for patients with severe thrombocytopenia. Lancet 2012; 380: 1309–16

Conclusioni:

- Nei pazienti con LAM, ad elevato rischio di sanguinamento, usare il valore soglia di 10.000 Plts/μL per la profilassi;

- E' possibile utilizzare una strategia più restrittiva in pazienti stabili non sanguinanti, anche se la conta piastrinica al mattino è < 10.000/μL

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A No-Prophylaxis Platelet-Transfusion Strategy for Hematologic Cancers

TOPPS (trial of prophylactic platelets) (2006-2011)

Multicentrico (14 centri in UK e Australia)

Randomizzato

Non-inferiorità

Endpoint primario: sanguinamento di grado ≥ 2 WHO valutato fino a 30gg dalla randomizzazione

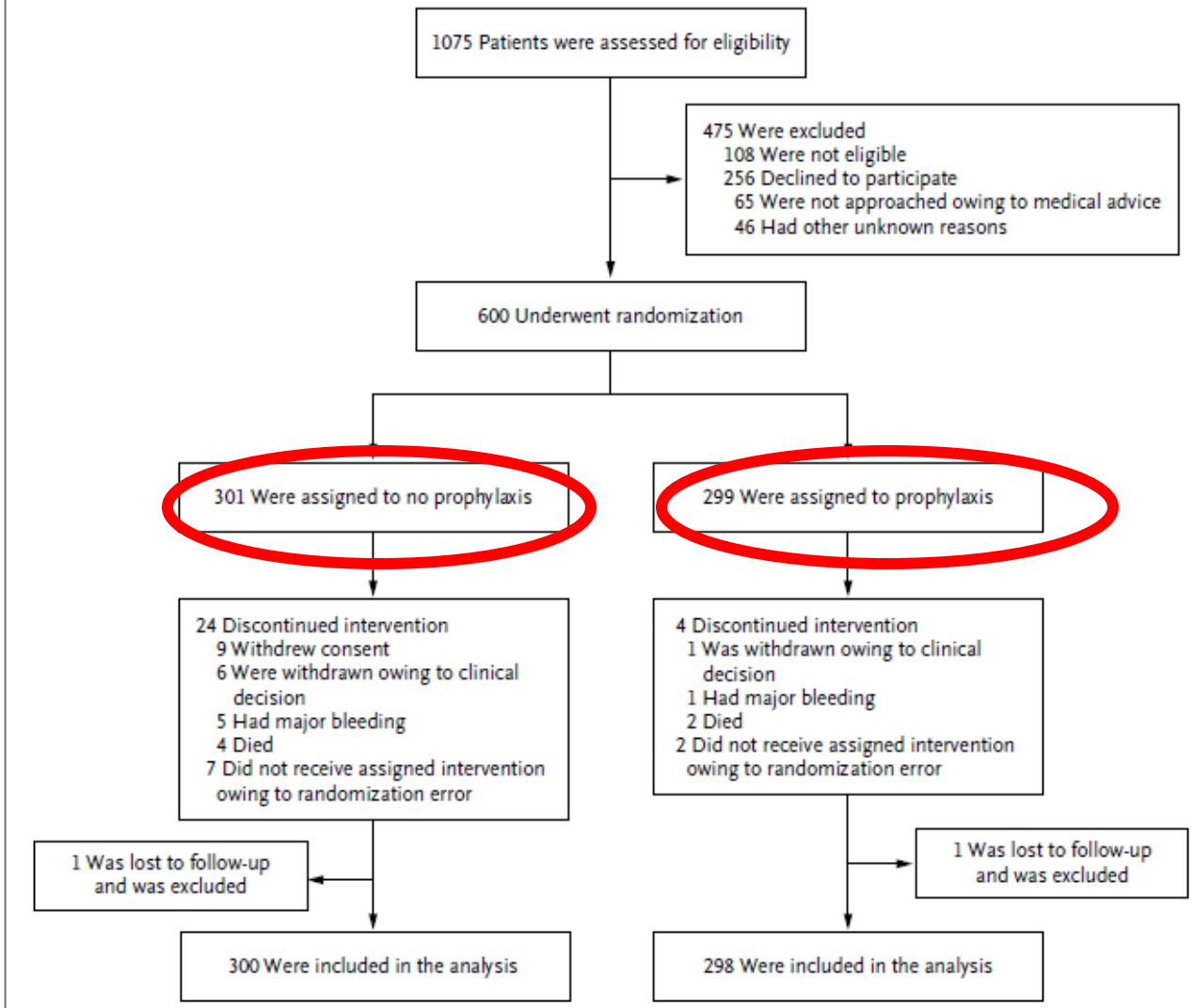

Figure 1. Study Enrollment and Randomization.

Of 1075 patients screened, 301 patients were randomly assigned to no prophylaxis and 299 to prophylaxis; 1 patient in each study group withdrew immediately after randomization. A total of 546 patients were enrolled in the United Kingdom and 54 in Australia.

Conclusioni

PROFILASSI SI: lievemente superiore rispetto alla NO profilassi nel proteggere dal sanguinamento i pazienti oncoematologici (riduzione emorragie del 7%) soprattutto in caso di leucemia acuta (non differenze nei pazienti autoBMT)

Strategia trasfusionale: mirata al tipo di patologia oncoematologica

Sulla frequenza del **sanguinamento** hanno una fondamentale importanza i trattamenti ricevuti dai pazienti: nel **57%** autoBMT, nel **79%** alloBMT e nel **73%** CHT

ORIGINAL ARTICLE

Italian daily platelet transfusion practice for haematological patients undergoing high dose chemotherapy with or without stem cell transplantation: a survey by the GIMEMA Haemostasis and Thrombosis Working Party

Giuseppe Tagariello[1], Giancarlo Castaman[2], Anna Falanga[3], Rita Santoro[4], Mariasanta Napolitano[5], Sergio Storti[6], Dino Veneri[7], Marco Basso[1], Laura Candiotto[1], Cristina Tassinari[1], Augusto B. Federici[8], Valerio De Stefano[6], and the GIMEMA Haemostasis and Thrombosis working party (see full list of contributors at the bottom)

Blood Transfus 2016; 14: 521-6 DOI 10.2450/2016.0321-15

QUESTIONARIO PIASTRINOPENIE POST-HDCHT/ASCT

1)vengono trasfuse piastrine

□ sempre < 20.000 □ sempre < 10.000

2) Viene verificata la risposta alla trasfusione piastrinica

□ Dopo 1 h □ dopo 24 h □ mai

4) I pazienti che non rispondono alla trasfusione piastrinica vengono trasfusi secondo i cut off definiti (v. sopra) solo al bisogno

5) Quanti pazienti vengono sottoposti a HD-CHT nella struttura in un anno?

6) Quanti CP vengono trasfusi in totale in un anno a questi pazienti?

7) Quanti CP da pool e quanti da aferesi?

Table II - Clinical and laboratory data on platelet transfusion criteria in 2013 in Italy.

Data from 18 haematology departments	
Patients undergoing high-dose chemotherapy/BMT	2,396
PC transfused per high-dose chemotherapy/BMT (ratio)	3.9
Total transfused PC	23,162
Platelet count triggers for transfusion	**N (%)**
Always with platelet count $\leq 10\times10^9$/L	17 (95%)
In symptomatic patients with platelet count between 10×10^9/L and 20×10^9/L	13 (72%)
Always with platelet count $\leq 20\times10^9$/L	1 (5%)
Definition of "symptomatic"	**N (%)**
Fever, even <38 °C	3 (17%)
Fever >38° C	13 (72%)
All bleeding	11 (61%)
According to WHO bleeding score (WHO≥2)	6 (33%)

PC: platelet concentrate; BMT: bone marrow transplantation.

Table III - Efficacy assessment and platelet transfusion criteria*.

Efficacy assessment (platelet count)	**N (%)**
After 1 hour	2 (11%)
After 24 hours	16 (89%)
Never	2 (11%)
Corrected count increment*	**N (%)**
Yes, after 1 hour	2 (11%)
Yes, after 24 hours	5 (28%)
No, refractoriness assessed only empirically	12 (67%)
No, refractoriness not considered	2 (11%)
Platelet transfusion in patients defined refractory	**N (%)**
When platelet count $\leq 10\times10^9$/L	3 (15%)
When platelet count between 10x10^9/L and 20×10^9/L	2 (10%)
When platelet count $\leq 20\times10^9$/L	1 (5%)
Only in the case of bleeding	14 (70%)

*The total number of answers exceeds the number of Haematology Departments as some departments gave multiple answers.

$$CCI^{*} = \frac{\text{PC-post} - \text{PC-pre}}{\text{N° of platelets transfused } (x10^{11})} \times BSA^{**}$$

*CCI (correct count increment) dovrebbe essere

> 7,500 a 1 h e
➢4,500 a 24 h

**BSA (m^2) = ([Height(cm) x Weight(kg)]/ 3600)^{½}

Platelets Concentrates (PC)

- PC from a single unit of whole blood:
  $0.45 - 0.85 \times 10^{11}$
- PC from a buffy coat pool: minimum content
  2.5×10^{11} **(equivalente circa a un concentrato da piastrinoaferesi)**

- PC from apheresis: minimum content
  3×10^{11}

- PC from plasmaplateletapheresis or from a multicomponent sample: minimum content
  2×10^{11}

Total number, source and ABO compatibility of platelet concentrates transfused in 18 Italian Haematology Departments during 2013.

Total platelet concentrates (average 1,287/centre; range, 300-4,100)	23,162
Type of concentrate	
Pool	38%
Apheresis	62%
ABO-compatible	**N (%)**
Yes	4 (25%)
No	3 (20%)
Partially	11 (55%)

Table I - WHO Bleeding Score.

Grade 0	No bleeding
Grade 1	Petechiae, ecchymosis, occult blood in body secretions, etc.
Grade 2	Evidence of gross haemorrhage, not requiring red cell transfusion
Grade 3	Haemorrhage requiring transfusion
Grade 4	Life-threatening haemorrhage

In Italy during 2013 about 200,000 platelet transfusions were carried out, 38% prepared from pooled buffy coats (cost approximately 123 Euro each) and 62% obtained by apheresis (245 Euro each), giving a total cost of around 40 million Euros. As there is no evidence that apheresis-derived platelets are better than pooled platelets, the cheaper option should be used in clinical practice[29].

Ann Int Med Clinical Guidelines
11 November 2014

In its recent guidelines[21], the American Association of Blood Banks still recommends transfusing hospitalised adult patients with a platelet count of $\leq 10 \times 10^9$/L to reduce the risk of spontaneous bleeding. Using this clinical practice, approximately 2.2 million platelet units are transfused annually in the USA at an expense of nearly one billion dollars[26]

Prophylactic platelet transfusions in patients with blood malignancies: cost analysis of a randomized trial

Helen E. Campbell[1], Lise J. Estcourt[2,3,4], Elizabeth A. Stokes[1], Charlotte A. Llewelyn[2,3,4], Michael F. Murphy[2,3,4], Erica M. Wood[5], and Simon J. Stanworth[2,3,4] for the TOPPS Study Investigators

pooled or apheresis equivalent, but $268 pool of 4 vs $566 apheresis”

Costi Regione Veneto CP anno 2013 Contabilità analitica

Pool da buffy coat	**€ 114,04**
Aferesi	**€ 249,69**

Nella nostra survey, sebbene i dati siano parziali e non espressione dell'intera situazione italiana, sembra emergere una maggiore prudenza (si trasfondono più concentrati)

3.6/ciclo di CHT

vs

	Terapia	Profilassi	
N° trasfusioni Plts/pz	1,6	2,4	Wandt H, 2012
	1,7	3,0	Stanworth SJ, 2013

REVIEW

CME Platelet transfusion: a systematic review of the clinical evidence

Ambuj Kumar,[1,2] Rahul Mhaskar,[1] Brenda J. Grossman,[3] Richard M. Kaufman,[4] Aaron A.R. Tobian,[5] Steven Kleinman,[6] Terry Gernsheimer,[7] Alan T. Tinmouth,[8] and Benjamin Djulbegovic,[1,2] on behalf of AABB Platelet Transfusion Guidelines Panel*

TRANSFUSION 2015;55:1116–1127

TABLE 1. Summary of evidence from RCTs on main outcomes

Question domain	Comparison	Outcome, number of studies (number of patients)	Summary effect, OR (95% CIs)	Quality	Comments
Prophylaxis	Prophylaxis vs. therapeutic	Major bleeding, 3 (1047)[12-14]	0.53 (0.32-0.87)	Moderate	Favors prophylaxis
Prophylaxis	Prophylaxis vs. therapeutic	All-cause mortality, 4 (1076)[12-15]	0.72 (0.34-1.55)	Low	No difference (wide CI)*
Prophylaxis	Prophylaxis vs. therapeutic	Mortality from bleeding, 4 (1074)[12-15]†	0.54 (0.09-3.10)	Low	No difference (wide CI)
Optimal threshold	$<20\times10^9/30\times10^9$ vs. $<10\times10^9$/L	Major bleeding, 4 (658)[16-19]	0.74 (0.41-1.35)	Moderate	No difference (wide CI)
Optimal threshold	$<20\times10^9$ vs. $<10\times10^9$/L	All-cause mortality, 3 (492)[17-19]	0.7 (0.4-1.22)	Moderate	No difference (wide CI)
Optimal threshold	$<20\times10^9/30\times10^9$ vs. $<10\times10^9$/L	Mortality from bleeding, 4 (658)[16-19]	0.37 (0.02-9.22)	Moderate	No difference (wide CI)
Optimal dose	Standard dose 2.2×10^{11}-2.6×10^{11}/m² vs. low dose 1.1×10^{11}-1.3×10^{11}/m²	Major bleeding, 4 (1132)[20-23]	0.91 (0.70-1.19)	Moderate	No difference (wide CI)
Optimal dose	Standard dose 2.2×10^{11}-2.6×10^{11}/m² vs. low dose 1.1×10^{11}-1.3×10^{11}/m²	All-cause mortality, 3 (1070)[21-23]	0.43 (0.13-1.42)	Low	No difference (wide CI)
Optimal dose	Standard dose 2.2×10^{11}-2.6×10^{11}/m² vs. low dose 1.1×10^{11}-1.3×10^{11}/m³	Mortality from bleeding, 3 (1070)[21-23]	Not pooled/no events in either arm	Low	No difference (wide CI)
Treatment‡	PLT/FFP vs. no specific coagulation therapy	All-cause mortality, 1 (22)[24]	2.22 (0.37-13.18)	Very low	No difference (wide CI)

* See discussion.
† Per-protocol analysis.
‡ Patients with DIC.

Cochrane Database of Systematic Reviews

Alternatives, and adjuncts, to prophylactic platelet transfusion for people with haematological malignancies undergoing intensive chemotherapy or stem cell transplantation

- artificial platelet substitutes
- platelet-poor plasma
- fibrinogen concentrate
- recombinant activated factor VII
- desmopressin (DDAVP)
- thrombopoietin (TPO) mimetics

2016

Open Access Protocol

BMJ Open 2016

Rationale and design of platelet transfusions in haematopoietic stem cell transplantation: the PATH pilot study

Jason Tay,[1,2,3] David Allan,[2] Sara Beattie,[4] Christopher Bredeson,[2,3] Dean Fergusson,[2,3] Dawn Maze,[5] Mitchell Sabloff,[2] Kednapa Thavorn,[3] Alan Tinmouth[2,3]

Strengths and limitations of this study

- Pilot randomised study (Vanguard design) to better assure feasibility and inform the design of a larger randomised study in recipients of autologous haematopoietic stem cell transplantation.
- First study in autologous haematopoietic stem cell transplantation to evaluate a strategy of prophylactic tranexamic acid with prophylactic platelet transfusions to prevent bleeding.
- First prospective study to concurrently use two bleeding scales—WHO and Bleeding Severity Measurement Scale (BSMS) to better appreciate clinically relevant bleeding.
- The trial will collect health-related quality of life data using a variety of validated scales within the context of bleeding risk and autologous haematopoietic stem cell transplantation.
- A limitation of this study is the absence of a 'third' control arm, where participants only receive therapeutic platelets (without prophylactic platelets or prophylactic tranexamic acid.

Conclusions

Our survey suggests that, in routine daily practice, Italian haematologists adopt the worldwide criterion of a platelet count cut-off when deciding whether to transfuse platelet concentrates, but they pay less attention to the WHO recommendations on platelet transfusions for bleeding and on monitoring refractoriness. This causes an excess of platelet transfusions, more frequently prepared by apheresis than from pooled donors, with a resulting increase of costs and waste of public health resources. The GIMEMA Haemostasis and Thrombosis