The role of platelets: hemostasis and transfusion therapy

Moderators: Manuel Quintana Díaz and Juan Ramón Fernández Villanueva

Monday, June 16, 2025

1. INTRODUCTION

Manuel Quintana Díaz

The use of platelets in Spain is currently excessive, and the trend is to keep on growing. Moreover, although not as much as red blood cell transfusion, platelet transfusion is associated to certain problems, such as fever reactions, allergic reactions, and TRALI—Transfusion-Related Acute Lung Injury.

The article by Blumberg et al., entitled *Platelet Transfusions: The Good, the Bad, and the Ugly,* summarizes the issues related to platelet transfusion that must be tackled[1]:

THE GOOD

- Altruistic donation
- Sound evidence to prevent bleeding if < $10x10^9$/L
- Low doses are equally effective
- Deciding about the transfusion considering the clinical history and the absolute figure

THE BAD

- Unjustified use if originating from apheresis
- Liberal transfusions increase bleeding and mortality
- When stored, they become proinflammatory and dysfunctional
- It has an immunological role o review

THE UGLY

- Ignoring the ABO group can cause refractoriness and damages
- Refractoriness can be prevented with an ABO-identical and well-performed leukoreduction
- ABO incompatibility may lead to bleeding, sepsis, and death
- Potential solutions (washing or plasma reduction) are expensive and are not always carried out

Questions arising from platelet transfusion

Impact?	Clinical, emotional, and ethical consequences?	Is it a good practice if it does not improve outcomes or prevents damage?	Can do less be better?

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2. ROLE OF PLATELETS IN HEMOSTASIS AND MONITORING: NUMBER OR FUNCTION?

Rocío Amézaga Menéndez

Platelets have multiple roles in the body, beyond hemostasis regulation:

Hemostasis	Immunity	Inflammation	Endothelial repair

Platelet alterations are associated with bleeding, thrombosis, and organ failure. Thus, both the **number of platelets** and their **functionality** must be assessed.

THROMBOCYTOPENIA[2-4]

PREVALENCE	DEFINITIONS	EVOLUTION	PROGNOSIS
43-67% patients in ICU	Absolute if < 150,000 / µL	Decrease up to day 4-5	Good, if >30x 10^9/L
20% develop it during hospitalization	Relative if there is a 30-50% drop	Recovery after days 7-10	Bad, if < 6x 10^9/L
			Increase in mortality if it persists > 4 days

Often, decisions are made in a thrombocytopenia situation that may not be the right ones and that are related to an alert:

- Postpone prophylactic heparin
- Postpone lumbar punctures
- Transfuse the patient without bleeding
- Not placing emergency central venous catheters
- Preventing anticoagulation in patients with deep vein thrombosis

In these contexts, knowing the causes for platelet decrease and the clinical context is as relevant as knowing the figure. Sepsis is the most common cause for thrombocytopenia[4,5].

↓ Production	Myelosuppression, nutritional deficiency, pregnancy, hematologic diseases, etc.
↑ Consumption or destruction	Sepsis, disseminated intravascular coagulation, autoimmunity, microvascular thrombosis, hemorrhages, drugs, etc.
Distribution / sequestration	Splenomegaly, hypersplenism, hypothermia, etc.
Dilution	Massive transfusion, fluid resuscitation, ECMO, etc.

It is also crucial to determine their functionality, even if it is within normal, based on the presence of the following clinical situations[3,4]:

- Absence of bleeding, petechias, or thrombosis
- Clinical stability
- Known compensatory mechanisms, such as young reactive platelets, adapted chronic thrombocytopenia or transitory states without actual hemostasis activation

In some situations, thrombosis may appear in patients with a low platelet count[4]:

Anomalous activation	Heparin-induced thrombocytopenia, disseminated intravascular coagulation, sepsis
Immunothrombosis	Sepsis, thrombotic microangiopathy, COVID
Intravascular consumption	Disseminated intravascular coagulation
Extracorporeal factors	CRRT, ECMO

THROMBOCYTOSIS

CAUSES	DEFINITION	EVOLUTION
Acute inflammation	> 450 x10^9/L	It is usually benign and transitory
Trauma		Thrombotic risk if there are added factors
Sepsis		Considering risk if 1000x10^9/L
Surgeries		Considering risk in an oncological or myeloproliferative context, or with previous thrombosis

In conclusion, it is necessary to take into account the following:

- Identifying and treating the cause of the platelet disorder
- Individualizing thresholds and treating patients, not figures
- Assessing the presence of bleeding, the platelet function, and the context before transfusing a patient

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3. THROMBOELASTOGRAPHY IN THE TRANSFUSION DECISION

Ainhoa Serrano Lázaro

Platelet transfusion is still an uncertain decision that must be frequently taken in the ICU setting. Besides the number of platelets, it is crucial to assess their function and the patient's overall coagulation state, since a platelet count within normal limits does not guarantee proper function.

In this context, thromboelastography (viscoelastic tests) is useful to make safe guided decisions on platelet transfusion, because it provides an estimation of how platelets function in an actual clot, and whether they provide real-time strength to every specific patient.

Thromboelastography provides a context for the count and allows an individualized goal-directed approach. The most commonly used viscoelastic tests are TEG® and ROTEM®.

Differences between TEG/ROTEM and specific platelet function tests:

TEG/ROTEM	SPECIFIC PLATELET FUNCTION TESTS
• They assess the whole blood and coagulation in an integrated manner and in real time. • They spot alterations between platelets, coagulation factors, and fibrinogen.	• They assess platelet function under controlled conditions and without integrating other components. • They assess adhesion, aggregation, and response to specific agonists. • Types: - Optical aggregometry, PFA-100 - VerifyNow and Multiplate, which are fast and can be helpful in the OR.
Useful to manage massive hemorrhage or surgery	**Useful to know the bleeding risk in antiaggregated patients**

There are intermediary modules supplementing TEG/ROTEM, which provide, in parallel to the viscoelastic information, the platelet function test for patients treated with antiaggregants:

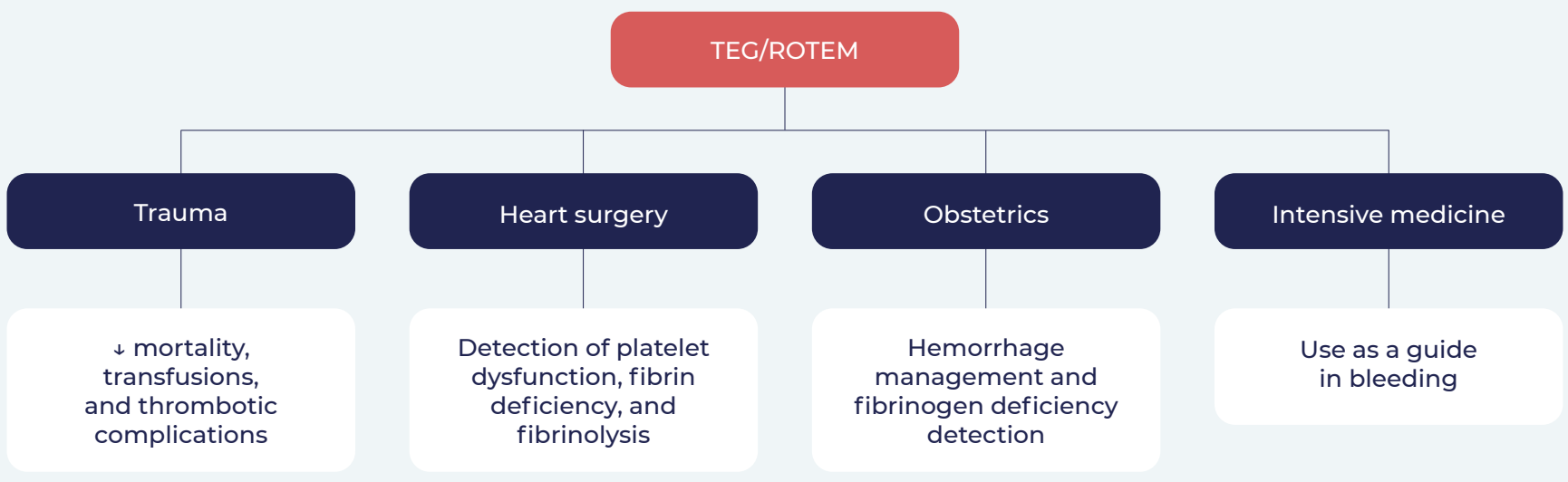
ROTEM platelet	TEG Platelet Mapping

Pros and cons of TEG/ROTEM versus traditional methods:

PROS	LIMITATIONS
Fast (results in 10 min) Functional dynamic information Holistic assessment of the whole hemostatic system Reduction of unnecessary transfusions Hemostatic treatment personalization	Context-based interpretation There is no standardization between sites Poor detection of adhesion/activation alterations and poor distinction between platelet dysfunction and dysfibrinogenemia False negatives if there are antiaggregant treatments Costs and availability

Thromboelastography should not replace clinical assessment, and a trained team is required to interpret and verify results. Clinical judgment and experience are required to make good clinical decisions.

Clinical practice guidelines recommend thromboelastography as a validated tool with sound evidence in areas such as trauma, heart surgery, obstetric hemorrhage[6], and cirrhosis[7]:



ESAIC, 2022	The use of ROTEM/TEG is recommended in surgery, trauma, and critical bleeding.
European Trauma Guidelines, 2023	ROTEM/TEG is a superior tool to INR or prothrombin time.
AHA, 2021	The use of ROTEM/TEG is recommended in cardiovascular surgery.

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4. THROMBOCYTOPENIA AND OUR FEARS: WHEN TO TRANSFUSE, HOW MUCH, AND WHAT CAN BE REVERTED?

María Gero Escapa

Thrombocytopenia is a common problem in critical patients, with diverse causes, and which may lead to serious consequences.

Platelet transfusion is the primary treatment, but it comes with certain drawbacks:

- Efficacy only in patients with low counts (< 10 x10^9/L) or platelet function disorders.
- Platelets are a valuable yet perishable resource.
- Their origin can change, but they are therapeutically equivalent products, with similar side effects:

WHOLE BLOOD DONATIONS | **APHERESIS**

- The process for their preservation and storage is complex: leukoreduction, continuous stirring, pollution detection or reduction systems, etc.
- Recommendations in current guidelines are based in the limited evidence, and their indications are not well defined.
- Transfusion thresholds[8,9] are just a figure, and they do not consider platelet functionality and patient circumstances.

There are four scenarios for platelet transfusion[9]:

Prophylactic transfusion		Therapeutic transfusion	
Hemorrhage prevention in patients with severe thrombopenia	Before an invasive procedure	Grade 2-4 hemorrhages (according to WHO)[10]	Massive hemorrhage /Hemorrhagic shock

According to the PLOT-ICU study[11]:

23% of ICU patients with thrombocytopenia receive platelets

64% of transfusions are prophylactic

It is essential to personalize the treatment for each patient, considering the platelet count, their function, and hemorrhagic and thrombotic risks.

PLATELET TRANSFUSION IS INDICATED IN MASSIVE HEMORRHAGE

Early transfusion is recommended as a part of massive transfusion protocols, particularly in patients with severe trauma, regardless of the platelet count [9].

The recommendations and suggestions in the HEMOMAS-II document are the following[12]:

Active hemorrhage	Massive bleeding and y traumatic brain injury/ocular trauma	Neurosurgical or ocular posterior pole intervention	Active bleeding not stopping with 50 x 10^9	Major invasive procedure	Multiple trauma, even with no bleeding
Transfusion to keep the 50 x 10^9/L threshold	Transfusion to keep the 100 x 10^9/L threshold	Transfusion to keep the 100 x 10^9/L threshold	Transfusion to keep the 100 x 10^9/L threshold	Transfusion to reach the 50 x 10^9/L threshold	Transfusion to reach the 50 x 10^9/L threshold

PLATELET TRANSFUSION IS INDICATED TO CHANNEL A CENTRAL VENOUS CATHETER (CVC).

- In a multi-site randomized controlled clinical trial, it was observed that discontinuing prophylactic transfusion before placing a CVC with a 10-50 x 10^9/L count leads to more hemorrhages related to CVC than prophylactic transfusion[13].

Hemorrhage relative risk 2-4: 2.45 (90% CI 1.27 -4.70)

PLATELET TRANSFUSION IS NOT INDICATED FOR REVERSION OF PLATELET ANTIAGGREGANTS[14–17]

No improvement has been observed in patient outcomes with[18]:

- Traumatic brain injury
- Spontaneous intracranial hemorrhages, which in some cases include deterioration of neurological recovery.

PLATELET TRANSFUSION IS NOT INDICATED FOR REVERSION IN PATIENTS WITH MASSIVE HEMORRHAGE.

In antiaggregated patients with massive hemorrhage, administering desmopressin is suggested, and in patients with intracranial hemorrhage, platelet transfusion should be avoided, unless they require neurosurgery[12].

- An early transfusion is suggested in patients with a hemorrhage clearly related to antiaggregants, preferably having monitored the platelet function[12].

PLATELET TRANSFUSION IS NOT INDICATED FOR REVERSION IN PATIENTS WITH BRAIN HEMORRHAGE.

The *European Stroke Association* calls into question the efficacy and safety of desmopressin in patients with intracranial hemorrhage related with the antiaggregant treatment, and it also rejects the use of platelets[14].

Dosing of platelet transfusion:

1 apheresis or 1 mix of 4-6 recovered units → 30-50 x 10^9/L increase in the count after 10-60 min → Consider refractoriness if:
- CCI* is <7.5 repeatedly or
- CCI* is <4.5 after 18-24 h

*Platelet Corrected Count Increment (CCI) = [(post-transfusion platelet count - pre-transfusion platelet count) x body surface area] / number of transfused platelets.

In general, platelet transfusion indications should be better defined to prevent unnecessary transfusions and to obtain improved clinical outcomes. However, further studies are required to determine the best strategies and to minimize the associated risks.

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