Indicaciones de la administración de fibrinógeno en base a los distintos test viscoelásticos

Juan V. Llau

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Profesor Asociado de Anestesiología

Universidad de Valencia

Conflicto de intereses en relación con esta actividad

Compensación económica por participación en actividades educacionales y/o de consultoría promovidas por

CSL Behring

Octapharma

Werfen

Ferrer

Hemosonics

Últimos 3 años

Agradecimientos

Agradecimiento especial a todos los colegas que colaboran conmigo en el estudio de la hemostasia, de la detección y tratamiento de sus complicaciones, de los que he aprendido tanto y sin cuyo apoyo y concurso desinteresados hubiera sido imposible para mí entenderlas

Punto de partida

Anaesthesia 2023, 78, 93–104 doi:10.1111/anae.15864

Review Article

Major haemorrhage: past, present and future

A. Shah,[1] V. Kemer,[2] S. J. Stanworth[3] and S. Agarwal[4]

Gastroenterology Report, 11, 2023, goad011

REVIEW ARTICLE

An update on the management of non-variceal upper gastrointestinal bleeding

Ali A. Alali[1,*] and Alan N. Barkun[2]

[1]Division of Gastroenterology, Department of medicine, Faculty of Medicine, Kuwait University, Kuwait; [2]Division of Gastroenterology, McGill University Health Center, McGill University, Montreal, Canada

Intensive Care Med
https://doi.org/10.1007/s00134-023-06980-6

REVIEW

How to manage coagulopathies in critically ill patients

Julie Helms[1,2*], Toshiaki Iba[3], Jean Marie Connors[4], Satoshi Gando[5,6], Marcel Levi[7,8], Ferhat Meziani[1,2] and Jerrold H. Levy[9]

Rossaint et al. Critical Care (2023) 27:80
https://doi.org/10.1186/s13054-023-04327-7

Critical Care

GUIDELINES Open Access

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

Rolf Rossaint[1*], Arash Afshari[2], Bertil Bouillon[3], Vladimir Cerny[4,5], Diana Cimpoesu[6], Nicola Curry[7,8], Jacques Duranteau[9], Daniela Filipescu[10], Oliver Grottke[1], Lars Grønlykke[11], Anatole Harrois[9], Beverley J. Hunt[12], Alexander Kaserer[13], Radko Komadina[14], Mikkel Herold Madsen[2], Marc Maegele[15], Lidia Mora[16], Louis Riddez[17], Carolina S. Romero[18], Charles-Marc Samama[19], Jean-Louis Vincent[20], Sebastian Wiberg[11] and Donat R. Spahn[13]

EJA

Eur J Anaesthesiol 2023; 40:29–38

OPEN

REVIEW ARTICLE

Haemostatic support in postpartum haemorrhage

A review of the literature and expert opinion

Stefan Hofer, Jan Blaha, Peter W. Collins, Anne-Sophie Ducloy-Bouthors, Emilia Guasch, Francesco Labate, Filipa Lança, Lill Trine Nyfløt, Kostja Steiner and Marc Van de Velde

EJA

Eur J Anaesthesiol 2023; 40:226–304

GUIDELINES

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

Second update 2022

Sibylle Kietaibl, Aamer Ahmed, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa, Giedrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C. Filipescu, Dietmar Fries, Anne Godier, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan V. Llau, Jens Meier, Zsolt Molnar, Lidia Mora, Niels Rahe-Meyer, Charles M. Samama, Ecaterina Scarlatescu, Christoph Schlimp, Anne J. Wikkelsø and Kai Zacharowski

Revista Española de Anestesiología y Reanimación

DOCUMENTO DE CONSENSO

Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva. Primera actualización 2023 (documento HEMOMAS-II)☆

Juan V. Llau[a,*], César Aldecoa[b], Emilia Guasch[c], Pascual Marco[d], Pilar Marcos-Neira[e], Pilar Paniagua[f], José A. Páramo[g], Manuel Quintana[h], F. Javier Rodríguez-Martorell[i] y Ainhoa Serrano[j]

Punto de partida

Anaesthesia 2023, 78, 93–104 doi:10.1111/anae.15866

Review Article

Major haemorrhage: past, present and future

A. Shah,[1] V. Kerner,[2] S. J. Stanworth[3] and S. Agarwal[4]

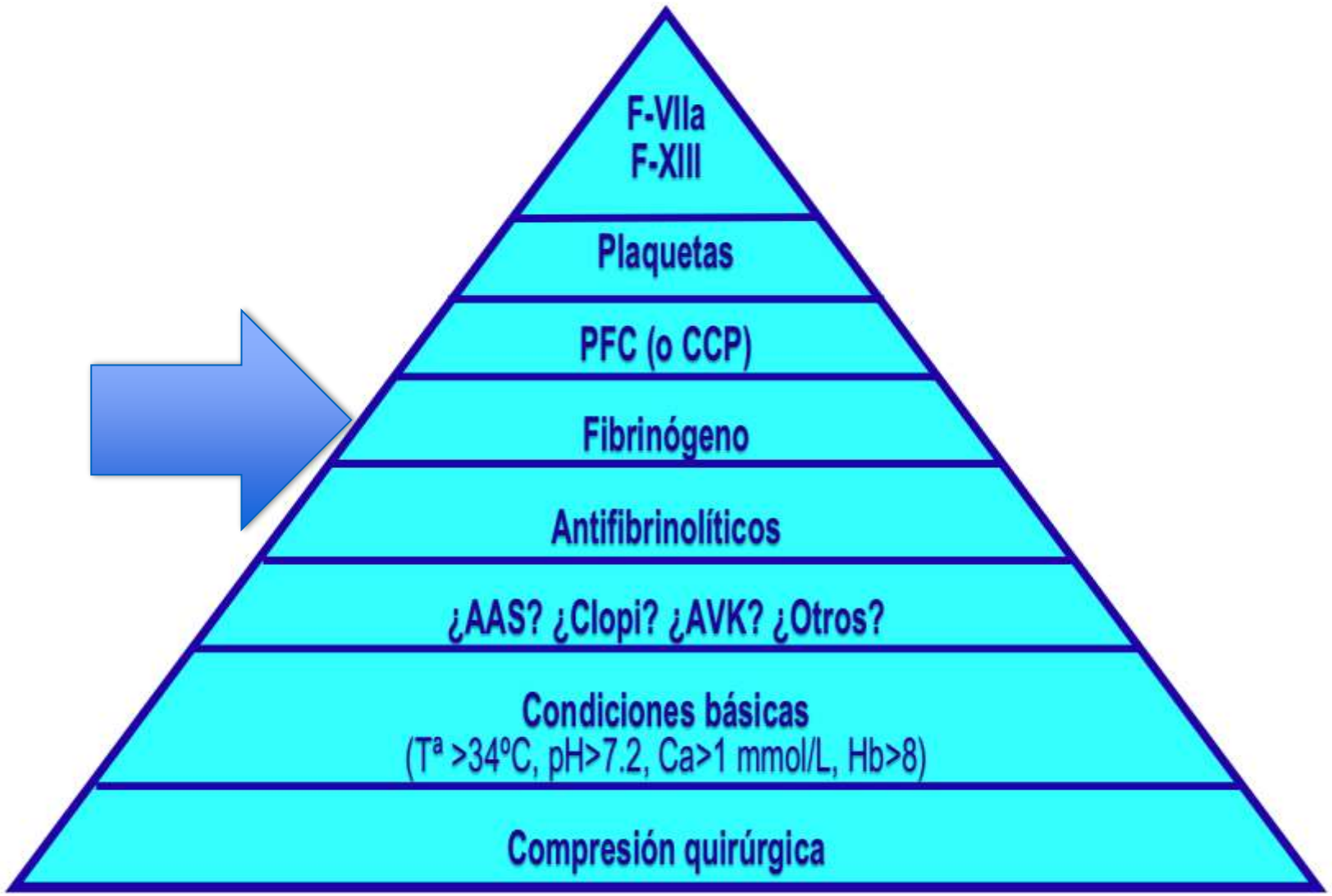
La Hemorragia masiva es una causa muy importante de morbimortalidad en todo el mundo, cuyo manejo óptimo ha variado sustancialmente en los últimos años

Capacidad de mejora

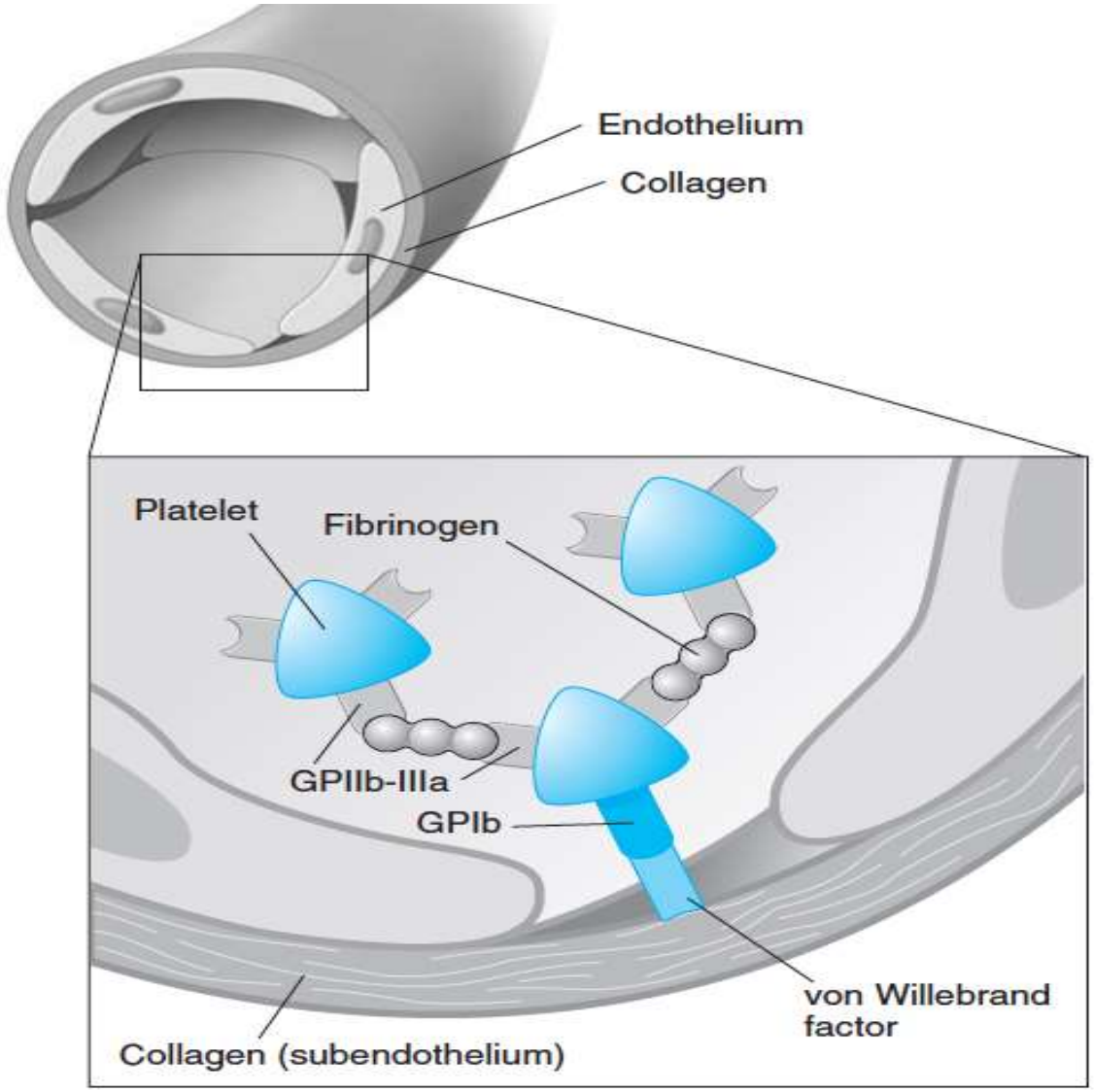
MANEJO ÓPTIMO DE LA HEMORRAGIA GRAVE

- Reconocimiento precoz
- Protocolización de la respuesta (PTM)
- Reanimación hemostática
- Disponibilidad de recursos: cirugía y RX intervencionista
- Prevención de complicaciones

El fibrinógeno en la reanimación hemostática



Modelo celular de la hemostasia



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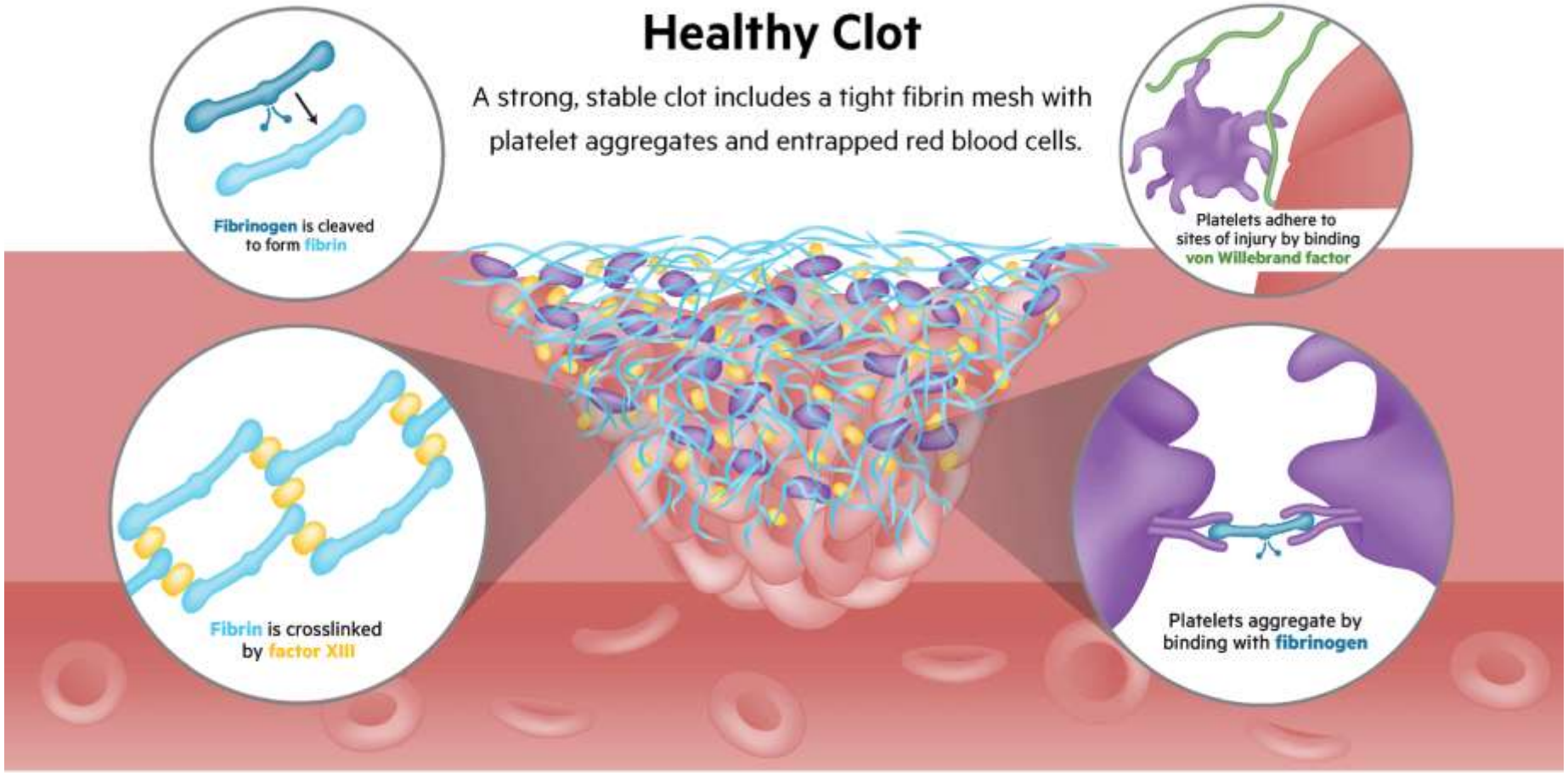
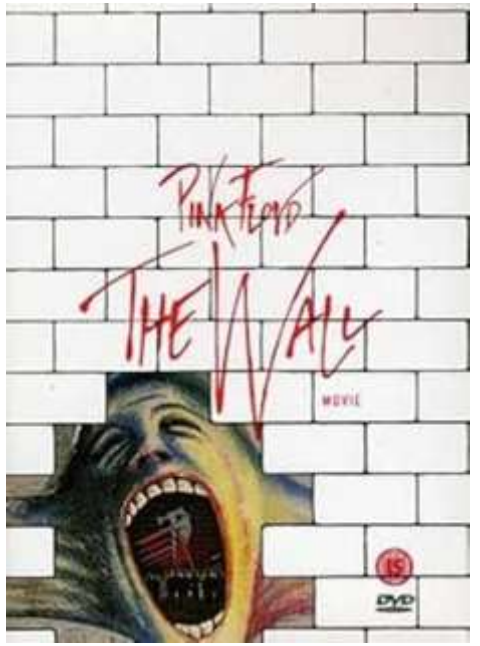


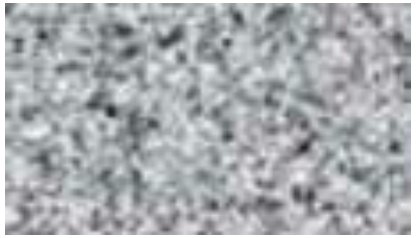
Fibrinógeno y plaquetas: “el muro”



¿Es posible compensar un recuento bajo de plaquetas con fibrinógeno?

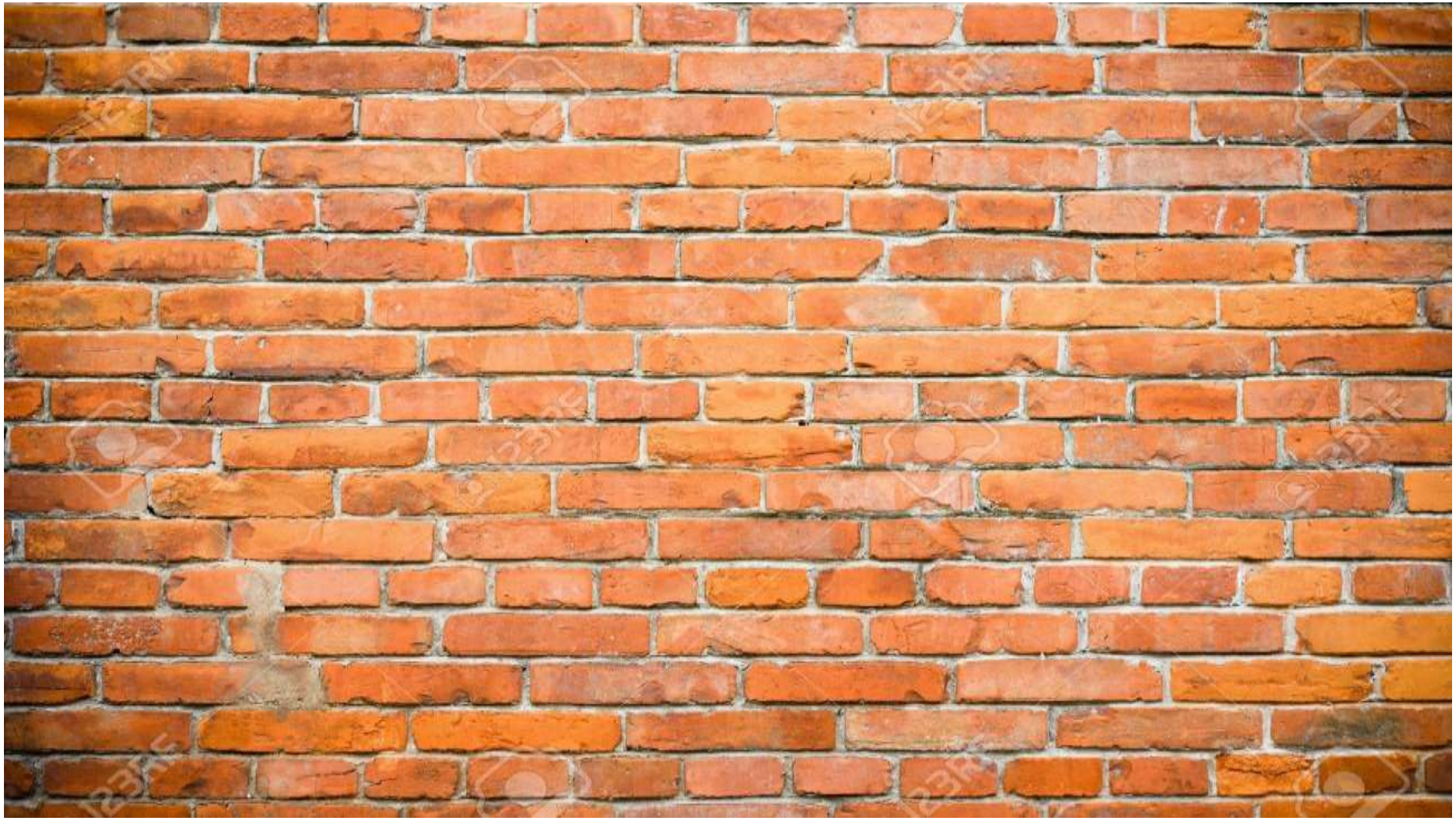
“TEORÍA DEL MURO”

Plaqueta

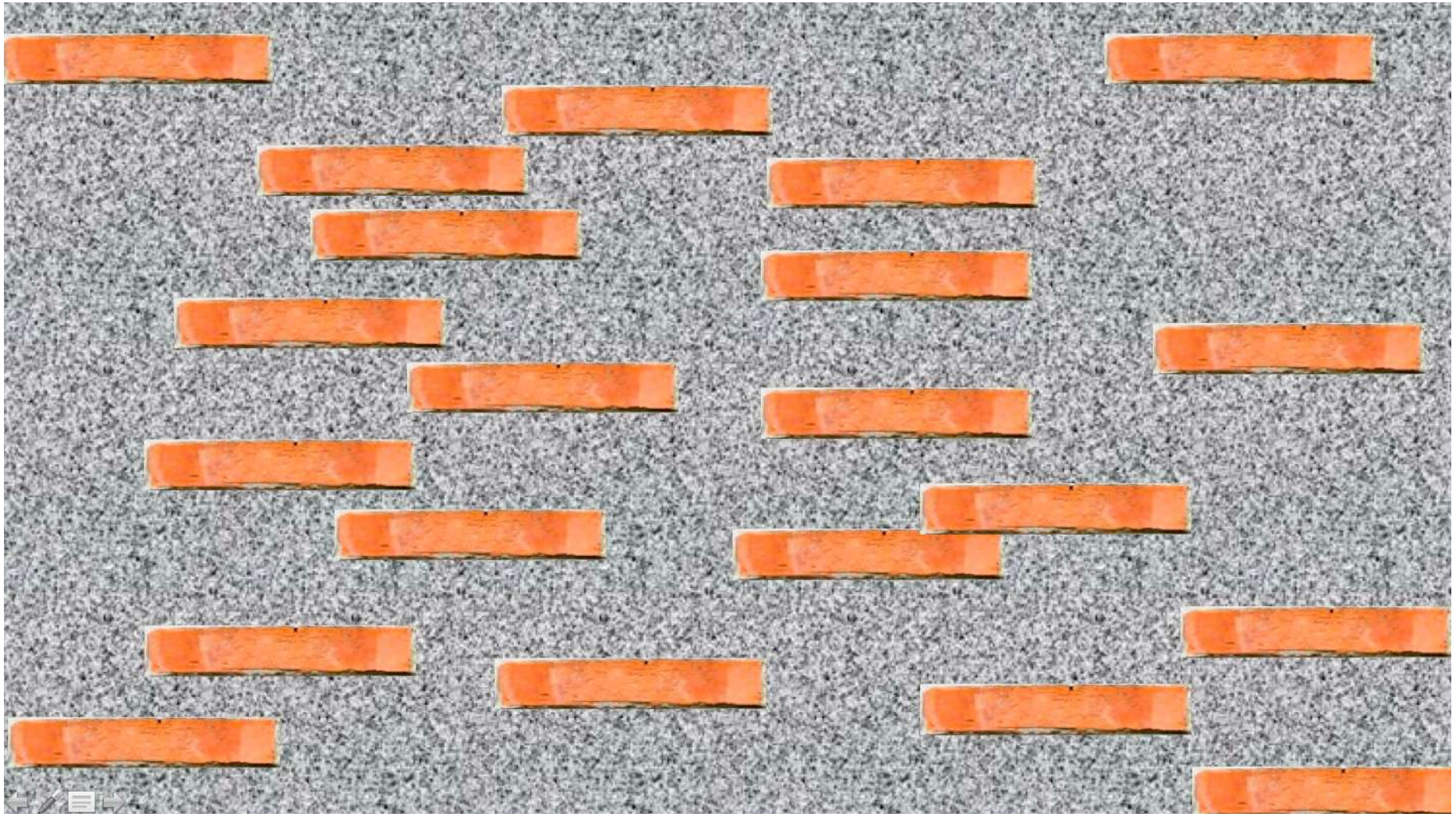


Fibrinógeno

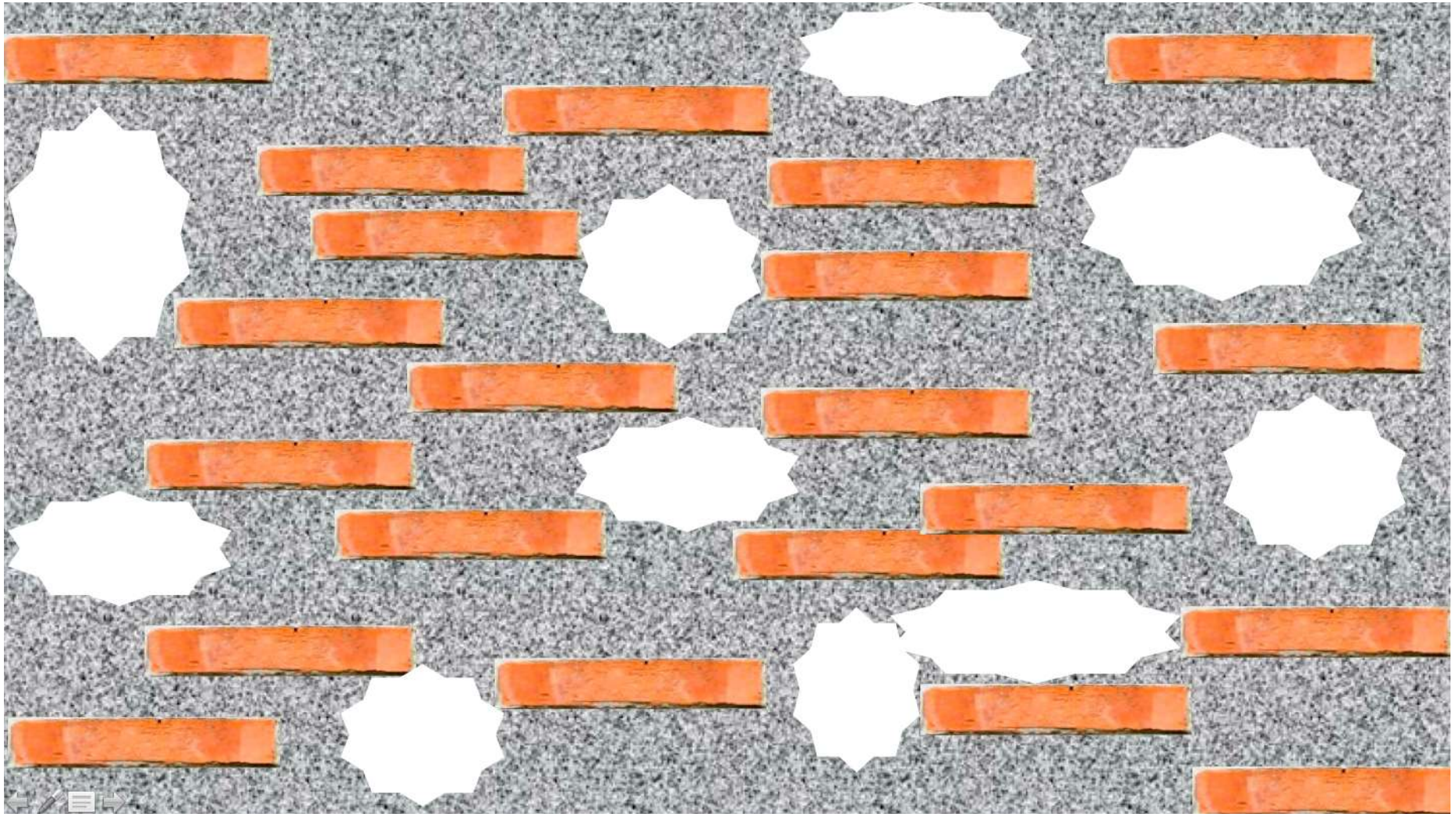
Fibrinógeno y plaquetas: “el muro”



Fibrinógeno y plaquetas: “el muro”



Fibrinógeno y plaquetas: “el muro”



Fibrinógeno: administración precoz

EJA

Eur J Anaesthesiol 2021; **38**:348–357

OPEN

ORIGINAL ARTICLE

Efficacy of prehospital administration of fibrinogen concentrate in trauma patients bleeding or presumed to bleed (FIinTIC)

A multicentre, double-blind, placebo-controlled, randomised pilot study

Bernhard Ziegler, Mirjam Bachler, Hubert Haberfellner, Christian Niederwanger, Petra Innerhofer, Tobias Hell, Marc Kaufmann, Marc Maegele, Uriel Martinowitz, Carolin Nebl, Elgar Oswald, Herbert Schöchl, Bettina Schenk, Markus Thaler, Benjamin Treichl, Wolfgang Voelckel, Ivana Zykova, Christine Wimmer, Dietmar Fries, the FIinTIC study group*

BACKGROUND Trauma-induced coagulopathy (TIC) substantially contributes to mortality in bleeding trauma patients.

OBJECTIVE The aim of the study was to administer fibrinogen concentrate in the prehospital setting to improve blood clot stability in trauma patients bleeding or presumed to bleed.

DESIGN A prospective, randomised, placebo-controlled, double-blinded, international clinical trial.

SETTING This emergency care trial was conducted in 12 Helicopter Emergency Medical Services (HEMS) and Emergency Doctors' vehicles (NEF or NAW) and four trauma centres in Austria, Germany and Czech Republic between 2011 and 2015.

PATIENTS A total of 53 evaluable trauma patients aged at least 18 years with major bleeding and in need of volume therapy were included, of whom 28 received fibrinogen concentrate and 25 received placebo.

INTERVENTIONS Patients were allocated to receive either fibrinogen concentrate or placebo prehospital at the scene or during transportation to the study centre.

MAIN OUTCOME MEASURES Primary outcome was the assessment of clot stability as reflected by maximum clot firmness in the FIBTEM assay (FIBTEM MCF) before and after administration of the study drug.

RESULTS Median FIBTEM MCF decreased in the placebo group between baseline (before administration of study treatment) and admission to the Emergency Department, from a median of 12.5 [IQR 10.5 to 14] mm to 11 [9.5 to 13] mm ($P = 0.0226$), but increased in the FC Group from 13 [11 to 15] mm to 15 [13.5 to 17] mm ($P = 0.0062$). The median between-group difference in the change in FIBTEM MCF was 5 [3 to 7] mm ($P < 0.0001$). Median fibrinogen plasma concentrations in the fibrinogen concentrate Group were kept above the recommended critical threshold of 2.0 g l^{-1} throughout the observation period.

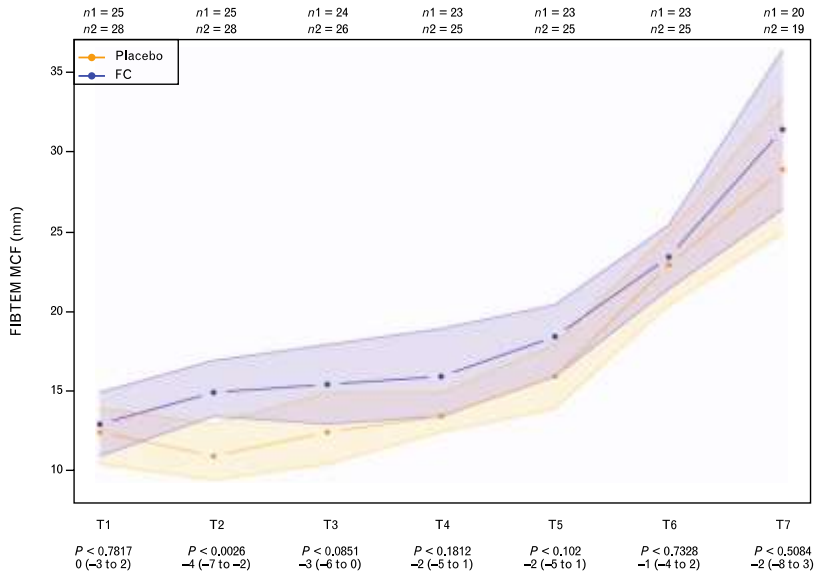
CONCLUSION Early fibrinogen concentrate administration is feasible in the complex and time-sensitive environment of prehospital trauma care. It protects against early fibrinogen depletion, and promotes rapid blood clot initiation and clot stability.

TRIAL REGISTRY NUMBERS EudraCT: 2010-022923-31 and ClinicalTrials.gov: NCT01475344.

Published online 28 October 2020

* Supplemental Digital Content 1, http://links.lww.com/EJA/A391 for a full list of the study investigators.

Fig. 3 Changes in FIBTEM maximum clot firmness (FIBTEM MCF) between baseline (T1) and 7 days posttrauma (T7)



Data are presented as median [IQR] (boxes; as well as minimum and maximum plus outliers as dots). *P* values are given with difference between groups and 95% CI. Horizontal dashed red lines show boundaries of the normal range. FC, Factor Concentrate group; n1, Placebo group; n2, FC group.

Fibrinógeno: directrices de uso

Fibrinogen Supplementation and Its Indications

Oliver Grottke, MD, PhD[1] Shuba Mallaiah, MD[2] Keyvan Karkouti, MD[3] Fuat Saner, MD[4] Thorsten Haas, MD[5]

Semin Thromb Hemost 2020;46:38–49.

Adequate plasma levels of fibrinogen are essential for clot formation, and in severe bleeding, fibrinogen reaches a critically low plasma concentration earlier than other coagulation factors. Although the critical minimum concentration of fibrinogen to maintain hemostasis is a matter of debate, many patients with coagulopathic bleeding require fibrinogen supplementation. Among the treatment options for fibrinogen supplementation, fibrinogen concentrate may be viewed by some as preferable to fresh frozen plasma or cryoprecipitate. The authors review major studies that have assessed fibrinogen treatment in trauma, cardiac surgery, end-stage liver disease, postpartum hemorrhage, and pediatric patients. Some but not all randomized controlled trials have shown that fibrinogen concentrate can be beneficial in these settings. The use of fibrinogen as part of coagulation factor concentrate based therapy guided by point-of-care viscoelastic coagulation monitoring (ROTEM [rotational thromboelastometry] or TEG [thromboelastography]) appears promising. In addition to reducing patients' exposure to allogeneic blood products, this strategy may reduce the risk of complications such as transfusion-associated circulatory overload, transfusion-related acute lung injury, and thromboembolic adverse events. Randomized controlled trials are challenging to perform in patients with critical bleeding, and more evidence is needed in this setting. However, current scientific rationale and clinical data support fibrinogen repletion in patients with ongoing bleeding and confirmed fibrinogen deficiency.

Niveles adecuados de fibrinógeno para hemostasia

En HM, el nivel plasmático de fibrinógeno baja rápidamente

Se debe usar en el contexto de una estrategia multimodal

Dudas en el empleo profiláctico

Mejor si se usa en terapia guiada por objetivos (test viscoelásticos)

TVE en las guías

EJA

Eur J Anaesthesiol 2023; 40:226–304

GUIDELINES

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

Second update 2022

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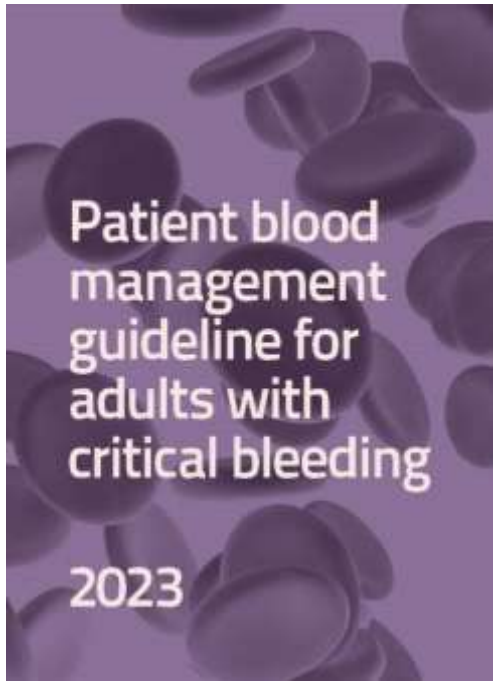
Rossaint et al. Critical Care (2023) 27:80
https://doi.org/10.1186/s13054-023-04327-7

Critical Care

GUIDELINES Open Access

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

Rolf Rossaint[1*], Arash Afshari[2], Bertil Bouillon[3], Vladimir Cerny[4,5], Diana Cimpoesu[6], Nicola Curry[7,8], Jacques Duranteau[9], Daniela Filipescu[10], Oliver Grottke[1], Lars Grønlykke[11], Anatole Harrois[9], Beverley J. Hunt[12], Alexander Kaserer[13], Radko Komadina[14], Mikkel Herold Madsen[2], Marc Maegele[15], Lidia Mora[16], Louis Riddez[17], Carolina S. Romero[18], Charles-Marc Samama[19], Jean-Louis Vincent[20], Sebastian Wiberg[11] and Donat R. Spahn[13]



Revista Española de Anestesiología y Reanimación 70 (2023) 409–421

Revista Española de Anestesiología y Reanimación

www.elsevier.es/redar

DOCUMENTO DE CONSENSO

Documento multidisciplinar de consenso sobre el manejo de la hemorragia masiva. Primera actualización 2023 (documento HEMOMAS-II)☆

Juan V. Llau[a,*], César Aldecoa[b], Emilia Guasch[c], Pascual Marco[d], Pilar Marcos-Neira[e], Pilar Paniagua[f], José A. Páramo[g], Manuel Quintana[h], F. Javier Rodriguez-Martorell[i] y Ainhoa Serrano[j]

Patient blood management guideline for adults with critical bleeding

Biswadev Mitra[1,2], Margaret Jorgensen[3], Michael C Reade[4,5], Anastazia Keegan[6,7], Anthony Holley[4,5], Shannon Farmer[8,9], Nichole Harvey[10], James Winearls[2,11], Michael Parr[12,13,14,15], Craig J French[16,17], for the Clinical and Consumer Reference group for the update of Patient Blood Management Guidelines (Module 1: Critical Bleeding/Massive Transfusion)*

MJA 220 (4) • 4 March 2024

TVE en las guías

documento HEMOMAS-II

Recomendación 19

En el paciente con hemorragia grave, se recomienda la monitorización precoz de la hemostasia para optimizar la administración de hemocomponentes y fármacos prohemostáticos, guiando mediante algoritmos un tratamiento individualizado basado preferentemente en los resultados de test viscoelásticos (1B), o en su defecto, de test de coagulación convencionales. (1C)

Abstract

Introduction: The management of patients with critical bleeding requires a multidisciplinary approach to achieve haemostasis, optimise physiology, and guide blood component use. The 2011 *Patient blood management guidelines: module 1 — critical bleeding/massive transfusion* were updated and published. Systematic reviews were conducted for pre-specified research questions, and recommendations were based on meta-analyses of included studies.

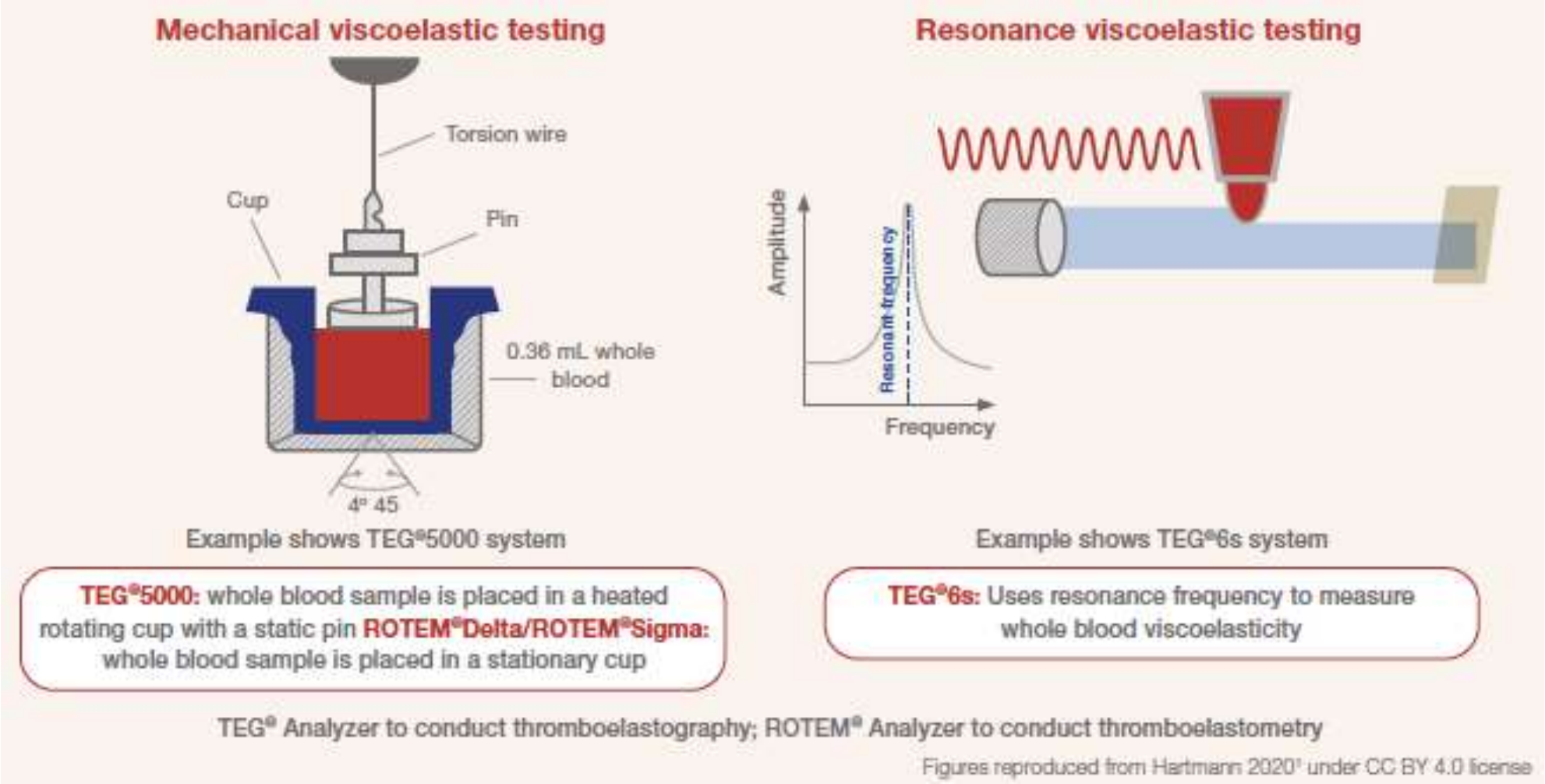
Main recommendations: The critical bleeding/massive transfusion guideline includes seven recommendations and 11 good practice statements addressing:

- major haemorrhage protocols (MHPs) facilitating a multidisciplinary approach to haemorrhage control, correction of coagulopathy and normalisation of physiological derangement;
- measurement of physiological, biochemical and metabolic parameters in critical bleeding/massive transfusion;
- the optimal ratio of red blood cells to other blood components;
- the use of tranexamic acid;
- viscoelastic haemostatic assays; and
- cell salvage.

Changes in management as a result of the guideline: The new guideline recommends MHPs be established as standard of care in all institutions managing patients with critical bleeding. In addition to routine physiological markers, the new guideline recommends temperature, biochemistry and coagulation profiles be measured early and frequently, providing parameters that define critical derangements. Ratio-based MHPs should include no fewer than four units of fresh frozen plasma and one adult unit of platelets for every eight units of red blood cells. In the setting of trauma and obstetric haemorrhage, administration of tranexamic acid within three hours of bleeding onset is recommended. The use of recombinant activated factor VII (rFVIIa) is not recommended. There was insufficient evidence to make recommendations on the use of viscoelastic haemostatic assays or cell salvage as part of MHPs.

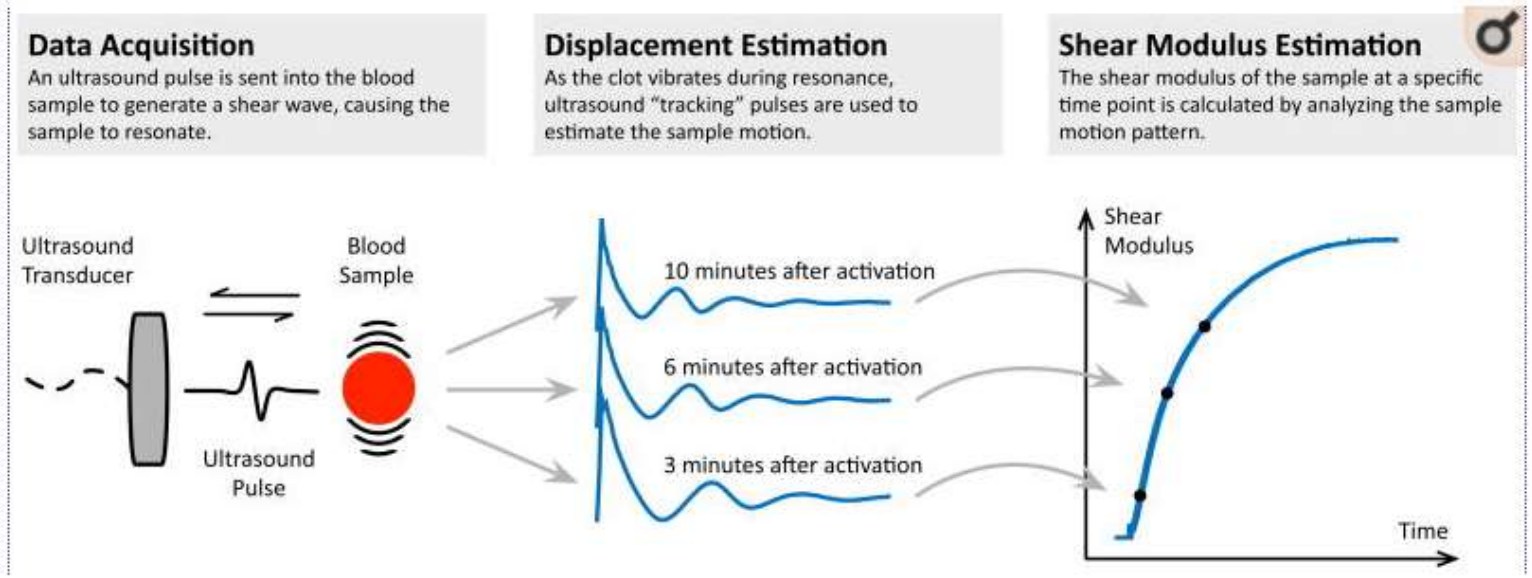
MJA 220 (4) • 4 March 2024

Conocer el funcionamiento de los TVE



Hartman J et al. *https://doi.org/10.1016/j.rpth.2022.100031*

Conocer el funcionamiento de los TVE

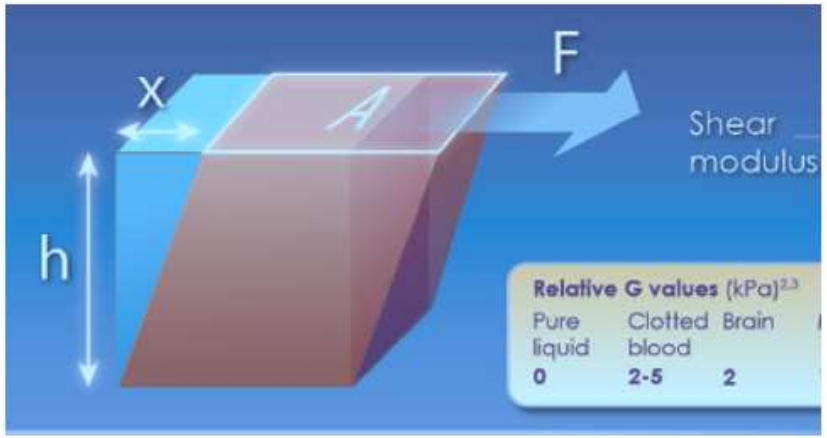


Schematic representation of SEER Sonorheometry. The technology is composed of three fundamental steps, as represented by the three panels in this figure. First, an ultrasound pulse is transmitted in the blood sample to generate a shear wave, causing the sample to resonate (left panel). A series of ultrasound "tracking" pulses is then sent within the sample and the returning echoes are used to estimate the sample motion (middle panel). The shape of the estimated displacement curve is directly related to the shear modulus of the sample. The time-displacement curve can be compared to theoretical models to determine the actual shear modulus for that specific point in time. This process is repeated every 4 seconds to form a signature curve that shows shear modulus vs time (right panel).

Conocer el funcionamiento de los TVE

QUANTRA
- AUTOMATICO
- NUEVO METODO DE MEDICION (SEER)
- **MEDICION DE LA ELASTICIDAD**

Aparente mejor detección de la formación de coágulos débiles



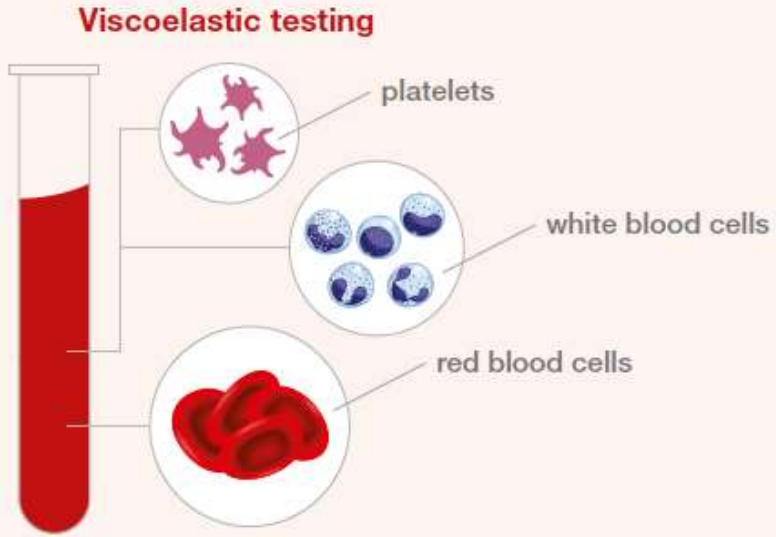
Medida Directa de la Elasticidad

"La elasticidad es una propiedad física real del coágulo"

Roman M. Sniecinski, MD,* and Kenichi A. Tanaka, MD, MSc†

Fibrinógeno y TVE

Advantages of viscoelastic testing compared with conventional coagulation testing [5]



Viscoelastic tests	Conventional laboratory coagulation assays
Whole blood sample	Platelet-poor plasma sample
Can be viewed and evaluated at the point-of-care	Tests take place in a central laboratory
Results within minutes	Longer turn-around time
Holistic overview of *ex vivo* clotting	Snapshot of individual steps in clotting process

Hartman J et al. *https://doi.org/10.1016/j.rpth.2022.100031*

Fibrinógeno y TVE

Assay	TEG® assays (activator)	ROTEM® assays (activator)	Interpretation of assay
Contact activation pathway	Kaolin TEG® (Kaolin)	INTEM® (ellagic acid)	Assesses the contact activation pathway (intrinsic pathway) partially measured by aPTT
Tissue factor (TF) activation pathway	–	EXTEM® (tissue factor)	Assesses the tissue factor activated pathway (extrinsic pathway) partially measured by PT
Contact activation + TF pathway	RapidTEG® (Tissue factor + kaolin)	–	Assesses both activation pathways
Heparinase	Kaolin TEG® with lyophilized heparinase	HEPTEM® (ellagic acid + lyophilized heparinase)	Assesses the presence of systemic heparin via comparison with the Kaolin/INTEM assay
Fibrinogen	TEG® Functional Fibrinogen (tissue factor + abciximab)	FIBTEM® (tissue factor + cytochalasin D)	Uses a platelet inhibitor to assess the relative contribution of fibrinogen to clot strength independent of platelets
Native whole blood sample	Native TEG®	NATEM®	Used for custom hemostasis tests. Not for clinical use due to the long reaction rate
Platelet function via AA and ADP activation	TEG® PlateletMapping®	No platelet function test exists on the platform; however, it can be used in conjunction with VerifyNow™ & Multiplate® platelet function impedance aggregometry analysis	Platelet receptor-specific tracing to identify levels of platelet inhibition and aggregation

Hartman J et al. *https://doi.org/10.1016/j.rpth.2022.100031*

Fibrinógeno y TVE

ALMAS
Algoritmos de Manejo de Sangrado

Log Out

Reversión AVK

Reversión ACODs

Hemorragia masiva

Información de interés

Atras

1 DIAGNÓSTICO DE HEMORRAGIA MASIVA

2 ACTIVACIÓN DEL PROTOCOLO DE TRANSFUSIÓN MASIVA

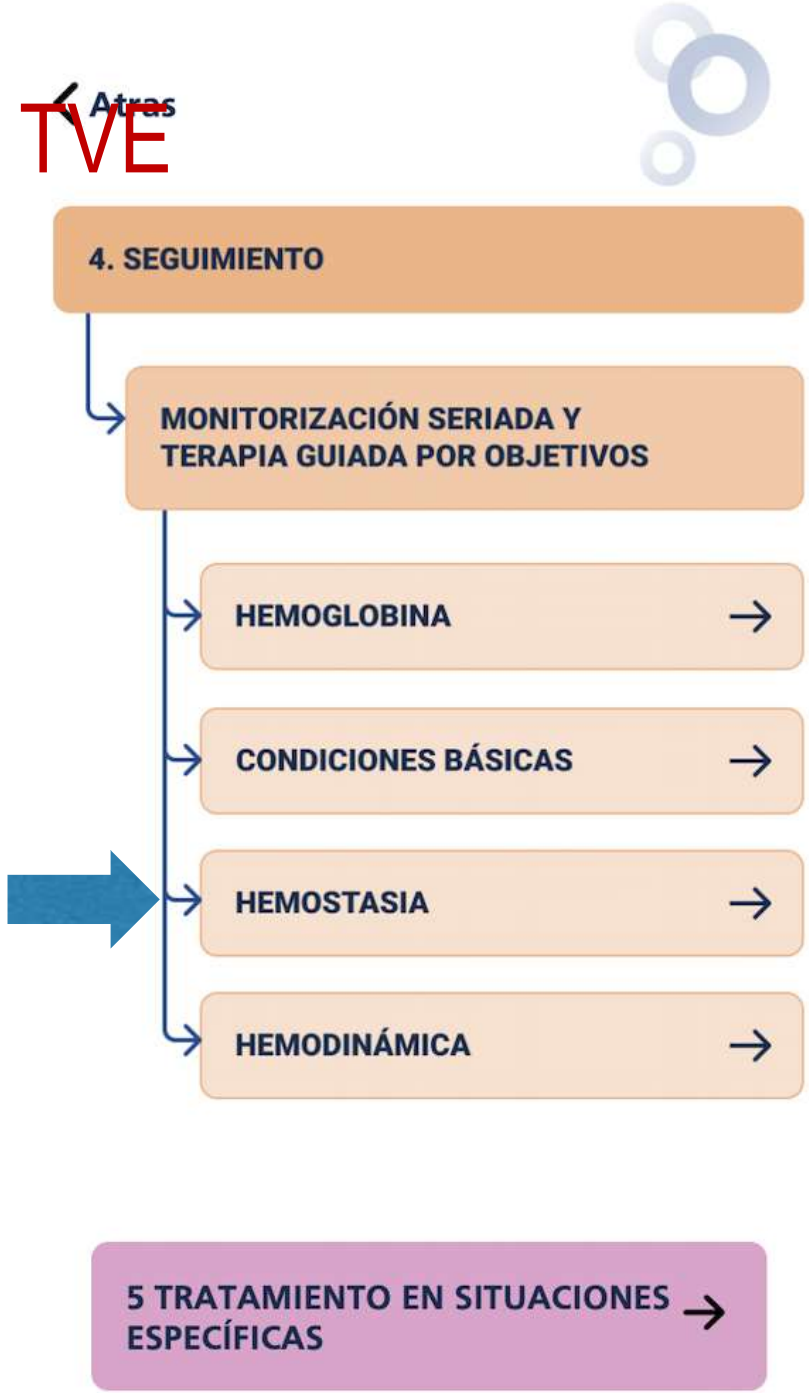
3 RESUCITACIÓN INICIAL

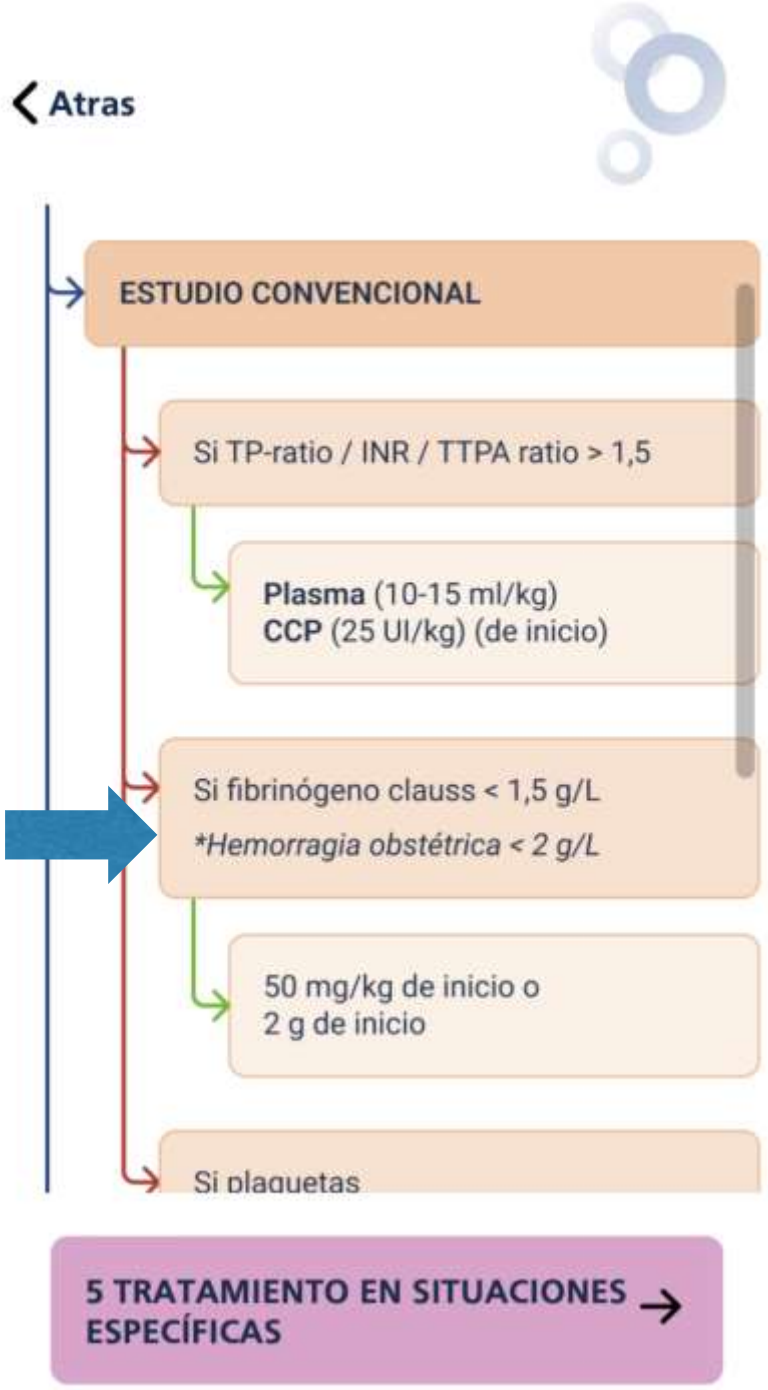
4 SEGUIMIENTO

5 TRATAMIENTO EN SITUACIONES ESPECÍFICAS

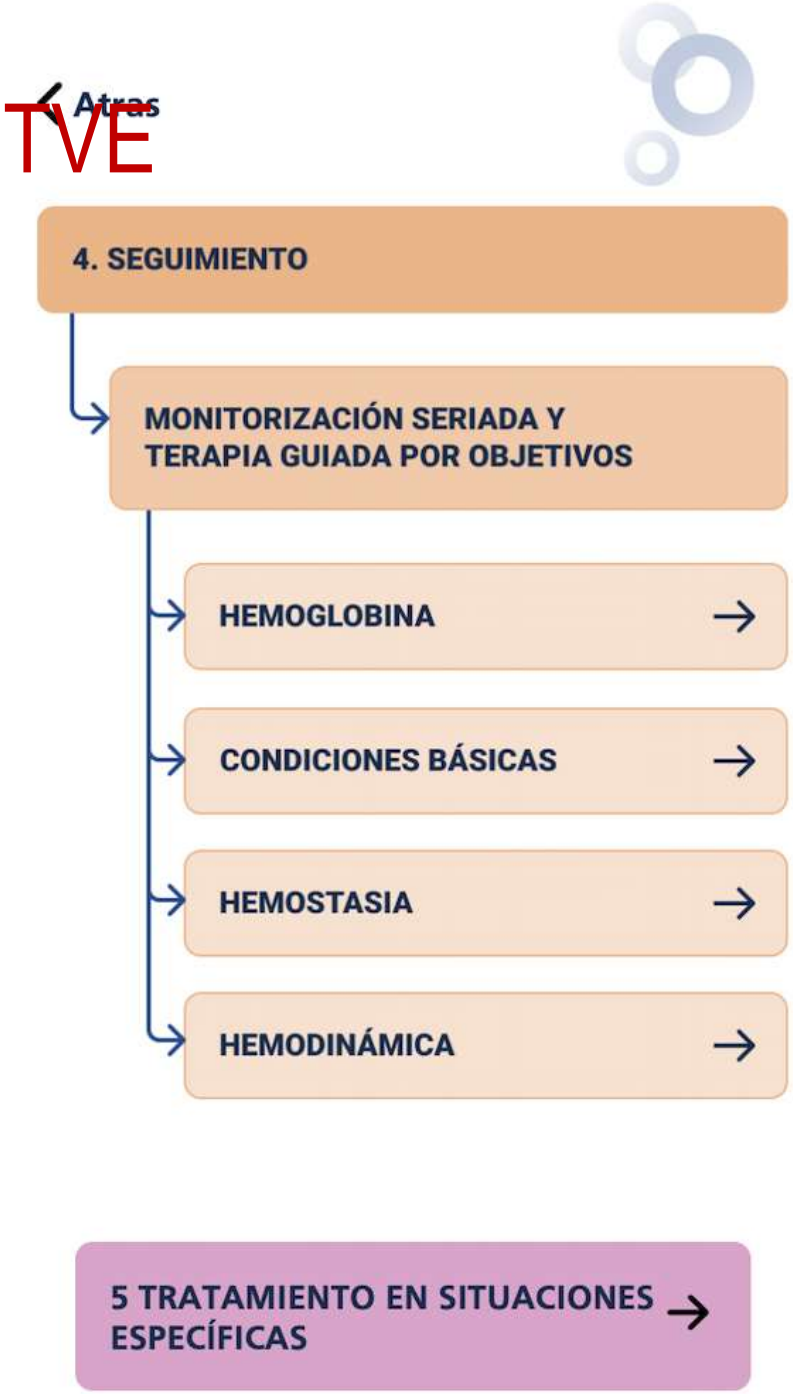
Con la colaboración de
octapharma

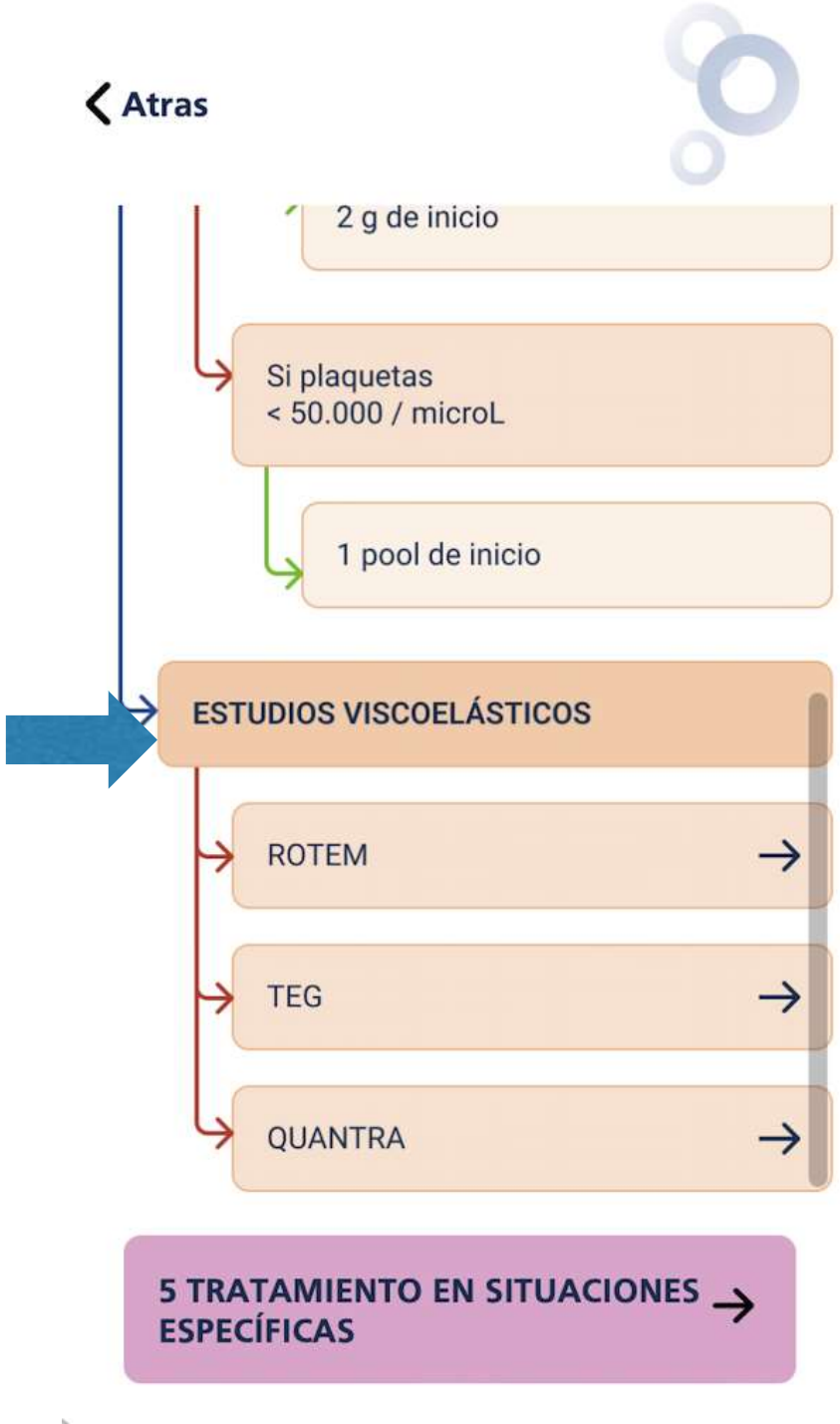
Fibrinógeno y TVE





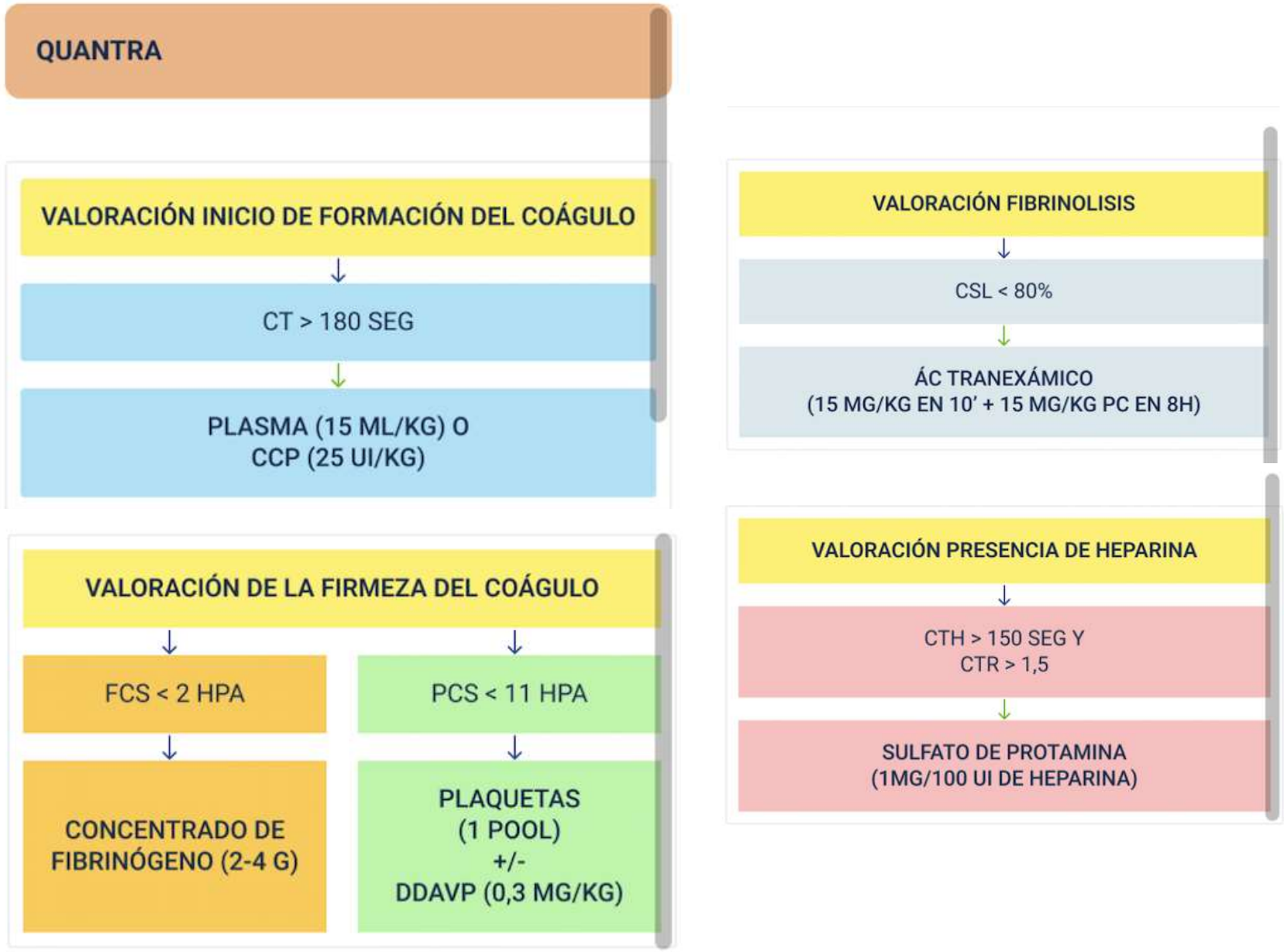
Fibrinógeno y TVE





Fibrinógeno y TVE

Fibrinógeno y TVE



Fibrinógeno y TVE: toma de decisiones

Recomendación 33

En un paciente con sangrado activo, se recomienda la administración de concentrado de fibrinógeno si los niveles plasmáticos (funcional de Clauss) están por debajo de 1,5-2,0 g/L, o el A5 en el FIBTEM es inferior a 7-9 mm o, por equivalencia, la amplitud máxima MA_{CFF} es inferior a 10 mm. (1C)

En la fase inicial del sangrado masivo, sobre todo si es debido a un traumatismo grave, se recomienda la administración de concentrado de fibrinógeno junto a concentrado de hematíes como alternativa a la estrategia de reanimación hemostática, incluso sin necesidad de resultados de los TVE o de coagulación. (1C)

El umbral para la administración de fibrinógeno es controvertido. El nivel plasmático no debe ser inferior a 1,5 g/L[30,4,13,19,45,68–70] correspondiendo a un A5-FIBTEM inferior a 7 mm, aunque se ha propuesto un umbral de 8-9 mm en algunos escenarios clínicos[70]. En el TEG®, por equivalencia, se correspondería con una amplitud máxima (MA_{CFF}) 10 mm.

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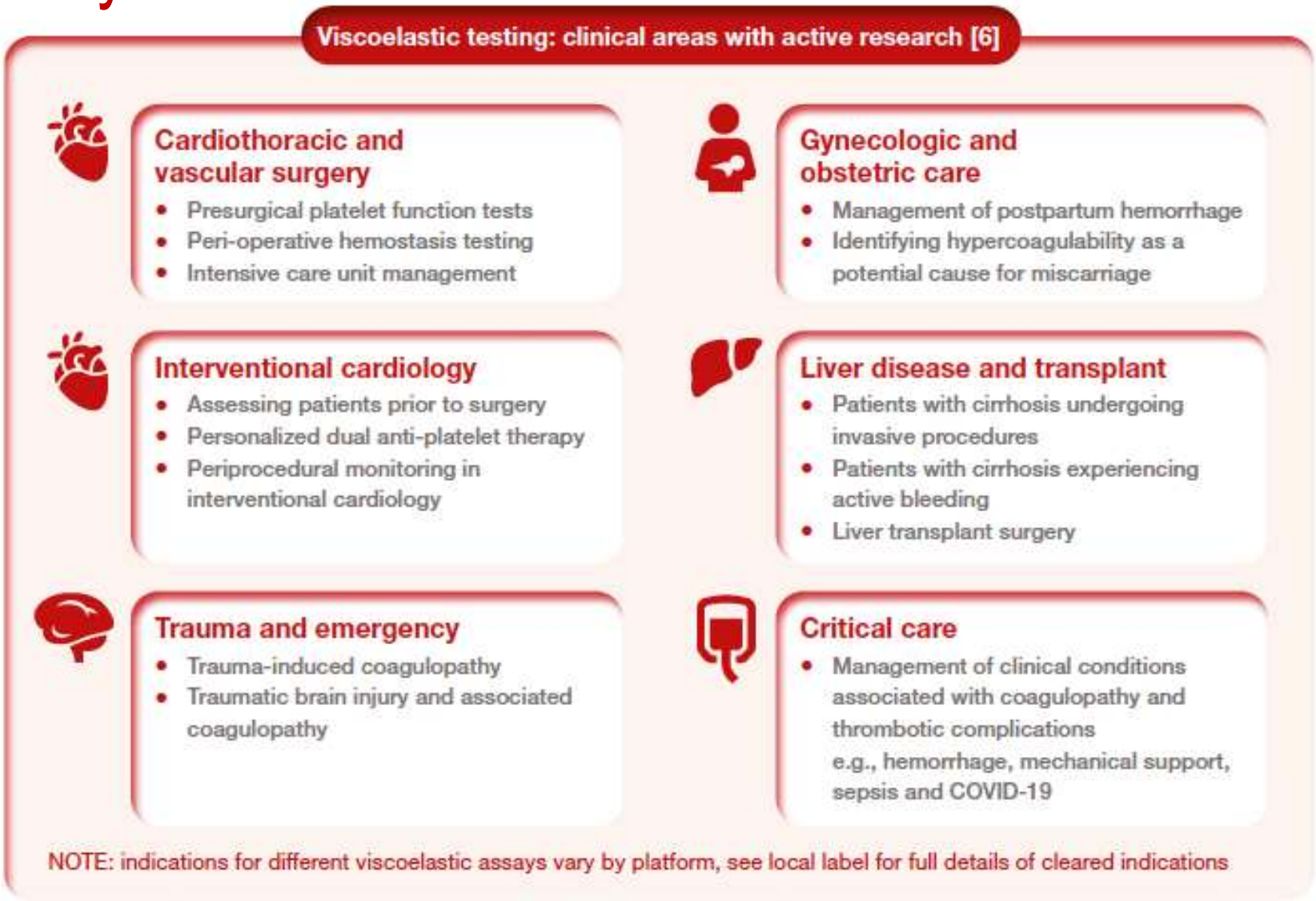
Fibrinógeno y TVE: toma de decisiones

Table 2. Societies' Guidelines on Coagulation Factor Substitution and Antifibrinolytic Therapy[9,13-17]

Medical Area	Obstetrics (Postpartum Hemorrhage)	Trauma	Cardiac Surgery with Cardiopulmonary Bypass	
Fibrinogen concentrate cryoprecipitate	Fibrinogen ROTEM viscoelastic amplitude at 5 min < 7 mm Fibrinogen ROTEM viscoelastic amplitude at 5 min < 12 mm (in ongoing bleeding)	Major bleeding with functional fibrinogen deficit (plasma Clauss fibrinogen concentration <1.5 g/l) Fibrinogen ROTEM maximum clot firmness < 8 to 10 mm* Functional fibrinogen < 12 mm*	Fibrinogen ROTEM viscoelastic amplitude at 10 min < 10 mm; tissue factor–activated ROTEM viscoelastic amplitude at 10 min < 40 mm TEG maximum amplitude < 40 mm; functional fibrinogen < 8 mm	Fibrinogen ROTEM maximum clot firmness ≤4 to 6 mm recommended Fibrinogen ROTEM maximum clot firmness 6 to 8 mm considered Fibrinogen ROTEM maximum clot firmness > 9 mm targeted
No fibrinogen concentrate	Fibrinogen ROTEM > 12 mm			Fibrinogen ROTEM maximum clot firmness > 14 mm

Erdoes G et al. Anesthesiology 2021 - 135;2:342-9

Fibrinógeno y TVE



Hartman J et al. *https://doi.org/10.1016/j.rpth.2022.100031*

Mensajes para llevar a casa

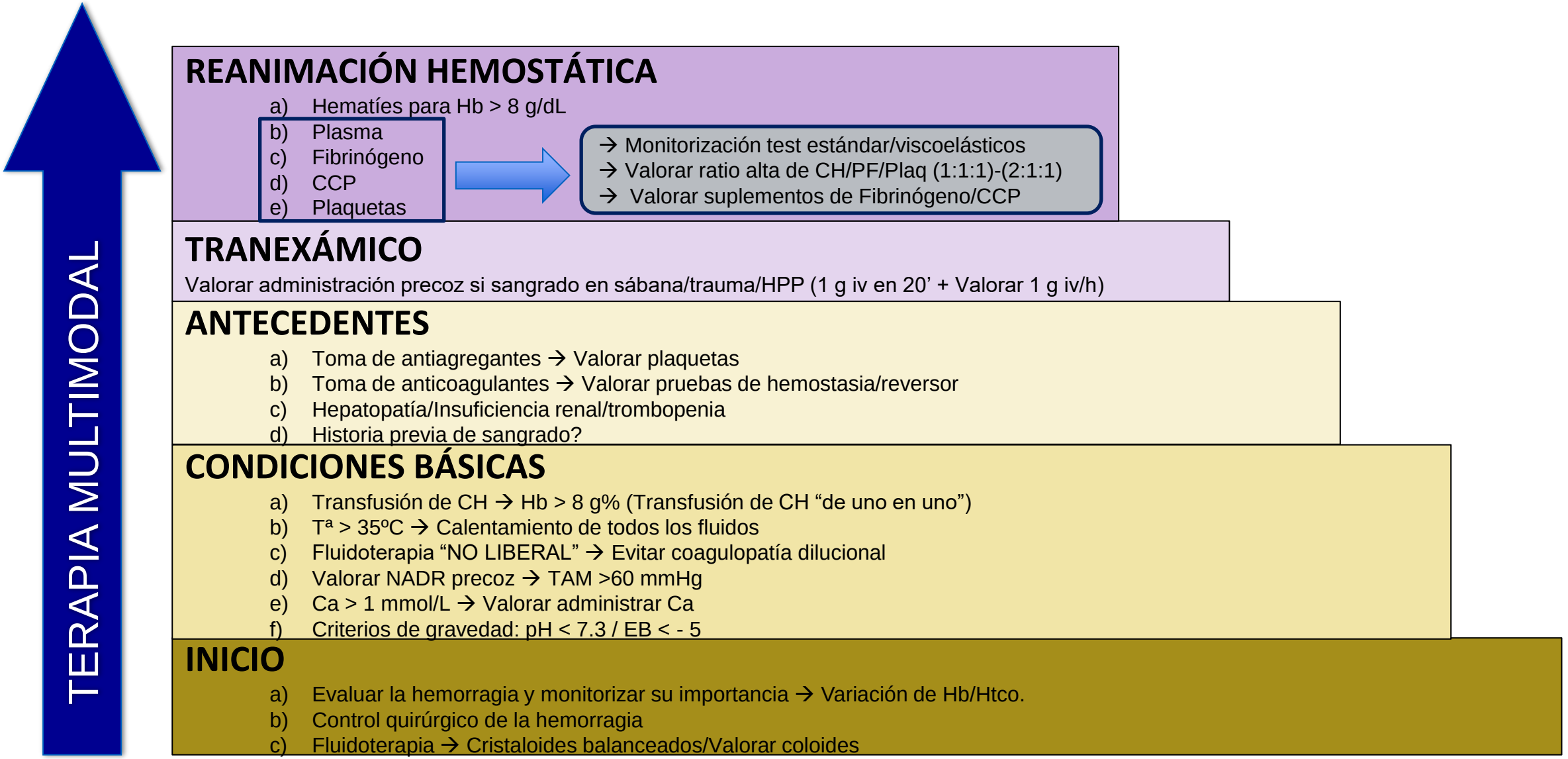
1. La administración precoz y efectiva de fibrinógeno es de crucial importancia para limitar la pérdida de sangre y minimizar el riesgo de complicaciones en una HM, probablemente porque disminuye la coagulopatía inducida al mejorar la fuerza del coágulo (demostrado en test viscoelásticos)

2. La administración profiláctica no es una opción preferente y no se recomienda de forma general

3. El aumento de fibrinógeno plasmático no se consigue de forma adecuada en base a la administración de PFC

4. Si bien su administración debe ser precoz, es altamente recomendable que se realice en base a los resultados de monitorización.

Reanimación hemostática



Indicaciones de la administración de fibrinógeno en base a los distintos test viscoelásticos

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