Valencia, 11 de febrero de 2013

Actualización del manejo de la hemorragia masiva

Juan V. Llau
S. Anestesiología - HCU Valencia
Prof. Asociado Dept. Fisiología - Universidad de Valencia

juanvllau@gmail.com

Conflicto de intereses

Definir hemorragia masiva...

Definir hemorragia masiva...

La definición de sangrado masivo se puede hacer en función de diferentes parámetros...

Definir hemorragia masiva...

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Descenso de la hemoglobina...

Definir hemorragia masiva...

La definición de sangrado masivo se puede hacer en función de diferentes parámetros...

Descenso de la hemoglobina...
Volumen de hemoderivados transfundido...

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Definir hemorragia masiva...

La definición de sangrado masivo se puede hacer en función de diferentes parámetros...

Descenso de la hemoglobina...
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Sangre recolectada en drenajes...

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...en 2 horas

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...en 6 horas

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Volumen de hemoderivados transfundido...
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...en 2 horas
...en 6 horas
...en 24 horas

Definir hemorragia masiva...

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Volumen de hemoderivados transfundido...
Sangre recolectada en drenajes...

...en 2 horas
...en 6 horas
...en 24 horas
...

Definir hemorragia masiva...

Definitions

Massive bleeding is defined as one of the following [49,50]:

1 Loss of entire blood volume within 24 h (10 U of packed RBC in a patient weighing 70 kg).
2 Loss of 50% of blood volume within 3 h.
3 Blood loss at a rate of 150 mL min^{-1}.
4 Blood loss at a rate of 1.5 mL kg^{-1} min^{-1} for ≥20 min.

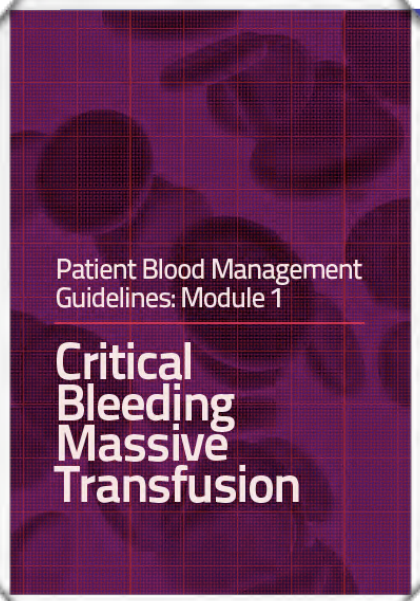
U. MARTINOWITZ* and M. MICHAELSON

Journal of thrombosis and Haemostasis 2005; 3: 640-8

Definir hemorragia masiva...

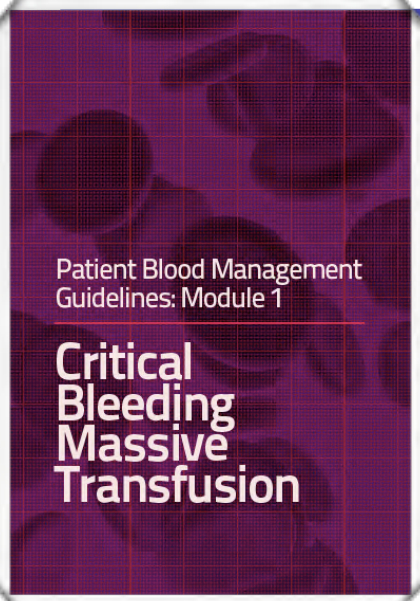
Definitions of massive haemorrhage vary and have limited value. The Working Party suggests that the nature of the injury will usually alert the anaesthetist to the probability of massive haemorrhage and can be arbitrarily considered as a situation where 1–1.5 blood volumes may need to be infused either acutely or within a 24-h period.

Definir hemorragia masiva...



Australian Government
National Health and Medical Research Council

Definir hemorragia masiva...



Australian Government
National Health and Medical Research Council

3.1.2 Massive transfusion

Massive transfusion has been defined based on the volume of blood loss or on the volume transfused. The most widely used definition proposes the loss or transfusion of one blood volume (about 7% of body weight in adults) over 24 hours;[11-14] or approximately 10 units of red blood cells (RBCs). Alternative, 'real time' definitions include replacement of half a blood volume within 4 hours,[15,16] or blood loss of more than 150 mL per minute.[13]

The different definitions reflect the diverse clinical scenarios in which critical bleeding occurs. Ultimately, the importance of defining critical bleeding or massive transfusion is to facilitate early recognition of this condition, or its potential, so that appropriate management can be instituted.

Definir hemorragia masiva...

3.1.2 Massive transfusion

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Definir hemorragia masiva...

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The different definitions reflect the diverse clinical scenarios in which critical bleeding occurs. Ultimately, the importance of defining critical bleeding or massive transfusion is to facilitate early recognition of this condition, or its potential, so that appropriate management can be instituted.

Definitions (see Chapter 3.1)

'Critical bleeding' may be defined as major haemorrhage that is life threatening and likely to result in the need for massive transfusion.

'Massive transfusion' may be defined:

- in adults, as a transfusion of half of one blood volume in 4 hours, or more than one blood volume in 24 hours (adult blood volume is approximately 70 mL/kg)
- in children, as a transfusion of more than 40 mL blood/kg (blood volume of children older than neonates is approximately 80 mL/kg).

Fisiopatología

British Journal of Anaesthesia **111** (S1): i71–i82 (2013)
doi:10.1093/bja/aet376

Update on massive transfusion

H. P. Pham[1,2] and B. H. Shaz[1,3*]

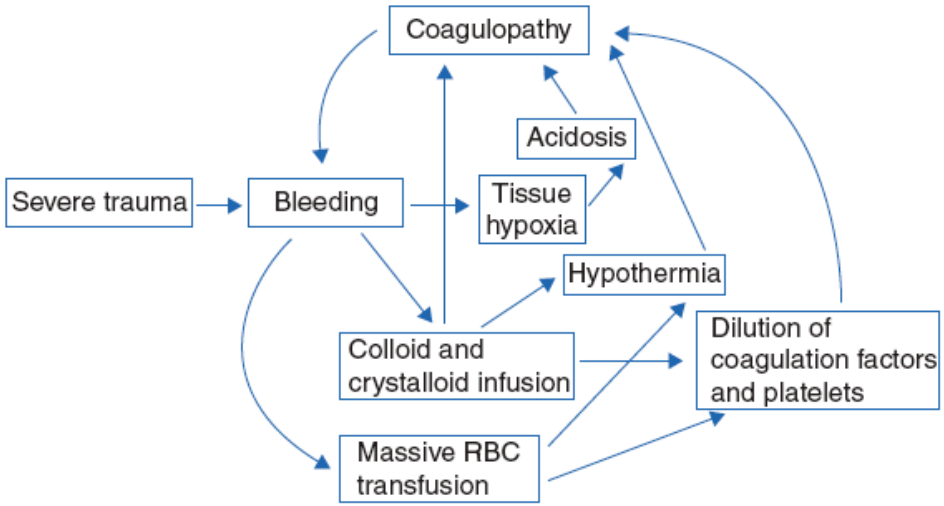
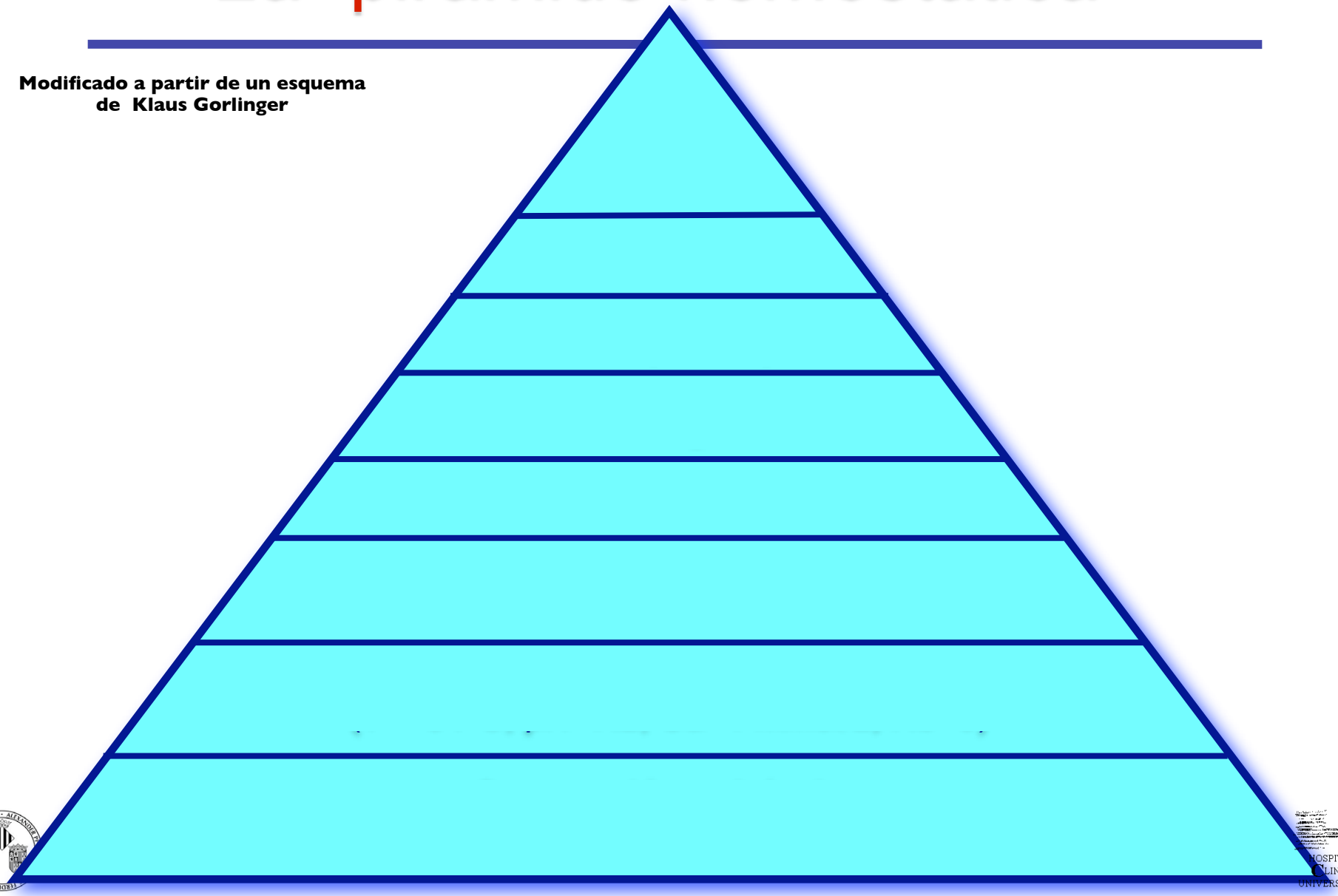


Fig 1 Pathogenesis of haemostasis abnormality in MT. Dilutional coagulopathy, activation of inflammatory mediators, hyperfibrinolysis, thrombocytopathy, and metabolic abnormalities (hypothermia, hypocalcaemia, and acidosis) all contribute to the pathogenesis of the haemostasis abnormality in massive haemorrhage.

La “pirámide hemostática”

Modificado a partir de un esquema de Klaus Gorlinger



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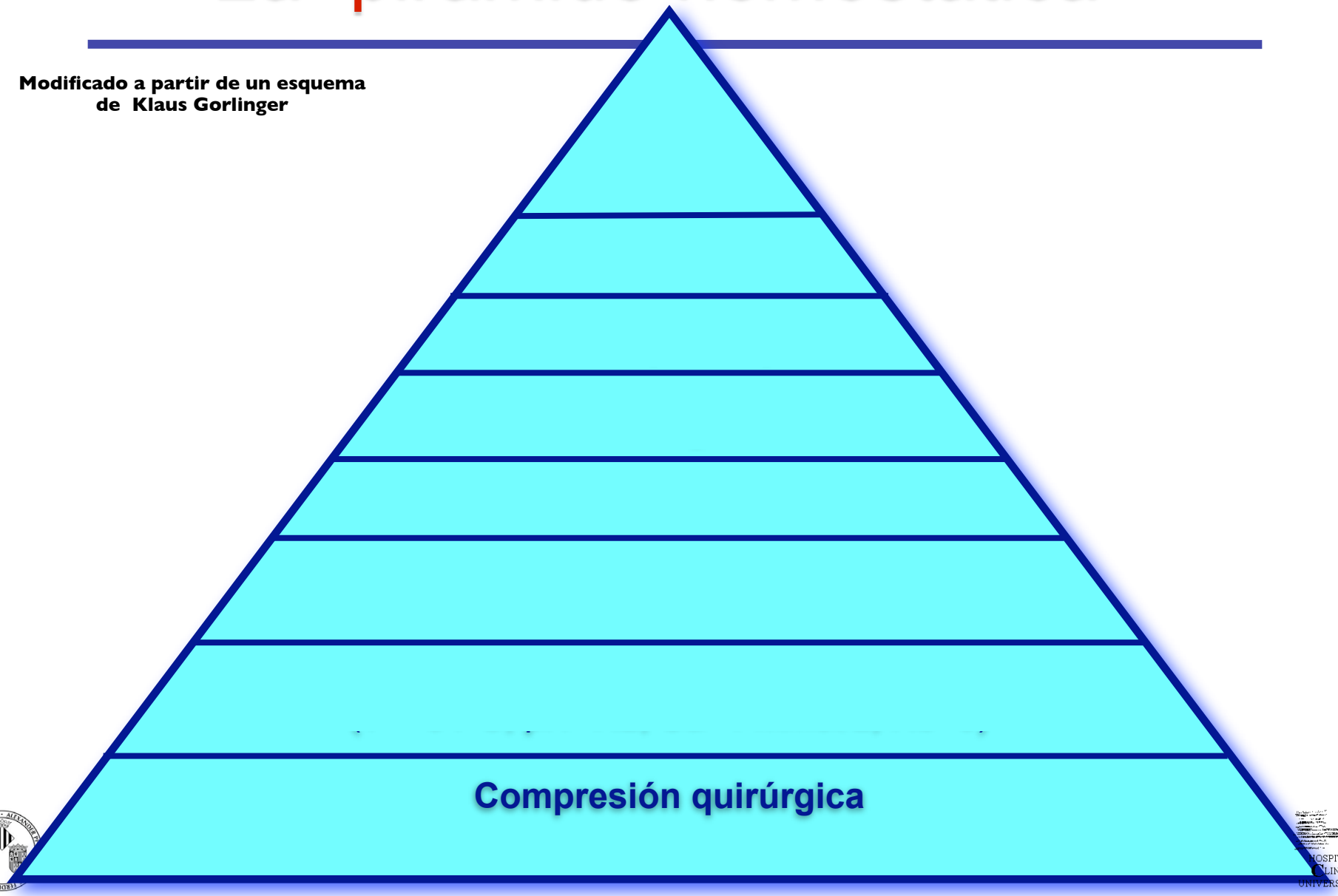

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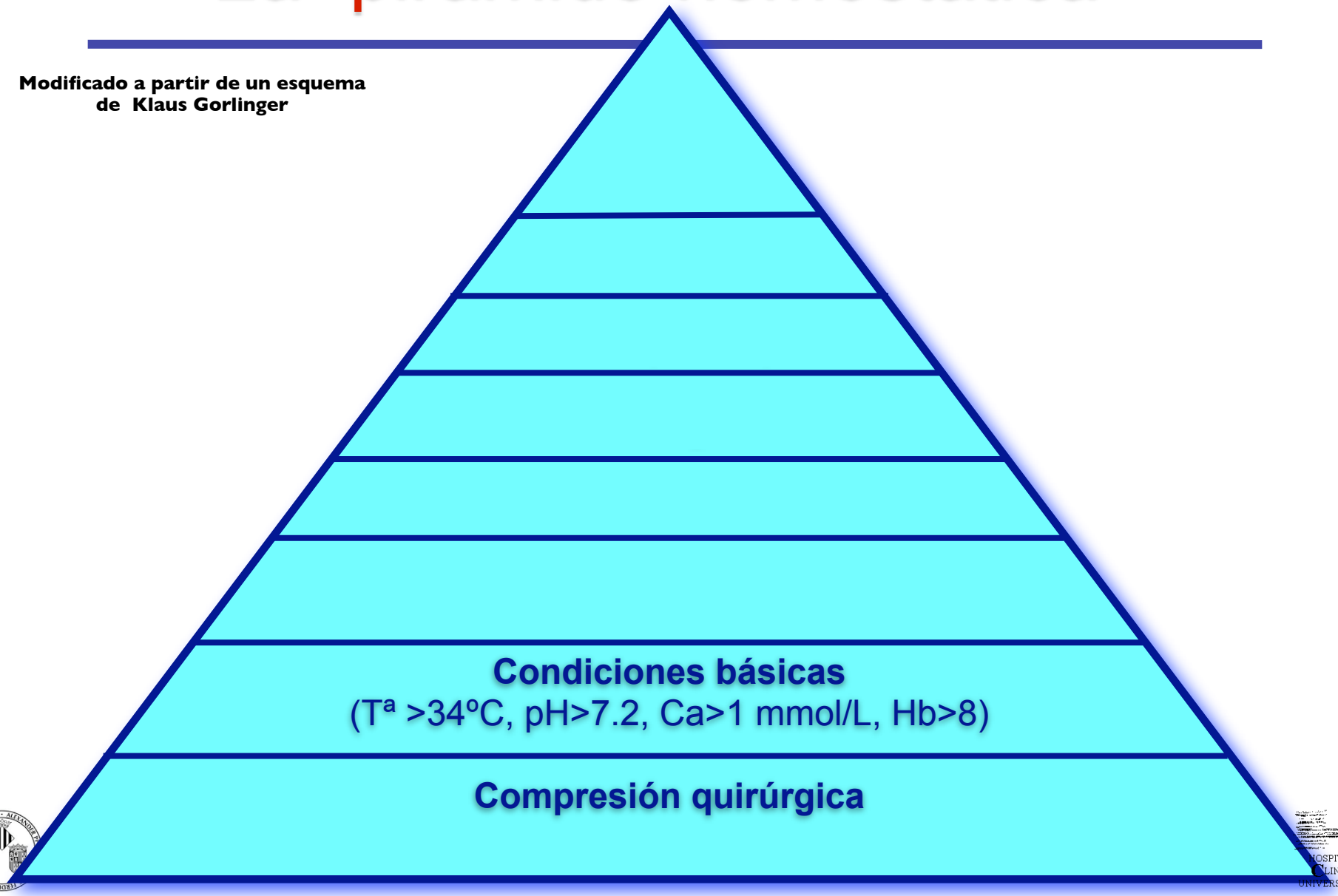

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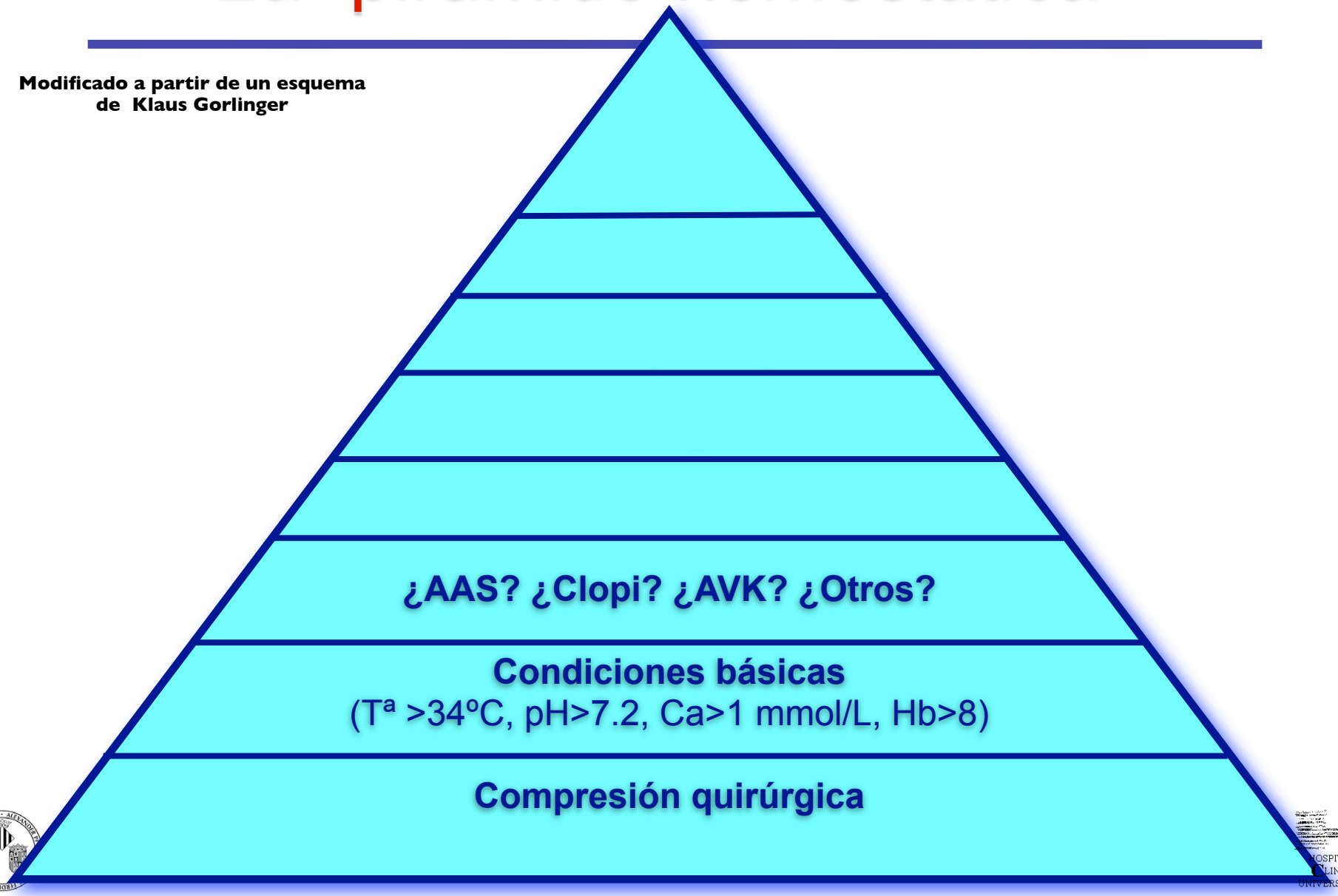

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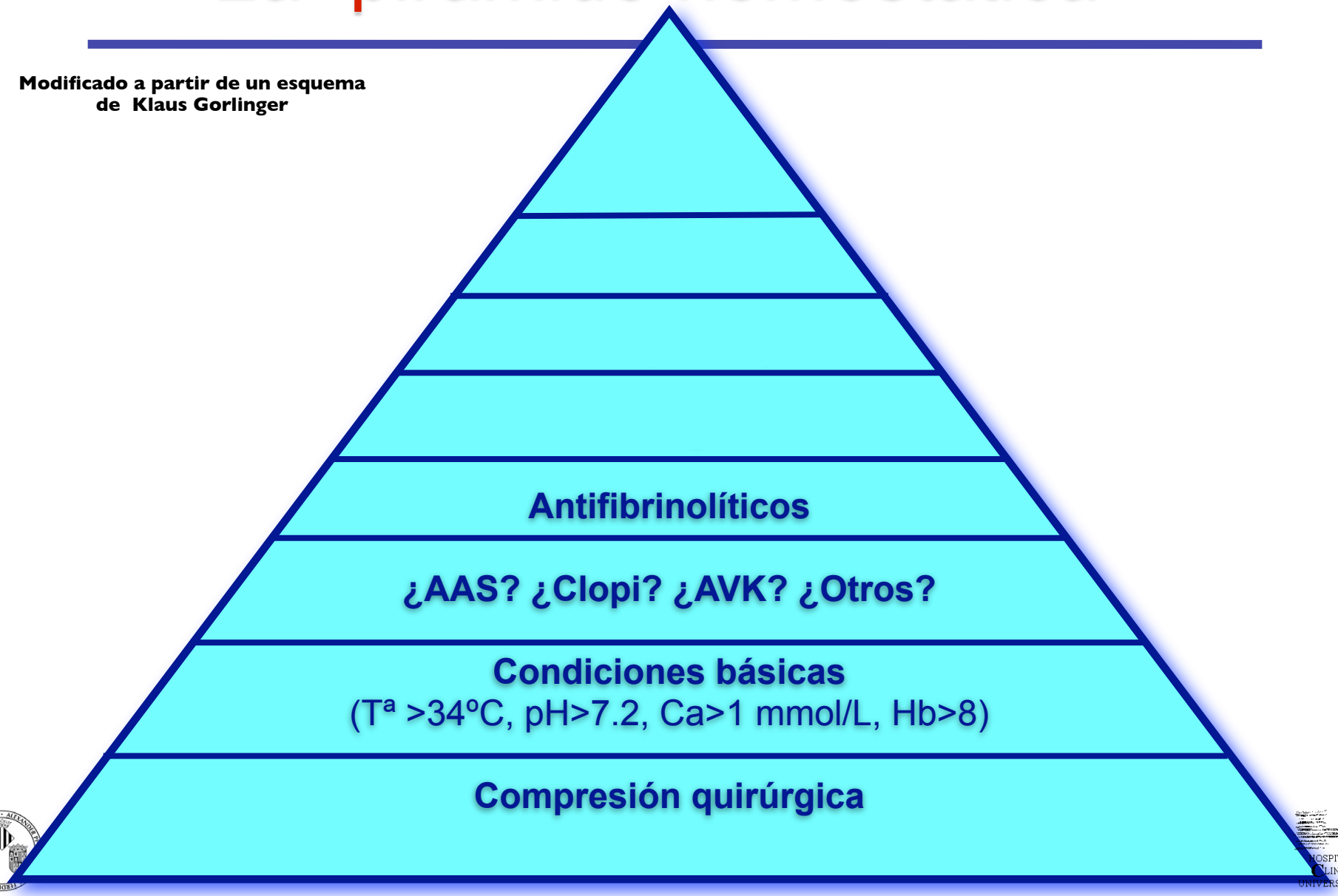

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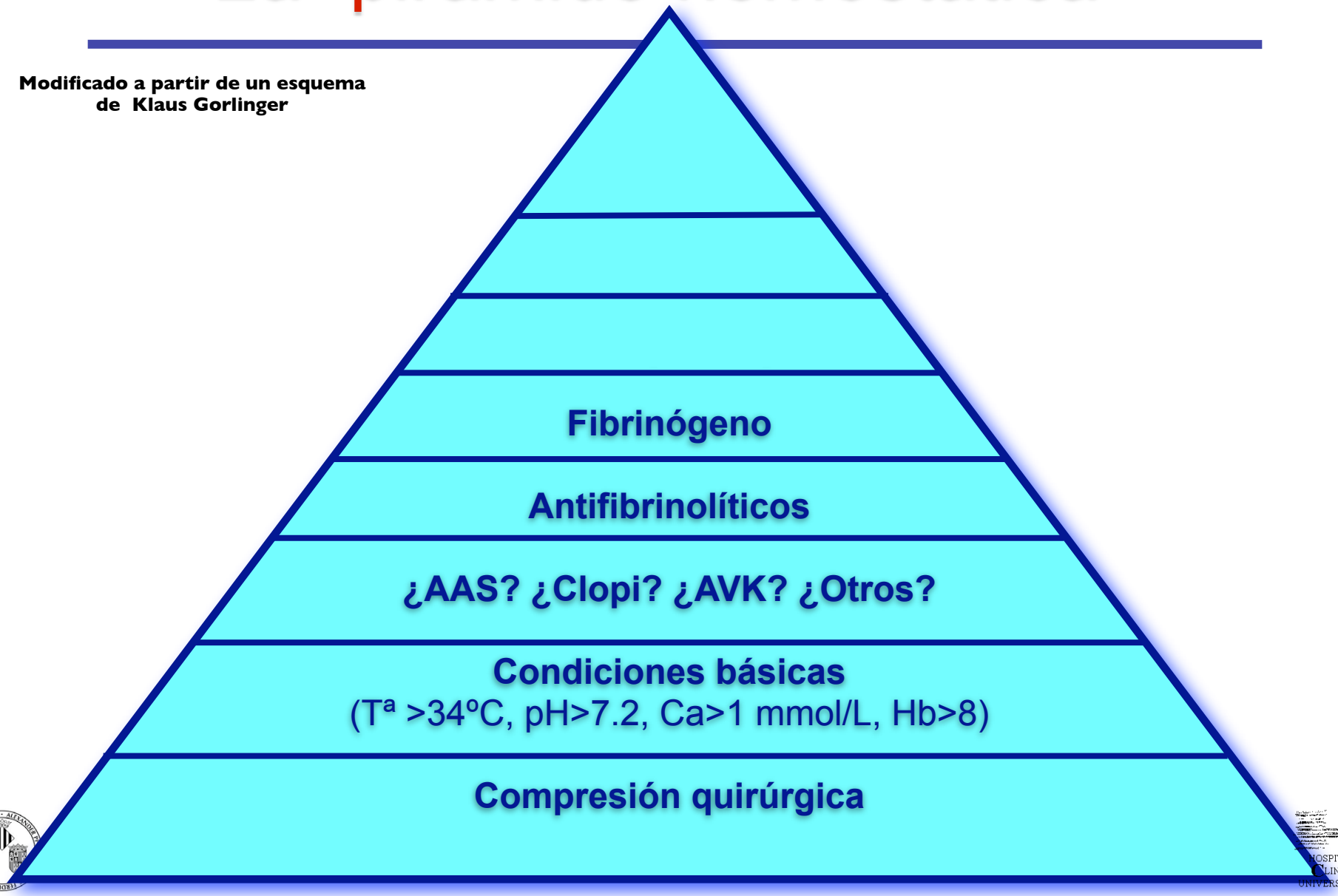

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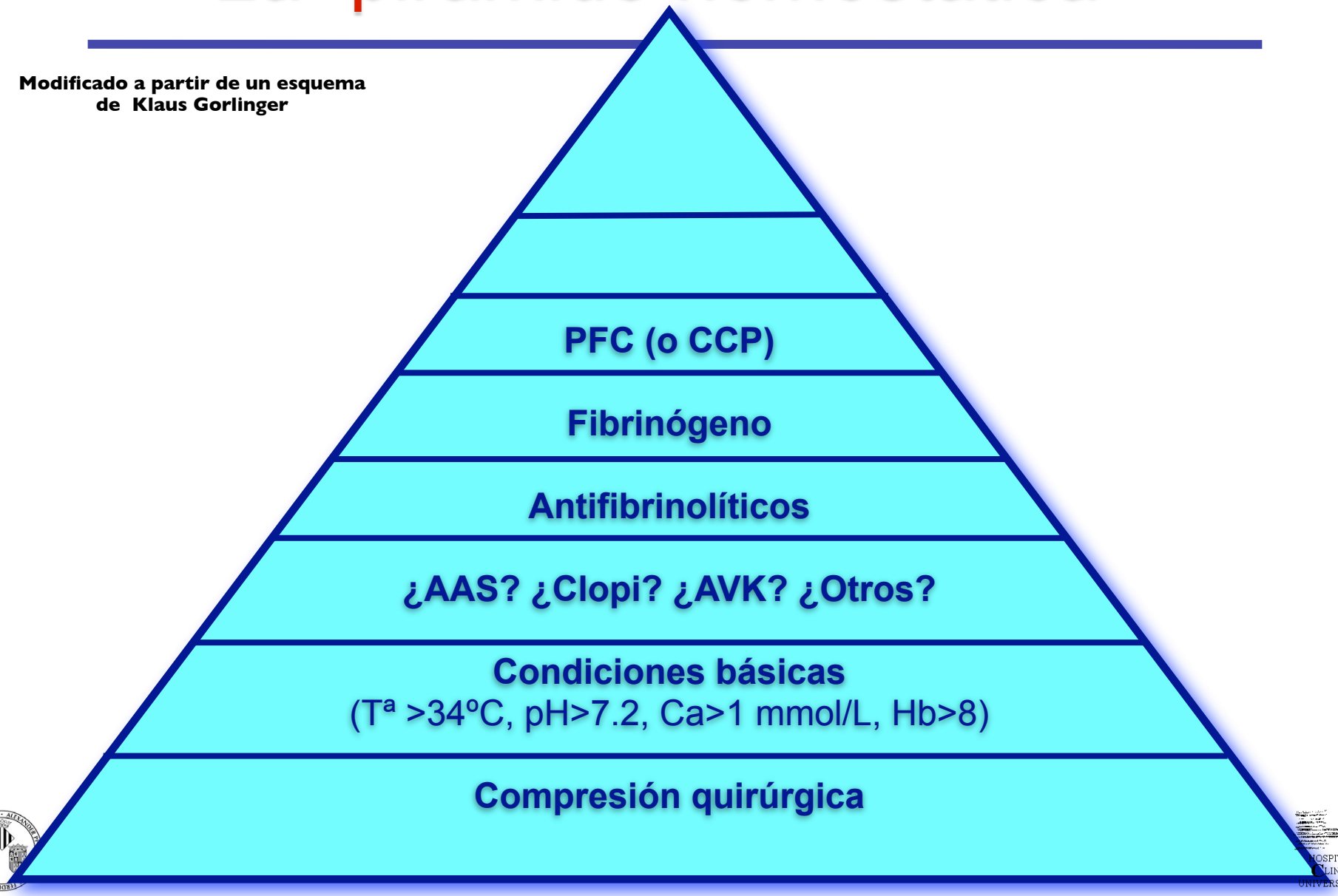

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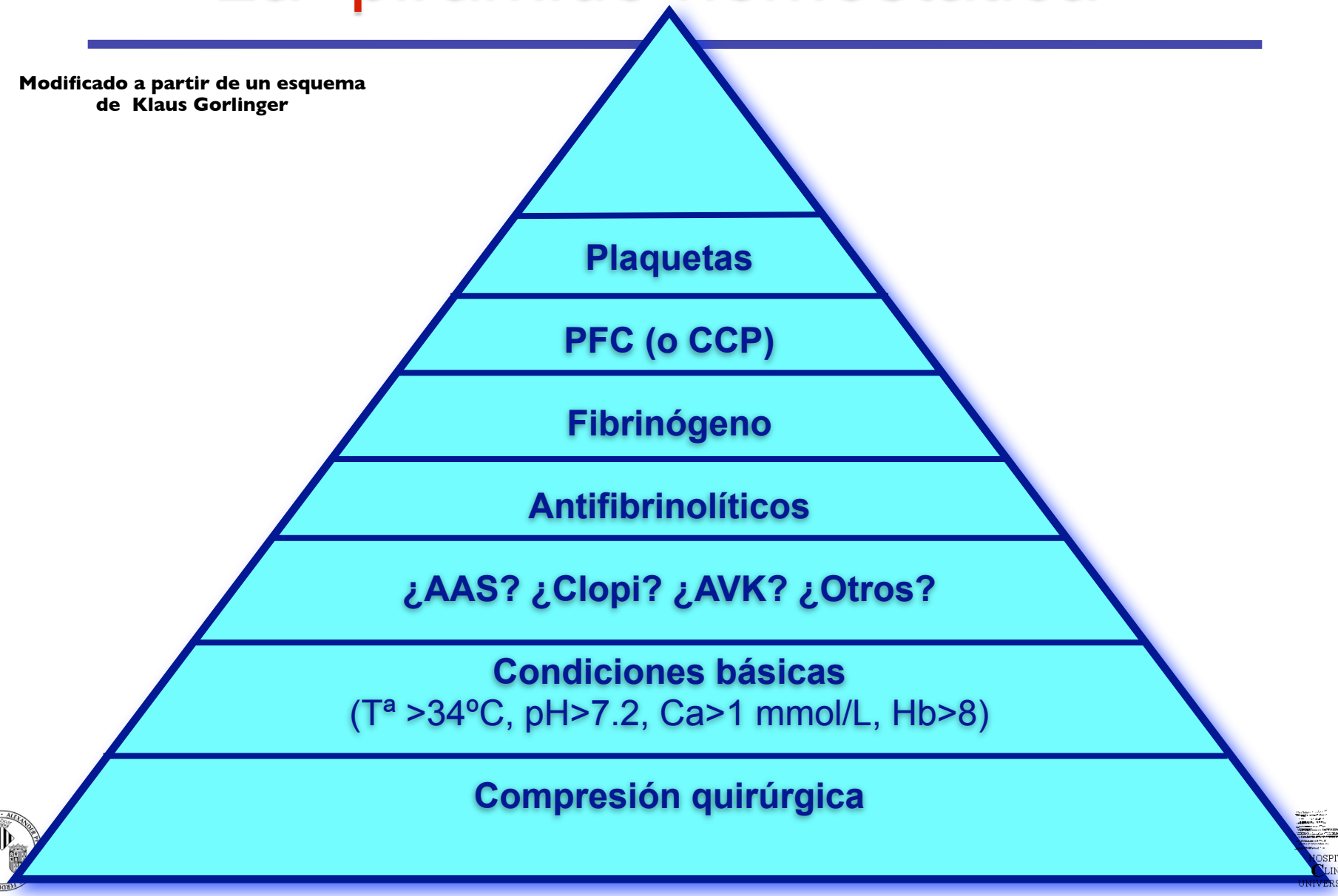

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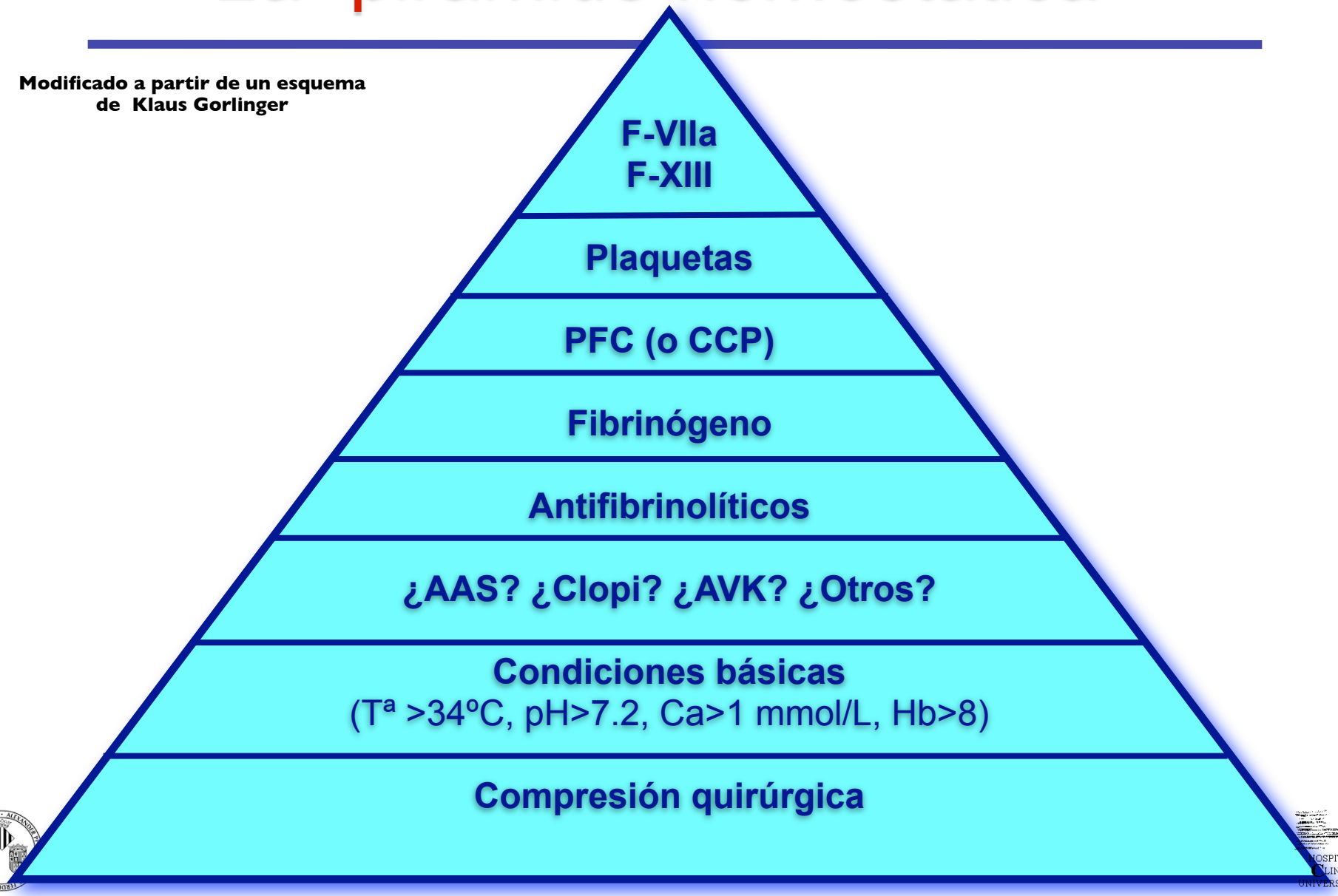

Últimas recomendaciones

EJA

Eur J Anaesthesiol 2013; **30**:1–112

GUIDELINES

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santullano, Edoardo De Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juul Wikkelsø, Patrick Wouters and Piet Wyffels

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Monitoring tissue perfusion

We recommend repeated measurements of a combination of haematocrit/haemoglobin, serum lactate, and base deficit in order to monitor tissue perfusion, tissue oxygenation and the dynamics of blood loss during acute bleeding. These parameters can be extended by measurement of cardiac output, dynamic parameters of volume status (e.g. stroke volume variation, pulse pressure variation) and central venous oxygen saturation. **1C**

EJA

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Coagulation management

We recommend treatment with fibrinogen concentrate if significant bleeding is accompanied by at least suspected low fibrinogen concentrations or function. **1C**

We recommend that a plasma fibrinogen concentration $<1.5–2.0\,g\,l^{-1}$ or ROTEM/TEG signs of functional fibrinogen deficit should be triggers for fibrinogen substitution. **1C**

We suggest an initial fibrinogen concentrate dose of $25–50\,mg\,kg^{-1}$. **2C**

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We recommend that patients on oral anticoagulant therapy should be given prothrombin complex concentrate (PCC) and vitamin K before any other coagulation management steps for severe perioperative bleeding. **1B**

We suggest that PCC (20–30 IU kg^{-1}) can also be administered to patients not on oral anticoagulant therapy in the presence of an elevated bleeding tendency and prolonged clotting time. Prolonged INR/PT alone is not an indication for PCC, especially in critically ill patients. **2C**

We suggest that off-label administration of recombinant activated factor VII (rFVIIa) can be considered for bleeding which cannot be stopped by conventional, surgical or interventional radiological means and/or when comprehensive coagulation therapy fails. **2C**

EJA

Eur J Anaesthesiol 2013; **30**:1–112

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Antifibrinolytics and tranexamic acid

We recommend the consideration of tranexamic acid ($20–25\,mg\,kg^{-1}$). **1A**

We suggest the use of DDAVP under specific conditions (acquired von Willebrand syndrome). There is no convincing evidence that DDAVP minimises perioperative bleeding or perioperative allogeneic blood transfusion in patients without a congenital bleeding disorder. **2B**

Correction of confounding factors

We recommend maintaining perioperative normothermia because it reduces blood loss and transfusion requirements. **1B**

We suggest that rFVIIa may be used in treatment of patients with hypothermic coagulopathy. **2C**

While pH correction alone cannot immediately correct acidosis-induced coagulopathy, we recommend that pH correction should be pursued during treatment of acidotic coagulopathy. **1C**

We recommend that rFVIIa should only be considered alongside pH correction. **1C**

We suggest that calcium should be administered during massive transfusion if Ca^{2+} concentration is low, in order to preserve normocalcaemia ($\geq 0.9\,mmol\,l^{-1}$). **2B**

PFC vs CCP

Perioperative use of prothrombin complex concentrates

M. J. COLOMINA [1], A. DÍEZ LOBO [2], I. GARUTTI [3], A. GÓMEZ-LUQUE [4], J. V. LLAU [5], E. PITA [6]

[1]Department of Anesthesiology, Vall d'Hebron University Hospital; Area of Orthopedic Surgery, Barcelona, Spain; [2]Department of Anesthesiology, Segovia General Hospital, Segovia, Spain; [3]Department of Anesthesiology, "Gregorio Marañón" General University Hospital, Madrid, Spain; [4]Department of Anesthesiology, Virgen de la Victoria University Hospital, Malaga University, Malaga, Spain; [5]Department of Anesthesiology, Valencia Clinical University Hospital "San Vicente Mártir" Catholic University, Valencia, Spain; [6]Department of Anesthesiology, A Coruña University Hospital Complex, Coruña, Spain

TABLE III.—*Differences between fresh frozen plasma and prothrombin complex concentrates.*

	FFP	PPC
Volume to be administered	Large (approximately 30-fold greater)	Small
Availability	Minimum 30 min	Immediate
Administration rate	Slow	Fast (*)
Viral inactivation	Methylene blue	Two steps
Specific blood group	Yes	No
Risk of TRALI	Yes	No
Hypocalcemia by citrate	Yes	No
Thrombogenicity risk	No	Yes
Factor content	All	II, VII, IX, X

FFP: fresh frozen plasma; PCC: prothrombin complex concentrate; TRALI: transfusion-related acute lung injury.
(*) Infusion rate varies for the different PCCs, with accepted rates of 3 mL/min for Octaplex, 5 mL/min for Prothromplex NF, and a maximum of 8.4 mL/min for Beriplex.

PFC vs CCP

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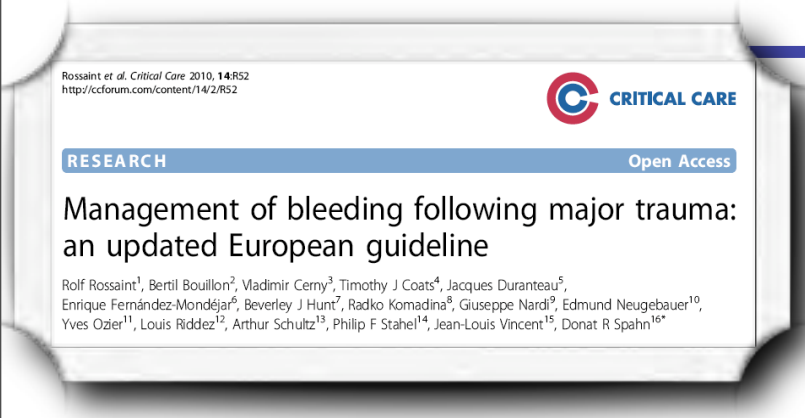
TABLE II.—*Contents in coagulation and anticoagulant factors of fresh frozen plasma and prothrombin complex concentrates marketed in Spain (data in IU/mL).*

	FFP (*) (IU/mL)	PROTHROMPLEX INF (IU/mL)	BERIPLEX (IU/mL)	OCTAPLEX (IU/mL)
F-II	1	30	20-48	11-38
F-VII	1	25	10-25	9-24
F-IX	1	30	20-31	25
F-X	1	30	22-60	18-30
Protein C	1	>20	15-45	7-31
Protein S	1	14-16	13-26	7-32
AT	1	0.75-1.5	9.2-1.5	—
Heparin	—	15.5	0.4-2.0	5-12.5
Viral inactivation/ elimination	MB —	Steam treatment Nanofiltration	Pasteurization Nanofiltration	Solvent-detergent Nanofiltration

FFP: fresh frozen plasma; MB: methylene blue; AT: antithrombin.
(*) By definition, FFP consists of 1 IU/mL of each of the stable and labile coagulation factors (±25%), except for fibrinogen. (Prothrombin complex concentrate data based on manufacturer information and on the labels of the different products available at www.agemed.es)

Evidencias y controversias



Rossaint *et al. Critical Care* 2010, **14**:R52
http://ccforum.com/content/14/2/R52

CRITICAL CARE

RESEARCH Open Access

Management of bleeding following major trauma: an updated European guideline

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3], Timothy J Coats[4], Jacques Duranteau[5], Enrique Fernández-Mondéjar[6], Beverley J Hunt[7], Radko Komadina[8], Giuseppe Nardi[9], Edmund Neugebauer[10], Yves Ozier[11], Louis Riddez[12], Arthur Schultz[13], Philip F Stahel[14], Jean-Louis Vincent[15], Donat R Spahn[16*]

Recommendation 24 We recommend early treatment with thawed FFP in patients with massive bleeding (Grade 1B). The initial recommended dose is 10 to 15 ml/kg. Further doses will depend on coagulation monitoring and the amount of other blood products administered (Grade 1C).

Evidencias y controversias

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CURRENT OPINION

Managing clotting: a North American perspective

Roman M. Sniecinski[a], *Keyvan Karkouti*[b,c], *and Jerrold H. Levy*[a]

Curr Opin Anesthesiol 2012, 25:74–79

Many guidelines recommended a dose of 10–15 mL.kg^{-1} [39]; however, Stanworth *et al.* and others have shown this dose may not be adequate to achieve a clinically meaningful change in coagulation factor levels [40▪▪,41], anticipating that higher doses (30 ml/kg) would be needed, which represent a disturbing amount of fluid in cardiovascular compromised patients. The

Evidencias y controversias

Coagulation management in massive bleeding

Matthew J. Griffee[a], Thomas G. DeLoughery[b] and Per A. Thorborg[a]

Current Opinion in Anaesthesiology 2010, 23:263–268

Although the primary indications for PCC are warfarin reversal and treatment of bleeding in hemophiliac patients with inhibitors, PCC has been used in the setting of massive bleeding after cardiac, vascular, and other surgery [28]. PCC used to treat perioperative bleeding refractory to FFP, platelets, and cryoprecipitate resulted in hemostasis in 78% of patients and was associated with reduced transfusion requirements [28]. More recent PCC products are believed to be less thrombogenic than older PCC formulations [27•].

Evidencias y controversias

British Journal of Anaesthesia **111** (S1): i71–i82 (2013)
doi:10.1093/bja/aet376

Update on massive transfusion

H. P. Pham[1,2] and B. H. Shaz[1,3*]

Prothrombin complex concentrate (PCC) has been used to treat congenital coagulation disorders and for warfarin reversal in patients with active bleeding or undergoing urgent procedures. PCC contains factors II, VII, IX, and X, and proteins C and S, with variations in the amount of factors between different products; thus, it is important to know which PCC product is available at the institution. PCC can be three-factor, such as Profilnine SD (Grifols Biologicals, Los Angeles, CA, USA) (lacking factor VII), or four-factor, such as Kcentra (CSL Behring, King of Prussia, PA, USA). To date, there has not been any prospective randomized controlled trial to evaluate the efficacy and safety of PCC in massively bleeding patients. In addition, PCC might be associated with thromboembolic risk as shown in animal studies.[74 75] Hence, it is advisable to discuss the risks and benefits of using PCC as an adjunctive therapy in any institutionally MTP and it is recommended that PCC usage should be continually evaluated.

Complejo protrombínico

Perioperative use of prothrombin complex concentrates

M. J. COLOMINA [1], A. DÍEZ LOBO [2], I. GARUTTI [3], A. GÓMEZ-LUQUE [4], J. V. LLAU [5], E. PITA [6]

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Indications

Accepted indications

Administration of PCCs is indicated for:

1) prophylaxis and treatment for bleeding in patients with congenital deficiencies of factors of the prothrombin complex (factors II, VII, IX, and X) in the absence of specific factors (recommendation 1B);

2) prophylaxis and treatment of bleeding in patients with acquired deficiencies of factors of the prothrombin complex (overall recommendation in this indication 1B).

Fibrinógeno

Rossaint et al. Critical Care 2010, 14:R52
http://ccforum.com/content/14/2/R52

CRITICAL CARE

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Fibrinogen and cryoprecipitate

Recommendation 26 We recommend treatment with fibrinogen concentrate or cryoprecipitate if significant bleeding is accompanied by thrombelastometric signs of a functional fibrinogen deficit or a plasma fibrinogen level of less than 1.5 to 2.0 g/l (Grade 1C). We suggest an initial fibrinogen concentrate dose of 3 to 4 g or 50 mg/kg of cryoprecipitate, which is approximately equivalent to 15 to 20 units in a 70 kg adult. Repeat doses may be guided by thrombelastometric monitoring and laboratory assessment of fibrinogen levels (Grade 2C).

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Fibrinógeno

The early use of fibrinogen, prothrombin complex concentrate, and recombinant-activated factor VIIa in massive bleeding

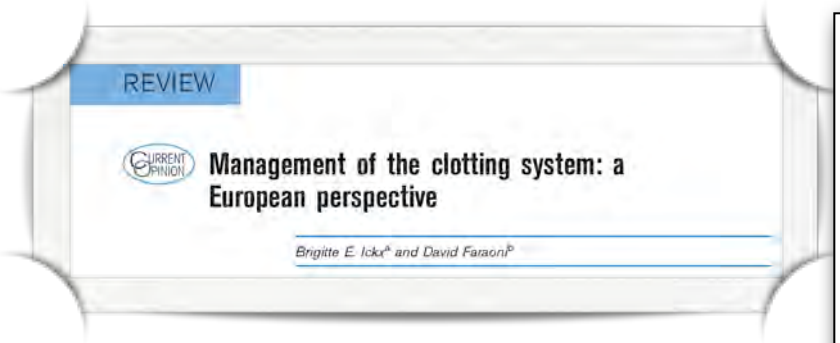
Dietmar Fries

TRANSFUSION 2013;53:91S-95S.

FIBRINOGEN CONCENTRATE

In severe traumatized and massively bleeding patients, fibrinogen usually reaches critical levels at an early stage. Clinical data from gynecology,[8] neurology,[9] and cardiac surgery[10] show that the perioperative and postoperative hemorrhagic tendency is increased when fibrinogen levels are below 150-200 mg/dL. Data on the efficacy of fibrinogen concentrates in acquired fibrinogen deficiency are limited. In vitro studies and experimental investigations, as well as reports from postmarketing surveillance and retrospective data analyses,[11-17] have shown consistently that fibrinogen can increase clot firmness and improves survival of severely injured massively bleeding patients or soldiers.[18] Four small prospective clinical studies examined the use of fibrinogen concentrate (thrombelastometry [ROTEM, TEM Innovation, Munich, Germany], assisted in two studies). In all four studies, coagulation was optimized, perioperative bleeding was reduced by 32%, and transfusion requirement was significantly reduced.[19-22]

Fibrinógeno


REVIEW

Management of the clotting system: a European perspective

Brigitte E. Ickx[a] and David Faraoni[b]

Curr Opin Anesthesiol 2012, 25:80–85

On the basis of previous guidelines, the targeted plasmatic fibrinogen concentration is 1 g/l in a bleeding patient [39]. Plasma fibrinogen replacement may be achieved either with FFP, cryoprecipitates (which are no longer available in many European countries), or fibrinogen concentrates. Twenty-five times more volume is needed to reach the same amount of fibrinogen using FFP compared with fibrinogen concentrates [41]. Moreover, viroinactivated fibrinogen concentrates obtained from human plasma are safer than FFP and cryoprecipitates and can be rapidly reconstituted. Decreased plasmatic fibrinogen levels have been associated with increased bleeding after cardiac surgery [44–46]. In animal experiments and in-vitro studies, fibrinogen supplementation has been shown to counteract both dilutional coagulopathy and impaired hemostasis caused by PLT deficiency [47,48]. For these reasons, some authors argue that the targeted concentration should be increased to 1.5–3 g/l [49,50]. To date, data on this hemostatic agent are limited and further investigations are needed to assess its safety.

Tranexámico

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

CRASH-2 trial collaborators*

www.thelancet.com Published online June 15, 2010 DOI:10.1016/S0140-6736(10)60835-5

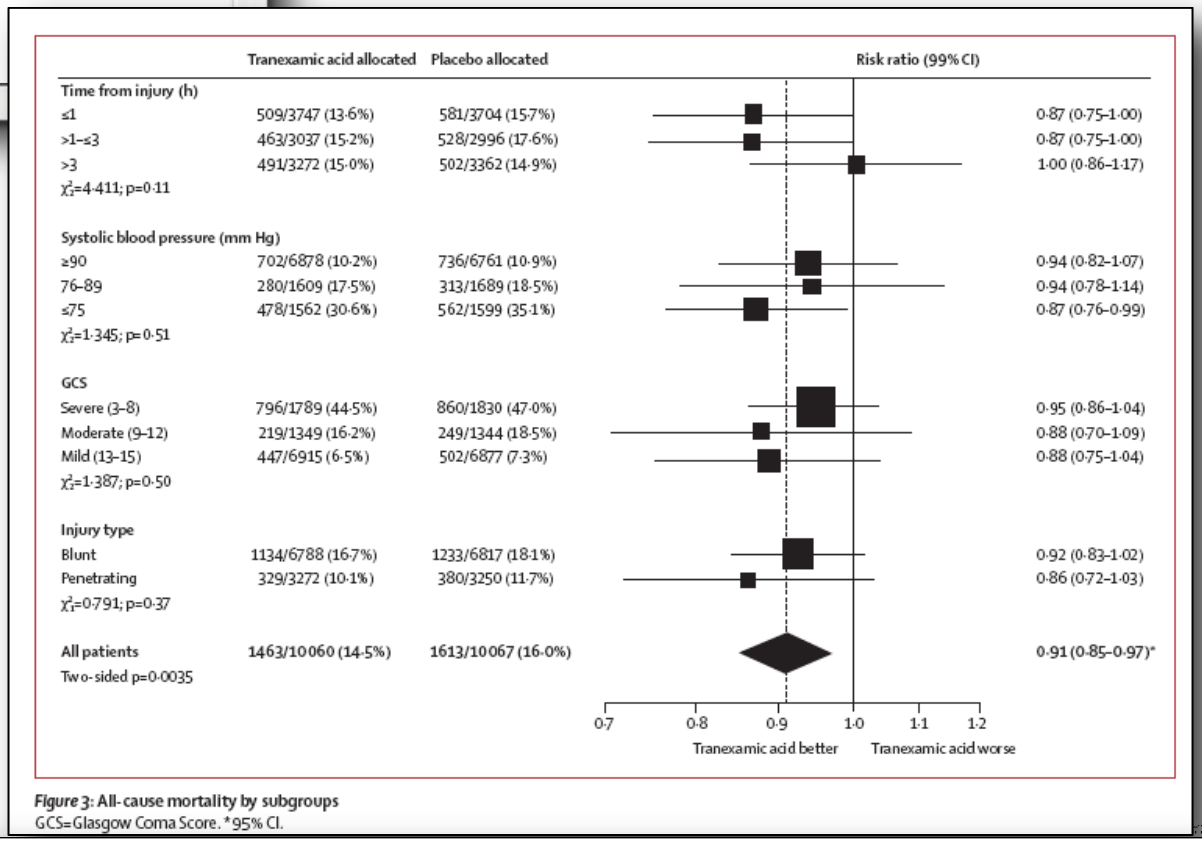


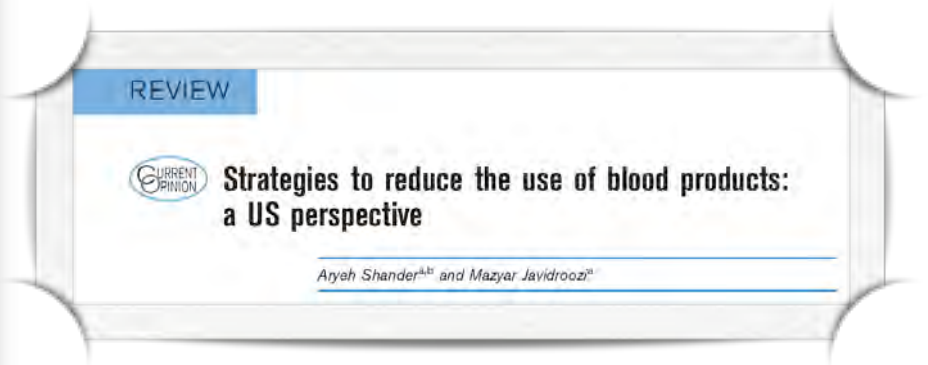
Figure 3: All-cause mortality by subgroups
GCS=Glasgow Coma Score. *95% CI.

Interpretation Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.

F VIIa

Recombinant activated factor VII (rFVIIa) – approved in the USA for treatment or prevention of bleeding in hemophilia and congenital factor VII deficiency – has been increasingly investigated and used on an 'off-label' basis as a hemostatic agent [62]. A systematic review of 25 trials on off-label use of rFVIIa to control or prevent bleeding concluded that rFVIIa reduced blood loss and RBC transfusions, but had no benefit in terms of reducing mortality [63], whereas another systematic review indicated no mortality benefits but increased thromboembolic risk [64]. These findings were partially corroborated by another meta-analysis of four randomized trials on prophylactic use of rFVIIa in patients undergoing liver surgery, which could not identify any benefits [65]. Most recently, a randomized trial in actively bleeding major trauma patients indicated that rFVIIa reduced transfusion, but did not impact mortality and tended to be associated with more thromboembolic events [66].

Thromboembolic events are the major safety concern of rFVIIa and meta-analysis of 35 randomized trials has indicated that off-label use of high doses of rFVIIa was associated with increased risk of arterial (but not venous) thromboembolic events [67▪▪]. Available data do not support routine off-label use of rFVIIa. Off-label use of fibrinogen concentrate as a


REVIEW

CURRENT OPINION

Strategies to reduce the use of blood products: a US perspective

Aryeh Shander[a,b] and Mazyar Javidroozi[a]

Fórmula 1:1:1


CRITICAL CARE

REVIEW

Clinical review: Canadian National Advisory Committee on Blood and Blood Products – Massive Transfusion Consensus Conference 2011: report of the panel

Question 1. Formula-driven resuscitation as the standard of care: is there sufficient evidence to justify 1:1:1 formula-driven resuscitation as the standard of care for bleeding trauma patients?

Recommendation of the Consensus Panel

As a result of the above considerations, especially the limited scientific evidence, the panel concluded that 1:1:1 formula-driven care cannot be recommended as a national standard of care for Canada. Practice recommendations for transfusion support are offered in the Discussion.

Fórmula 1:1:1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Fórmula 1:1:1

New developments in massive transfusion in trauma

Sarah E. Greer[a], Kurt K. Rhynhart[a], Rajan Gupta[a] and Howard L. Corwin[b]

Current Opinion in Anaesthesiology 2010, 23:246–250

Summary

As optimal resuscitation strategies continue to evolve, recent efforts have focused on early and aggressive treatment of coagulopathy, with higher ratios of plasma and platelets to red blood cells transfused. Early evidence suggests that such strategies have a beneficial outcome in regards to trauma-related mortality.

Fórmula 1:1:1

Managing clotting: a North American perspective

Roman M. Sniecinski[a], *Keyvan Karkouti*[b,c], *and Jerrold H. Levy*[a]

Curr Opin Anesthesiol 2012, 25:74–79

this setting, protocols using specified ratios of fresh frozen plasma (FFP) and platelets are transfused following red blood cell units often in a 1 : 1 : 1 ratio [7]. In trauma and with massive hemorrhage, fixed transfusion ratios are reported to improve survival, and multiple civilian studies have suggested improved outcome with earlier and increased use of plasma and platelets, but studies in this area are preliminary in nature and sometimes contradictory [6,7]. Thus, further studies are needed before higher platelet and plasma ratios can be recommended. As suggested by Holcolmb, a multicenter prospective observational study is underway with randomized trials planned to determine optimal plasma : platelet : red blood cell transfusion ratios.

Fórmula 1:1:1

CURRENT OPINION

Plasma/platelets/red blood cell ratio in the management of the bleeding traumatized patient: does it matter?

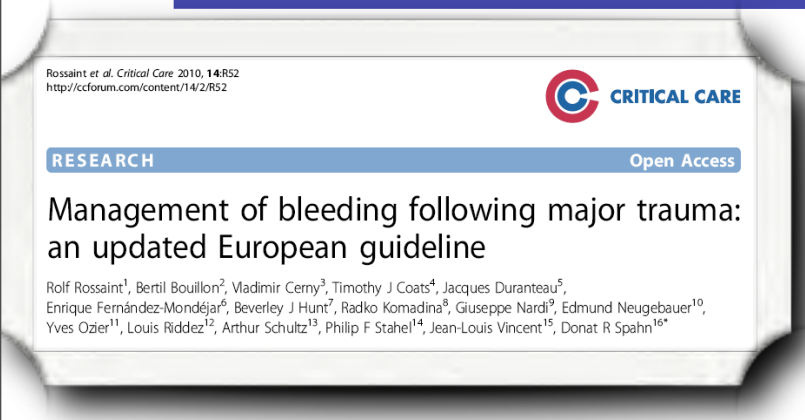
Anne Godier[a], Charles-Marc Samama[a], and Sophie Susen[b,c]

Curr Opin Anesthesiol 2012, 25:242–247

KEY POINTS

- A growing body of evidence supports that high FFP/PLT/RBC ratios improve survival of the massively transfused trauma patient.
- Acting quickly is critical as there is a temporal relationship between aggressive plasma transfusions and survival.
- Reducing transfusion delay can be achieved through massive transfusion protocol implementations, which incorporate local agreements with blood banks and trauma packs.
- Thawed plasma and freeze-dried plasma allow immediate delivery of plasma.
- Immediate delivery of blood products should be provided to the right, accurately screened patients in organized trauma systems.

Hb objetivo



Rossaint *et al. Critical Care* 2010, **14**:R52
http://ccforum.com/content/14/2/R52

CRITICAL CARE

RESEARCH Open Access

Management of bleeding following major trauma: an updated European guideline

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3], Timothy J Coats[4], Jacques Duranteau[5], Enrique Fernández-Mondéjar[6], Beverley J Hunt[7], Radko Komadina[8], Giuseppe Nardi[9], Edmund Neugebauer[10], Yves Ozier[11], Louis Riddez[12], Arthur Schultz[13], Philip F Stahel[14], Jean-Louis Vincent[15], Donat R Spahn[16*]

Erythrocytes

Recommendation 21 We recommend a target haemoglobin (Hb) of 7 to 9 g/dl (Grade 1C).

Rationale Erythrocytes contribute to haemostasis by influencing the biochemical and functional responsiveness of activated platelets via the rheological effect on platelet margination and by supporting thrombin generation [221]; however, the optimal Hct or Hb concentration required to sustain haemostasis in massively bleeding patients is unclear. Further investigations into the role of the Hb concentration on haemostasis in massively transfused patients are therefore warranted.

Hb objetivo

Rossaint et al. Critical Care 2010, 14:R52
http://ccforum.com/content/14/2/R52

CRITICAL CARE

RESEARCH Open Access

Management of bleeding following major trauma: an updated European guideline

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3], Timothy J Coats[4], Jacques Duranteau[5], Enrique Fernández-Mondéjar[6], Beverley J Hunt[7], Radko Komadina[8], Giuseppe Nardi[9], Edmund Neugebauer[10], Yves Ozier[11], Louis Riddez[12], Arthur Schultz[13], Philip F Stahel[14], Jean-Louis Vincent[15], Donat R Spahn[16*]

Despite the lack of high-level scientific evidence for a specific Hb transfusion trigger in patients with TBI, these patients are currently transfused in many centres to achieve an Hb of approximately 10 g/dl [239]. This might be justified by the recent finding that increasing the Hb from 8.7 to 10.2 g/dl improved local cerebral oxygenation in 75% of patients [158]. In another preliminary study in patients with TBI, one to two RBC transfusions at a Hb of approximately 9 g/dl transiently (three to six hours) increased cerebral oxygenation, again in approximately 75% of patients [240,241]. A storage time of more than 19 days precluded this effect [240]. In another recent study, cerebral tissue oxygenation, on average, did not increase due to an increase in Hb from 8.2 to 10.1 g/dl [242]. Nevertheless, the authors came to the conclusion based on multivariable statistical models that the changes in cerebral oxygenation correlated significantly with Hb concentration [242]. This conclusion, however, was questioned in the accompanying editorial [243].

CCP: seguridad

Abstract

Prothrombin complex concentrates (PCCs) are used mainly for emergency reversal of vitamin K antagonist therapy. Historically, the major drawback with PCCs has been the risk of thrombotic complications. The aims of the present review are to examine thrombotic complications reported with PCCs, and to compare the safety of PCCs with human fresh frozen plasma. The risk of thrombotic complications may be increased by underlying disease, high or frequent PCC dosing, and poorly balanced PCC constituents. The causes of PCC thrombogenicity remain uncertain but accumulating evidence indicates the importance of factor II (prothrombin). With the inclusion of coagulation inhibitors and other manufacturing improvements, today's PCCs may be considered safer than earlier products. PCCs may be considered preferable to fresh frozen plasma for emergency anticoagulant reversal, and this is reflected in the latest British and American guidelines. Care should be taken to avoid excessive substitution with prothrombin, however, and accurate monitoring of patients' coagulation status may allow thrombotic risk to be reduced. The risk of a thrombotic complication due to treatment with PCCs should be weighed against the need for rapid and effective correction of coagulopathy.

CCP: seguridad

Prothrombin complex concentrates in emergency bleeding disorders

George M. Rodgers*

Am. J. Hematol. 87:898–902, 2012.

Thrombotic complications

PCC use has been associated with the emergence of serious thrombotic events, especially at high doses and in patients with severe liver disease [2]. Thrombotic complications that have been linked to PCC therapy include venous thromboembolism, disseminated intravascular coagulation, microvascular thrombosis, and myocardial infarction [4]. Results of a recent literature search revealed that the incidence of thromboembolic events with PCC treatment was ~ 1.8% in patients receiving 4-factor PCCs and 0.7% in patients receiving 3-factor PCCs [56]. These findings suggest that the risk of thromboembolic complications with the use of PCCs is low, but not clinically insignificant. In clinical studies of PCCs, patients manifesting an elevated risk of thrombotic events usually have a relevant medical history or current illness, and these underlying thrombotic risk factors may become clinically salient when VKA-related anticoagulation is reversed [4]. In newer PCCs, the inclusion of proteins C, S, and Z, among other anticoagulation factors depleted by VKAs, may represent a more balanced approach that, in theory, could mitigate thrombotic risks [4].

CCP: seguridad

Safety of prothrombin complex concentrates for rapid anticoagulation reversal of vitamin K antagonists

A meta-analysis

Francesco Dentali[1]; Chiara Marchesi[1]; Matteo Giorgi Pierfranceschi[2]; Mark Crowther[3]; David Garcia[4]; Elaine Hylek[5]; Daniel M. Witt[6,7]; Nathan P. Clark[6]; Alessandro Squizzato[1]; Davide Imberti[8]; Walter Ageno[1]

doi:10.1160/TH11-01-0052
Thromb Haemost 2011; 106: 429–438

Summary

Prothrombin complex concentrates (PCCs) are recommended as the treatment of choice in warfarin-related coagulopathy. However, the risk of thromboembolic complications associated with their use is not well defined. We performed a meta-analysis to estimate the rate of thromboembolic complications in patients receiving vitamin K antagonists (VKAs) treated with PCCs for bleeding or before urgent surgery. Medline and Embase databases were searched. Two reviewers performed study selection and extracted data independently. Studies providing data on incidence of thromboembolic complications in VKA-treated patients were eligible for the study. Weighted mean proportion of the rate of thromboembolic complications and the mortality rate were calculated. Twenty-seven studies (1,032 patients) were included. Seven studies used 3-factor, and 20 4-factor PCCs. Twelve patients had a thromboembolic complication (weighted mean 1.4%; 95% CI 0.8–2.1), of which two were fatal. The incidence of thromboembolic events was 1.8% (95% CI 1.0–3.0) in patients treated with 4-factor PCCs, and 0.7% (95% CI 0.0–2.4) in patients treated with 3-factor PCCs. Total mortality rate was 10.6% (95% CI 5.9–16.6). In conclusion, our results suggest there is a low but quantifiable risk of thromboembolism in VKA-treated patients receiving PCCs for anticoagulation reversal. These findings should be confirmed in randomised, controlled trials.

Keywords

Prothrombin complex concentrates, PCC, coumarins, thromboembolic complications, haemorrhage

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CCP: seguridad

Circulation

American Heart Association

Efficacy and Safety of a 4-Factor Prothrombin Complex Concentrate in Patients on Vitamin K Antagonists Presenting With Major Bleeding: A Randomized, Plasma-Controlled, Phase IIIb Study

Ravi Sarode, Truman J. Milling, Jr, Majed A. Refaai, Antoinette Mangione, Astrid Schneider, Billie L. Durn and Joshua N. Goldstein

Circulation. 2013;128:1234-1243; originally published online August 9, 2013; doi: 10.1161/CIRCULATIONAHA.113.002283

Table 8. Summary of AEs (Intention-to-Treat Safety Population)

AE	No. (%) of Patients 4F-PCC (n=103)	Plasma (n=109)
Any nonserious AE*	66 (64.1)	71 (65.1)
Related AE†	10 (9.7)	23 (21.1)
AE leading to treatment discontinuation	0	3 (2.8)
Serious AE*	32 (31.1)	26 (23.9)
Related serious AE†	2 (1.9)	4 (3.7)
AEs of interest		
Deaths to day 30	6 (5.8)	5 (4.6)
Deaths to day 45	10 (9.7)	5 (4.6)
Related deaths (to day 45)‡	1 (1.0)	0
Thromboembolic AE	8 (7.8)	7 (6.4)
Related thromboembolic AE†	4 (3.9)	3 (2.8)
Fluid overload or similar cardiac event	5 (4.9)	14 (12.8)
Related fluid overload or similar cardiac event†	0	7 (6.4)

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CCP: seguridad

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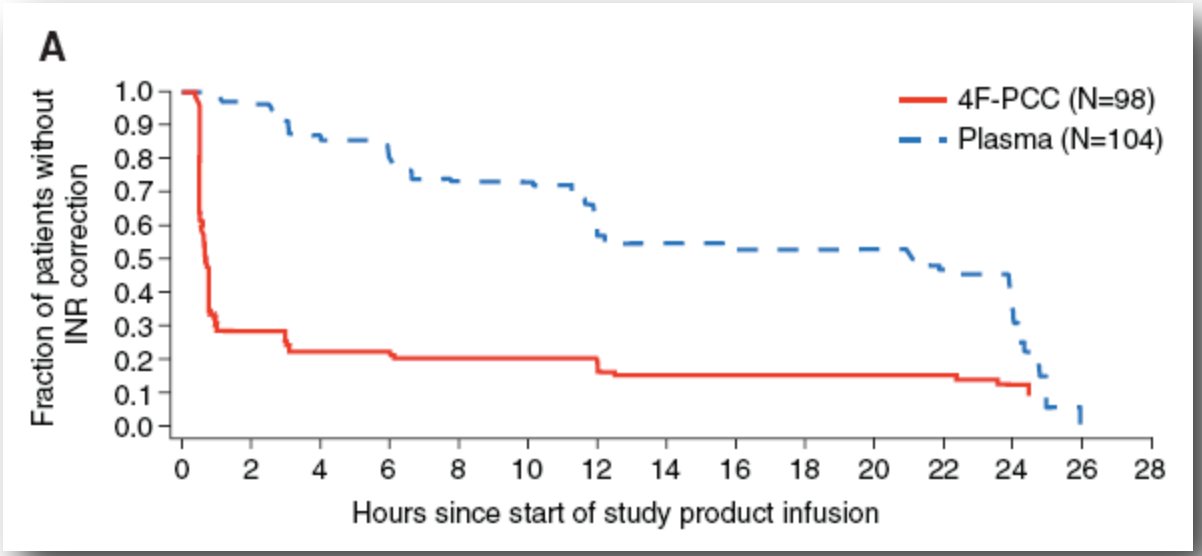
doi: 10.1161/CIRCULATIONAHA.113.002283

Table 4. Study Product Infusion Details and Details of Concomitant Packed Red Blood Cell Use (Intention-to-Treat Efficacy Population)

Parameter	4F-PCC (n=98)	Plasma (n=104)
Study product*		
Duration, median (range), min	17.0 (7–288)	148.0 (26–928)
Total volume, median (range), mL	99.4 (50–230)	813.5 (400–1525)
Infusion rate, median (range), IU/min for 4F-PCC, mL/min for plasma	154.1 (7.3–307.1)	6.6 (1.1–38.8)



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CCP: seguridad

Sørensen et al. Critical Care 2011, 15:201
http://ccforum.com/content/15/1/201

CRITICAL CARE

REVIEW

Clinical review: Prothrombin complex concentrates - evaluation of safety and thrombogenicity

Benny Sørensen[1*], Donat R Spahn[2], Petra Innerhofer[3], Michael Spannagl[4] and Rolf Rossaint[5]

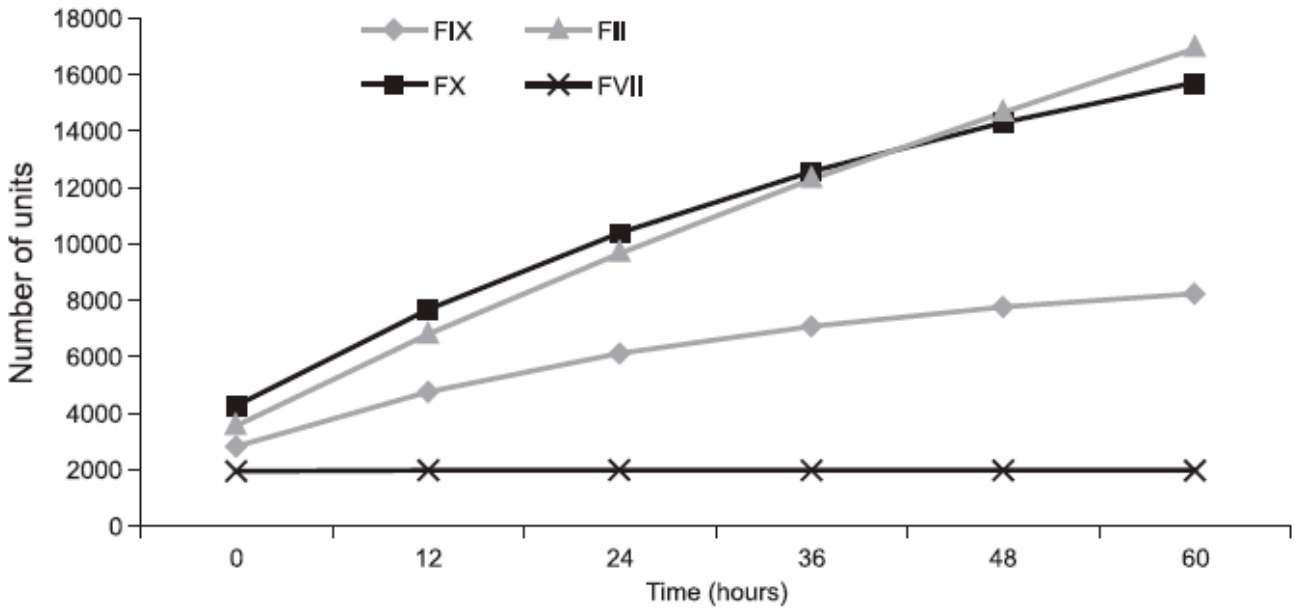

Figure 1. Coagulation factors accumulate differently when a prothrombin complex concentrate is administered repeatedly. Illustration of how coagulation factors accumulate differently when a prothrombin complex concentrate (PCC) is administered repeatedly due to their different half-lives. The example shows the theoretical accumulation of factors in plasma sampled immediately after dosing when 40 units/kg four-factor PCC is given every 12 hours to a 70 kg patient.

Protocolos de Transfusión Masiva

British Journal of Anaesthesia **111** (S1): i71–i82 (2013)
doi:10.1093/bja/aet376

Update on massive transfusion

H. P. Pham[1,2] and B. H. Shaz[1,3]*

Massive transfusion protocols

One way to coordinate the care for patients requiring MT is to develop an institutional MTP to facilitate communication between different services (trauma, nursing, transfusion medicine, and other laboratories), avoid delay in clinical care, laboratory testing and blood product transfusion, and nursing care. MTP is a way to assure good patient care by having a standard protocol on specific actions to take for each service involved. MTPs have demonstrated improved patients survival and reduced rates of organ failure and post-trauma complications.[29] The development, implementation, and continuous improvement of an MTP require ongoing collaboration between different clinical services. When developing an MTP, determining quality indicators will enable clear parameters to track and trend, such as the time for products preparation and issue, product wastage, laboratory turnaround time, laboratory values, and indications for MTP in order to continuously improve the MTP. An MTP should have the following components:

(i) When and who should initiate MTP.
(ii) Notification of the transfusion service and laboratory regarding start and stop of MTP.
(iii) Laboratory testing algorithm [prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen level, blood gas, and complete blood count], and thromboelastography if available.
(iv) Blood product preparation and delivery (i.e. predetermined transfusion packages).
(v) Other patient care needs (such as blood warmers, nursing care).

Conclusiones - recomendaciones

- Importancia de los factores básicos
- Importancia de un protocolo de TM
- Hemostáticos precoces
- Ac. Tranexámico en politrauma
- Reanimación hipotensiva y Cirugia de Contencion de Daños
- Antecedentes: valoración de tratamiento especifico para tomadores de AAP o ACO y otros escenarios
- Valorar CCP y Fibrinógeno
- Monitorización de la hemostasia: ROTEM si posible

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Valencia, 11 de febrero de 2013

Actualización del manejo de la hemorragia masiva

Juan V. Llau
S. Anestesiología - HCU Valencia
Prof. Asociado Dept. Fisiología - Universidad de Valencia

juanvllau@gmail.com

Valencia, 11 de febrero de 2013

Actualización del manejo de la hemorragia masiva

Muchas gracias por vuestra atención

Juan V. Llau
S. Anestesiología - HCU Valencia
Prof. Asociado Dept. Fisiología - Universidad de Valencia

juanvllau@gmail.com