Actualités du traumatisé sévère

Quelle stratégie transfusionnelle en 2015 ?

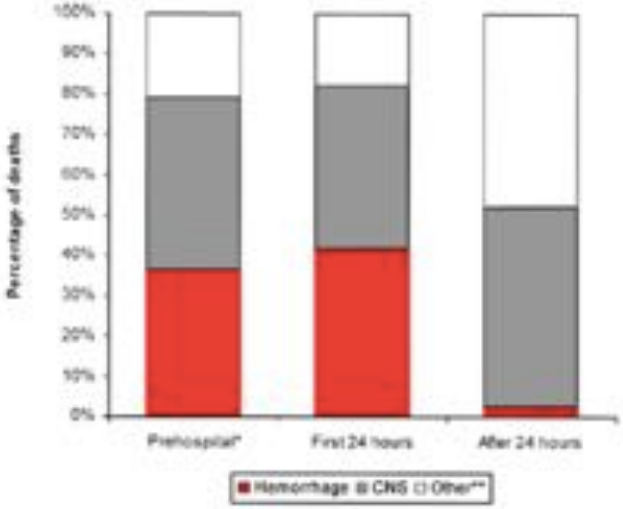
Avril 2015

PY CORDIER
Service de réanimation
HIA Laveran, Marseille

Introduction

Choc hémorragique

- 2ème cause de décès des traumatisés
- 1ère cause de décès évitables

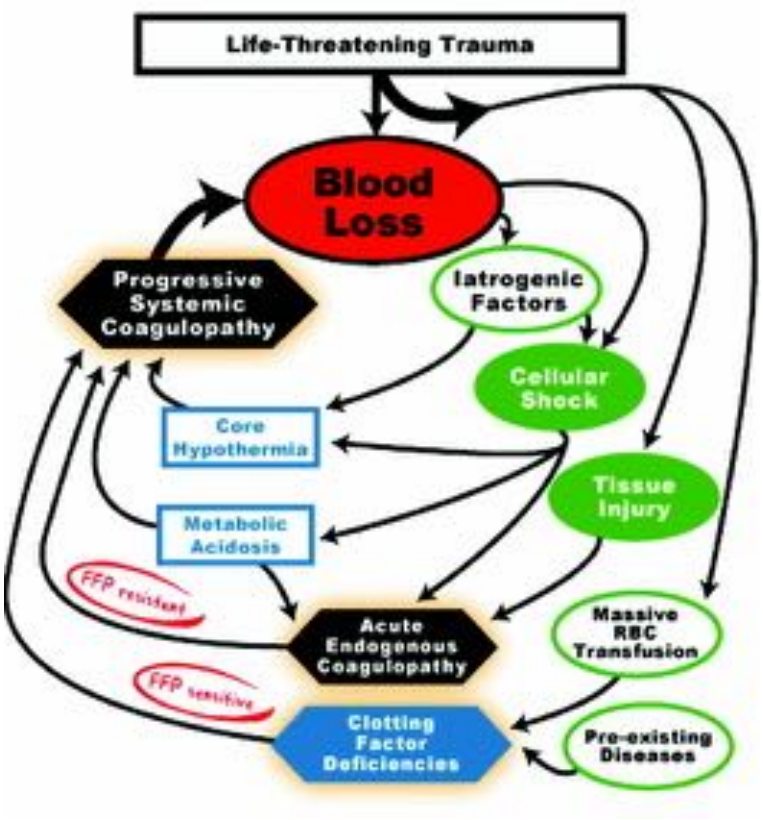


Impact of Hemorrhage on Trauma Outcome

Kauvar, et al. Journal of Trauma. 2006

Introduction

Triade létale



« the lethal triad of

hypothermia, acidosis and coagulopathy

is associated with a

significant increase in mortality »

Damage Control Resuscitation

Holcomb, et al. Journal of Trauma. 2007

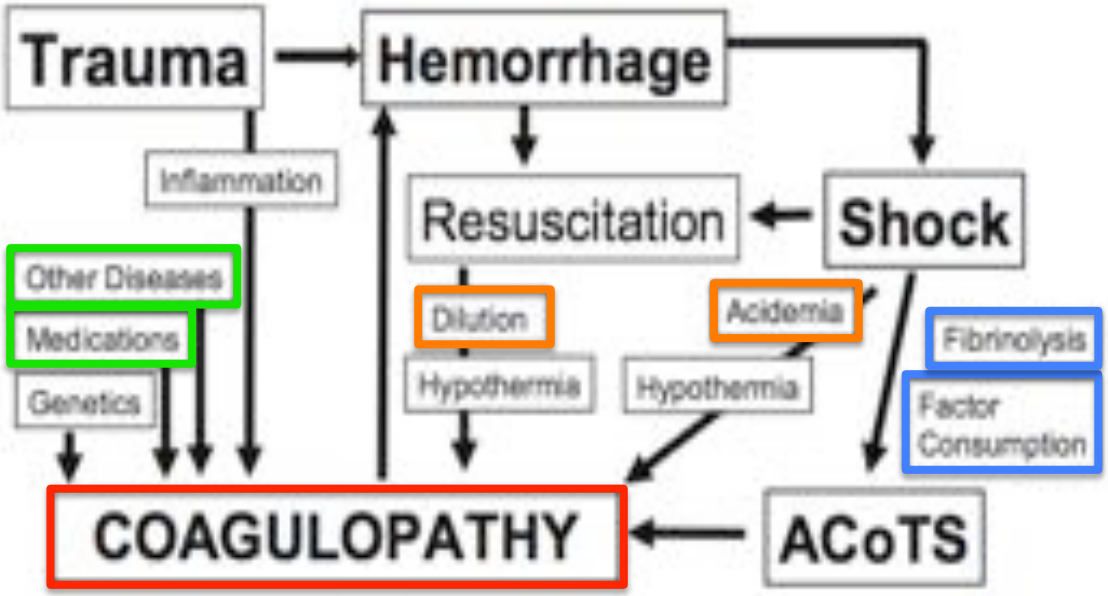
Introduction

Coagulopathie post-traumatique

Review Article

The Journal of TRAUMA® Injury, Infection, and Critical Care

The Coagulopathy of Trauma: A Review of Mechanisms

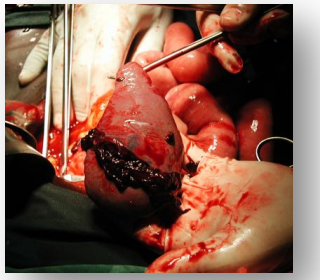


Hess, et al. Journal of Trauma 2008

Introduction

Stratégie de Damage control

Damage Control
Ground Zero



Damage Control Surgery

Second look chirurgical

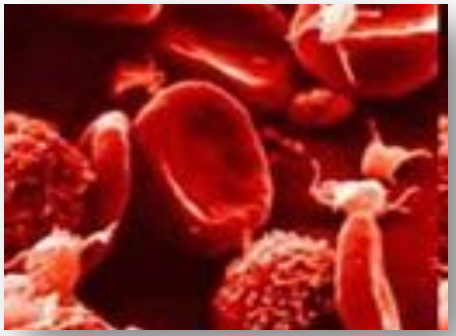
Damage Control Resuscitation

Réanimation transfusionnelle

« Damage control hématologique »

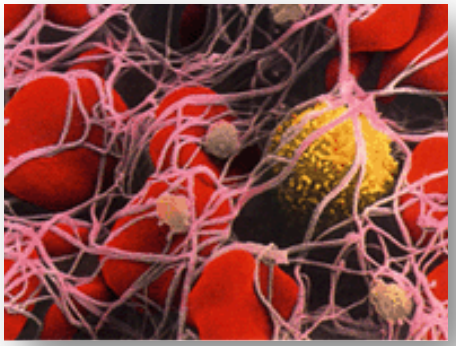
Réanimation transfusionnelle

Objectifs



Restaurer le pouvoir oxyphorique

- **Transfusion érythrocytaire**



Traiter la coagulopathie

- Transfusion **plasma** et **plaquettes**
- Administration **agents pro coagulants**

Réanimation transfusionnelle

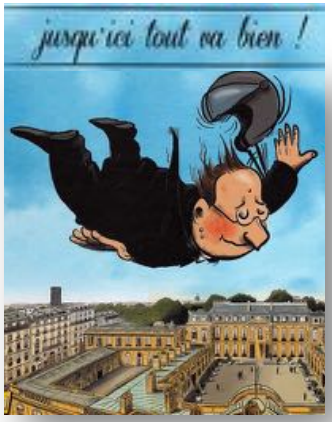
Stratégie

Objectifs transfusionnels

connus chez patients stabilisés…

…Seuils transfusionnels

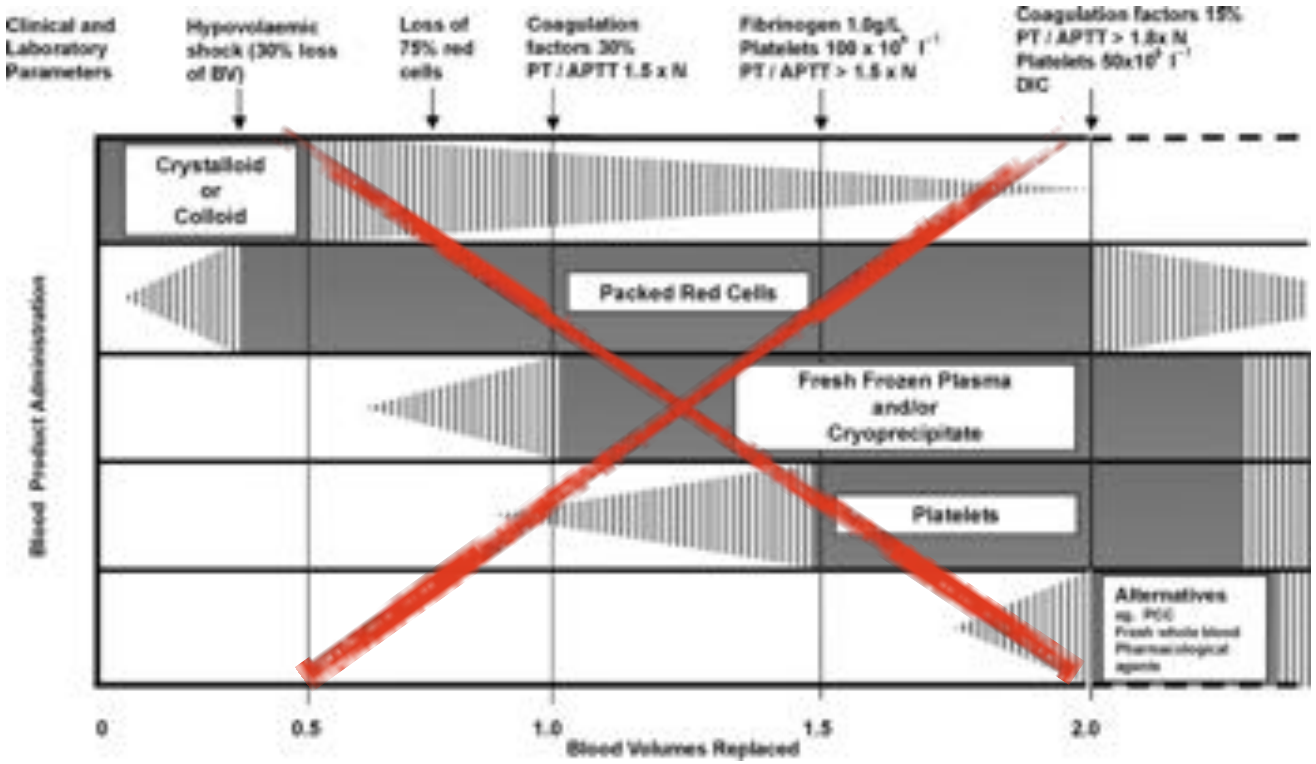
inadaptés au contexte d'une hémorragie active



- **Anticipation** des besoins transfusionnels
- **Protocole transfusionnels** basés sur des **ratios**

Réanimation transfusionnelle

Stratégie



Massive blood transfusion in the elective surgical setting.

Erber, et al. Transfus Apher Sci. 2002

Stratégie transfusionnelle

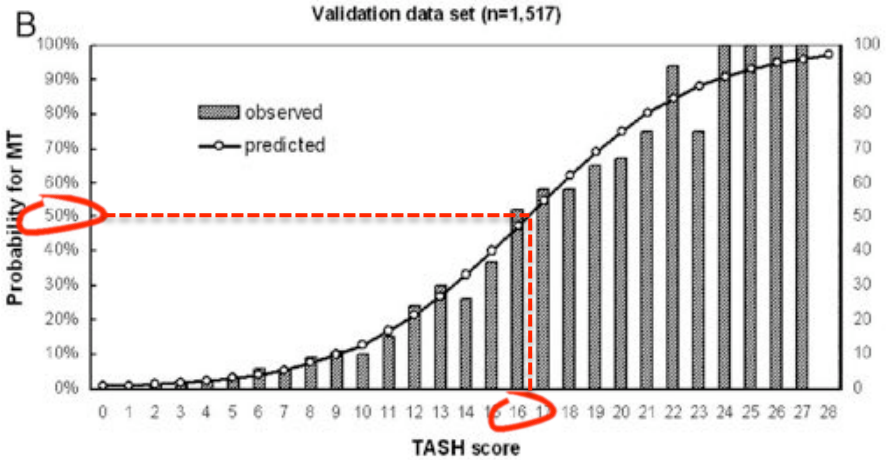
Anticiper les besoins transfusionnels

Identifier les patients à risque de transfusion massive

Table 3 Final TASH Score

Variable	Value	Points
Hemoglobin (mg/dL)	<7	8
	<9	6
	<10	4
	<11	3
	<12	2
Base excess (mmol/L)	<−10	4
	<−6	3
	<−2	1
Systolic blood pressure (mm Hg)	<100	4
	<120	1
Heart rate (beats/min)	>120	2
Free intraabdominal fluid (e.g. by FAST)		
Extremities		3
Clinically instable pelvic fracture		6
Clinically femur fracture open/dislocated		3
Male patient		1

FAST, focused assessment sonography in trauma.



Trauma Associated Severe Hemorrhage (TASH)-Score

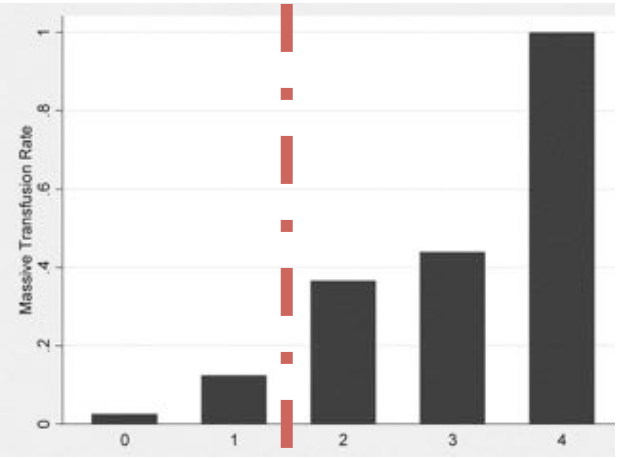
Yücel, et al. Journal of Trauma, 2006

Stratégie transfusionnelle

Anticiper les besoins transfusionnels

Early Prediction of Massive Transfusion in Trauma: Simple as ABC (Assessment of Blood Consumption)?

1. Penetrating mechanism
2. ED SBP of 90 mmHg or less
3. ED HR of 120 bpm or greater
4. Positive FAST



Nunez, et al. Journal of Trauma, 2009

Stratégie transfusionnelle

Anticiper les besoins transfusionnels

Early Predictors of Massive Transfusion in Combat Casualties

	Value	Odds ratio	95% CI
HGB (g/dL)	≤11	7.7	5.0–11.9
INR	>1.5	5.9	3.5–10.2
Penetrating mechanism	Yes	2.6	1.4–4.8

HGB, hemoglobin; INR, International Normalized Ratio.

Schreiber, et al. J Am Coll Surg, 2007

Stratégie transfusionnelle

Standardiser les pratiques

Procédure locale de gestion de l'hémorragie massive

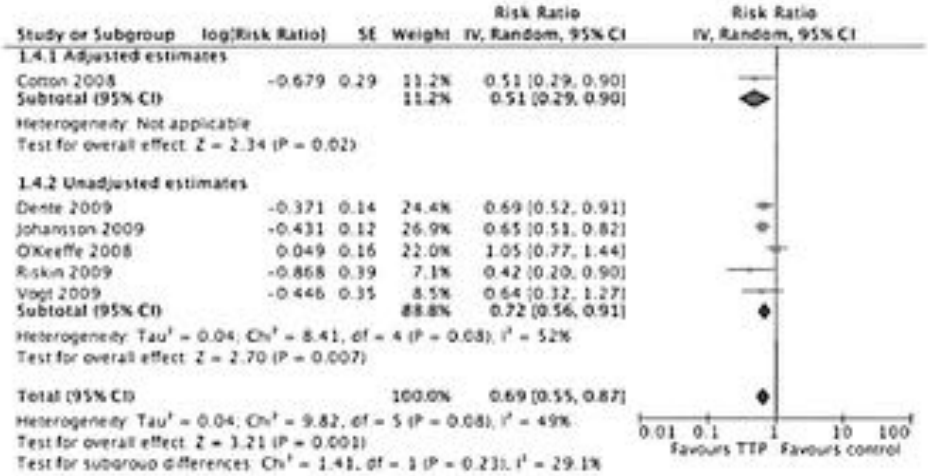
- Critères de déclenchement
- Quantité de PSL et d'agents hémostatiques
- **Ratios transfusionnels**, séquence d'administration
- Distribution conjointe en « packs transfusionnels »
- Procédure de délivrance rapide
- Procédure de délivrance en l'absence de résultats immuno hématologiques

RFE SFAR 2014

Stratégie transfusionnelle

Standardiser les pratiques

The use of trauma transfusion pathways for blood component transfusion in the civilian population: a systematic review and meta-analysis*



Study or Subgroup	log(Risk Ratio)	SE	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 Adjusted estimates				
Cotton 2008	-0.679	0.29	11.2%	0.51 [0.29, 0.90]
Subtotal (95% CI)			11.2%	0.51 [0.29, 0.90]
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.34 (P = 0.02)				
1.4.2 Unadjusted estimates				
Dente 2009	-0.371	0.14	24.4%	0.69 [0.52, 0.91]
Johansson 2009	-0.431	0.12	26.9%	0.65 [0.51, 0.82]
O'Keeffe 2008	0.049	0.16	22.0%	1.05 [0.77, 1.44]
Riskin 2009	-0.868	0.39	7.1%	0.42 [0.20, 0.90]
Vogt 2009	-0.446	0.35	8.5%	0.64 [0.32, 1.27]
Subtotal (95% CI)			88.8%	0.72 [0.56, 0.91]
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 8.41$, df = 4 (P = 0.08); $I^2 = 52\%$				
Test for overall effect: Z = 2.70 (P = 0.007)				
Total (95% CI)			100.0%	0.69 [0.55, 0.87]
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 9.82$, df = 5 (P = 0.08); $I^2 = 49\%$				
Test for overall effect: Z = 3.21 (P = 0.001)				
Test for subgroup differences: $Chi^2 = 1.41$, df = 1 (P = 0.23), $I^2 = 29.1\%$				

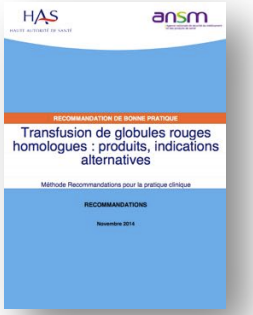
- **Diminution significative de la mortalité** et de la consommation de plasma
- Diminution *(NS)* de la consommation de CGR

Vogt, et al. Transfusion Medicine. 2012

Transfusion érythrocytaire

- **Urgence vitale immédiate :** le délai d'obtention des CGR prime sur le délai d'obtention des résultats immuno-hématologiques
- Transfusion CGR O RH1 KEL-1 (CGR O RH-1 KEL-1 pour les femmes jusqu'à la fin de la période procréatrice)

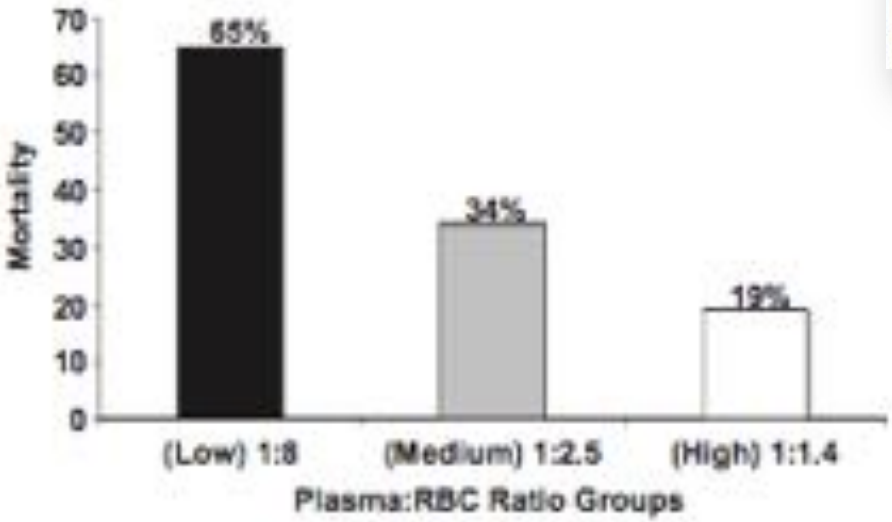
HAS, Novembre 2014



Traitement de la coagulopathie

Transfusion de plasma

Stratégie basée sur des ratios



The Journal of TRAUMA® Injury, Infection, and Critical Care

The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital

Borgman, et al. Journal of trauma, 2007

Traitement de la coagulopathie

Transfusion de plasma

Revue générale

Le ratio transfusionnel PFC/CGR 1/1 : un phénomène de mode basé sur des preuves ?

1/1 plasma to red blood cell ratio: An evidence-based practice?

A. Godier [a], Y. Ozier [b], S. Susen [c,*], pour le Groupe d'intérêt en hémostase périopératoire (GIHP)

Godier, et al. AFAR, 2011

The Journal of TRAUMA® *Injury, Infection, and Critical Care*

The Relationship of Blood Product Ratio to Mortality: Survival Benefit or Survival Bias?

Snyder, et al. Journal of trauma, 2009

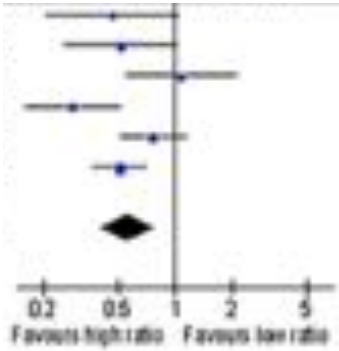
Traitement de la coagulopathie

Transfusion de plasma

Review

Meta-analysis of plasma to red blood cell ratios and mortality in massive blood transfusions for trauma[☆,☆☆]

Aneel Bhangu[a], Dmitri Nepogodiev[a], Heidi Doughty[b], Douglas M. Bowley[a,*]



- 6 études, 1885 patients, ISS comparables
- **Meilleure survie à J30 pour ratio > 1:2**
- Pas de bénéfice supplémentaire pour ratio 1:1

Bhangu, et al. Injury, 2013

→ Ratio 1:2 à 1:1

→ Administration **précoce** de plasma

Traitement de la coagulopathie

PLYO

Plasma lyophilisé (PLYO) - French Lyophilised Plasma (FLYP)

ORIGINAL ARTICLE

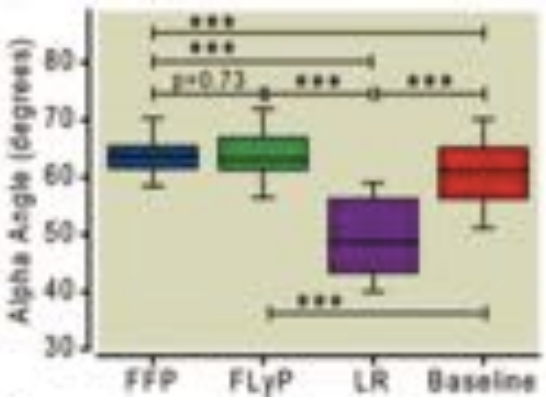
The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service

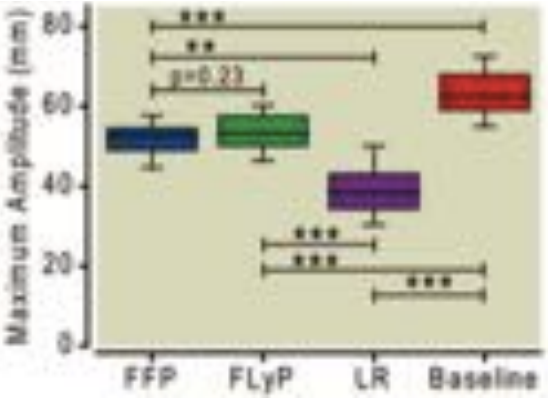
- **Plasma « *AB-like* »** compatible avec tous les groupes sanguins
- Stockage 2 ans à température ambiante
- Reconstitution en moins de 6 minutes

Saillol,et al. Transfusion, 2013

Traitement de la coagulopathie

PLYO





In vitro hemostatic properties of french lyophilized plasma

Martinaud, et al. Anesthesiology, 2012

Traitement de la coagulopathie

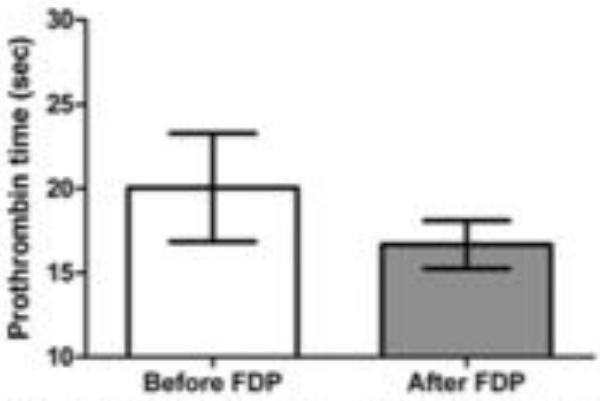
PLYO

Transfusion PLYO à l'HMC KAIA (02/2010 – 02/2011)

ORIGINAL ARTICLE

Use of Freeze-Dried Plasma in French Intensive Care Unit in Afghanistan

- 87 patients – 57 survivants
- 3,5 PLYO en moyenne



Martinaud, et al. Journal of trauma, 2011

Traitement de la coagulopathie

PLYO en pratique civile

Recommandation n°19 : **Mettre en place un PHRC portant sur le plasma lyophilisé dans le secteur de l'anesthésie réanimation et développer une coopération entre EFS et CTSA dans ce sens.**

La filière du sang en France. *Rapport parlementaire, 2013*

Nombreuses applications potentielles :

- Attente décongélation plasma frais
- Etablissements dépourvus de dépôt de sang
- Médecine préhospitalière, médecine de catastrophe

Service de santé des armées

2014 : Etude PREHO-PLYO

CTSA JEAN JULLIARD

Traitement de la coagulopathie

Transfusion de plaquettes

ANESTHESIA & ANALGESIA

current data support the use of plasma:RBC:platelet ratio of 1:1:1.

Shaz,et al. 2009

- Objectifs transfusionnels connus
- Stratégie basée sur des **ratios**
- Transfusion à envisager **dès le deuxième pack transfusionnel**
- Intérêt chez patients sous **antiagrégants plaquettaires**

R28
Platelets
***

Platelets should be administered to maintain a platelet count above 50×10^9/l. A platelet count above 100×10^9/l in patients with ongoing bleeding and/or traumatic brain injury may be maintained. An initial dose of 4-8 platelet concentrates or one aphaeresis pack may be used.

Spahn,et al. 2013

Traitement de la coagulopathie

Transfusion de plaquettes

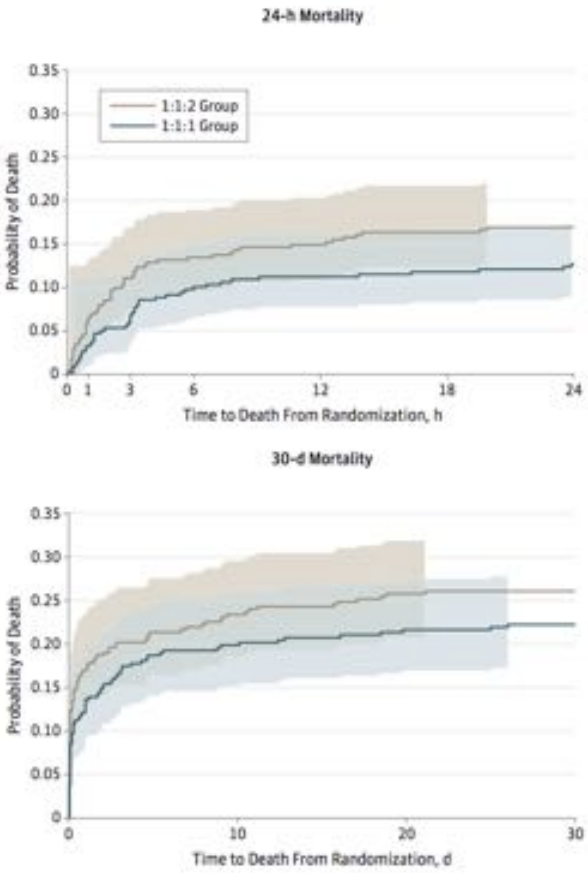
Original Investigation

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma

The PROPPR Randomized Clinical Trial

- 680 patients
- Etude prospective, 12 centres
- Ratio 1:1:1 *vs* 1:1:2
- **Pas de différence de mortalité**

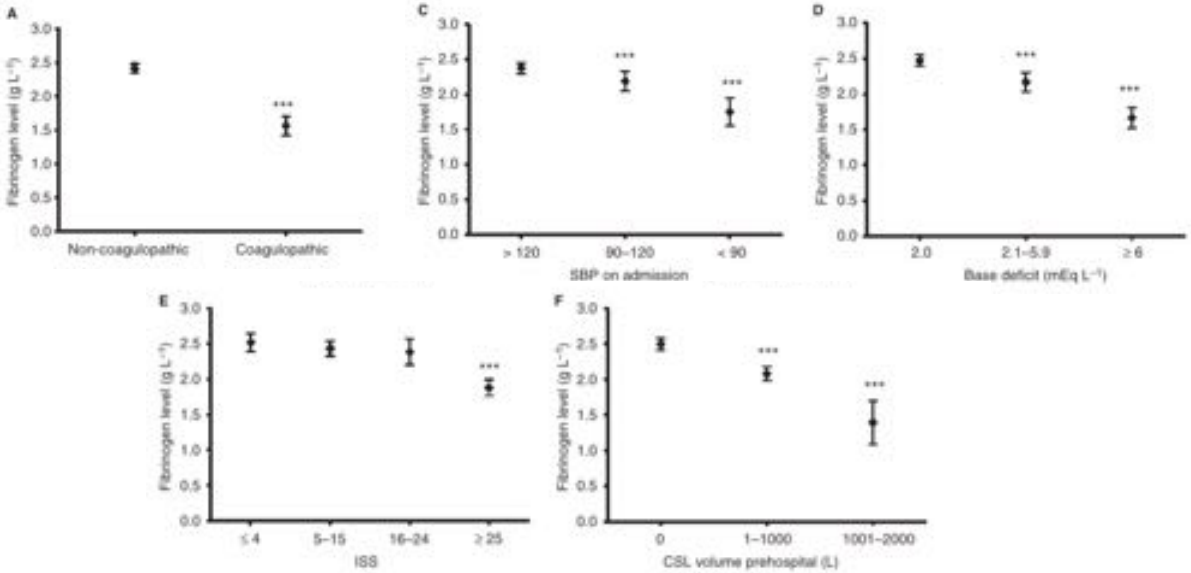
Holcomb,et al. JAMA, 2015



Traitement de la coagulopathie

Fibrinogène

Hypofibrinogénémie chez les patients traumatisés



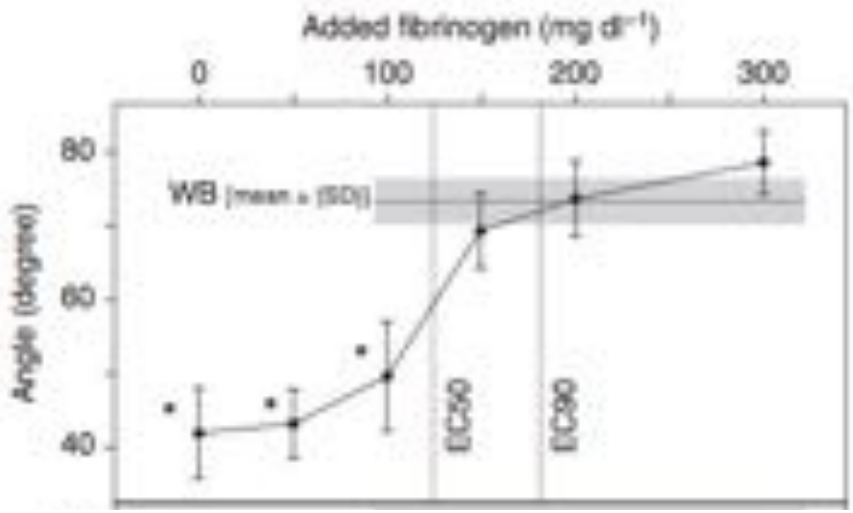
Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes

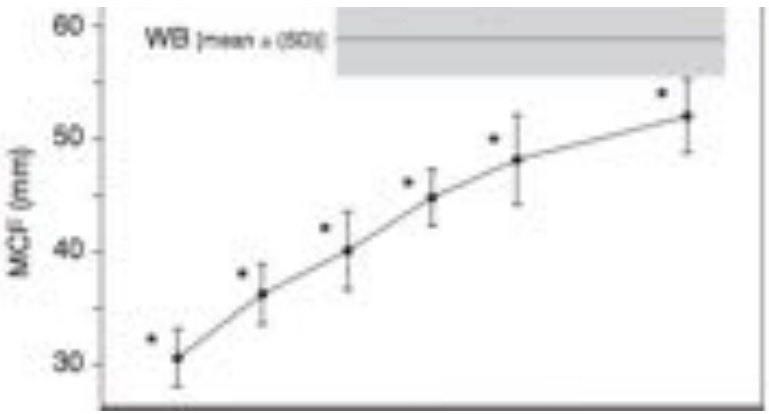
Rourke, et al. Journal of Thrombosis and Haemostasis, 2012

Traitement de la coagulopathie

Fibrinogène

Fibrinogène : concentration cible





Finding the optimal concentration range for fibrinogen replacement after severe haemodilution: an in vitro model

Bolliger, et al. BJA, 2009

Traitement de la coagulopathie

Fibrinogène

Apport de fibrinogène

	Four-unit window	Eight-unit window	Twelve-unit window
Fibrinogen levels (g L^{-1})			
Whole cohort	1.5 (1.2–1.8)	1.5 (1.1–2.0)	1.3 (1.0–1.7)
Received PRBCs alone	1.2 (1.0–1.8)	0.5 (0.4–0.6)	1.0§
PRBCs plus fibrinogen in any form	1.6 (1.4–1.8)^{NS}	1.5 (1.2–2.0)*	1.3 (1.0–1.7)^{NS}
PRBCs plus fibrinogen from FFP or PLTs alone	1.6 (1.4–1.9)	1.5 (1.1–1.5)	1.0 (0.8–1.0)
PRBCs plus fibrinogen from cryoprecipitate and FFP/PLTs¶	1.4 (1.2–1.7)^{NS1}	1.7 (1.3–2.0)^{NS1}	1.6 (1.1–1.9)^{NS1}

Rourke, et al. Journal of Thrombosis and Haemostasis, 2012

- **Monitorer** et **compenser** les hypofibrinogénémies < 1,5 – 2g/L
- Administration de **concentrés de fibrinogène** – dose initiale 3g

Traitement de la coagulopathie

Anti-fibrinolytiques

CRASH2

- 1g sur 10min puis 1g sur 8H
- **Réduction de la mortalité** de 30%

Shakur, et al. Lancet 2010

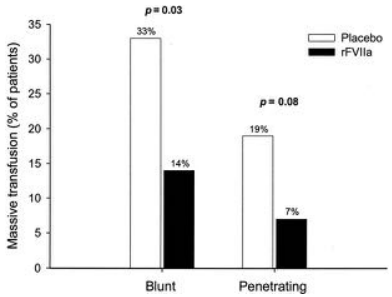
	Tranexamic acid allocated	Placebo allocated	Risk ratio (99% CI)
Time from injury (h)			
≤1	509/3747 (13·6%)	581/3704 (15·7%)	0·87 (0·75–1·00)
>1–≤3	463/3037 (15·2%)	528/2996 (17·6%)	0·87 (0·75–1·00)
>3	491/3272 (15·0%)	502/3362 (14·9%)	1·00 (0·86–1·17)

Intérêt d'une **administration précoce !**

Traitement de la coagulopathie

Facteur rVIIa

- Diminution des besoins transfusionnels pour les **traumatismes fermés**
- Pas de différence de survie



Boffard, et al. Journal of Trauma 2005

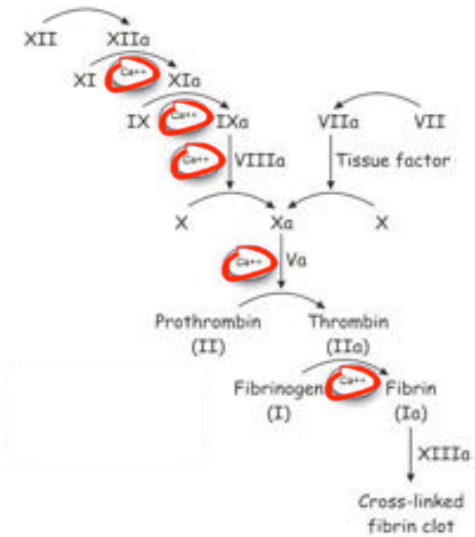
- Efficacité non clairement démontrée
- Coût important
- Place en **seconde intention**

Recommendations on the use of recombinant activated factor VII as an adjunctive treatment for massive bleeding. A European perspective.

Vincent, et al. AFAR 2006

Traitement de la coagulopathie

Calcium



- Hypocalcémie fréquente par **dilution**, **consommation** et **chélation**

  => Diminution de la contractilité myocardique

  => Vasoplégie

  => Troubles de l'hémostase

- Monitorer et supplémenter en cas de transfusion massive

Early hypocalcemia in severe trauma.

Vivien, et al. Crit Care Med, 2005.

Monitorage de la coagulation

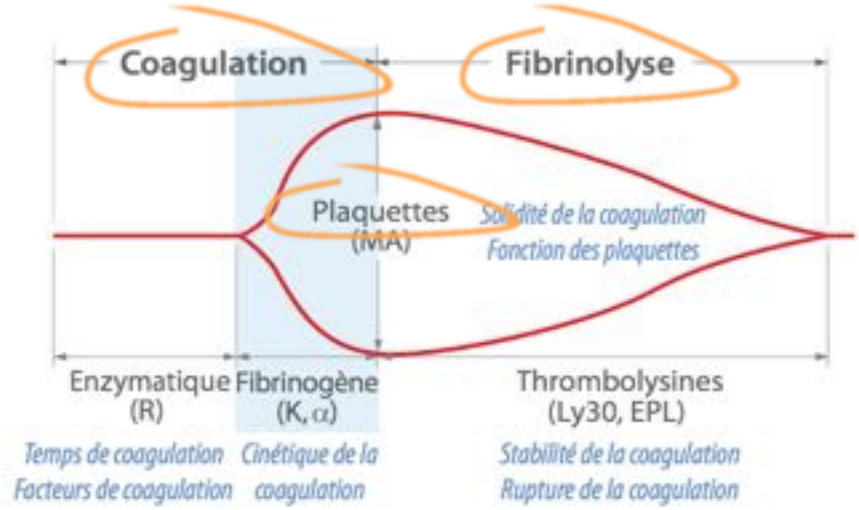
Etude des caractéristiques visco-élastiques du caillot

Monitorage de la coagulation

Thromboélastogramme

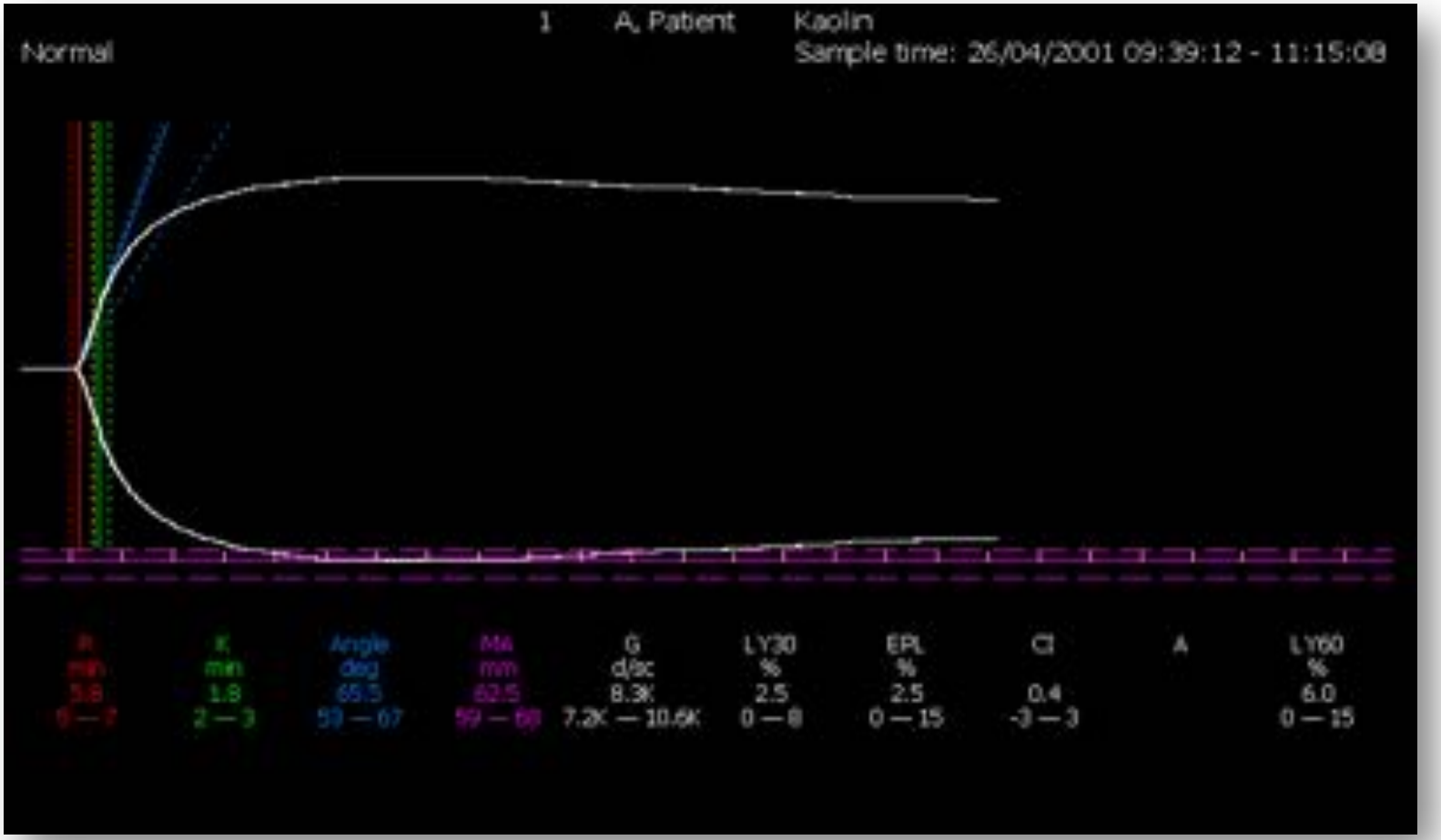
Caractéristiques visco-élastiques du caillot : Thromboélastogramme

- Monitorage **global** de la coagulation, sur **sang total**
- Analyse **fonctionnelle** du processus hémostatique
- Résultats rapides et en **temps réel**



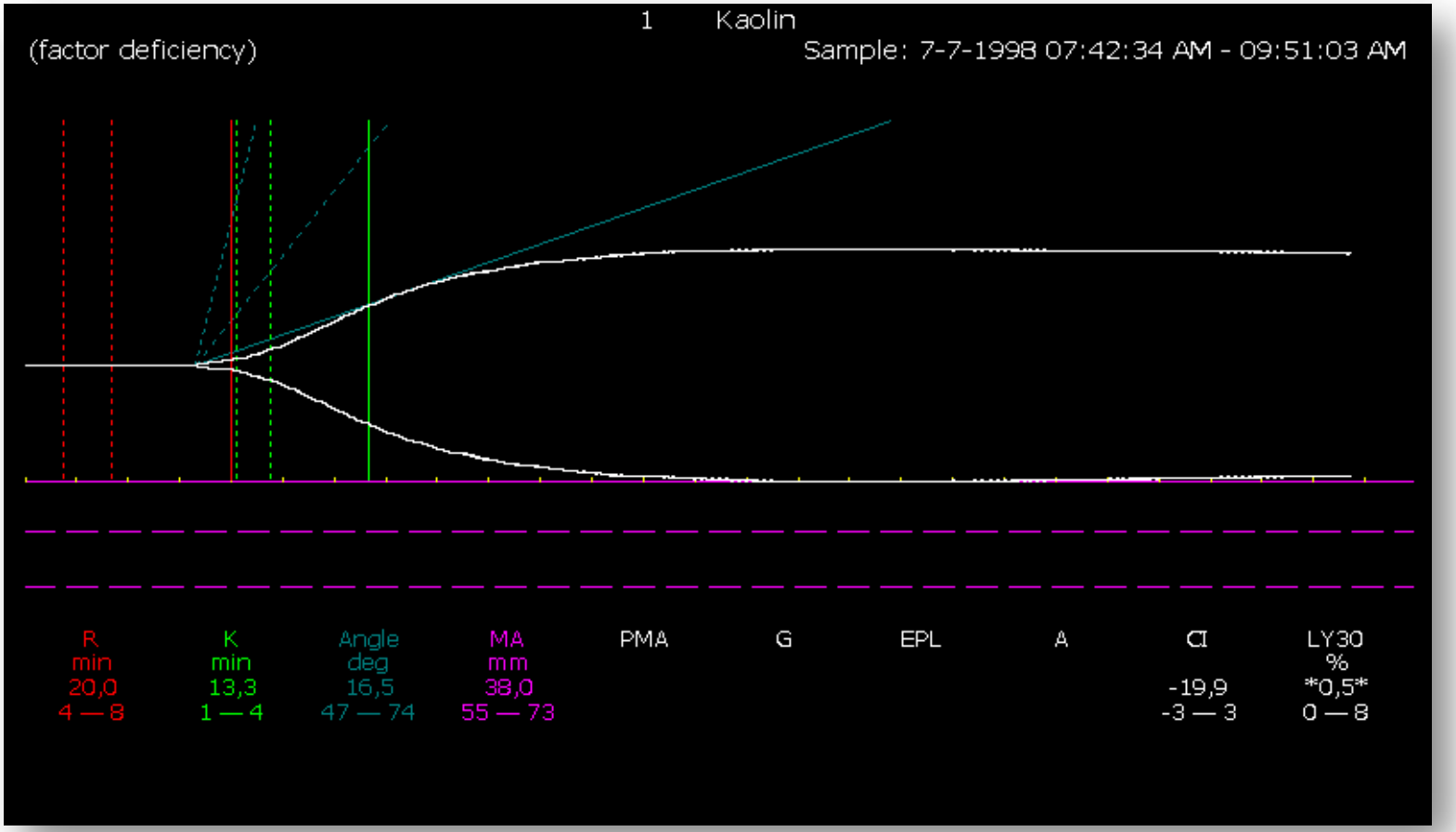
Thromboélastogramme

Tracé normal



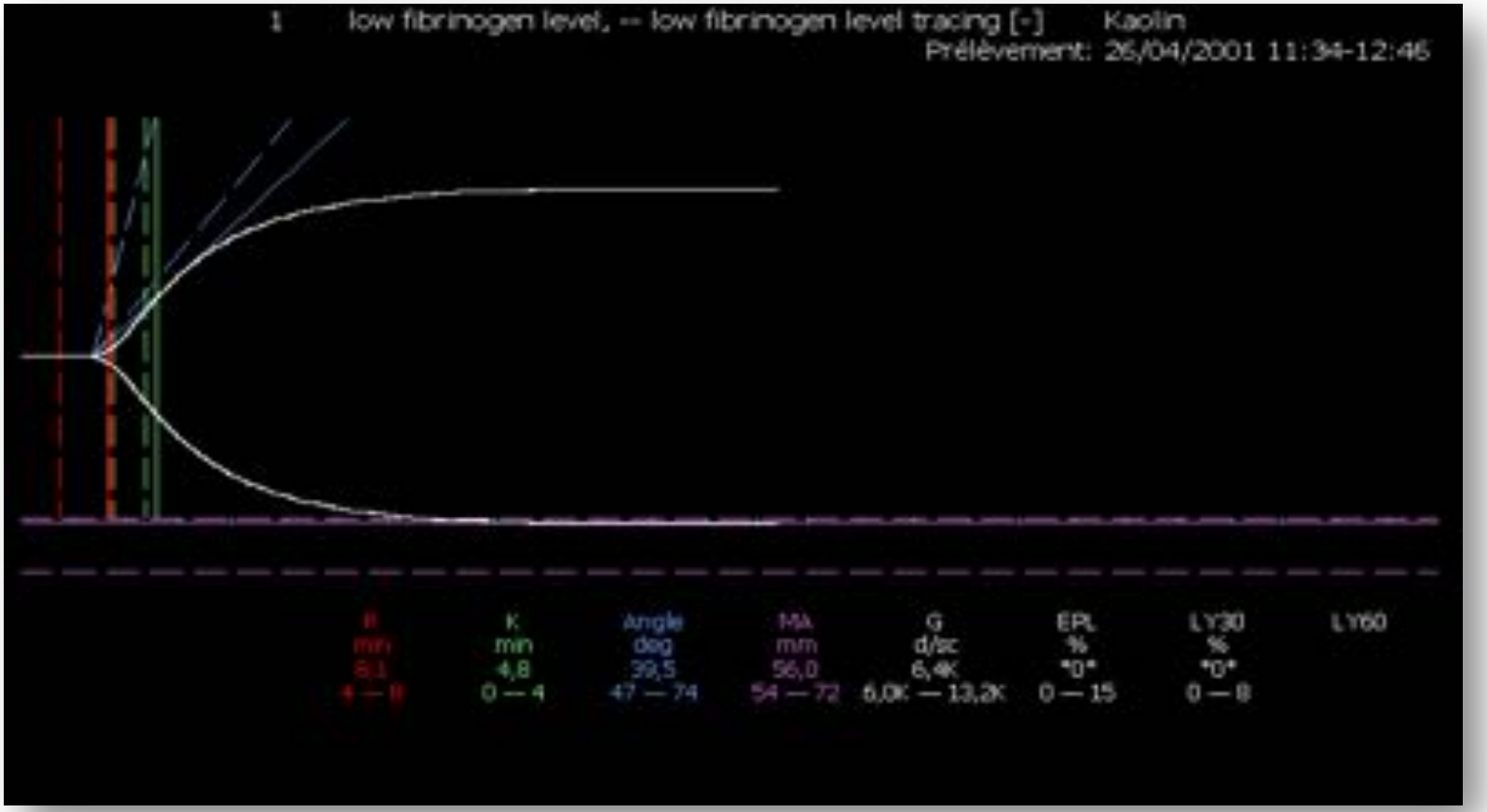
Thromboélastogramme

Défaut d'initiation et d'amplification



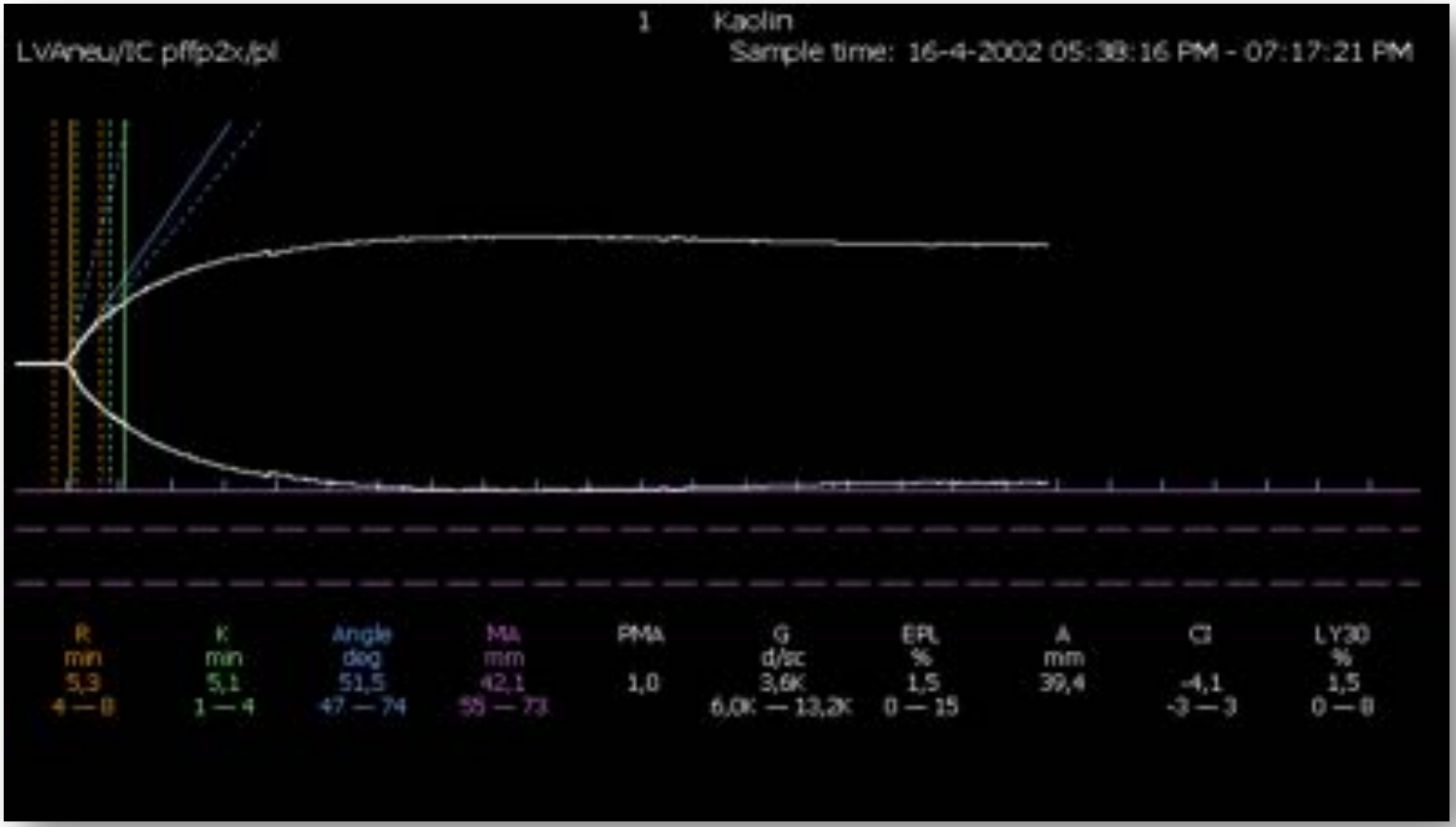
Thromboélastogramme

Défaut d'amplification



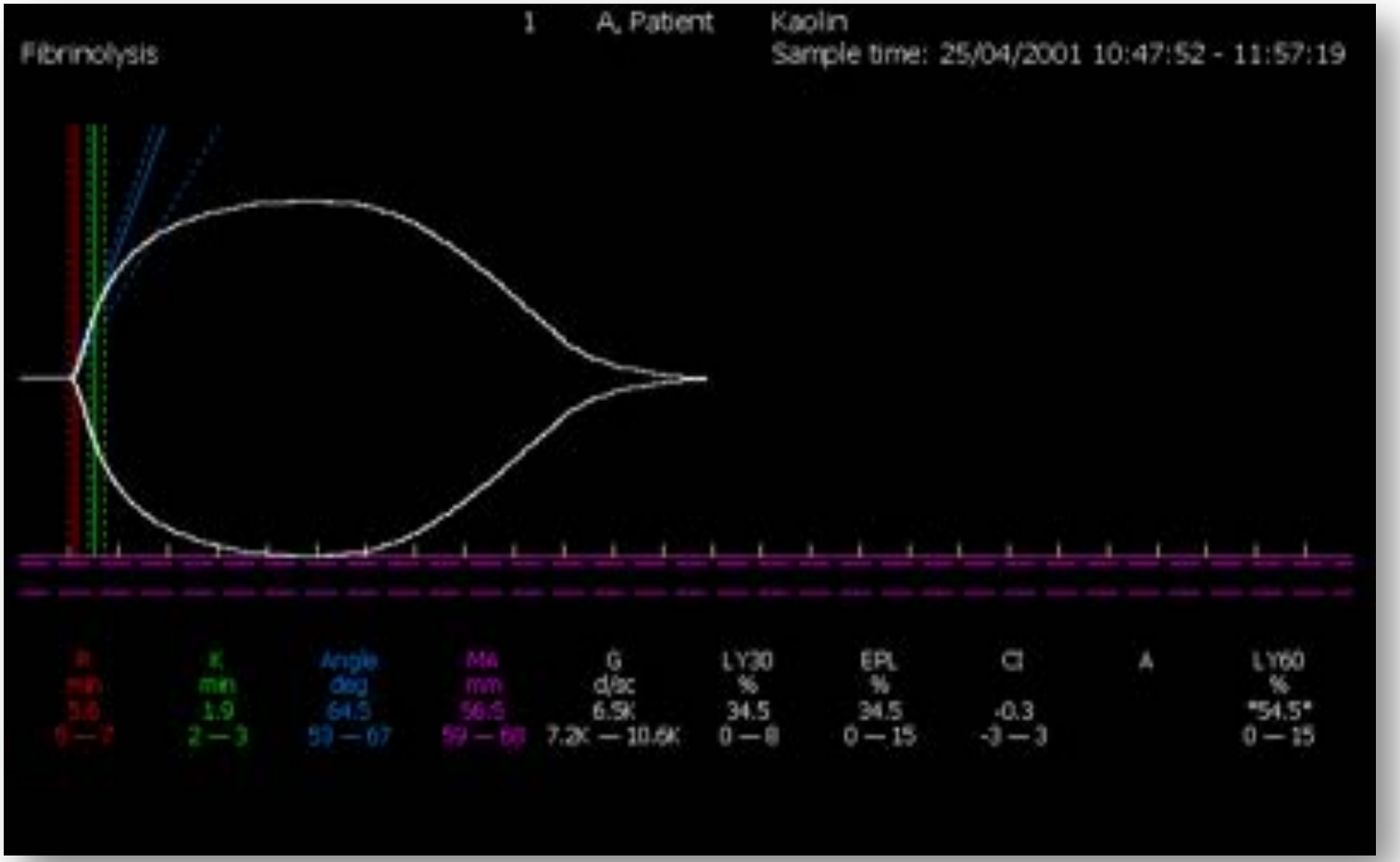
Thromboélastogramme

Défaut plaquettes



Thromboélastogramme

Fibrinolyse primaire



Thromboélastogramme

Rapidité des résultats

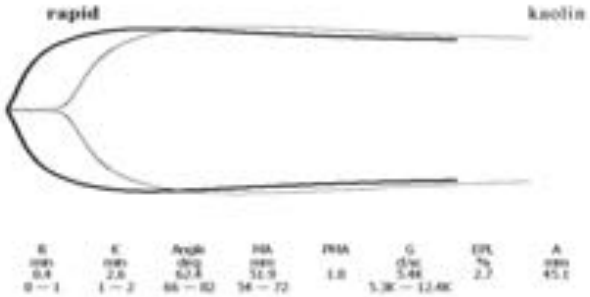
Procedures and Techniques

The Journal of TRAUMA® Injury, Infection, and Critical Care

Can RapidTEG Accelerate the Search for Coagulopathies in the Patient With Multiple Injuries?

Délai médian admission – résultat définitif :

- RapidTEG : 30 minutes
- TEG kaolin : 42 minutes
- Biologie conventionnelle : 62 minutes



Jeger, et al. Journal of trauma 2009

Thromboélastogramme

Anticiper une transfusion massive

Admission Rapid Thrombelastography Can Replace Conventional Coagulation Tests in the Emergency Department

Experience With 1974 Consecutive Trauma Patients

- Corrélation entre paramètres du TEG et tests habituels
- **Angle α** plus sensible que l'INR pour prédire une transfusion massive
- **MA** plus sensible que la numération plaquettaire pour prédire une transfusion plaquettaire

Holcomb, et al. Annals of surgery 2012

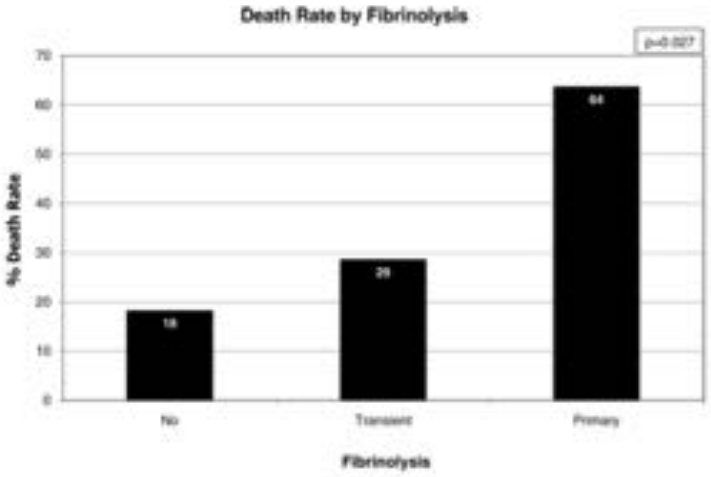
Thromboélastogramme

Monitorer la fibrinolyse

ORIGINAL ARTICLES

Primary Fibrinolysis Is Integral in the Pathogenesis of the Acute Coagulopathy of Trauma

- **34% de fibrinolyse** chez les traumatisés sévères nécessitant une transfusion massive
- Fibrinolyse plus fréquente en cas **d'hypotension, d'hypothermie, d'acidose métabolique**



Kashuk, et al. Annals of surgery 2010

Thromboélastogramme

Stratégie transfusionnelle

TEG-guided resuscitation is superior to standardized MTP resuscitation in massively transfused penetrating trauma patients

- Stratégie à la liberté du clinicien **avec monitorage du TEG**
- Puis mise en place d'un protocole de transfusion massive avec **ratios 1:1:1**

	Blunt MOI			Penetrating MOI, %		
	PreMTP, %	MTP, %	*p*	PreMTP, %	MTP, %	*p*
30-Day mortality						
≥6U RBC	30	25	0.59	23	31	0.24
≥10U RBC	41	39	0.91	33	54	0.04*

Tapia, et al. Journal of trauma 2013

Thromboélastogramme

Stratégie transfusionnelle

Vox Sanguinis (2009) **96**, 111–118

ORIGINAL PAPER

© 2008 The Author(s)
Journal compilation © 2008 International Society of Blood Transfusion
DOI: 10.1111/j.1423-0410.2008.01130.x

Effect of Haemostatic Control Resuscitation on mortality in massively bleeding patients: a before and after study

- ✓ Etude avant-après mise en place d'un protocole de transfusion massive
- ✓ 1er Pack : 5 CGR, 5 PFC, 2 CUP
- ✓ Puis **algorithme basé sur le TEG**

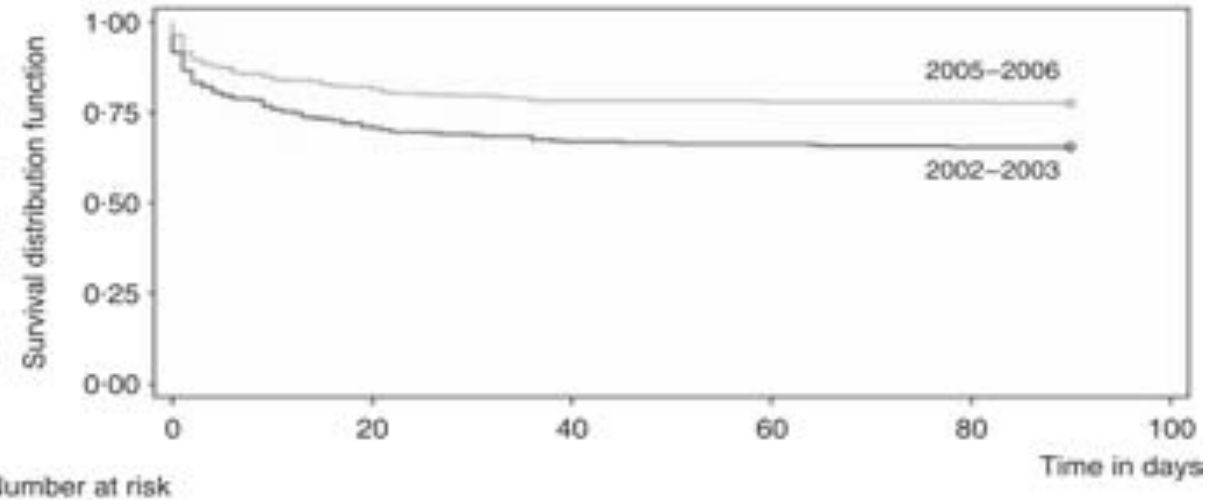
TEG Parameter	Treatment
R 11–14 min	2 × FFP or 10 ml/kg
R > 14 min	4 × FFP or 20 ml/kg
MA 46–50 mm	1 platelet concentrate
MA < 46 mm	2 platelet concentrates
Angle < 52	2 × FFP or fibrinogen
Ly30 > 8%	Antifibrinolytics

Johansson, et al. Vox sanguinis 2009

Thromboélastogramme

Stratégie transfusionnelle

Résultats



Number at risk

2005–2006	442	385	362	352	347	345	345	344	343	343
2002–2003	390	308	281	267	257	255	255	255	255	255

Log-rank, $P < 0{\cdot}0001$

Johansson, et al. Vox sanguinis 2009

Transfusion en situation d'exception

Transfusion de sang total

The Journal of TRAUMA® *Injury, Infection, and Critical Care*

Fresh Whole Blood Transfusion: A Controversial Military Practice

David S. Kauvar, MD, John B. Holcomb, MD, Gary C. Norris, MPH, and John R. Hess, MD

- Pratique du SSA en opérations extérieures, dérogation au Code de la Santé Publique
- Indications :
  - **collectives** (afflux saturant, pénurie de PSL)
  - **individuelles** (coagulopathie, transfusion massive)

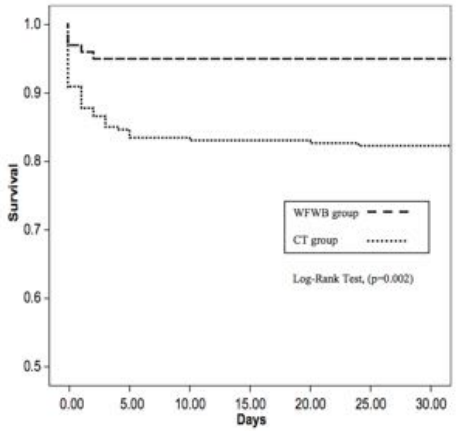
Transfusion en situation d'exception

Transfusion de sang total

Bénéfice individuel

Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries

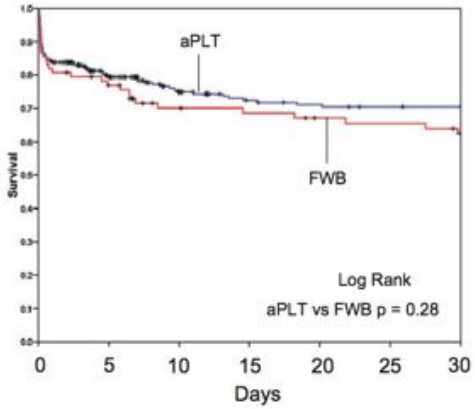
Spinella, et al. J Trauma 2009



Alternative à la transfusion plaquettaire

Comparison of platelet transfusion as fresh whole blood versus apheresis platelets for massively transfused combat trauma patients

Perkins, et al. Transfusion 2011



Transfusion en situation d'exception

Transfusion de sang total

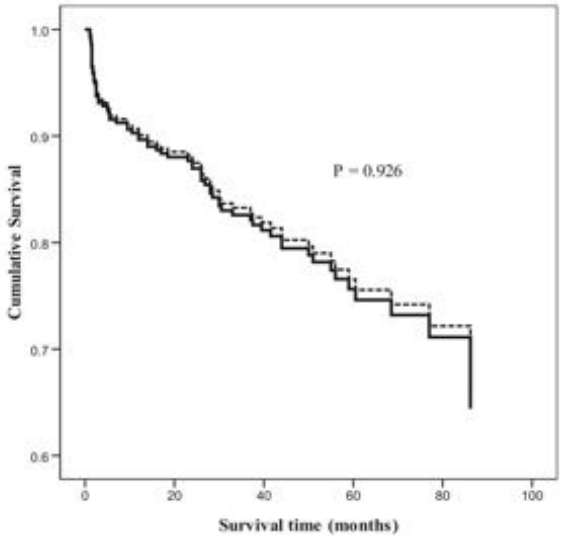
Warm fresh whole blood transfusion for severe hemorrhage: U.S. military and potential civilian applications

Spinella, et al. Critical Care Medicine 2008

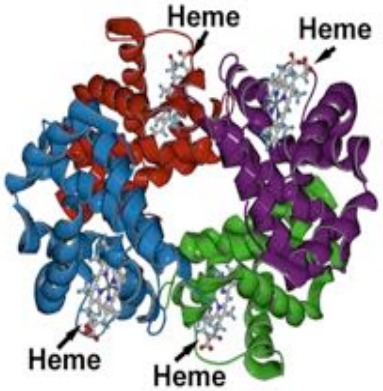
Lack of effect of unrefrigerated young whole blood transfusion on patient outcomes after massive transfusion in a civilian setting

- 353 transfusions massives
- **77 transfusions de sang total**

Ho KM et al. Transfusion. 2011



Conclusion



1. Prise en charge **standardisée**
2. **Anticipation** des besoins transfusionnels
3. Prise en charge précoce de la **coagulopathie**

Transfusion pré-hospitalière

Transfusion érythrocytaire

Transfusion pré-hospitalière

Plasma lyophilisé

SPECIAL REPORT

Point-of-injury use of reconstituted freeze dried plasma as a resuscitative fluid: A special report for prehospital trauma care

- Utilisation préhospitalière depuis janvier 2013 par *Israeli Defense Force Medical Corps*
- **LyoPlas** – produit par Croix Rouge Allemande

Glassberg, et al. Journal of trauma, 2013

Service de santé des armées

En France : étude PREHO-PLYO