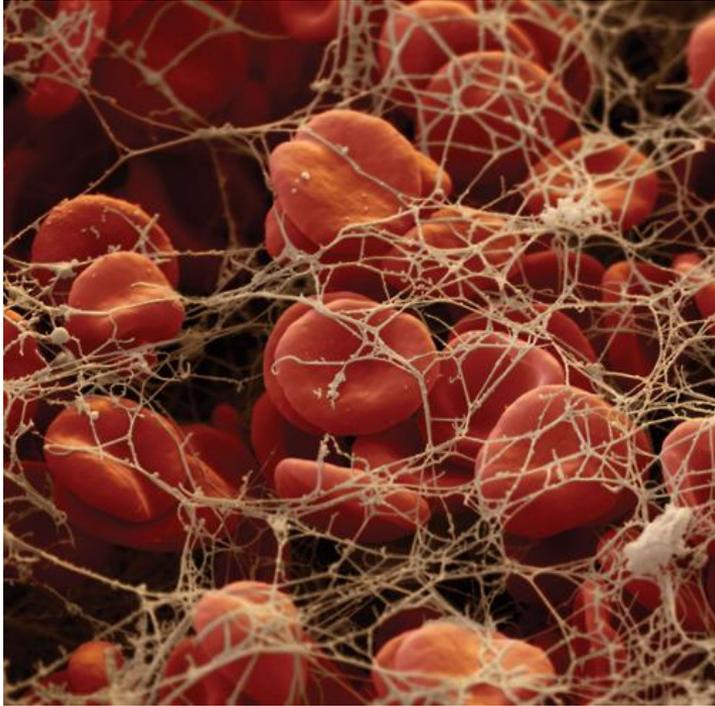


Fibrinogène et hémorragie du post-partum



1. Pourquoi le fibrinogène est arrivé jusque dans nos maternités ???

D Chassard, Lyon

Place du fibrinogène dans la cascade coagulation ?

Voie intrinsèque
VIII-IX-XI-XII

Voie tissulaire
Voie extrinsèque
VII

Activation
X

Activation thrombine

Fibrinogène

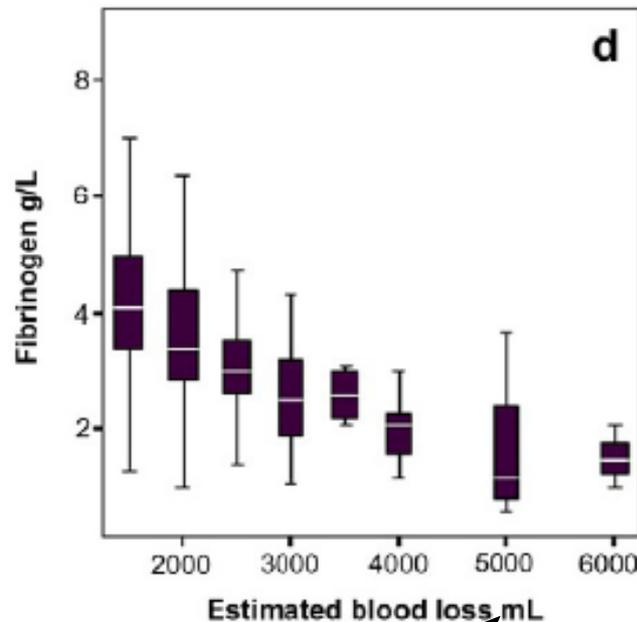
*Fibrinogène: premier facteur critique
à baisser en cas d'hémorragie/dilution*

Standard haemostatic tests following major obstetric haemorrhage

L. de Lloyd,^a R. Bovington,^b A. Kaye,^c R.E. Collis,^a R. Rayment,^b J. Sanders,^c A. Rees,^c P.W. Collins^b

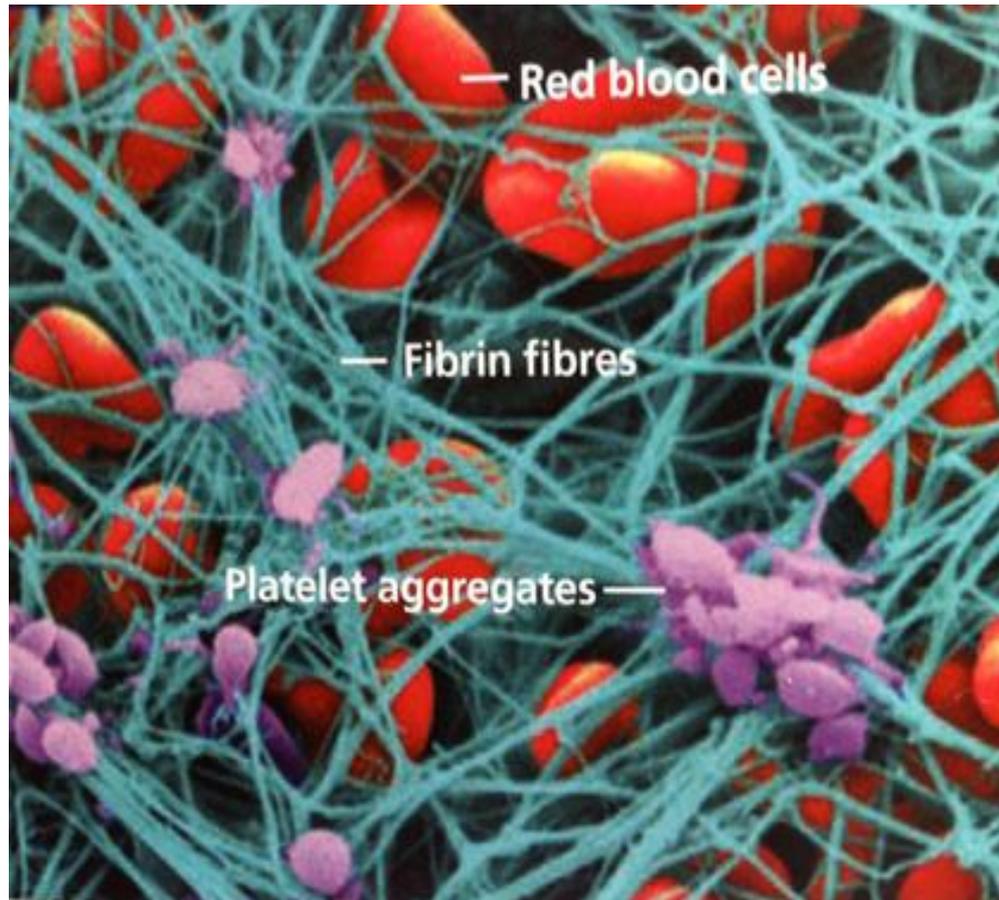
Department of^a Anaesthesia, ^bHaematology and ^cObstetrics and Gynaecology, University Hospital of Wales and School of Medicine, Cardiff, UK

Int J Obst Anesth 2011;20:135-41



Chute inexorable du fibrinogène au fur et à mesure de la perte sanguine

Ce qui arrête une hémorragie = un caillot...

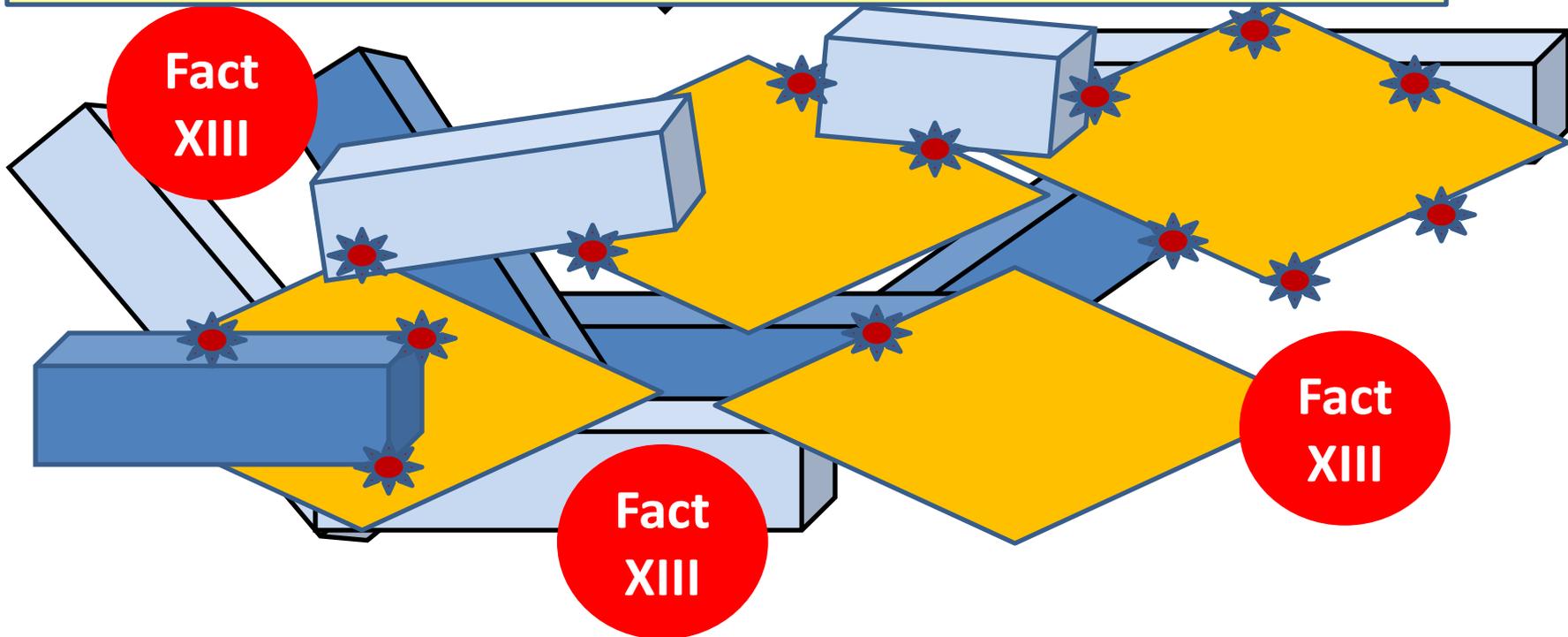


Facteurs limitants sur la formation du caillot

1. Pas les plaquettes car très nombreux récepteurs GP IIb IIIa (>40.000) sur leur surface
2. Pas la thrombine car 1 molécule de thrombine clive 1680 de fibrinogène
3. Le facteur XIII renforce la fermeté mais on peut tolérer un taux entre 5-10%

C'est le taux de fibrinogène qui est le plus important

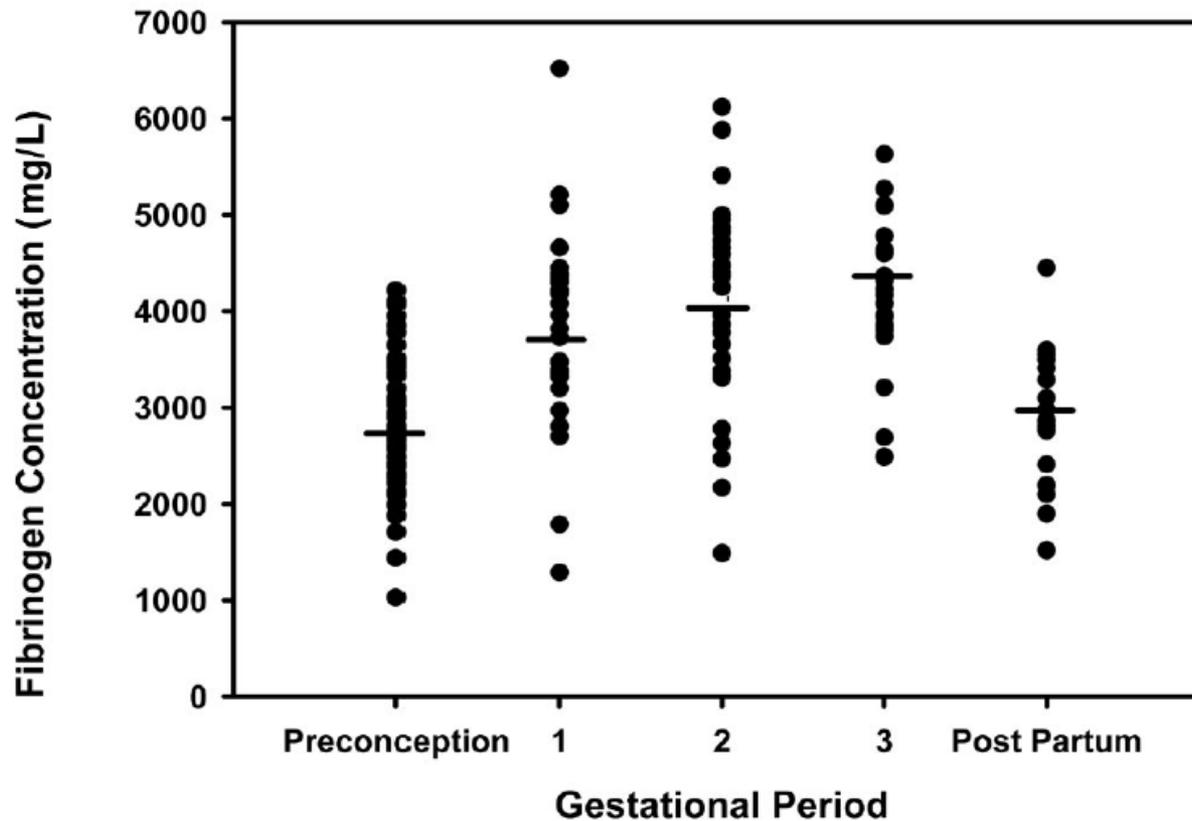
3b



D-Dimer Concentrations in Normal Pregnancy: New Diagnostic Thresholds Are Needed

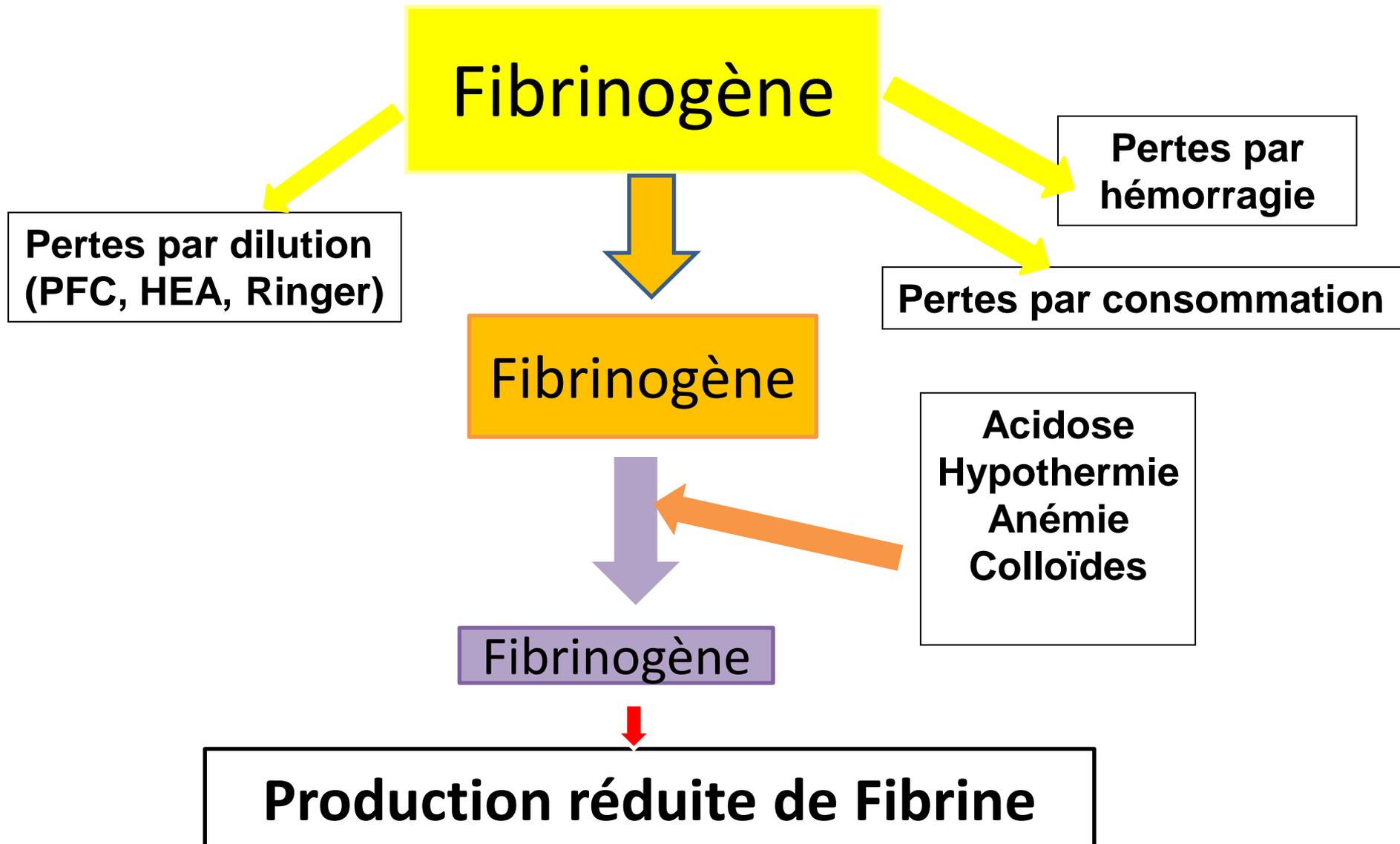
Clinical Chemistry 51:5
825–829 (2005)

JEFFREY A. KLINE,^{1*} GINGER W. WILLIAMS,² and JACKELINE HERNANDEZ-NINO²



Les taux de fibrinogène sont élevés en fin grossesse

Mécanismes de la chute précoce du fibrinogène



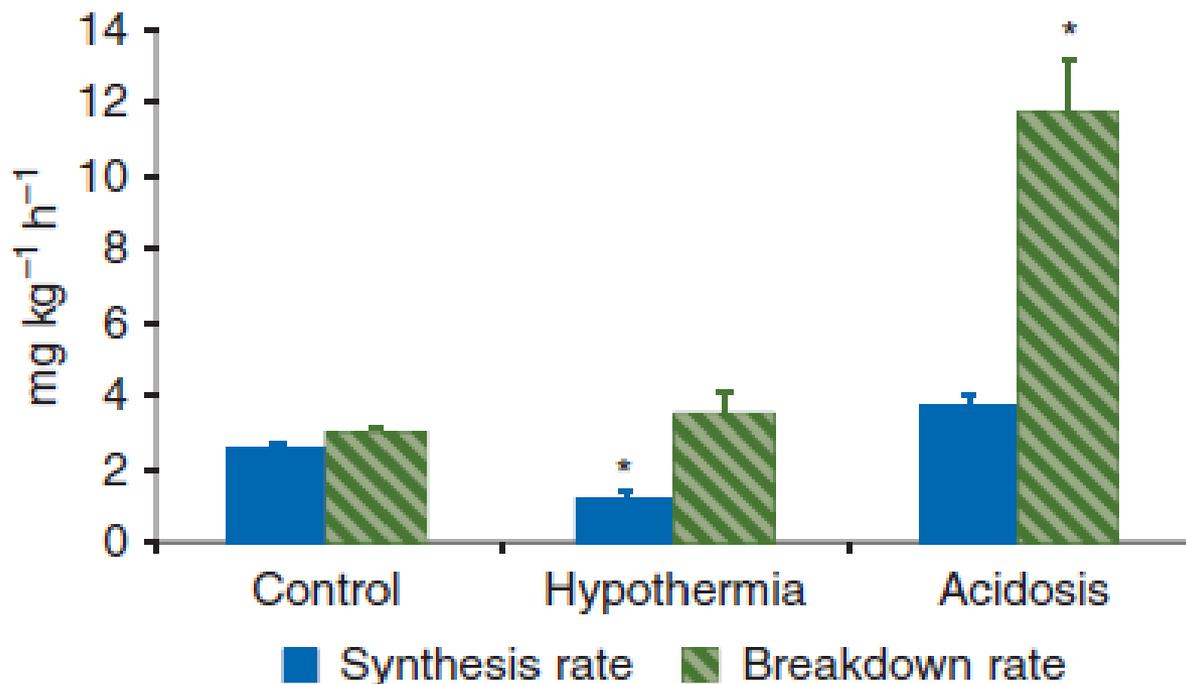


Fig 1 Changes in fibrinogen synthesis and breakdown in pigs after haemorrhage, hypothermia, and acidosis. Data from Martini and colleagues¹⁷ and Martini and Holcomb.¹⁸ * $P < 0.05$ compared with control values.

Le taux de fibrinogène préopératoire
ou per critique est-il prédictif
d'une complication hémorragique ?

Preoperative Fibrinogen Plasma Concentration Is Associated With Perioperative Bleeding and Transfusion Requirements in Scoliosis Surgery

Malin S. Carling, MD,* Anders Jeppsson, MD, PhD,† Per Wessberg, MD,* Anita Henriksson, RN,* Fariba Baghaei, MD, PhD,‡ and Helena Brisby, MD, PhD*

Spine 2011;36:549–555

TABLE 3. Pre- and Perioperative Variables in Patients With Extensive Red Blood Cell Transfusion (>2 U) and Patients With No or Limited Transfusion (≤2 U)

	Transfusion >2 U n = 13	Transfusion 0–2 U n = 69	<i>P</i>
Age (yr)	15 ± 2	16 ± 3	0.25
Gender (female)	12 (92%)	58 (84%)	<0.001
Body mass index	18 ± 1	21 ± 5	0.014
Surgical time (minutes)	205 ± 54	192 ± 49	0.37
Colloid prophylaxis	9 (69%)	19 (28%)	0.004
Fibrinogen (g/L)	2.5 ± 0.5	3.1 ± 0.6	0.002
Prothrombin time (INR)	1.1 ± 0.1	1.1 ± 0.1	0.67
aPTT (s)	36 ± 4	36 ± 3	0.63
Platelet count (>10 ⁹ /L)	285 ± 62	312 ± 70	0.20
Hemoglobin (g/L)	136 ± 8	137 ± 12	0.94
Total bleeding volume (mL)	2964 ± 1382	1286 ± 669	0.001

**Un taux pré-op bas
= plus
de transfusions
Péri-opératoires**



Plasma fibrinogen level, bleeding, and transfusion after on-pump coronary artery bypass grafting surgery: a prospective observational study

Martin Karlsson, Lisa Ternström, Monica Hyllner, Fariba Baghaei, Staffan Nilsson, and Anders Jeppsson

TRANSFUSION 2008

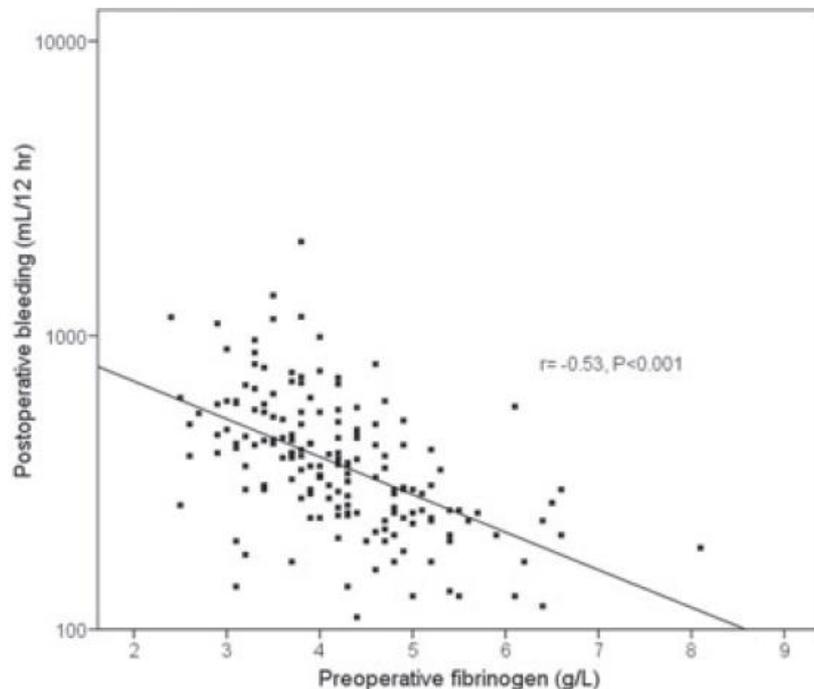


TABLE 2. Univariate correlation between clinical and laboratory variables and log bleeding after CABG

Variable	r Value	p Value
Age (years)	0.09	0.24
Sex	0.14	0.08
BMI (kg/m ²)	-0.15	0.06
Unstable angina	-0.009	0.90
Preoperative medication		
Aspirin	0.09	0.27
LMWH	0.13	0.09
Clopidogrel	-0.02	0.76
Warfarin	0.006	0.94
Hb (g/L)	-0.25	0.001
PLT count ($\times 10^9/L$)	-0.26	<0.001
aPTT (sec)	0.07	0.37
PT (INR)	0.05	0.49
Fibrinogen (g/L)	-0.53	<0.001
Number of anastomoses	0.11	0.16
ECC (min)	0.06	0.47
Aortic clamp time (min)	0.08	0.28

ECC = extracorporeal circulation; LMWH = low-molecular-weight heparin.

Un taux pré-op bas = plus d'hémorragies post-op

ORIGINAL ARTICLE

The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage

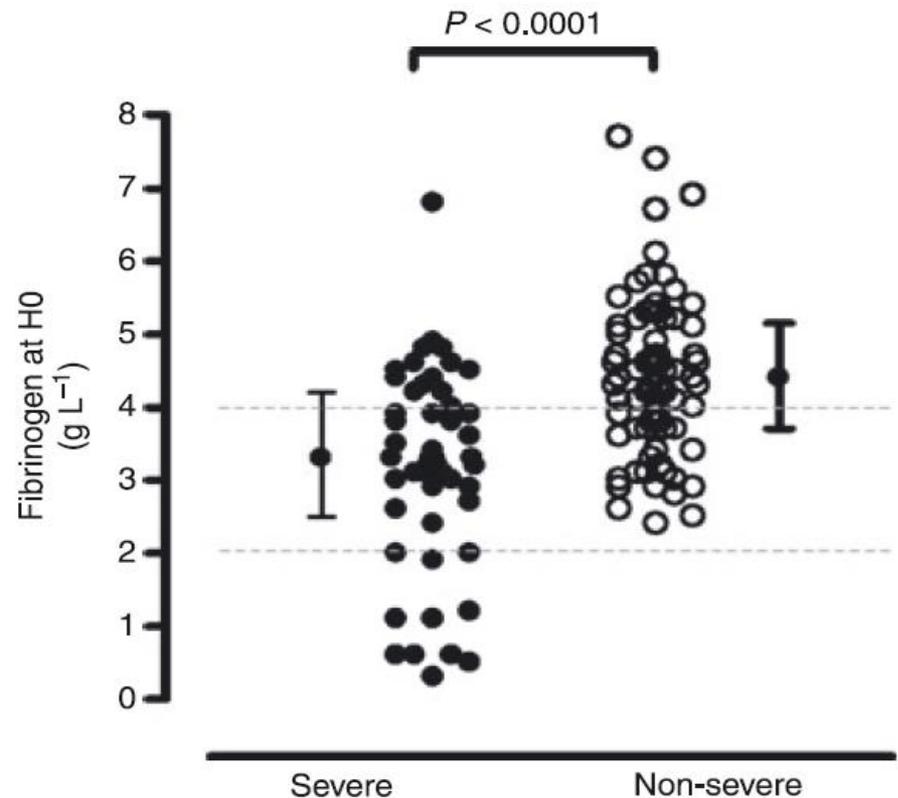
B. CHARBIT,*† L. MANDELBROT,‡ E. SAMAIN,§ G. BARON,¶ B. HADDAOUI,‡‡‡ H. KEITA,‡¶
O. SIBONY,** D. MAHIEU-CAPUTO,¶ M. F. HURTAUD-ROUX,** M. G. HUISSE,¶‡‡
M. H. DENNINGER,†‡‡ and D. DE PROST††††† FOR THE PPH STUDY GROUP

In multivariate analysis, fibrinogen was the **only marker** associated with the occurrence of severe PPH

At t0 (début Hrgie), the risk for severe PPH was **2.63-fold higher** for each 1 gL decrease of fibrinogen.

The negative predictive value of a fibrinogen concentration >4 gL was 79%

The positive predictive value of a concentration < 2 gL was 100%.



Etienne Gayat
Matthieu Resche-Rigon
Olivier Morel
Matthias Rossignol
Jean Mantz
Armelle Nicolas-Robin

Predictive factors of advanced interventional procedures in a multicentre severe postpartum haemorrhage study

Table 3 Univariate and multivariate estimated odds ratios for each of the five items included in the SPPH score. The results are expressed as median [first to third quartile]

Data collected on admission	Univariate analysis		Multivariate analysis	
	Odds ratio [95% CI]	<i>p</i> value	Odds ratio [95% CI]	<i>p</i> value
Abnormalities of placental implantation	4.83 [1.71–13.64]	0.003	7.05 [2.26–22.03]	0.0007
Prothrombin time <50% ^a	8.42 [3.86–18.36]	<0.0001	3.55 [1.38–9.17]	0.008
Heart rate >115 bpm	2.73 [1.51–4.95]	<0.0001	2.18 [1.03–4.62]	0.04
Fibrinogen <2 g/l 	5.02 [2.9–8.67]	<0.0001	2.75 [1.51–4.95]	0.005
Troponin I detectable	3.91 [2.32–6.59]	<0.0001	2.73 [1.51–4.95]	0.0009

^a Corresponding to an average threshold INR of 1.64 in the seven hospitals

Etienne Gayat
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Olivier Morel
Matthias Rossignol
Jean Mantz
Armelle Nicolas-Robin

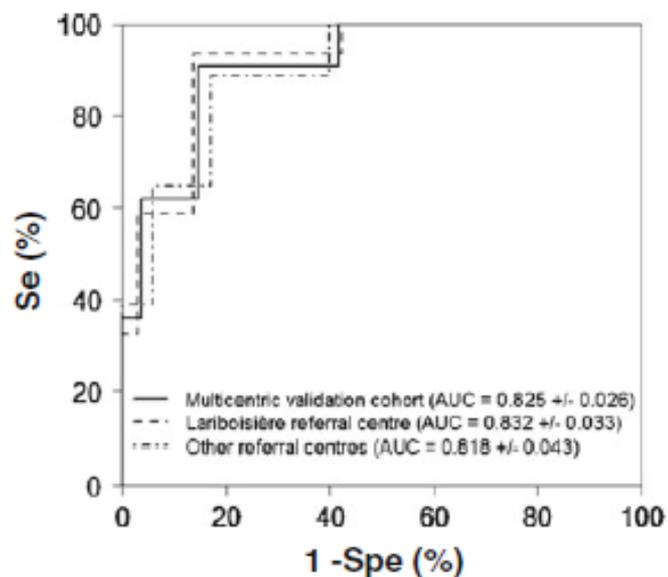
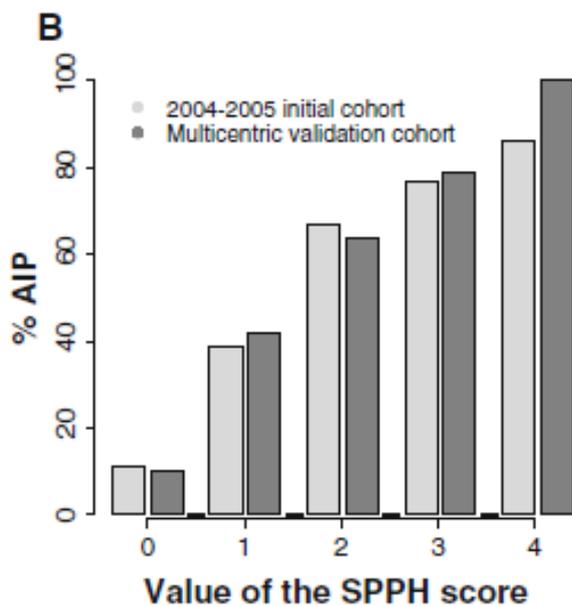
Predictive factors of advanced interventional procedures in a multicentre severe postpartum haemorrhage study

Fibrinogène inclus dans le score SPPH

A Sever Post Partum Hemorrhage (SPPH) Score

- Abnormalities of Placental implantation 0 or 1
- PT at admission < 50% 0 or 1
- HR at admission > 115 bpm 0 or 1
- Fibrinogene at admission < 2 gL⁻¹ 0 or 1
- Troponine I detectable at admission 0 or 1

Total score = 0 to 5



High Incidence of Myocardial Ischemia during Postpartum Hemorrhage

Peter C. J. Karpati, M.D.,* Mathias Rossignol, M.D.,† Marcus Pirot, M.D.,‡ Bernard Cholley, M.D., Ph.D.,† Eric Vicaut, M.D., Ph.D.,§ Patrick Henry, M.D., Ph.D.,|| Jean-Philippe Kévorkian, M.D.,# Patrick Schurando, M.D.,† Jacqueline Peynet, Ph.D.,** Denis Jacob, M.D.,†† Didier Payen, M.D., Ph.D.,‡‡ Alexandre Mebazaa, M.D., Ph.D.§§

Table 2. Comparison of Hemodynamic and Biochemical Variables on Admission and Discharge from the ICU

Variable	Values		
	ICU Admission	ICU Discharge	P

Systemic Blood

Le taux de fibrinogène bas est donc bien un marqueur de risque de complications

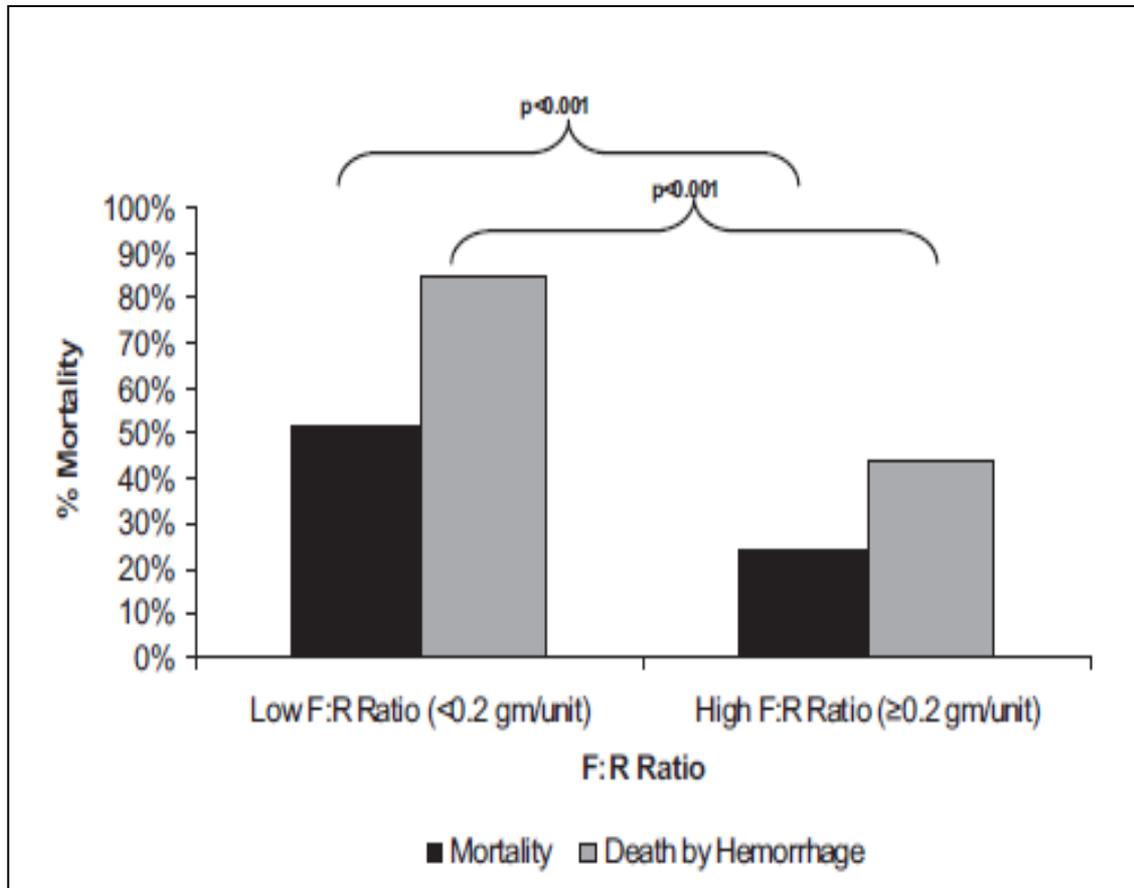
g/dl			
Prothrombin time, %	52 (34-67)	78 (68-91)	<0.001
 Fibrinogen, g/l	1.6 (0.9-2.5)	4.0 (3.1-5.0)	< 0.001

**Est-ce qu'un apport de fibrinogène
corrige les anomalies
de la coagulation et diminue
la transfusion ?**

The Ratio of Fibrinogen to Red Cells Transfused Affects Survival in Casualties Receiving Massive Transfusions at an Army Combat Support Hospital

J Trauma. 2008;64:S79 –S85.

Harry K. Stinger, MD, Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD,



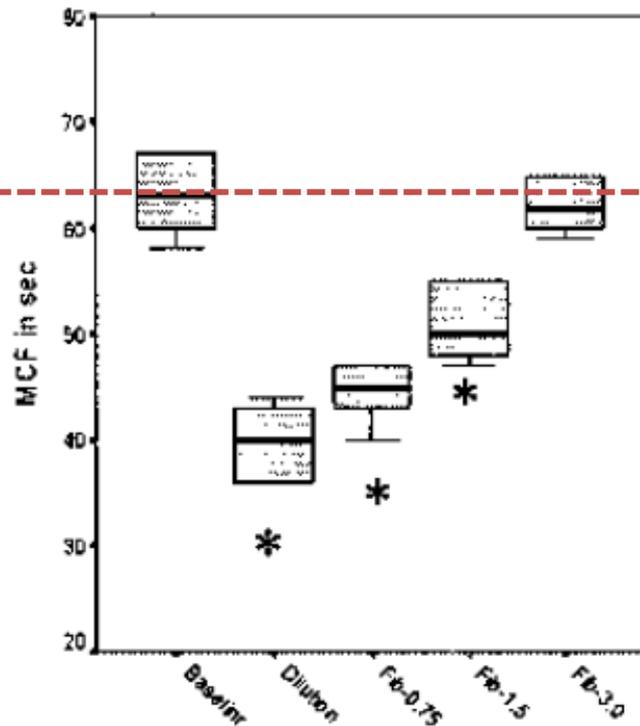
Moins de 200 mg de fibrinogène/CGR facteur indépendant péjoratif sur mortalité

The Effect of Fibrinogen Substitution on Reversal of Dilutional Coagulopathy: An *In Vitro* Model

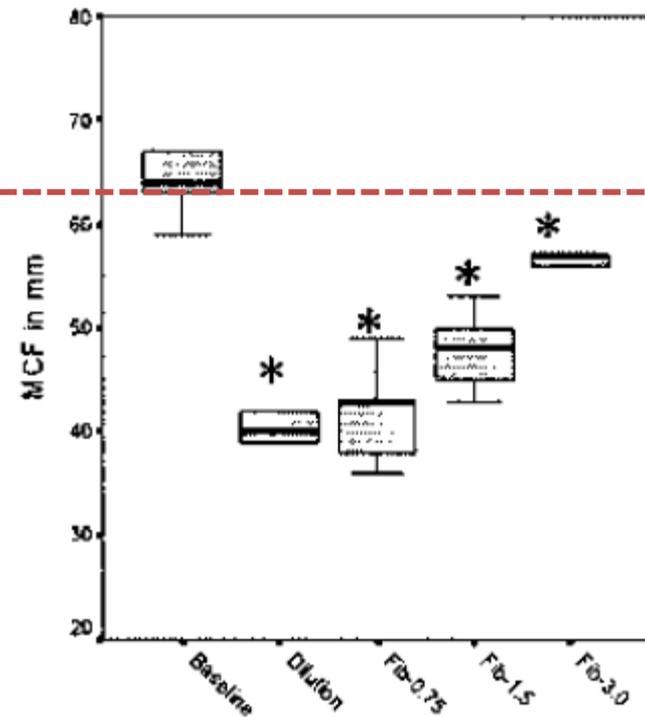
Dietmar Fries*, Petra Innerhofer*, Christian Reift, Werner Streift, Anton Klingler‡, Wolfgang Schobersberger§, Corinna Velik-Salchner*, and Barbara Friesenecker*

Anesth Analg 2006

Salé



HEA



Le fibrinogène corrige la perte de fermeté du caillot (Rotem) provoquée par une hémodilution (un peu moins celle des HEA)

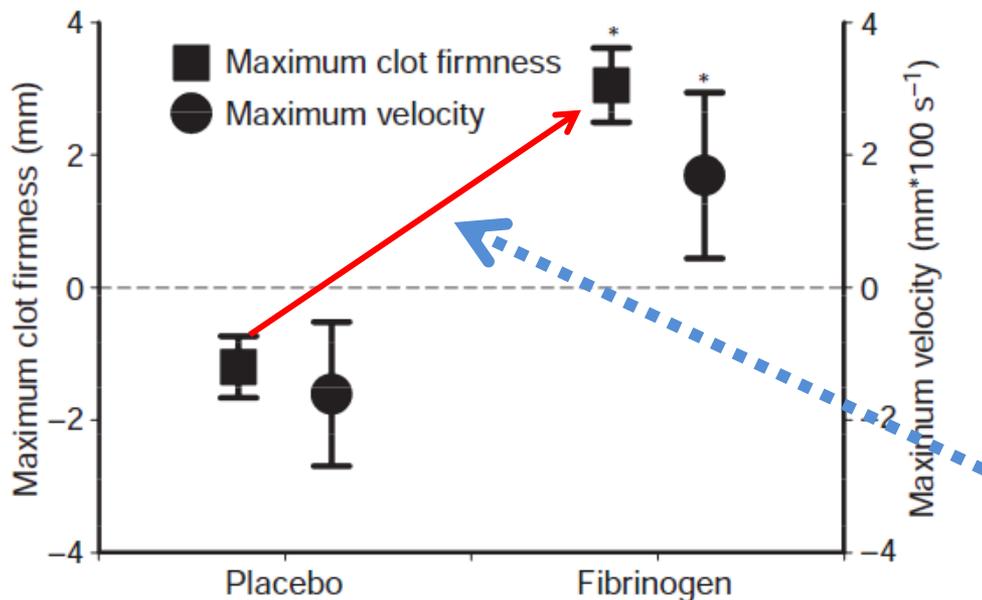
Fibrinogen substitution improves whole blood clot firmness after dilution with hydroxyethyl starch in bleeding patients undergoing radical cystectomy: a randomized, placebo-controlled clinical trial

C. FENGER-ERIKSEN,*† T. M. JENSEN,* B. S. KRISTENSEN,* K. M. JENSEN,‡ E. TØNNESEN,*
 J. INGER SLEV† and B. SØRENSEN†§

Les HEA diminuent la fermeté du caillot

Le FIB diminue la nécessité de la transfusion

Clot strength			
Maximum clot firmness (mm)	59.2 ± 5.8	50.6 ± 4.7	< 0.05*
Transfusion, red blood cells			
During operation	2.5 (0–6)	2 (0–5)	0.91
Postoperative period (48 h)	1.5 (0–2)	0 (0–2)	< 0.05*
Total	4.0 (0–6)	3.5 (0–5)	0.34

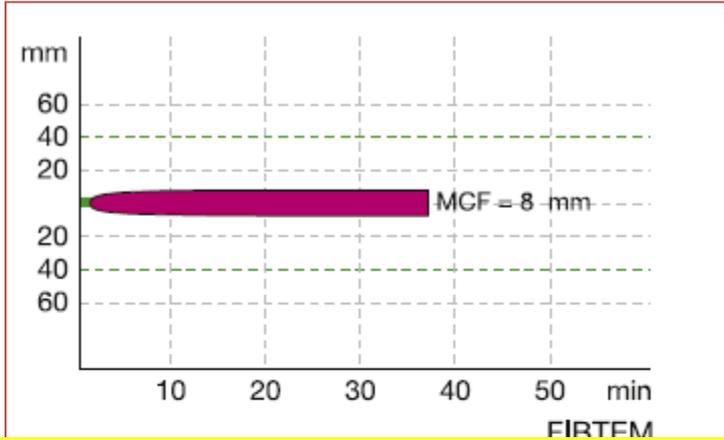


45 mL/kg corrigent les effets de la dilution par le Voluven (sur le Rotem),

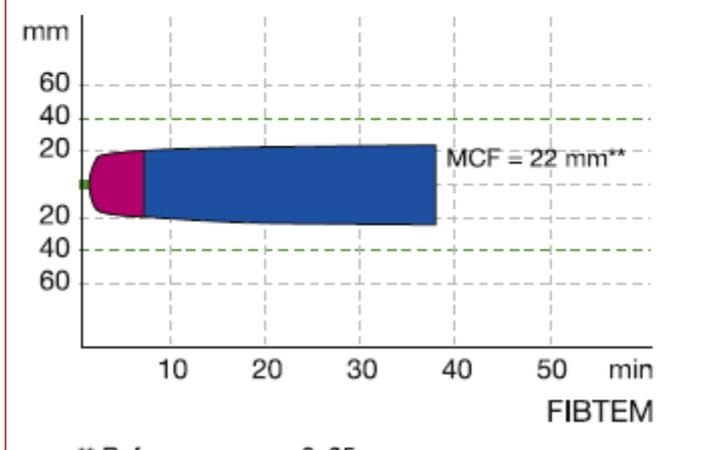
Thromboelastometry-guided administration of fibrinogen concentrate for the treatment of excessive intraoperative bleeding in thoracoabdominal aortic aneurysm surgery

JTCS 2009

Niels Rahe-Meyer, MD, MSc, PhD,^a Cristina Solomon, MD,^a Michael Winterhalter, MD,^a Siegfried Piepenbrock, MD,^a Kenichi Tanaka, MD, MSc, PhD,^b Axel Haverich, MD,^c and Maximilian Pichlmaier, MD^c



7.8 ± 2.7 g of fibrinogen concentrate

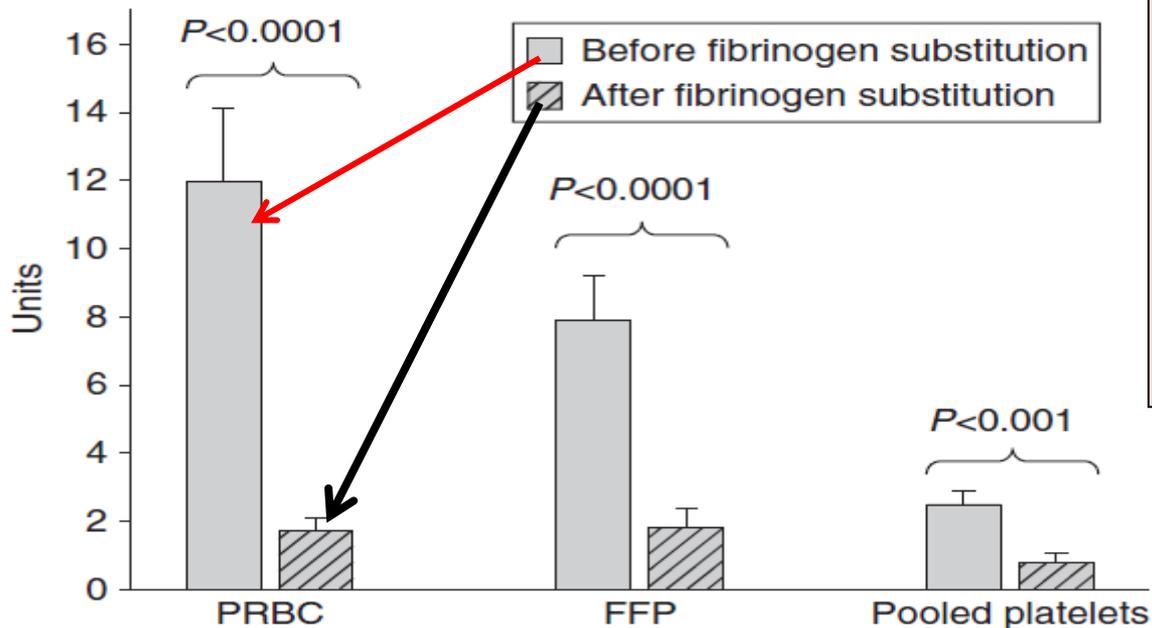


Patients without any allogeneic blood after CPB	0 (0%)	4 (66%)*
Units transfused/volume drained after CPB and during the first 24 h in ICU		
Red blood cells (U), mean	4.1	1.0*
Fresh frozen plasma (U), mean	9.1	1.0*
Platelet concentrate (U), mean	3.2	0.5*
Total blood cell concentrates (U), mean	16.4	2.5*

Le FB corrige le Rotem mais aussi diminue le recours aux différents dérivés du sang

Fibrinogen concentrate substitution therapy in patients with massive haemorrhage and low plasma fibrinogen concentrations

C. Fenger-Eriksen¹, M. Lindberg-Larsen¹, A. Q. Christensen¹, J. Ingerslev^{1*}
and B. Sørensen^{1 2}



Etude rétrospective:
Effets sur la transfusion
d'une perfusion
de fibrinogène.
(augmentation de 1g/L
du taux de fibrinogène:
passage de 1,4 à 2,4 g/L)

Fig 1 Blood product transfusion requirements—quantitative results. Use of RBC, FFP, and pooled platelet concentrates before and after fibrinogen substitution in surviving patients. $n=35$. Data presented as mean (SE) obtained during a time period of 24 h before and 24 h after fibrinogen substitution.

The use of fibrinogen concentrate to correct hypofibrinogenaemia rapidly during obstetric haemorrhage

S.F. Bell, R. Rayment,* P.W. Collins* R.E. Collis

*Department of Anaesthesia and *Department of Haematology, University Hospital of Wales, Cardiff, UK*

Table 1 Blood results of six patients with hypofibrinogenaemia

	Hb (g/dL)	Platelets ($\times 10^9/L$)	APTT (s)	PT (s)	Fibrinogen level (g/L)	Fibrinogen increase (g/L)*
Patient 1						
Initial	7.7	97	31	12	0.5	
150 min after fibrinogen	7.7	86	28	12	1	0.25
Patient 2						
Initial results	8.1	47	72	>150	<0.5	
180 min after fibrinogen	6.3	29	32	13.7	1.6	>0.37
Patient 3						
Initial results	8.3	134	25	13	0.5	
180 min after fibrinogen	7.7	80	29.5	13.1	1.4	0.3
Patient 4						
Initial results	6.6	106	48	15.6	1.3	
150 min after fibrinogen	8.5	57	36	12.8	3.4	0.53
Patient 5						
Initial results	6.7	94	55.4	13.9	1	
120 min after fibrinogen	7.5	134	35.3	14.5	1.7	0.23
120 min after 2 nd dose	7.2	78	30.2	10.3	1.8	0.05
Patient 6						
Initial results	12.9	136	42.6	14.4	1.2	
While receiving fibrinogen	9.8	80	28.8	12.8	1.6	
180 min after fibrinogen	11.3	73	29.9	13.2	2.6	0.5

* Baseline value

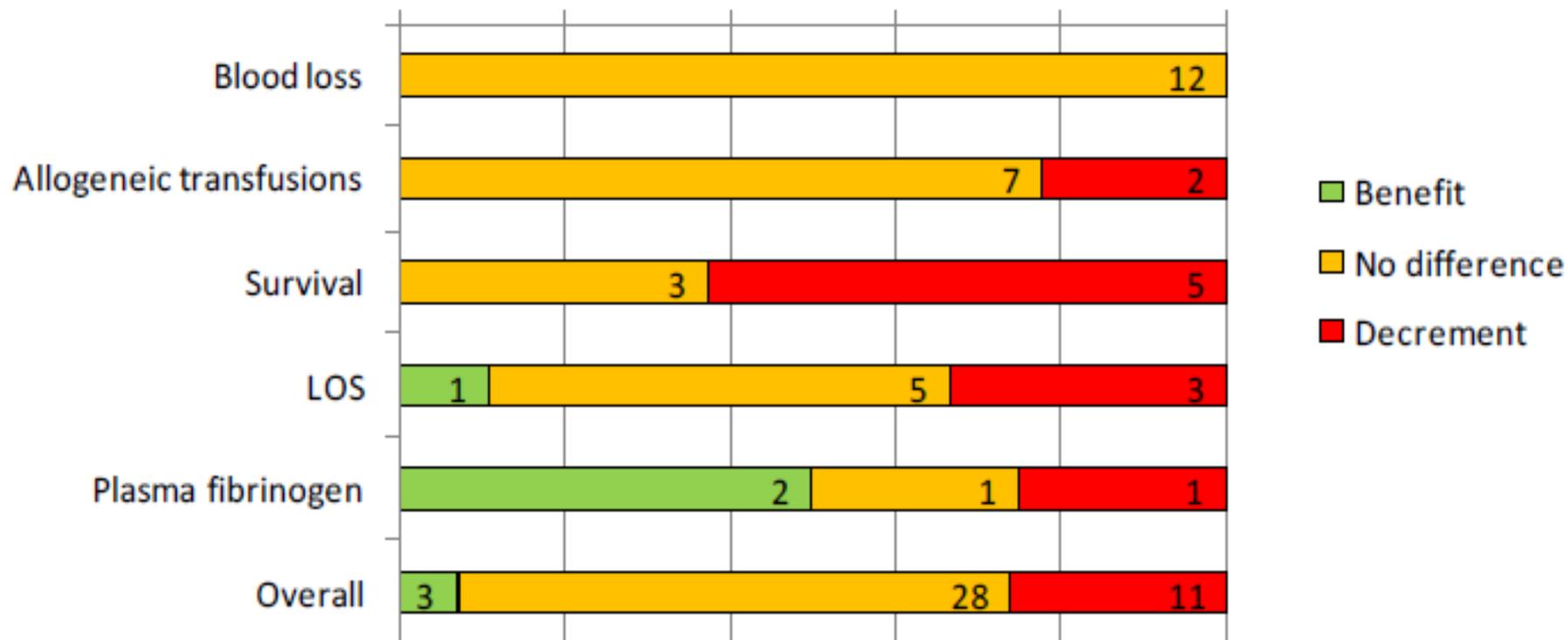
Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review

Sibylle Kozek-Langenecker^{1*}, Benny Sørensen^{2,3}, John R Hess⁴ and Donat R Spahn⁵

2c

Studies assessing FFP vs crystalloids/colloids/no FFP

0% 20% 40% 60% 80% 100%



Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review

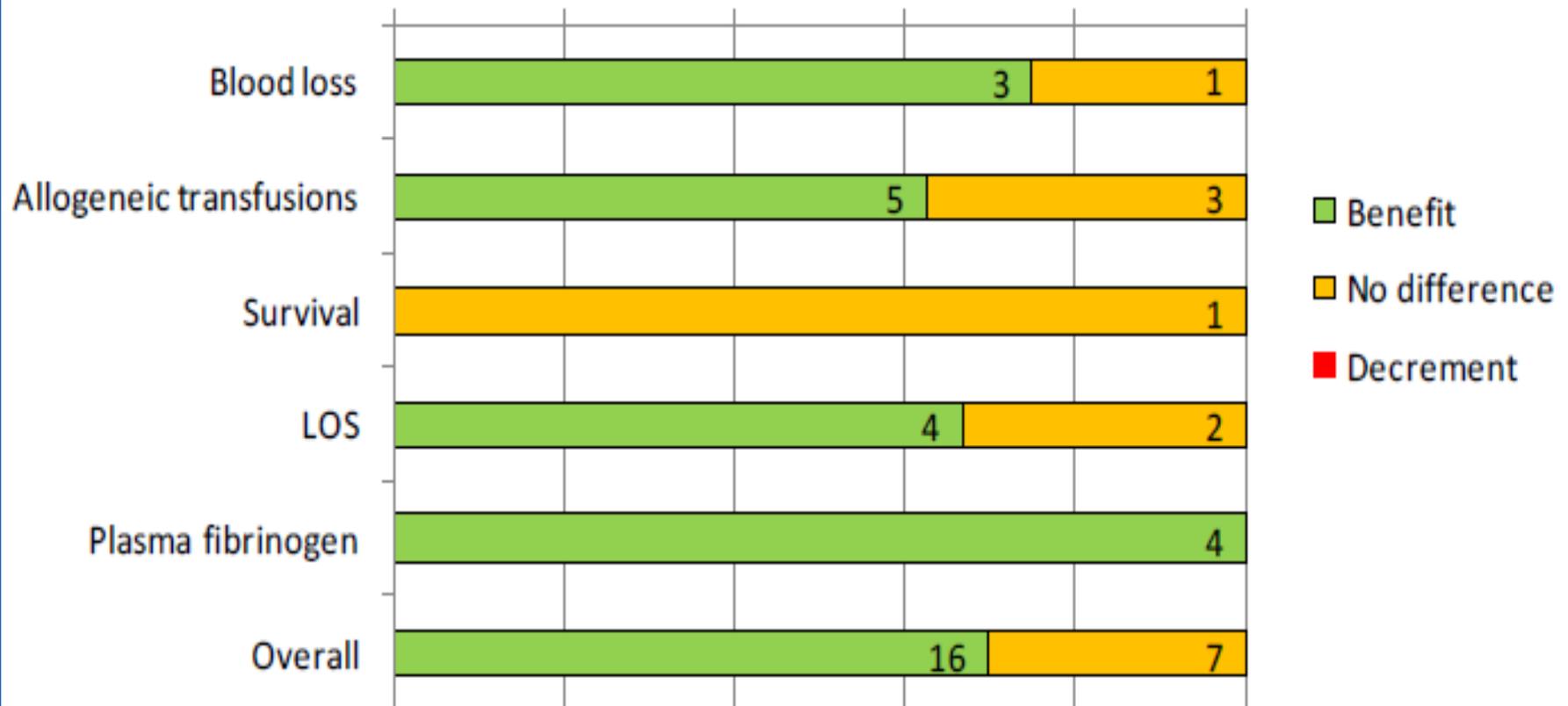
Critical Care 2011, 15:R239

Sibylle Kozek-Langenecker^{1*}, Benny Sørensen^{2,3}, John R Hess⁴ and Donat R Spahn⁵

2d

Studies assessing fibrinogen concentrate vs crystalloids/FFP/no fibrinogen concentrate

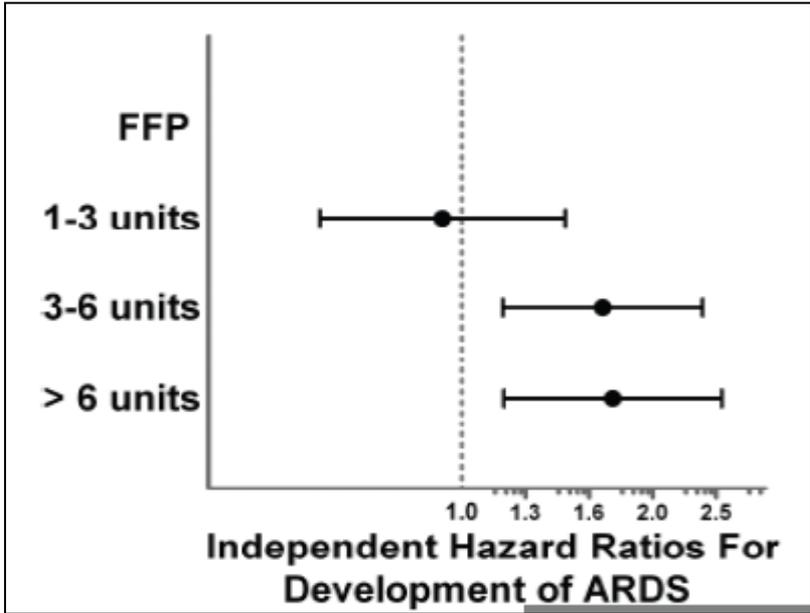
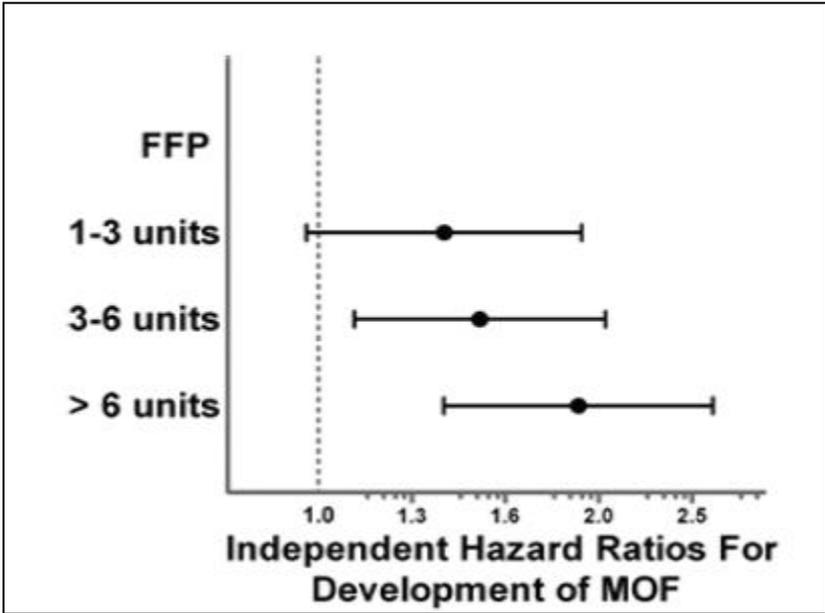
0% 20% 40% 60% 80% 100%



Fresh Frozen Plasma Is Independently Associated With a Higher Risk of Multiple Organ Failure and Acute Respiratory Distress Syndrome

Gregory A. Watson, MD, Jason L. Sperry, MD, MPH, Matthew R. Rosengart, MD, MPH, Joseph P. Minei, MD, Brian G. Harbrecht, MD, Ernest E. Moore, MD, Joseph Cuschieri, MD, Ronald V. Maier, MD, Timothy R. Billiar, MD, and Andrew B. Peitzman, MD, The Inflammation and the Host Response to Injury Investigators

J Trauma. 2009



Pourquoi du fibrinogène plus que des PFC ?

Temps de préparation court

Stockage in situ

Pas de risque viral prion

Pas d'immunisation

Pas de TRALI

Volume infusé < plasma: risque OAP par surcharge

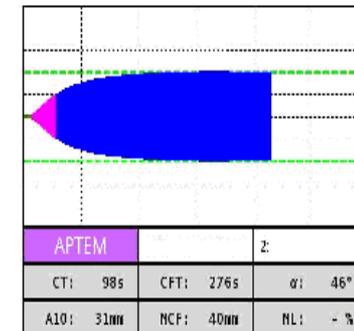
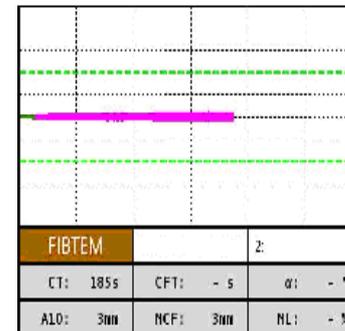
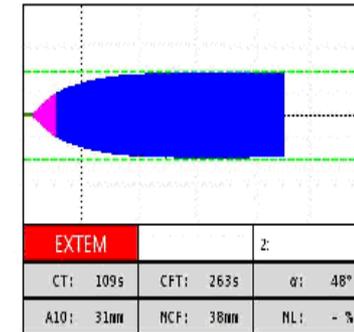
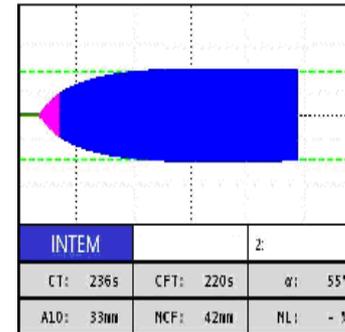
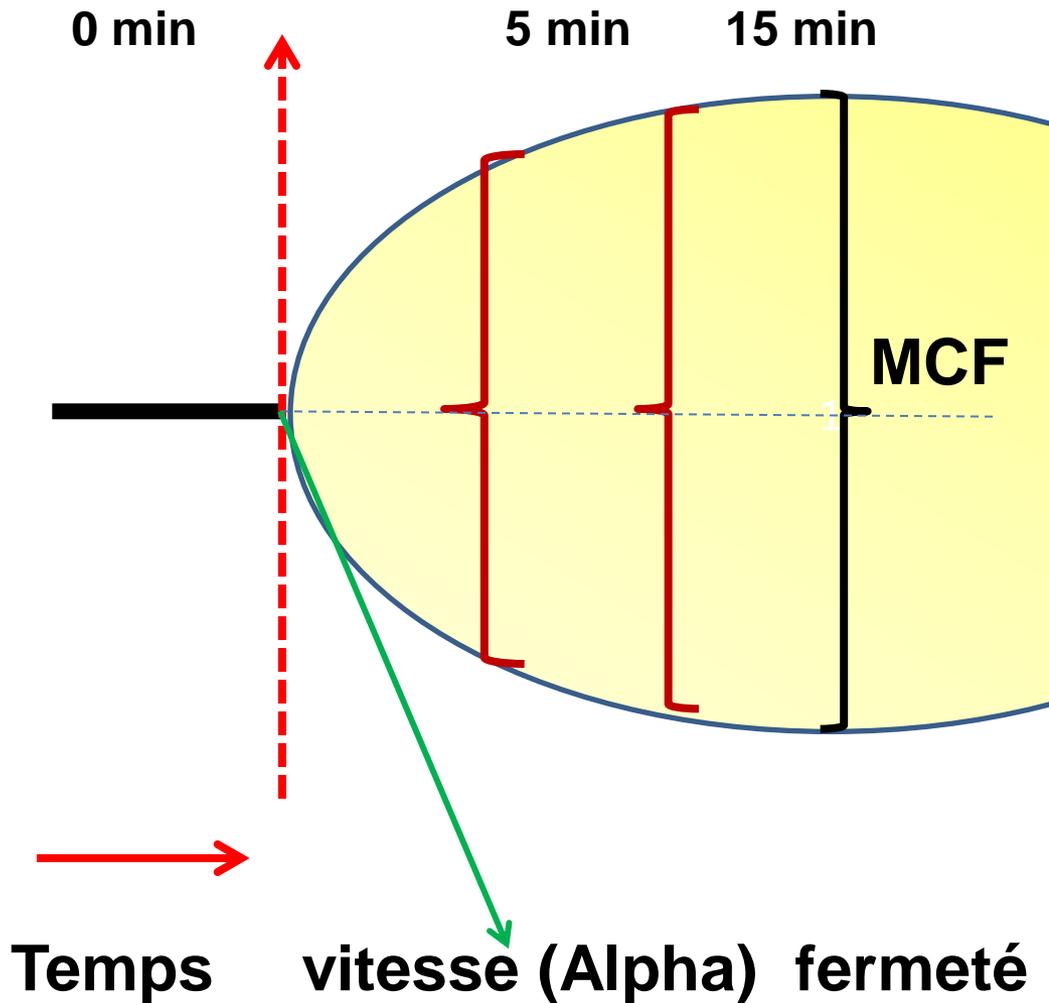
**Théoriquement 3 g de fibrinogène à perfuser pour
augmenter de 1 g le Fib circulant chez un adulte de 70 kg:**

PFC (0,5 g/L) = 6 poches = 1200 mL = 600 euros

Fibrinogène: 1,5 g/ 0,1 L = 2 flacons = 200 mL = 1500 euros

**Nos futures pratiques
à partir de ces données??**

Clot amplitude (fermeté): CA 5 et 15 min et MCF

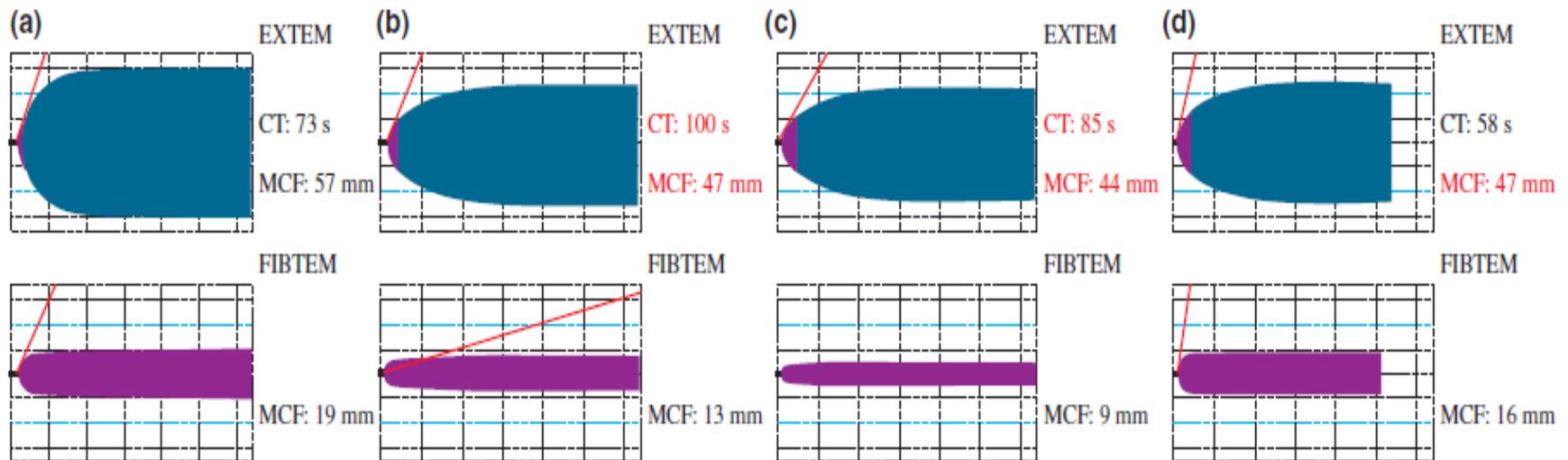


lyse

CASE REPORT

Use of rotation thromboelastometry (ROTEM[®]) to achieve successful treatment of polytrauma with fibrinogen concentrate and prothrombin complex concentrate

H. Schöchl,¹ L. Forster,¹ R. Woidke,² C. Solomon³ and W. Voelckel⁴



13 grammes fibrinogène !



Anaesthesia

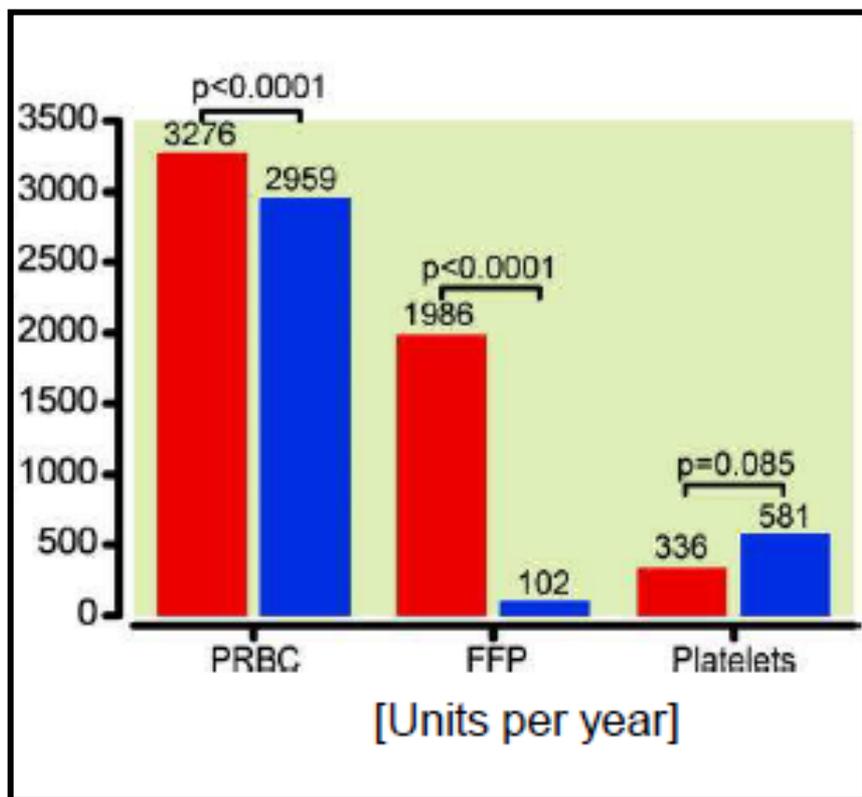
Journal of the Association of Anaesthetists of Great Britain and Ireland

Anaesthesia, 2010, 65, pages 199–203

First-line Therapy with Coagulation Factor Concentrates Combined with Point-of-Care Coagulation Testing Is Associated with Decreased Allogeneic Blood Transfusion in Cardiovascular Surgery

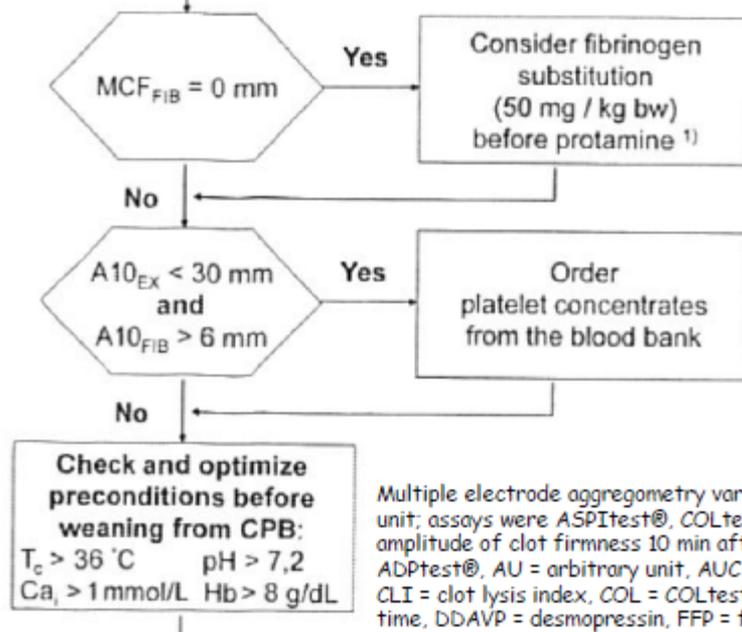
A Retrospective, Single-center Cohort Study

Görlinger, Klaus Dr. med*¹; Dirkmann, Daniel Dr. med†²; Hanke, Alexander A. Dr. med†³; Kamler, Markus PD Dr. med‡⁴; Kottenberg, Eva PD Dr. med*⁵; Thielmann, Matthias PD Dr. med‡⁶; Jakob, Heinz Prof. Dr. med§⁷; Peters, Jürgen Prof. Dr. med||⁸



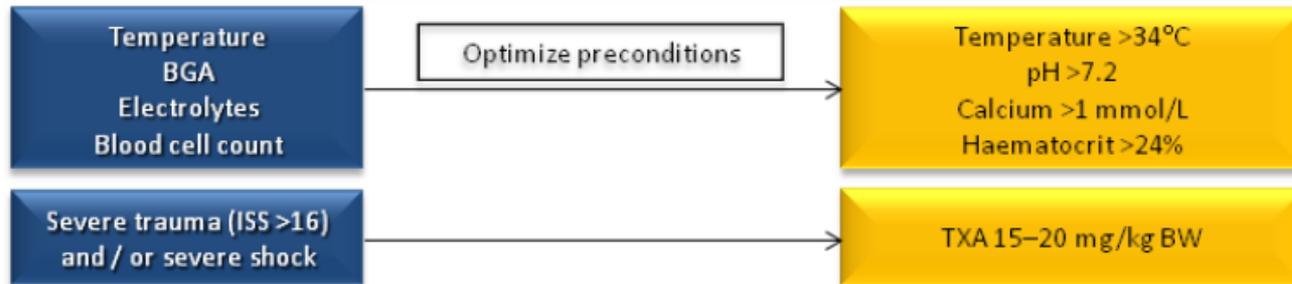
Diminution PGR/PFC Avec introduction fibrinogène+algorithme Rotem

ROTEM®-Analysis after declamping of the aorta

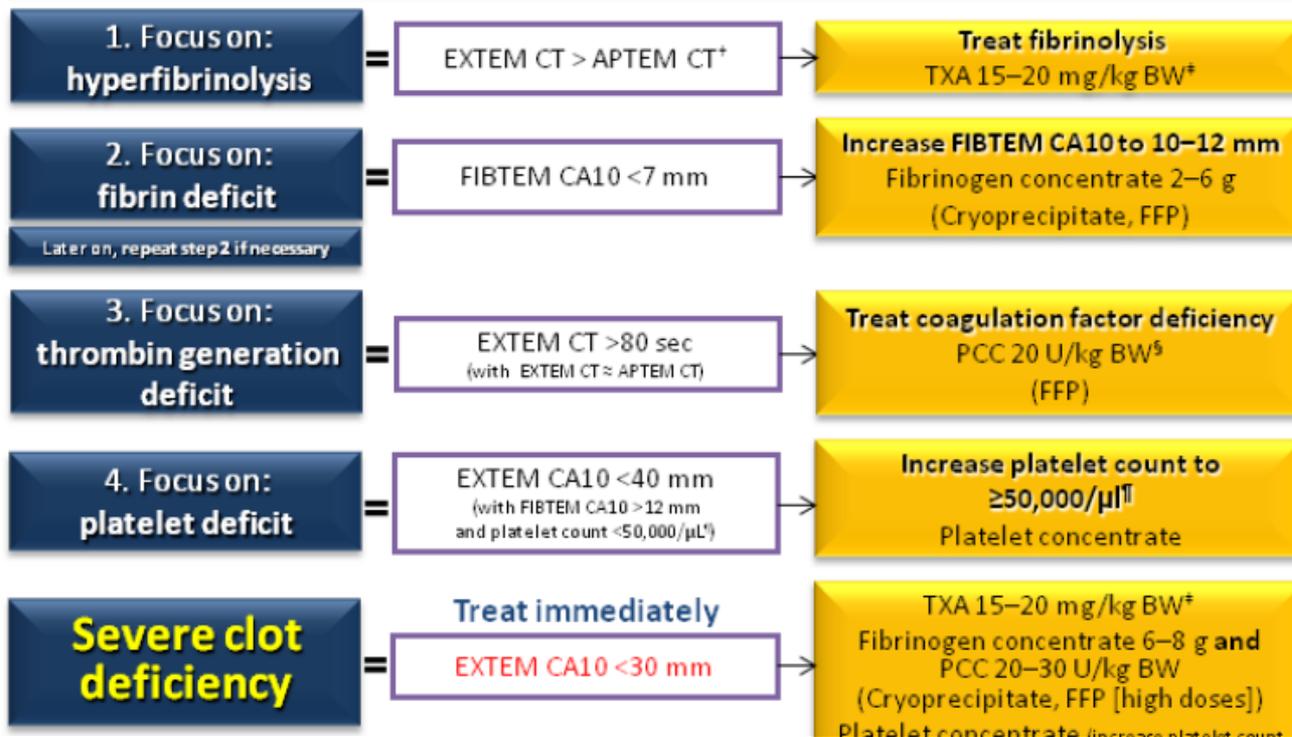


Multiple electrode aggregometry variables unit; assays were ASPiTest®, COLtest®, A amplitude of clot firmness 10 min after clo ADPtest®, AU = arbitrary unit, AUC = area CLI = clot lysis index, COL = COLtest®, CP time, DDAVP = desmopressin, FFP = fresh f factor VIII/von Willebrand factor concent MCF = maximum clot firmness, PCC = prothi

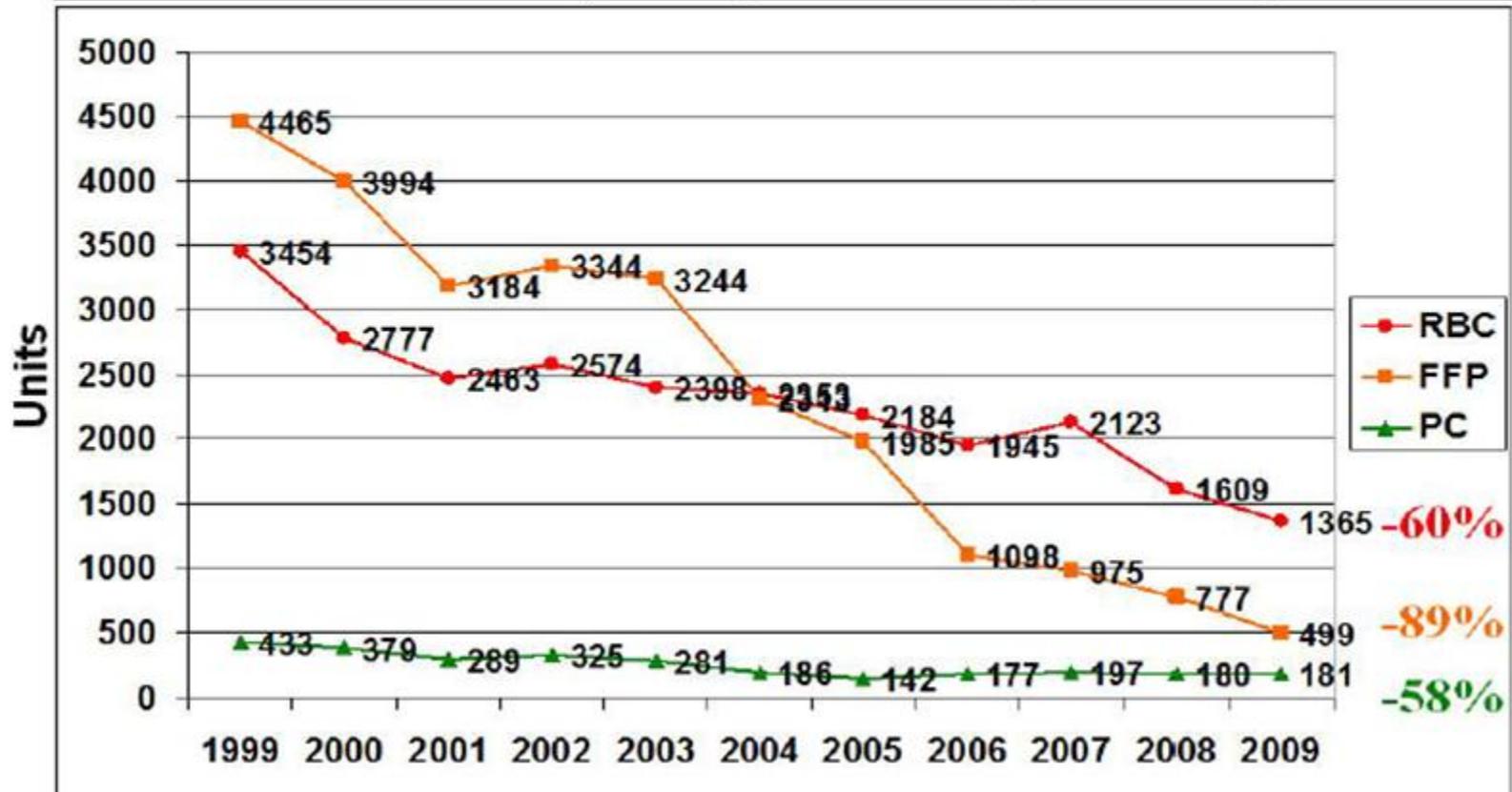
Algorithm for treating bleeding in patients with trauma-induced coagulopathy



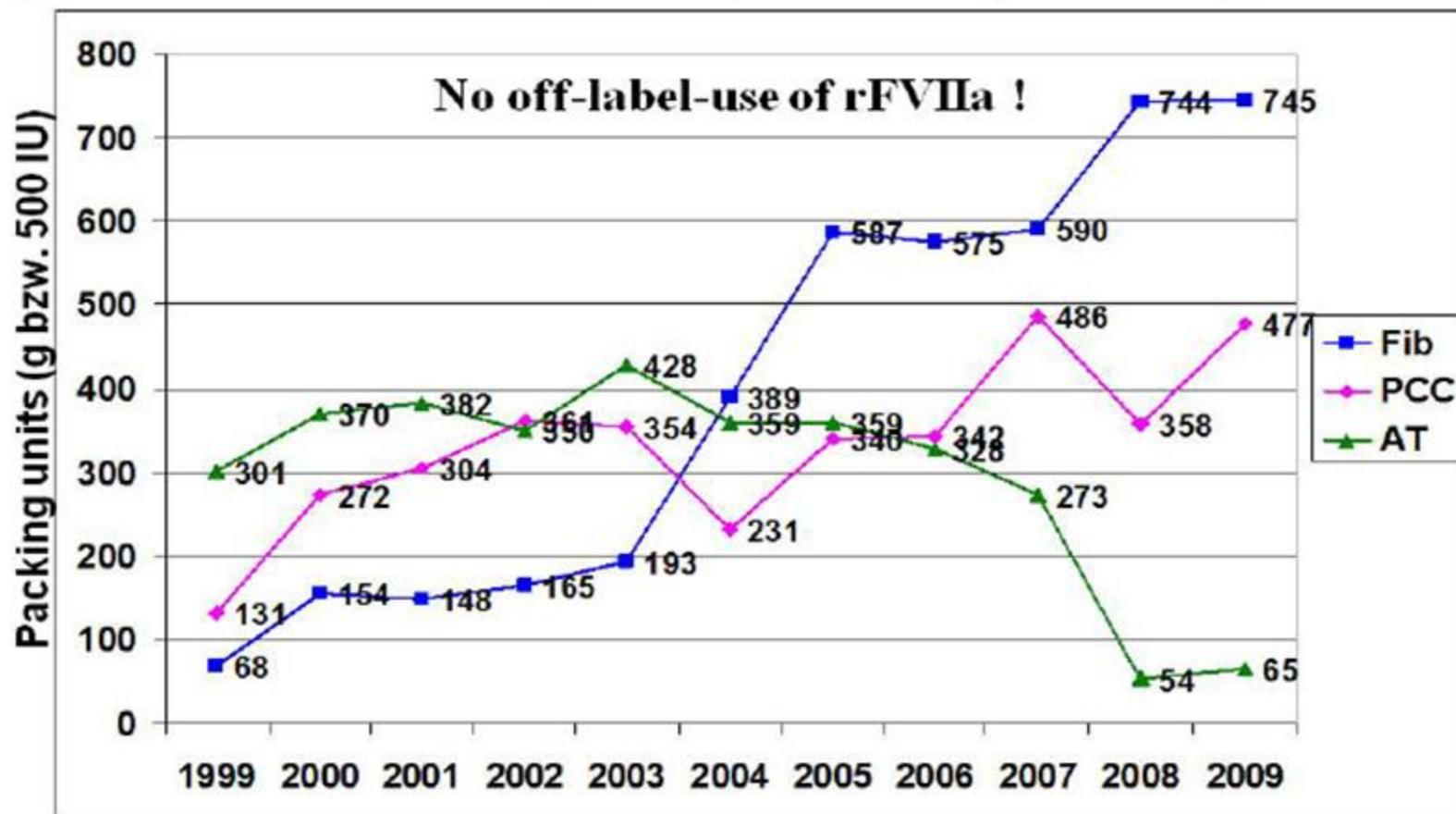
Run ROTEM (EXTEM, INTEM, FIBTEM, APTEM)*



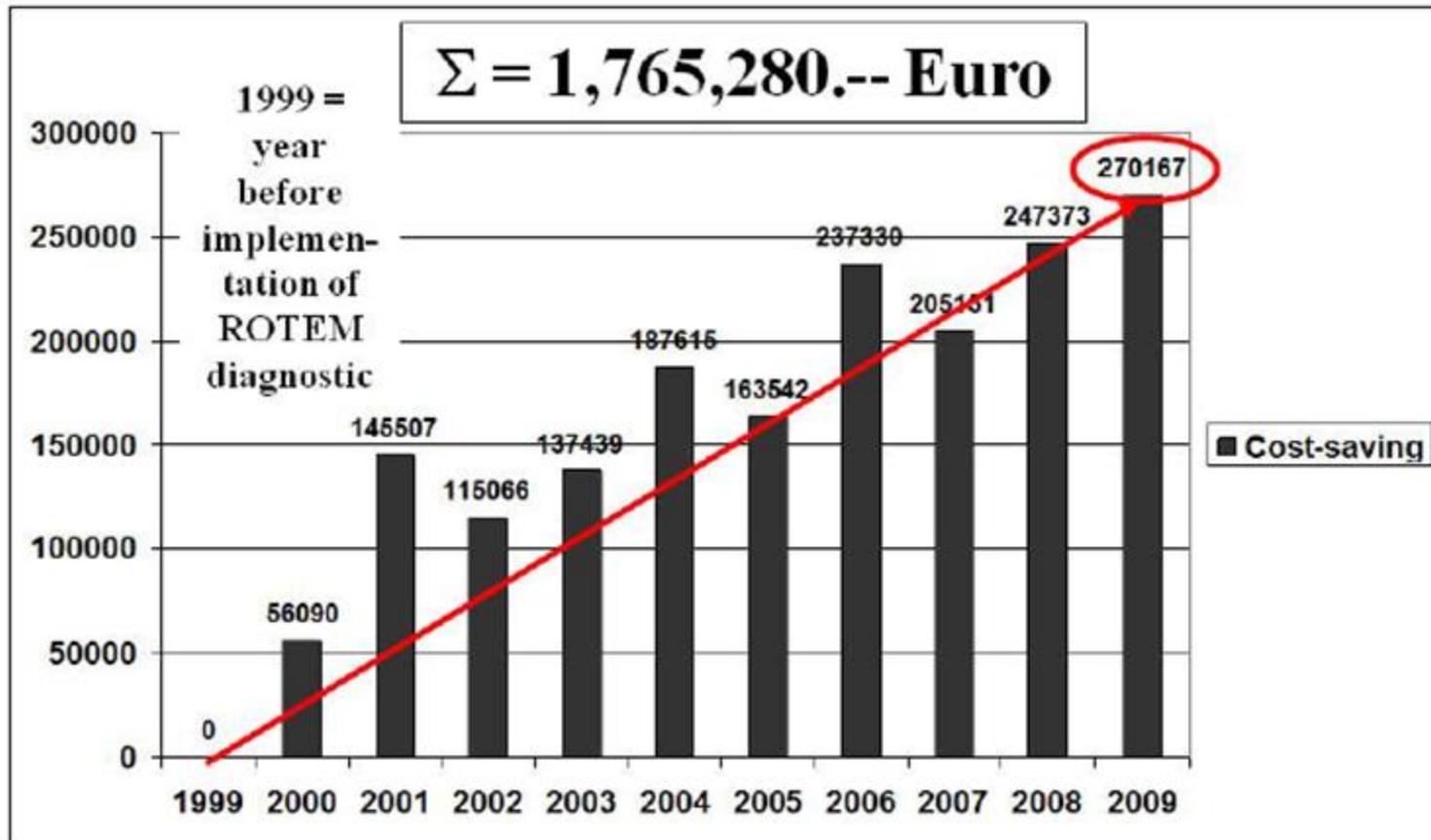
Intraoperative usage of blood products per year in visceral surgery and liver transplantation at University Hospital Essen, Germany



Intraoperative usage of coagulation factor concentrates per year in visceral surgery and liver transplantation at University Hospital Essen, Germany



Cummulative cost saving compared to 1999 in visceral surgery and liver transplantation at University Hospital Essen, Germany



	conventionnel	POC
CGR	18548	13175
PFC	13530	4885
PPSB	25755	15123
Fibrinogène	35882	27727#
Vlla	44544	5568
Total	155.431 €	75.397 €
Par patient	3109	1658



Plasma frais

Fibrinolyse

Fibrinogène

Fermeté Qualité

Systematic review of the efficacy and safety of fibrinogen concentrate substitution in adults

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Conclusion

In conclusion, evidence from four controlled trials suggests that the administration of fibrinogen concentrate improved clot firmness, decreased the need for other blood products and significantly reduced post-operative bleeding and drainage volume. In addition, it appeared to be safe. However, because all studies identified were of poor quality, these findings have to be confirmed by randomised controlled trials of sufficient size and long-term follow-up.

