Thromboélastographie et Coagulopathie Post Traumatique

Plus de MDS, Moins de PSL ?

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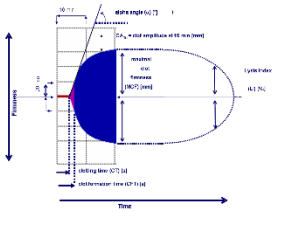
RESUVal
RESEAU DES URGENCES DE LA VALLÉE DU RHÔNE

Université Claude Bernard Lyon 1

Hospices Civils de Lyon



Déclaration de conflits d'intérêts

- ☐ **J'ai, ou ai eu** durant les trois dernières années, une affiliation, des intérêts financiers ou autres intérêts avec un organisme industriel ou commercial de type :
  - ☐ Rémunération / Bourse / Honoraires
  - ☐ Orateur / Consultant
  - ☐ Autre :

  Nom de l'organisme / des organismes : **Laboratoire LFB**

- ☐ **Je n'ai pas de conflit d'intérêt**

EPIDEMIOLOGIE

- Coagulopathie est **Fréquente**
  - 10 à 30 % des trauma sévères

Rugeri et al. JTH 2007

- Coagulopathie ↗ **Mortalité** (X 4)

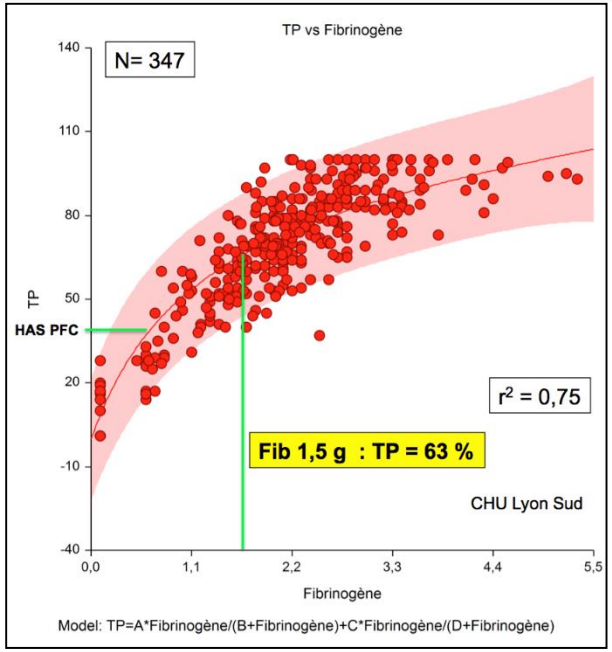
Brohi et al. J Trauma 2003

	Definition of coagulopathy	Number of patients	Percentage with coagulopathy	ISS	Mortality normal	Mortality coagulopathy
Brohi, 2003 [6]	PT >18 s or PTT >60 s	1088	24%	20[a]	11%	46%
MacLeod, 2003 [7]	PT >14 s or PTT >35 s	10 790	28%	9[a]	6%	19%
Maegele, 2007 [8•]	Quick test <70%	8724	34%	24[b]	8%	28%
Brohi, 2007 [9••]	PT >18 s or PTT >60 s[c]	208	10%	17[a]	8%	62%
Rugeri, 2007 [10•]	INR > 1.6 or PTT >60 s	88	28%	22[b]	n/a	n/a

Brohi et al. Curr Opin Crit Care 2007

KEY POINTS

CINETIQUE FIBRINOGENE

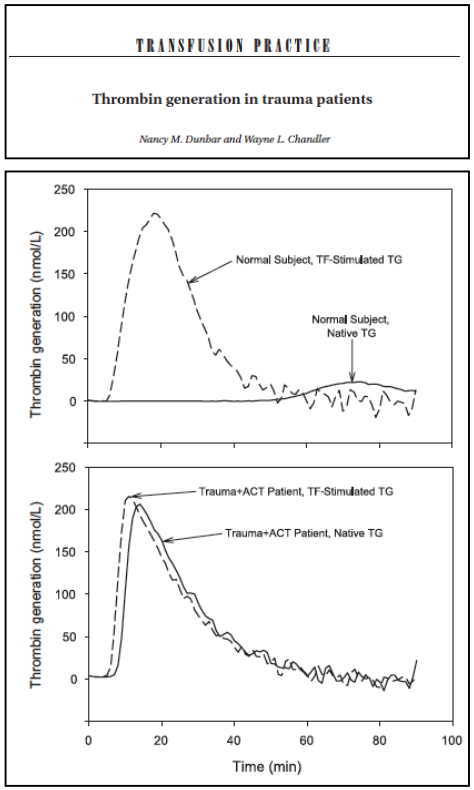


DÉCHOCAGE LYON SUD :

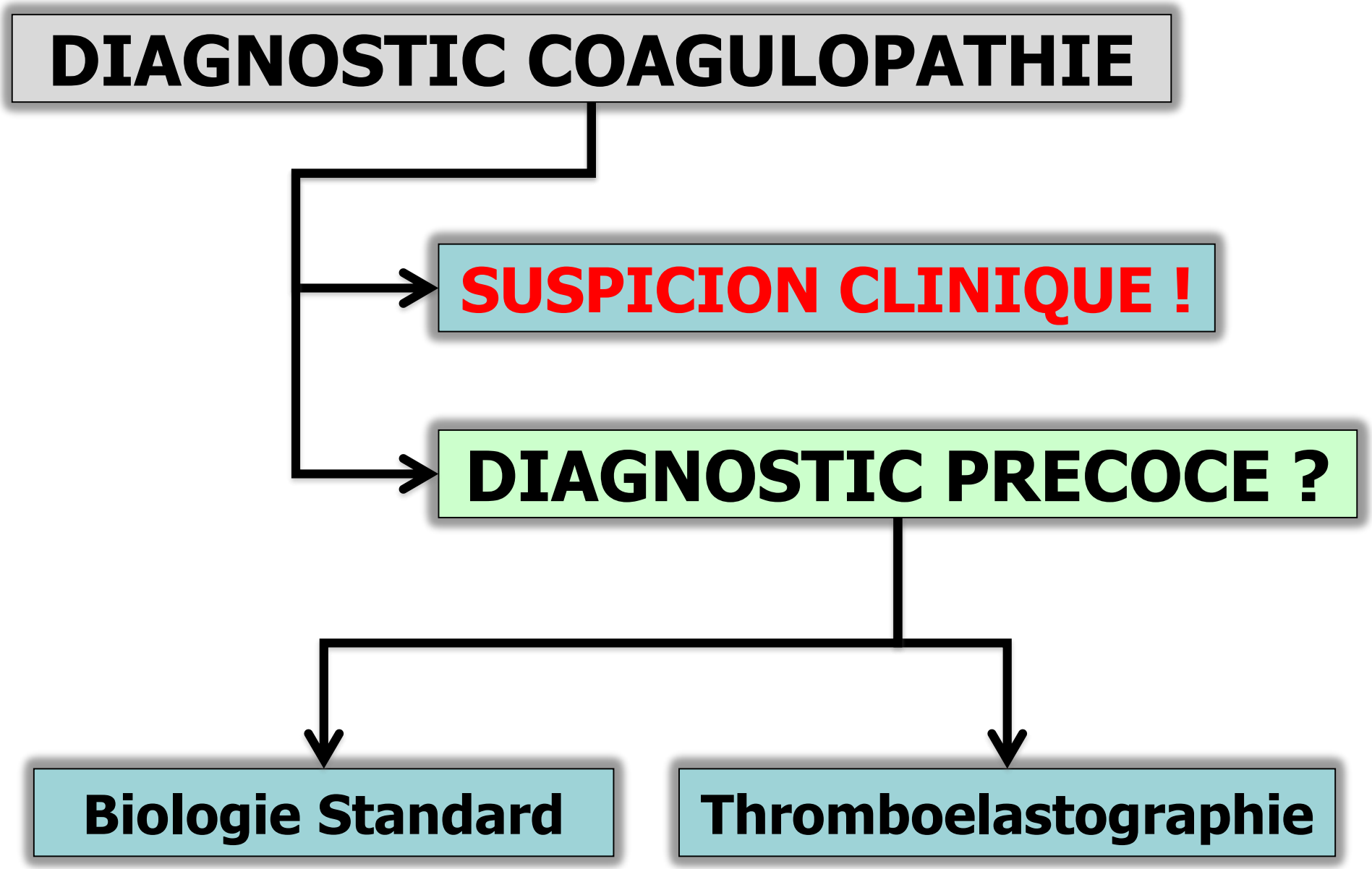
-Banque de donnée (01/2011-12/2014) = 1249 Patients

- Fibrinogène < 1,5 $g.l^{-1}$: 71 patients (20 %)
- TP< 40 : 35 patients (10 %)
- Plaquette < 100 : 14 patients (4 %)

GENERATION THROMBINE ↗



Conséquence Thérapeutique : PFC d'Abord ou C FIB ??


DIAGNOSTIC COAGULOPATHIE
SUSPICION CLINIQUE !
DIAGNOSTIC PRECOCE ?
Biologie Standard
Thromboelastographie

BIOLOGIE STANDARD

- **Bilan de coagulation standard : FIB+TP+PLT**
  - > 60 min …

Toulon et al. Thromb Haemost 2009 ; David et al. J Trauma, 2012

  - Tube coagulé, tube perdu …
  - Attendre la validation de l'Interne

British Journal of Anaesthesia **114** (2): 217–24 (2015)
Advance Access publication 8 September 2014 · doi:10.1093/bja/aeu303

BJA

Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence?

T. Haas[1*], D. Fries[2], K. A. Tanaka[3], L. Asmis[4], N. S. Curry[5] and H. Schöchl[6,7]

tings.[11 18 24 26 35–42] Based on the data of the present review, there is no high-quality evidence to support that the traditionally applied trigger levels of ≥1.5-fold prolongation of aPTT/PT or INR are of great help to diagnose whether a patient suffers

Prélevé le : 10/04/2014 15:40
Reçu le : 10/04/2014 15:50

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HEMOSTASE

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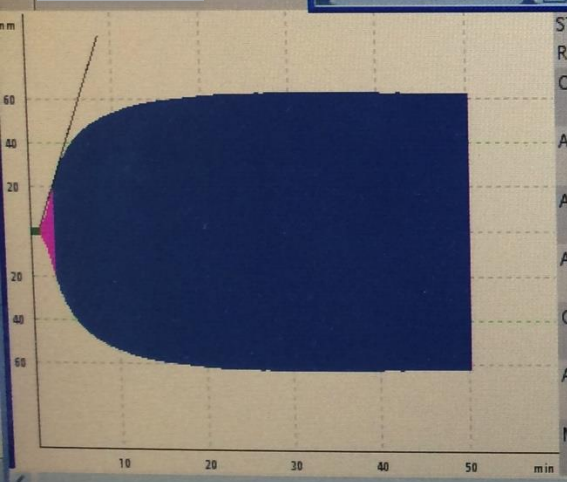
D.Massignon (04.78.86.11.77), MO.Geay (04.78.86.11.83)

Bilan de Coagulation

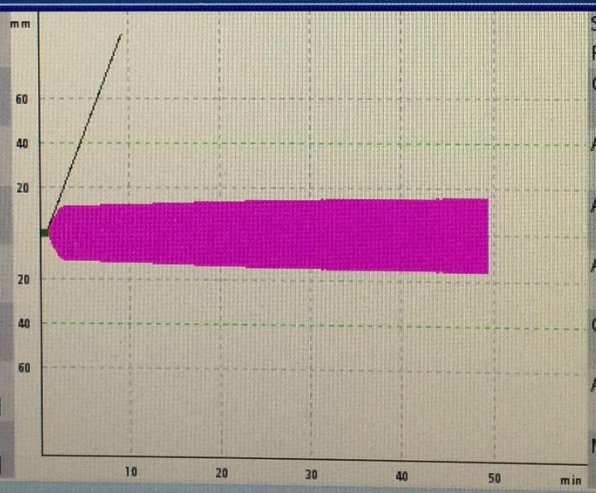
	Résultats	Unités	Valeurs de référence	Antériorités
TCA malade Méthode chronométrique. Sur STAR EVO.	En cours	s		
TCA témoin Méthode chronométrique. Sur STAR EVO.	En cours	s		
Ratio TCA	En cours		0.80-1.20	
Temps de Quick Méthode chronométrique. Sur STAR EVO.	En cours	s		
Temps de Quick Témoin Méthode chronométrique. Sur STAR EVO.	En cours	s		
Taux de Prothrombine Méthode chronométrique. Sur STAR EVO.	En cours	%	75-100	

1 sur 2

Antériorité (22 jours) | Imprimer | Fermer



ST: 16:20:50
RT: 00:50:44
CT: 67 s [0038 -- 0079]
A5: 45 mm
A10: 56 mm [0043 -- 0065]
A15: 60 mm [0048 -- 0069]
CFT: 92 s [0034 -- 0159]
A20: 62 mm [0050 -- 0071]
MCF: 63 mm [0050 -- 0072]



ST: 16:21:40
RT: 00:49:54
CT: 57 s
A5: 12 mm
A10: 13 mm [0007 -- 0023
A15: 14 mm
CFT: ---
A20: 14 mm [0008 -- 0024
MCF: 16 mm [0009 -- 0025

Retour au tableau des en cours

Nouvelle recherche

Intranet local

démarrer | CRISTALNET - Patien... | Résultat du patient C... | Consultation | 2855:0

2011

Functional definition and characterization of acute traumatic coagulopathy

Ross Davenport, BSc, MD, MRCS; Joanna Manson, MD, MRCS; Henry De'Ath, MD, MRCS; Sean Platton, MSc, CSci, FIBMS; Amy Coates, BSc; Shubha Allard, MD, FRCP, FRCPath; Daniel Hart, MD; Rupert Pearse, MD, FRCA; K. John Pasi, PhD, FRCP, FRCPath, FRCPCH; Peter MacCallum, MD, FRCP, FRCPath; Simon Stanworth, DPhil, MRCP, FRCPath; Karim Brohi, FRCA, FRCS

Coaguchek
INRatio
iStat …

EARLY PT MEASURE !?

- Potentially an interesting tool when a VCT is not available:
  - Rate of false negative is significant: 0.2-0.3 difference (depends to the ISI of your laboratory)
  - You may have a fibrinogen decrease and still a $PT_r < 1,5$
  - Available for Prehospital Setting
  - Allows rapid detection of patient taking VKA

2012

ORIGINAL ARTICLE

Utility of a Point of Care Device for Rapid Determination of Prothrombin Time in Trauma Patients: A Preliminary Study

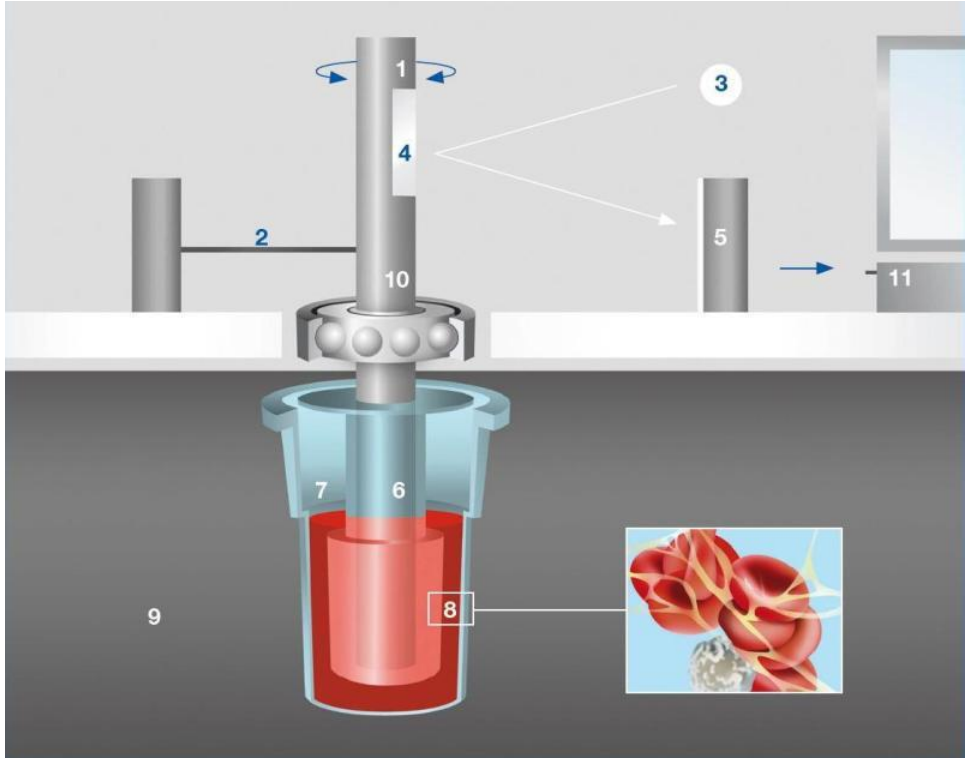
Jean-Stéphane David, MD, PhD, Albrice Levrat, MD, Kenji Inaba, MD, MSc, Caroline Macabeo, MD, Lucia Rugeri, MD, Oriane Fontaine, MD, Aurélie Cheron, MD, and Vincent Piriou, MD, PhD

Excellente VPN

INR = PTr

TECHNIQUES VISCO-ELASTIQUE

- **Sang Natif ou Citraté**



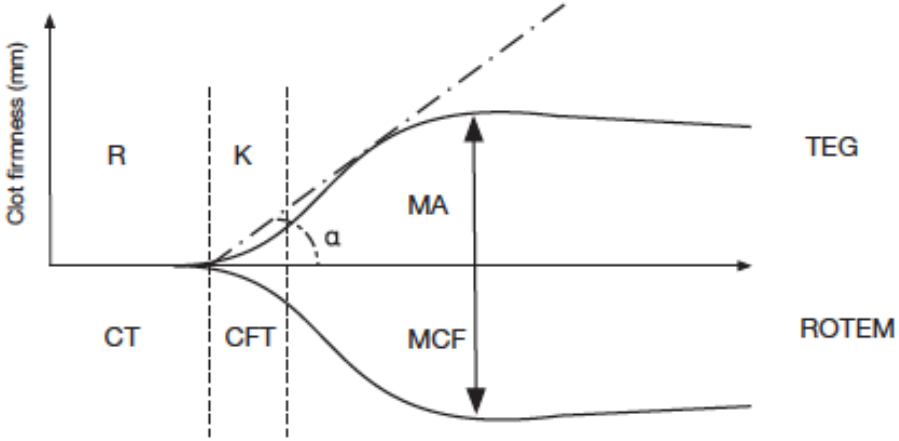
- **Inventé en 1948**
- **Ajout d'activateur**
- **ROTEM :** 4 activateurs
  - INTEM : Ac Ellagic (TCA)
  - **EXTEM** : Fact Tissulaire (TP)
  - **FIBTEM** : CytoChal. D (FIB)
  - APTEM : Aprotinine (F.LYSE)
- **TEG :** 1 activateur
  - **Kaolin (test classique)**
  - (rTEG (FT))
  - (Fibrinogène Fonctionnel)

bjh review

The place of viscoelastic testing in clinical practice

Gregory A. Hans[1] and Martin W. Besser[2]

[1]Department of Anaesthesia and Intensive Care Medicine, CHU of Liege, Liege, Belgium and [2]Department of Haematology, Addenbrooke's Hospital, Cambridge, UK

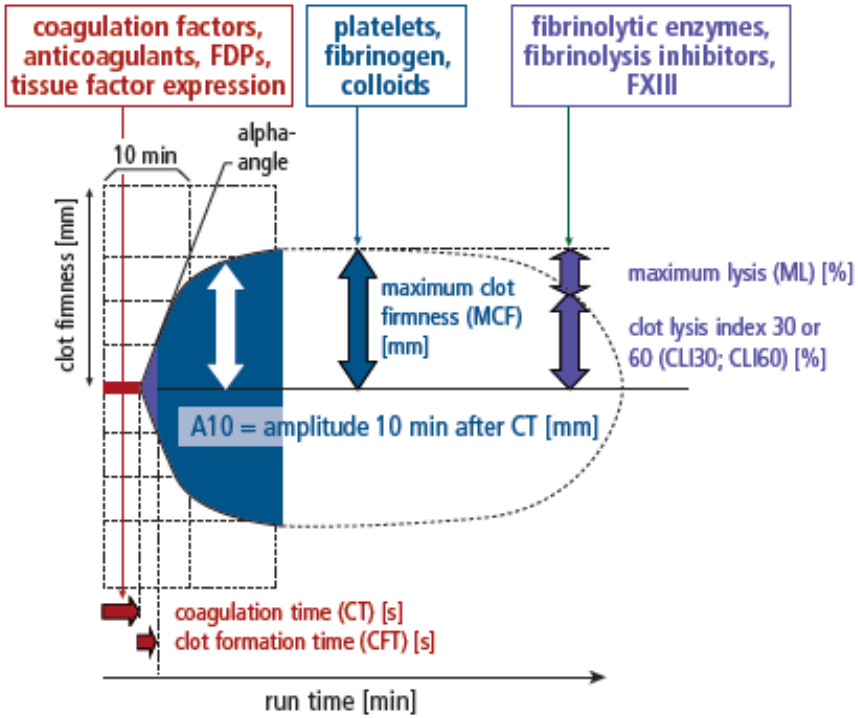


Thromboelastometry guided therapy of severe bleeding

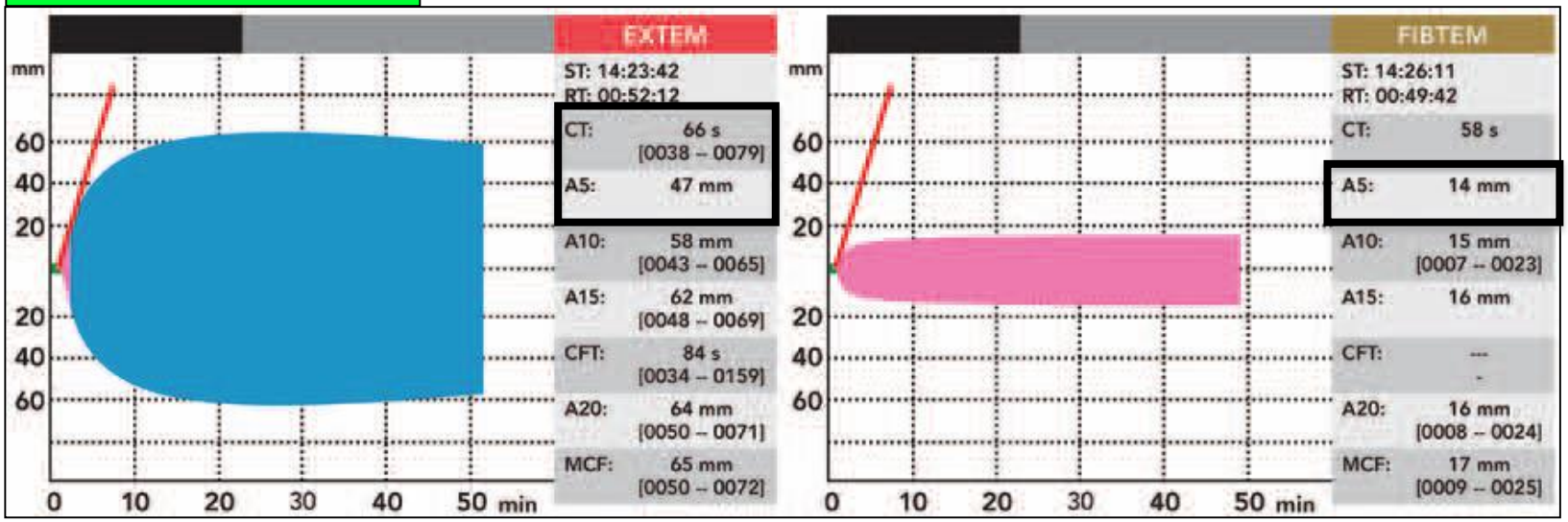
Essener Runde algorithm

H. Lier[1]; M. Vorweg[2]; A. Hanke[3]; K. Görlinger[4]

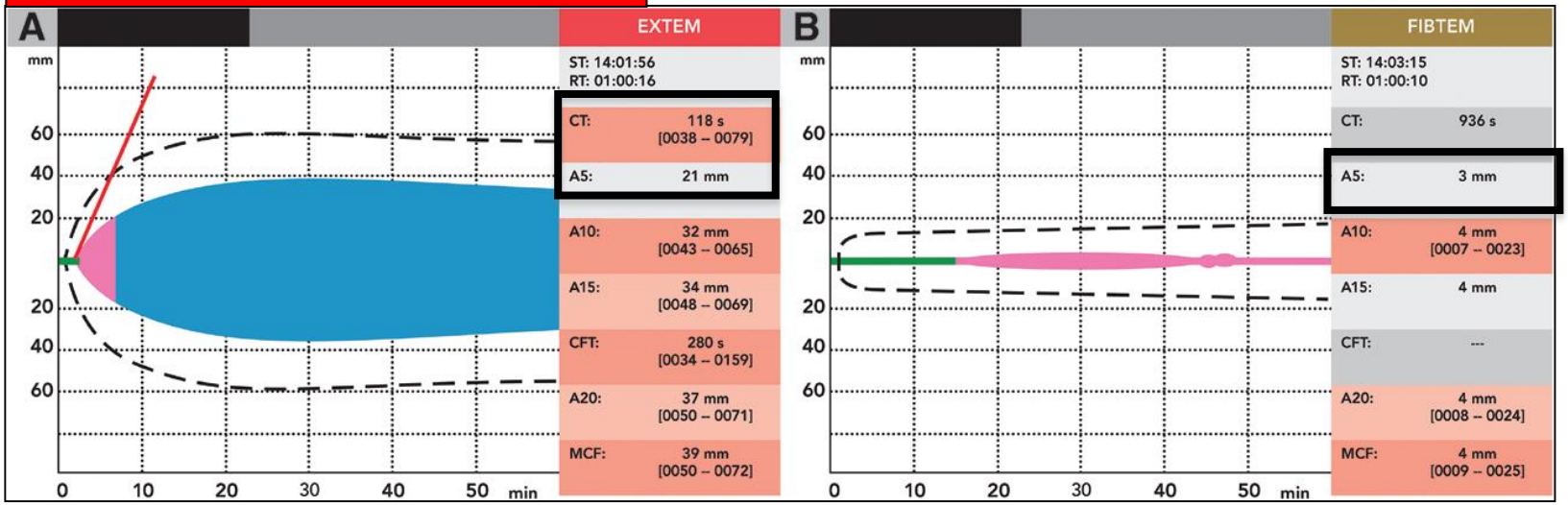
[1]Department of Anaesthesiology and Intensive Care Medicine, University Hospital Cologne, Germany; [2]Administrative Department OP-Management, Cologne City Hospitals, University of Witten / Herdecke, Cologne, Germany; [3]Department of Anaesthesiology and Intensive Care Medicine, Hannover Medical School, Hannover, Germany; [4]Tem International GmbH, Munich, Germany



TRACE NORMAL



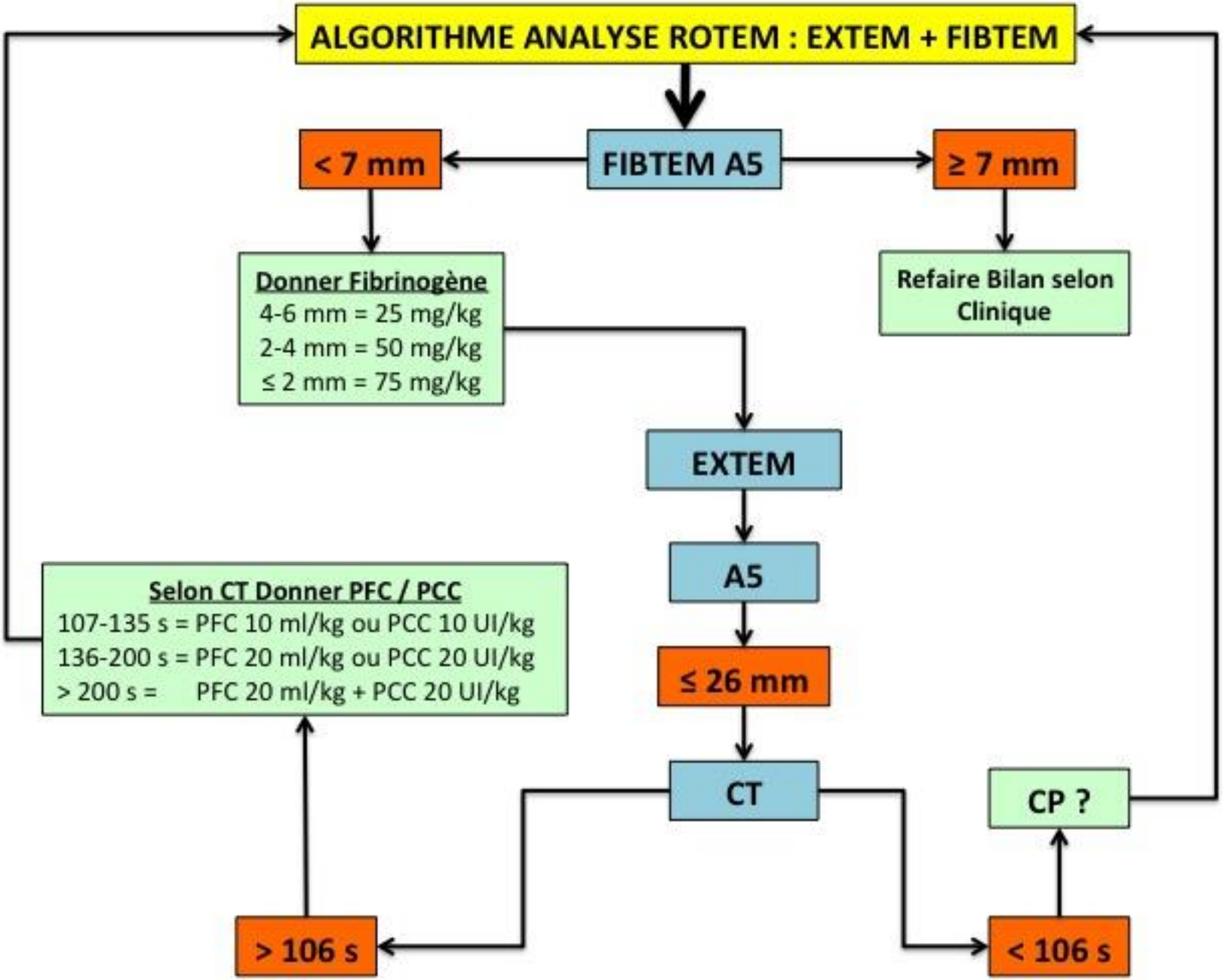
COAGULOPATHIE SEVERE



David et al. Anesthesiology 2013

<u>Lyon</u> : Prélèvement au Déchocage puis Tube Citraté au Labo
Tube Pneumatique (Pas de modification Amplitude !)

COLLABORATION +++ AVEC BIOLOGISTE


ALGORITHME ANALYSE ROTEM : EXTEM + FIBTEM
FIBTEM A5
< 7 mm
≥ 7 mm
Donner Fibrinogène
4-6 mm = 25 mg/kg
2-4 mm = 50 mg/kg
≤ 2 mm = 75 mg/kg
Refaire Bilan selon Clinique
EXTEM
A5
≤ 26 mm
CT
Selon CT Donner PFC / PCC
107-135 s = PFC 10 ml/kg ou PCC 10 UI/kg
136-200 s = PFC 20 ml/kg ou PCC 20 UI/kg
> 200 s = PFC 20 ml/kg + PCC 20 UI/kg
CP ?
> 106 s
< 106 s

TEG / ROTEM : Littérature ?

- + Rapide que Bio
- Correlation BS/TM
- Réduction PSL
- Baisse Couts
- Baisse LOS

Transfusion Medicine and Hemotherapy

Review Article · Übersichtsarbeit

Transfus Med Hemother 2012;39:104–113
DOI: 10.1159/000337186

Received: April 27, 2011
Accepted: August 1, 2011
Published online: March 8, 2012

Reduction of Fresh Frozen Plasma Requirements by Perioperative Point-of-Care Coagulation Management with Early Calculated Goal-Directed Therapy

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[a] Klinik für Anästhesiologie und Intensivmedizin, Universitätsklinikum Essen, Universität Duisburg-Essen, Germany
[b] Klinische Abteilung für Allgemeine und Chirurgische Intensivmedizin, Medizinische Universität Innsbruck, Austria
[c] Klinik für Anästhesiologie, Intensivmedizin und Schmerztherapie, Klinikum der Johann Wolfgang Goethe-Universität Frankfurt am Main,
[d] Klinik für Anästhesiologie und Intensivmedizin, Medizinische Hochschule Hannover, Germany
[e] Abteilung für Anästhesiologie und Intensivmedizin, AUVA Unfallkrankenhaus Salzburg und Ludwig Boltzmann Institut, AUVA Forschungszentrum für Traumatologie, Wien, Austria

Keywords
Thromboelastometry · Transfusion algorithms · Fibrinogen concentrate · Prothrombin complex concentrate · Transfusion-associated adverse events · Pharmacoeconomics

Schlüsselwörter
Thromboelastometrie · Transfusionsalgorithmen · Fibrinogenkonzentrat · Prothrombin-Komplex-Konzentrat · Transfusionsassoziierte Komplikationen · Pharmakoökonomie

Summary
Background: Massive bleeding and transfusion of packed red blood cells (PRBC), fresh frozen plasma (FFP) and platelets are associated with increased morbidity, mortality and costs. **Patients and Methods:** We analyzed the transfusion requirements after implementation of point-of-care (POC) coagulation management algorithms based on early, calculated, goal-directed therapy with fibrinogen concentrate and prothrombin complex concentrate (PCC) in different perioperative nonhuge trauma surgery, visceral and transplant surgery (VTS), cardiovascular surgery (CVS) and general and surgical intensive care medicinal at 3 different hospitals (AUVA Trauma Centre Salzburg, University Hospital Innsbruck and University Hospital Essen) in 2 different countries (Austria and Germany). **Results:** In all institutions, the implementation of POC coagulation management algorithms was associated with a reduction in the transfusion requirements for FFP by about 90% (Salzburg 94%, Innsbruck 88% and Essen 93%). Furthermore, PRBC transfusion was reduced by 8.4–62%. The incidence of intraoperative massive transfusion (>10 U PRBC) could be more than halved in VTS and CVS (7.58 vs. 0.88%, p < 0.0001 and 2.53 vs. 1.08%, p = 0.0097, respectively). Platelet transfusion could be reduced by 21–72%, except in CVS where it increased by 116% due to a 5-fold increase in patients with dual antiplatelet therapy (2.7 vs. 13.7%, p < 0.0001). **Conclusions:** The implementation of perioperative POC coagulation management algorithms based on early, calculated, goal-directed therapy with fibrinogen concentrate and PCC is associated with a reduction in the transfusion requirements for FFP, PRBC and platelets as well as with a reduced incidence of massive transfusion. Thus, the limited blood resources can be used more efficiently.

Zusammenfassung
Hintergrund: Sowohl schwere Blutungen als auch die Transfusion von Erythrozytenkonzentraten (EK), Frischplasma (FFP) und Thrombozytenkonzentraten (TK) sind mit einer Steigerung der Morbidität, der Mortalität und der Kosten assoziiert. **Patienten und Methoden:** Wir analysierten den Einfluss der Implementierung von Point-of-Care(POC)-Algorithmen zum Gerinnungsmanagement, basierend auf der frühzeitigen, kalkulierten, zielgerichteten Therapie mit Fibrinogenkonzentrat und Prothrombin-Komplex-Konzentrat (PPSB), auf den Transfusionsbedarf in unterschiedlichen perioperativen Bereichen (Unfallchirurgie, Viszeral- und Transplantationschirurgie, kardiovaskuläre Chirurgie und allgemeine und chirurgische Intensivmedizin) in 3 verschiedenen Kliniken (AUVA Traumazentrum Salzburg, Universitätsklinikum Innsbruck und Universitätsklinikum Essen) in 2 verschiedenen Ländern (Österreich und Deutschland). **Ergebnisse:** In allen Kliniken war die Implementierung der POC-Algorithmen zum Gerinnungsmanagement mit einer etwa 90%igen Reduktion des Transfusionsbedarfs an FFP assoziiert (Salzburg 94%, Innsbruck 88% und Essen 93%). Außerdem konnte die Zahl der transfundierten EK um 8.4–62% reduziert werden. Die Inzidenz von intraoperativen Massivtransfusionen (>10 EK) konnte in der Viszeral- und Transplantationschirurgie sowie in der kardiovaskulären Chirurgie mehr als halbiert werden (2,58 vs. 0,88%; p < 0,0001 bzw. 2,58 vs. 1,08%; p = 0,0097). Die Transfusion von TK konnte mit Ausnahme der kardiovaskulären Chirurgie um 21–72% reduziert werden. In Letzterer stieg der Verbrauch an TK aufgrund einer 5-fachen Zunahme der Patienten mit dualer antithrombotischer Therapie (2,7 vs. 13,7%; p < 0,0001) um 116% an. **Schlussfolgerungen:** Die Implementierung von POC-Algorithmen zum perioperativen Gerinnungsmanagement, basierend auf der frühzeitigen, kalkulierten, zielgerichteten Therapie mit Fibrinogenkonzentrat und PCC, ist mit einer Reduktion des Transfusionsbedarfs für EK, FFP und TK sowie mit einer Reduktion der Inzidenz von Massivtransfusionen assoziiert. Dadurch können die knappen Blutressourcen effizienter genutzt werden.

Introduction

In the last decade interest in trauma coagulopathy has increased with an awareness that 24–34% of patients[1–3] who arrive at major trauma centres have a coagulopathy. The proportion of patients exhibiting coagulopathy increases with injury severity score (ISS), and the presence of coagulopathy is independently associated with increased mortality.[4] Military rates of admission coagulopathy have been reported to be similar[5] to those seen in civilian practice. The aetiology of trauma coagulopathy is multi-factorial. Recently it has been suggested that in the early stages of acute trauma coagulopathy the clotting deficiency is a primary event related to tissue hypoxia.[6] In this phase there is an imbalance between anticoagulation, coagulation and fibrinolysis which favours anticoagulation and lysis.

In order to effectively treat trauma induced coagulopathy it is necessary to rapidly assess the patient's dynamically changing coagulation status and their response to treatment.[7–9] Conventional laboratory tests (PT/aPTT) are too long to provide meaningful guidance for the seriously injured patient.[8] In Afghanistan it generally took 40–60 min for a laboratory PT/aPTT result to be available at the patient bedside.[10] This delay rendered the result historical and of no value in guiding the initial, highly dynamic, treatment of these seriously injured patients. Viscoelastic methods potentially provide more rapid feedback and are therefore potentially more useful in determining contemporary coagulation status of the patient.[11–13] Key parameters include measures of clot initiation time, the dynamics of the clotting process and clot strength. Unfortunately it can take up to 45 min in our study, for a full picture to emerge in a coagulopathic patient, although interim values are reported sooner. The purpose of this

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0020-1383/$ – see front matter. Crown Copyright © 2012 Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.injury.2012.03.018

Please cite this article in press as: Woolley T, et al. Utility of interim ROTEM® values of clot strength, A5 and A10, in predicting final assessment of coagulation status in severely injured battle patients. Injury (2012), doi:10.1016/j.injury.2012.03.018

Schöchl et al. Critical Care 2011, 15:R83
http://ccforum.com/content/15/2/R83

CRITICAL CARE

RESEARCH · Open Access

Transfusion in trauma: thromboelastometry-guided coagulation factor concentrate-based therapy versus standard fresh frozen plasma-based therapy

Herbert Schöchl[1,2], Ulrike Nienaber[3], Marc Maegele[4], Gerald Hochleitner[2], Florian Primavesi[2], Beatrice Steitz[2], Christian Arndt[1], Alexander Hanke[5], Wolfgang Voelckel[2] and Cristina Solomon[6]*

Abstract
Introduction: Thromboelastometry (TEM)-guided haemostatic therapy with fibrinogen concentrate and prothrombin complex concentrate (PCC) in trauma patients may reduce the need for transfusion of red blood cells (RBC) or platelet concentrate, compared with fresh frozen plasma (FFP)-based haemostatic therapy.
Methods: This retrospective analysis compared patients from the Salzburg Trauma Centre (Salzburg, Austria) treated with fibrinogen concentrate and/or PCC, but no FFP (fibrinogen+PCC group, n = 80), and patients from the Traumaregister DGU® receiving ≥ 2 units of FFP, but no fibrinogen concentrate/PCC (FFP group, n = 601). Inclusion criteria were age 18-70 years, base deficit at admission ≥2 mmol/L, injury severity score (ISS) ≥16, abbreviated injury scale for thorax, or abdomen and/or extremity ≥3, and for head/neck < 5.
Results: For haemostatic therapy in the emergency room and during surgery, the FFP group (ISS 35.5 ± 10.5) received a median of 6 units of FFP (range: 2, 51), while the fibrinogen+PCC group (ISS 35.2 ± 12.5) received medians of 6 g of fibrinogen concentrate (range: 0, 15) and 1200 U of PCC (range: 0, 6600). RBC transfusion was avoided in 29% of patients in the fibrinogen+PCC group compared with only 3% in the FFP group (P< 0001). Transfusion of platelet concentrate was avoided in 91% of patients in the fibrinogen+PCC group, compared with 56% in the FFP group (P< 0001). Mortality was comparable between groups: 25% in the fibrinogen+PCC group and 10.0% in the FFP group (P = 069).
Conclusions: TEM-guided haemostatic therapy with fibrinogen concentrate and PCC reduced the exposure of trauma patients to allogeneic blood products.

Introduction

In patients with severe trauma, coagulopathy represents a frequent cause of death [1,2]. Prompt haemostatic intervention is necessary to prevent and correct life-threatening bleeding. Standard coagulation therapy consists of fresh frozen plasma (FFP), platelet concentrate and, in some countries, cryoprecipitate [3,4]. One approach proposed for preventing exsanguination has been to treat patients with a fixed ratio of FFP to red blood cells (RBC), but the optimal value of this ratio is still under debate [5-8]. It has been recently suggested that the time to intervention may also be an important determinant of patient outcomes [9,10].

Our group has been exploring goal-directed coagulation management using fibrinogen concentrate and prothrombin complex concentrate (PCC), administered as early as possible according to thromboelastometric (TEM) measurements [11,12]. This approach supports timely and aggressive correction of coagulopathy. It may also be considered as a strategy for reducing transfusion of allogeneic blood products: the need for FFP may be reduced by the administration of coagulation factors: fibrinogen, contained in fibrinogen concentrate, and factors II, VII, IX and X, contained in most PCCs. Furthermore, clinical and experimental data suggest that fibrinogen supplementation may also compensate for

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Full list of author information is available at the end of the article

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EAST 2015 PLENARY PAPER

All the bang without the bucks: Defining essential point-of-care testing for traumatic coagulopathy

Michael D. Goodman, MD, Amy T. Makley, MD, Dennis J. Hanseman, PhD, Timothy A. Pritts, MD, PhD, and Bryce R.H. Robinson, MD, *Cincinnati, Ohio*

BACKGROUND: Rapid assessment and treatment of coagulopathy reduces postinjury morbidity and mortality. Although thrombelastography (TEG) may be more accurate and efficient than conventional coagulation tests, it requires significant financial and personnel investments. We hypothesized that point-of-care international normalized ratio (POC INR) may provide a rapid and accurate alternative to TEG.
METHODS: A retrospective review of sequential trauma patients who underwent both POC INR and rapid TEG (r-TEG) testing upon presentation to a Level I trauma center from July 2012 to December 2013 was performed. POC INR was compared with r-TEG values (R value, K time, α angle, maximum amplitude, percent clot lysis in 30 minutes) and transfusion requirements. Vital signs, admission laboratory values, and injury severity were analyzed. POC INR and venous blood gas testing was performed in the emergency department. All results and Pearson correlations noted were significant ($P \leq 0.05$).
RESULTS: We identified 628 trauma patients with concomitant r-TEG and POC INR testing. Median Injury Severity Score (ISS) was 13, 20% arrived in shock (base value < −5), 23% were transfused, and 11% died. POC INR correlated with all r-TEG values, with stronger correlations for patients in shock. POC INR and r-TEG had similar correlations with blood products transfused at 4 hours and 24 hours, but only POC INR predicted substantial bleeding and massive transfusion. POC INR also correlated strongly with standard INR testing. POC INR test duration was less than 1 minute, compared with at least 30 minutes for r-TEG. Total cohort charges for POC INR were estimated at $21,980 versus $396,896 for r-TEG.
CONCLUSION: POC INR testing is faster and cheaper than r-TEG. In addition, POC INR correlates not only with r-TEG values but also with acute blood product transfusions. POC INR provides a practical alternative for rapid coagulopathy assessment in the trauma patient at institutions that lack TEG capability. *J Trauma Acute Care Surg.* 2015;79:117-124. Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.
LEVEL OF EVIDENCE: Diagnostic study, level III; Therapeutic/care management study, level IV.
KEY WORDS: INR; TEG; coagulopathy; massive transfusion.

Exsanguinating hemorrhage remains the leading cause of preventable death following injury.[1,2] In addition to rapid surgical control of hemorrhage, prompt identification and treatment of acute coagulopathy is necessary to avert ongoing blood loss. The presence and severity of acute traumatic coagulopathy (ATC) on admission are associated with increased transfusion requirements and mortality in trauma patients.[3–5] The rapid identification and treatment of coagulopathy by protocols and principles such as damage-control resuscitation can combat the lethal effects of ATC in both military and civilian populations.[6–14] Timely recognition of ATC may depend on the coagulation test performed upon arrival to the emergency department (ED). Plasma-based conventional coagulation tests (CCTs) are traditionally used and include prothrombin time (PT) and standardized international normalized ratio (INR), activated partial thromboplastin time, and fibrinogen level. Of these CCTs, INR alone has been included in a set of physiologic and hemodynamic triggers that correlate with the need for massive transfusion, including systolic blood pressure less than 90 mm Hg, hemoglobin less than 11 g/dL, temperature lower than 35.5°C, INR greater than 1.5, and base deficit of 6 or greater.[8,15] Admission INR has further been identified as the most predictive individual trigger for any transfusion, including the need for massive transfusion.[15]

Despite the universal availability and implementation of INR testing in hospital laboratories worldwide, recent literature suggests that CCTs may not be optimal for identification of acute coagulopathy in trauma patients. CCTs are in vitro acellular assessments of platelet-poor plasma that are neither time nor temperature sensitive.[16,17] There has been increased interest in whole-blood viscoelastic hemostatic assays, such as thromboelastography (TEG), to address the need for a rapid, real-time assessment of coagulopathy. Compared with CCTs, rapid TEG (r-TEG) values have been shown to be faster and less expensive measures of coagulopathy. TEG more strongly correlates with blood product transfusion in severely injured trauma patients and more accurately assesses coagulopathy in stable trauma and surgical patients when compared with CCTs.[16,17] However, TEG and other viscoelastic tests are subject to a unique set of preanalytic and analytic factors that may impact test reliability and reproducibility.[18] Sample storage time and the use of citrated samples can affect reproducibility of TEG results, and

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CRITICAL CARE

RESEARCH · Open Access

Goal-directed coagulation management of major trauma patients using thromboelastometry (ROTEM®)-guided administration of fibrinogen concentrate and prothrombin complex concentrate

Herbert Schöchl[1,2], Ulrike Nienaber[3], Georg Hofer[1], Wolfgang Voelckel[2], Csilla Jambor[4], Gisela Scharbert[1], Sibylle Kozek-Langenecker[3] and Cristina Solomon[4]*

Abstract
Introduction: The appropriate strategy for trauma-induced coagulopathy management is under debate. We report the treatment of major trauma using mainly coagulation factor concentrates.
Methods: This retrospective analysis included trauma patients who received > 5 units of red blood cell concentrate within 24 hours. Coagulation management was guided by thromboelastometry (ROTEM®). Fibrinogen concentrate was given as first-line haemostatic therapy when maximum clot firmness (MCF) measured by FIBTEM (fibrin-based test) was < 10 mm. Prothrombin complex concentrate (PCC) was given in case of recent coumarin intake or clotting time measured by extrinsic activation test (EXTEM) > 1.3 times normal. Lack of improvements in EXTEM MCF after fibrinogen concentrate administration was an indication for platelet concentrate. The observed mortality was compared with the mortality predicted by the trauma injury severity score (TRISS) and by the revised injury severity classification (RISC) score.
Results: Of 131 patients included, 128 received fibrinogen concentrate as first line therapy, 98 additionally received PCC, while 3 patients with recent coumarin intake received only PCC. Twelve patients received FFP and 29 received platelet concentrate. The observed mortality was 24.4%, lower than the TRISS mortality of 33.7% (P = 0.032) and the RISC mortality of 28.7% (P > 0.05). After excluding 17 patients with traumatic brain injury, the difference in mortality was 14% observed versus 27.8% predicted by TRISS (P = 0.0018) and 24.3% predicted by RISC (P = 0.014).
Conclusions: ROTEM®-guided haemostatic therapy, with fibrinogen concentrate as first-line haemostatic therapy and additional PCC, was goal-directed and fast. A favourable survival rate was observed. Prospective, randomized trials to investigate this therapeutic alternative further appear warranted.

Introduction

Coagulopathy has been shown to be present in approximately 25 to 35% of all trauma patients on admission to the emergency room (ER) [1,2]. This represents a serious problem for major trauma patients and accounts for 40% of all trauma-related deaths [3]. Coagulopathy forces a strategy of early and rapid haemostatic treatment to prevent exsanguination. Fresh frozen plasma (FFP) is part of the massive transfusion protocols in most trauma centres [3-5], although its efficacy is uncertain. Massive transfusion protocols that favour a red blood cell (RBC):FFP ratio of 1:1 have shown conflicting results [6-14]. In addition, there are well recognized risks associated with FFP administration in the trauma setting, such as acute lung injury, volume overload, and nosocomial infection [12,15-17]. According to the Serious Hazards of Transfu-

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CRITICAL CARE

RESEARCH · Open Access

Trauma-induced coagulopathy: impact of the early coagulation support protocol on blood product consumption, mortality and costs

Giuseppe Nardi[1*], Vanessa Agostini[2], Beatrice Rondinelli[3], Emanuele Russo[4], Barbara Bastianini[1], Giovanni Bini[4], Simona Bulgarelli[5], Emiliano Cingolani[1], Alessia Donato[5], Giorgio Gambale[5] and Giulia Ranaldi[5]

Abstract
Introduction: Hemorrhage is the principal cause of death in the first few hours following severe injury. Coagulopathy is a frequent complication of critical bleeding. A network of Italian trauma centers recently developed a protocol to prevent and treat trauma-induced coagulopathy. A pre-post cohort multicenter study was conducted to assess the impact of the early coagulation support (ECS) protocol on blood products consumption, mortality and treatment costs.
Methods: Adult trauma patients (Injury Severity Score (ISS) > 15) administered at least 1 unit of packed red blood cells (PRBCs) within 24 hours of an accident were included in the study. In 2011, patients with significant hemorrhaging were treated with early administration of plasma with the aim of achieving a high (≥ 1:2) plasma-to-PRBC ratio. In 2013, the ECS protocol was the treatment strategy. Outcome data, blood product consumption and treatment costs were compared between the two periods.
Results: The two groups were well matched for demographics, injury severity (ISS: 32.9 in 2011 versus 33.6 in 2013) and clinical and laboratory data on admission. In 2013, a 40% overall reduction in PRBCs was observed, together with a 65% reduction in plasma and a 52% reduction in platelets. Patients in the ECS group received fewer blood products: 6.51 units of PRBCs versus 8.14 units, plasma transfusions decreased from 8.98 units to 4.21 units ($P < 0.05$), and platelets fell from 4.14 units to 2.53 units ($P < 0.05$). Mortality in 2013 was 13.5% versus 20% in 2011 (13 versus 26 hospital deaths, respectively) (nonsignificant). When costs for blood components, factors and point-of-care tests were compared, a €76,342 saving in 2013 versus 2011 (23%) was observed.
Conclusions: The introduction of the ECS protocol in two Italian trauma centers was associated with a marked reduction in blood product consumption, reaching statistical significance for plasma and platelets, and with a non-significant trend toward a reduction in early and 28-day mortality. The overall costs for transfusion and coagulation support (including point-of-care tests) decreased by 23% between 2011 and 2013.

Introduction

Hemorrhage is the principal cause of death in the first few hours following severe injury. Coagulopathy is a frequent complication of hemorrhage and may occur in up to 35% of patients, even before hospital admission [1]. Recently, a multidisciplinary, pan-European group of experts launched the Stop the Bleeding Campaign [2], a campaign to counteract preventable deaths from uncontrolled bleeding following traumatic injury. The goal of the campaign is to reduce the number of patients who die within 24 hours after hospital admission (due to exsanguination) by a minimum of 20%. This goal was set in response to the updated European guidelines for management of bleeding and coagulopathy [3]. These guidelines recommend that every trauma facility implement an evidence-based treatment algorithm for the bleeding trauma patient and promote the use of treatment algorithms to guide clinical management.

The Italian Trauma Centers Network (TUN) responded to the recommendations by developing a treatment

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Goal-directed Hemostatic Resuscitation of Trauma-induced Coagulopathy

A Pragmatic Randomized Clinical Trial Comparing a Viscoelastic Assay to Conventional Coagulation Assays

Eduardo Gonzalez, MD, Ernest E. Moore, MD,*† Hunter B. Moore, MD,* Michael P. Chapman, MD,* Theresa L. Chin, MD,* Arsen Ghasabyan, MPH,* Max V. Wohlauer, MD,* Carlton C. Barnett, MD,*† Denis D. Bensard, MD,*† Walter L. Biffl, MD,*† Clay C. Burlew, MD,*† Jeffrey L. Johnson, MD,*† Fredric M. Pieracci, MD, MPH,*† Gregory J. Jurkovich, MD,*† Anirban Banerjee, PhD,* Christopher C. Silliman, MD, PhD,*‡§ and Angela Sauaia, MD, PhD*¶*

Background: Massive transfusion protocols (MTPs) have become standard of care in the management of bleeding injured patients, yet strategies to guide them vary widely. We conducted a pragmatic, randomized clinical trial (RCT) to test the hypothesis that an MTP goal directed by the viscoelastic assay thrombelastography (TEG) improves survival compared with an MTP guided by conventional coagulation assays (CCA).

Methods: This RCT enrolled injured patients from an academic level-1 trauma center meeting criteria for MTP activation. Upon MTP activation, patients were randomized to be managed either by an MTP goal directed by TEG or by CCA (ie, international normalized ratio, fibrinogen, platelet count). Primary outcome was 28-day survival.

Results: One hundred eleven patients were included in an intent-to-treat analysis (TEG = 56, CCA = 55). Survival in the TEG group was significantly higher than the CCA group (log-rank $P = 0.032$, Wilcoxon $P = 0.027$); 20 deaths in the CCA group (36.4%) compared with 11 in the TEG group (19.6%) ($P = 0.049$). Most deaths occurred within the first 6 hours from arrival (21.8% CCA group vs 7.1% TEG group) ($P = 0.032$). CCA patients required similar number of red blood cell units as the TEG patients [CCA: 5.0 (2–11), TEG: 4.5 (2–8)] ($P = 0.317$), but more plasma units [CCA: 2.0 (0–4), TEG: 0.0 (0–3)] ($P = 0.022$), and more platelets units [CCA: 0.0 (0–1), TEG: 0.0 (0–0)] ($P = 0.041$) in the first 2 hours of resuscitation.

Conclusions: Utilization of a goal-directed, TEG-guided MTP to resuscitate severely injured patients improves survival compared with an MTP guided by CCA and utilizes less plasma and platelet transfusions during the early phase of resuscitation.

Keywords: coagulopathy, fibrinolysis, goal-directed, resuscitation, thrombelastography, transfusion

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Injury is the second leading cause of death worldwide and the most common for individuals 15 to 49 years of age.[1–3] The burden of injuries has decreased due to strategies such as injury prevention, advanced prehospital care, regionalized trauma systems, damage control operative techniques, advances in critical care medicine, and rehabilitation with reintegration into society.[4,5] However, in both civilian and military trauma, uncontrolled bleeding remains the leading preventable cause of death, with as much as 40% of injury-related mortality due to hemorrhage.[6–9] This is largely attributed to the exacerbation of bleeding by dysfunctional hemostasis. In 25% to 35% of patients with severe trauma, this trauma-induced coagulopathy is already present upon arrival to the emergency department (ED).[10,11]

Traditionally, assessment of hemostasis in the injured has been made with conventional coagulation assays (CCA) such as the international normalized ratio (INR) of prothrombin time, partial thromboplastin time (PTT), platelet count, and fibrinogen concentration. Viscoelastic assays of hemostasis (VHA) such as thrombelastography (TEG) (Haemonetics Corp, Niles, IN) and rotational

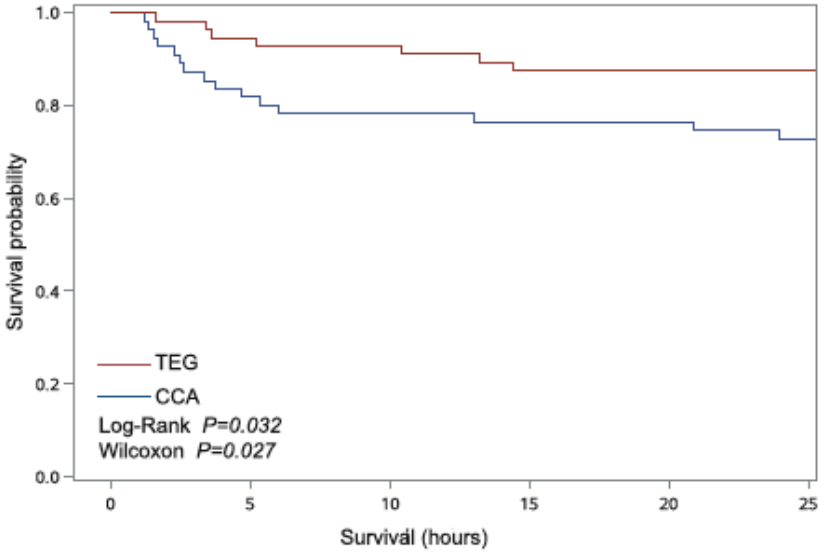

FIGURE 1. Kaplan-Meier estimates of survival by randomization group for patients analyzed as intention-to-treat. Survival in the TEG group was significantly higher than the CCA group (log-rank $P = 0.0324$, Wilcoxon $P = 0.0275$).

TABLE 2. Outcome of Mortality Stratified by Study Group

	Intention to Treat		
	CCA (N = 55)	TEG (N = 56)	*P*
Deaths, no. (% within group)	20 (36.4)	11 (19.6)	0.049
Time to death in hours from ED arrival, median (IQR)	4.2 (2.4–9.9)	10.4 (4.5–200.3)	0.181
Deaths occurring in the first 6 hours from ED arrival, no. (% within group)	12 (21.8)	4 (7.1)	0.032
Deaths occurring >6 h from ED arrival, no. (% within group)	8 (14.5)	7 (12.5)	0.785
Hemorrhagic deaths, no. (% within group)	11 (20.0)	5 (8.9)	0.110
TBI deaths, no. (% within group)	6 (10.9)	4 (7.1)	0.537
Organ failure, no. (% within group)	3 (5.5)	2 (3.6)	0.675

TRAITEMENT COAGULOPATHIE

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DOI 10.1186/s13054-016-1265-x

Critical Care

RESEARCH Open Access

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

Rolf Rossaint[1], Bertil Bouillon[2], Vladimir Cerny[3,4,5,6], Timothy J. Coats[7], Jacques Duranteau[8], Enrique Fernández-Mondéjar[9], Daniela Filipescu[10], Beverley J. Hunt[11], Radko Komadina[12], Giuseppe Nardi[13], Edmund A. M. Neugebauer[14], Yves Ozier[15], Louis Riddez[16], Arthur Schultz[17], Jean-Louis Vincent[18] and Donat R. Spahn[19*]

Abstract

Background: Severe trauma continues to represent a global public health issue and mortality and morbidity in trauma patients remains substantial. A number of initiatives have aimed to provide guidance on the management of trauma patients. This document focuses on the management of major bleeding and coagulopathy following trauma and encourages adaptation of the guiding principles to each local situation and implementation within each institution.

Methods: The pan-European, multidisciplinary Task Force for Advanced Bleeding Care in Trauma was founded in 2004 and included representatives of six relevant European professional societies. The group used a structured, evidence-based consensus approach to address scientific queries that served as the basis for each recommendation and supporting rationale. Expert opinion and current clinical practice were also considered, particularly in areas in

Recommandations formalisées d'experts

SFAR

Recommandations sur la réanimation du choc hémorragique

Guidelines on the treatment of hemorrhagic shock

Jacques Duranteau[a], Karim Asehnoune[b], Sébastien Pierre[c], Yves Ozier[d], Marc Leone[e], Jean-Yves Lefranc[f], et le groupe de travail de la Société française d'anesthésie et de réanimation (Sfar), de la Société de réanimation de langue française (SRLF), de la Société française de médecine d'urgence (SFMU) et du Groupe d'études sur l'hémostase et la thrombose (GEHT)*

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[f]Services des réanimations, division anesthésie réanimation douleur urgence, CHU Nîmes, Place du Pr Robert Debré, 30029 Nîmes cedex 9, France

CIBLES

- **CGR** pour Hgb 7 - 9 gr/dL
- **PFC/PCC** si TP < 40 %
  - PFC : 10-15 ml/kg
  - (PCC : 20-25 UI/kg)
- **Fibrinogène** si < 1.5 gr/L
  - < 50 kg : 1,5 gr
  - 50-80 kg : 3 gr
  - > 80 kg : 4,5 gr
- **Plaquette** > 50 G/L
  - > 100 Hémorragie active/TCG
- **Règle Transfusion Massive**
- **Adapter avec Biologie / 1-2 h**

2 SITUATIONS TRES DIFFERENTES …

CHOC HEMORRAGIQUE

COAGULOPATHIE

CHOC HEMORRAGIQUE

SITUATION CLINIQUE NON CONTROLEE

LABORATOIRE D'HEMATOLOGIE		
HEMOSTASE IMMEDIATE		
TCA malade	*	>180.0
TCA témoin		32.0
Ratio M/T		Non déterminé
Temps de Quick malade	*	>60.0
Temps de Quick témoin		12.4
Taux de prothrombine	*	<10
INR	*	>7.00(1)
Dans la surveillance des traitements AVK, seul		
Zone thérapeutique INR : 2 à 4.5		
Fibrinogène	*	<0.5
HEMATOLOGIE IMMEDIATE		
NUMERATION GLOBULAIRE		
LEUCOCYTES		6.06
Hématies	*	2.00
HEMOGLOBINE	*	5.7
Hématocrite	*	0.18
VGM		89.5
TGMH		28.5
CCMH		31.8
CVG		14.0
PLAQUETTES	*	54
Vol. plaquettaire		9.5

- **ASSOCIE LES PRODUITS !**
- PSL + Concentrés de Facteurs (Fibrinogène …)
- Hypothermie / Acidose + Hypocalcémie
- Hémostase : Chirurgie / Radiologie …
- **Protocole de Transfusion Massive = RATIO**
  - Composition : CGR/PFC/CP + Fibrinogène
  - Supplémentation en Calcium
  - **Règle sur mesure / poids supposé**
- Adaptation Biologique 2aire puis / 1-2h

European Guidelines – Crit Care 2016

RFE SFAR 2014

HGB 68
TP 17
Fibri < 0,5 g

NADN 6mg/h
RV > 5L

CHOC HEMORRAGIQUE : FIB + PFC + CGR + CP

CHOC HEMORRAGIQUE NON CONTROLE ?

PFC ?!

Ratio 1:1 ?
20-30 ml/Kg ?

1 PFC = + 2,5 % TP …

1- TT

2- ROTEM

Adaptation

TP 10 : 14
TP 20 : 8
TP 30 : 4
TP 40 : 0

STRATÉGIE RATIO 1:1 – 1:2

= Uniquement en cas de Transfusion Massive !!

VALIDITE EN EUROPE ??

ETUDES RATIO

- **PROPPR :** Pas de Fib
- **PROMT :** Peu de Fib (cryo)
- Fib **: Pas de CF US !**

- **PFC : très mx source Fib**

Collins PW et al. Brit J Anaesth 2014

REVIEW

Fixed ratio versus goal-directed therapy in trauma

Herbert Schöchl[a,b], Marc Maegele[c], and Wolfgang Voelckel[a]

Purpose of review
This article compares the strategy of a fixed transfusion ratio of plasma and platelet concentrates to red blood cells to reconstitute 'whole blood' with the concept of individualized goal-directed coagulation therapy (GDCT).

Recent findings
Current data suggest that an early and high ratio of plasma and platelet concentrate transfusion, predominantly in a fixed 1 : 1 : 1 ratio with red blood cells, is associated with improved outcome. However, the optimal ratio is still under discussion. Moreover, storage time considerably affects the hemostatic competence of these products and no universal standard for the composition of these 'transfusion packages' has been established. Some European trauma centers instituted the concept of GDCT in trauma patients, which is based on early diagnosis of the coagulation deficit using point-of-care viscoelastic tests (VETs). These tests provide rapid information about the underlying hemostatic deficiencies, allowing targeted coagulation therapy according to the individual deficits of the patient. Treatment algorithms have been established for the administration of coagulation factor concentrates, and plasma and platelet concentrate based on VET results.

Summary
Individualized GDCT, guided by VET, offers several advantages over fixed ratio coagulation therapy. Studies comparing both hemostatic strategies are warranted.

Keywords
goal-directed coagulation therapy, ratio-driven coagulation therapy, trauma-induced coagulopathy, viscoelastic tests

INTRODUCTION

Despite substantial improvement in acute trauma care, uncontrolled bleeding remains the primary cause of preventable death [1,2]. Most of these patients die within 3–6 h of hospital admission [3]. Thus, many trauma centers implement massive transfusion protocols to rapidly identify patients at risk for massive transfusion and administer hemostatic agents without substantial time delay [4,5]. Recent data suggest that early transfusion of high ratios of plasma and platelet concentrate, predominantly in a fixed 1 : 1 : 1 ratio with red blood cells (RBCs), is associated with improved outcome in patients with severe bleeding [6••].

Some European trauma units have established a more targeted approach to treat coagulopathic trauma victims. Viscoelastic tests (VETs), most commonly rotational thromboelastometry (ROTEM, TEM International GmbH, Munich, Germany) or thrombelastography (TEG, Haemonetics Corporation, Niles, Illinois, USA], are used to evaluate the hemostatic capacity of trauma patients. Tailored hemostatic therapy, largely consisting of purified coagulation factor concentrates (CFCs), can then be applied [7–13].

FIXED RATIO COAGULATION THERAPY

The concept of damage-control resuscitation has been adopted in many military and civilian trauma centers [14,15], and is essentially based on restricted fluid therapy, permissive hypotension, and consequent maintenance of normothermia [14]. Early and aggressive transfusion of plasma has been

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Correspondence to Herbert Schöchl, AUVA Trauma Centre Salzburg, Austria and Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, AUVA Research Centre, Donaueschingenstrasse 13, 1200 Vienna, Austria. Tel: +43.664 34 22 945; e-mail: herbert.schoechl@auva.at

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STRATEGIE A L'AVEUGLE

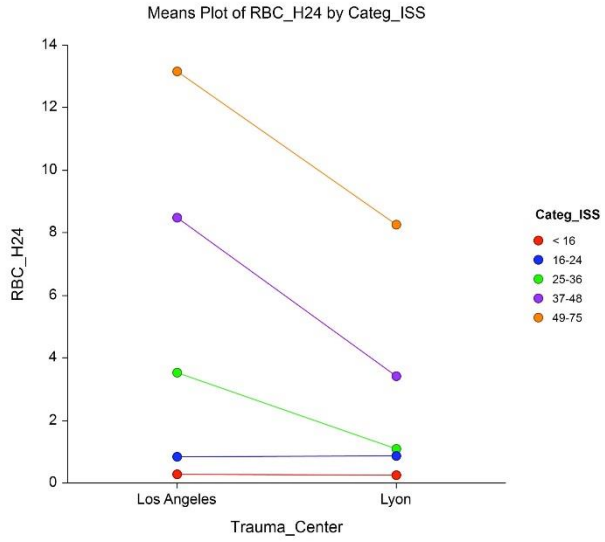
TRAITEMENT À L'AVEUGLE
« L'Abondance de la Mitraille compense l'Imprécision du Tir »
Michel Ney, Maréchal de France (1769-1815)

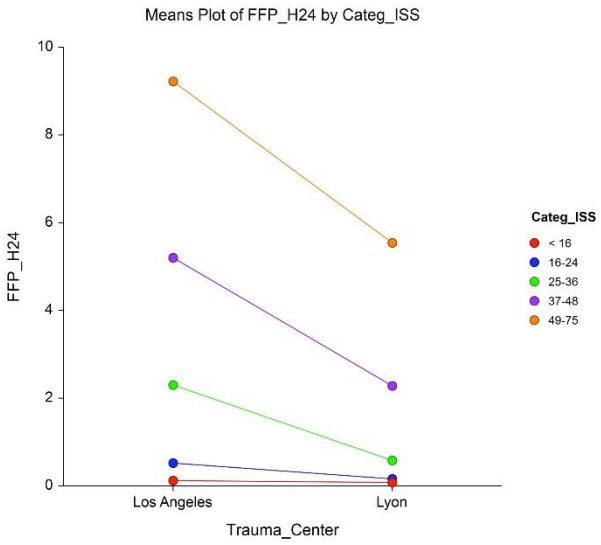
CGR / PFC / CP : Ratio

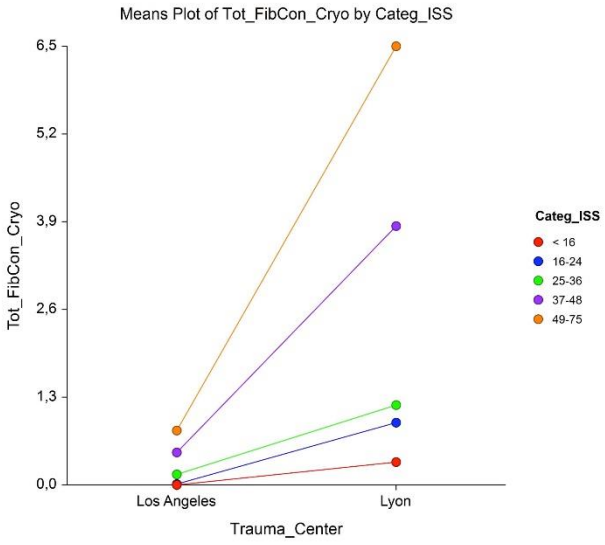
EARLY GOAL DIRECTED THERAPY

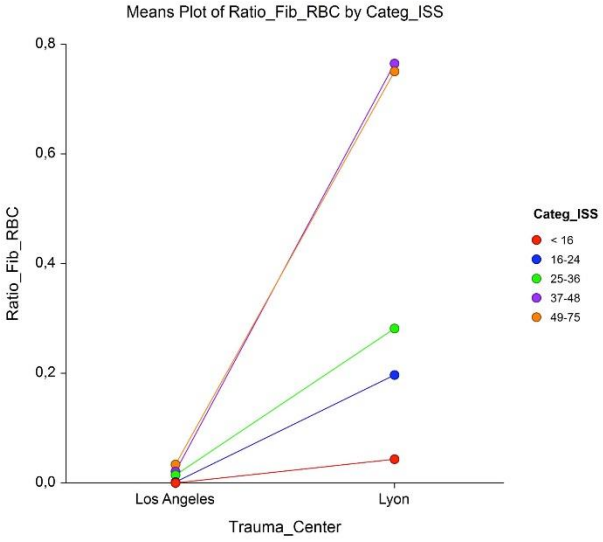
TRAITEMENT CIBLE
Définition Précise de la Cible puis Traitement Spécifique

TT Ciblé du Défect : FIB …









Analyse Multivariée « Transfusion Massive »		
N= 919	**OR**	**IC 95**
ISS	1,05	1,04-1,14
Shock Index	3,51	2,24-5,48
Ratio PFC:CGR	1,31	1,04-1,07
Ratio Fib:CGR	0,46	0,22-0,98
ROTEM (oui)	0,37	0,16-0,88

EXEMPLE CONCRET

AVP A7 – Ejecté, coincé sous VL

PEC SMUR :

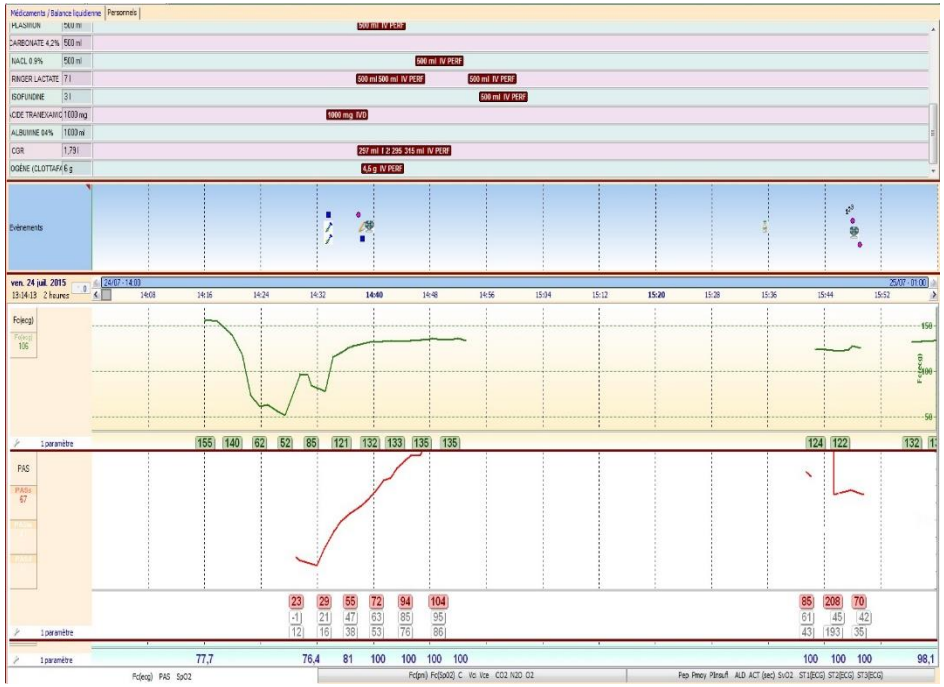
GCS 14, HD Stable
Hgb 104 / Délabrement 2 MS
TXA 1g / RV 2 L

TRANSPORT Hélico :

Dégradation …
Poursuite RV / + NADN

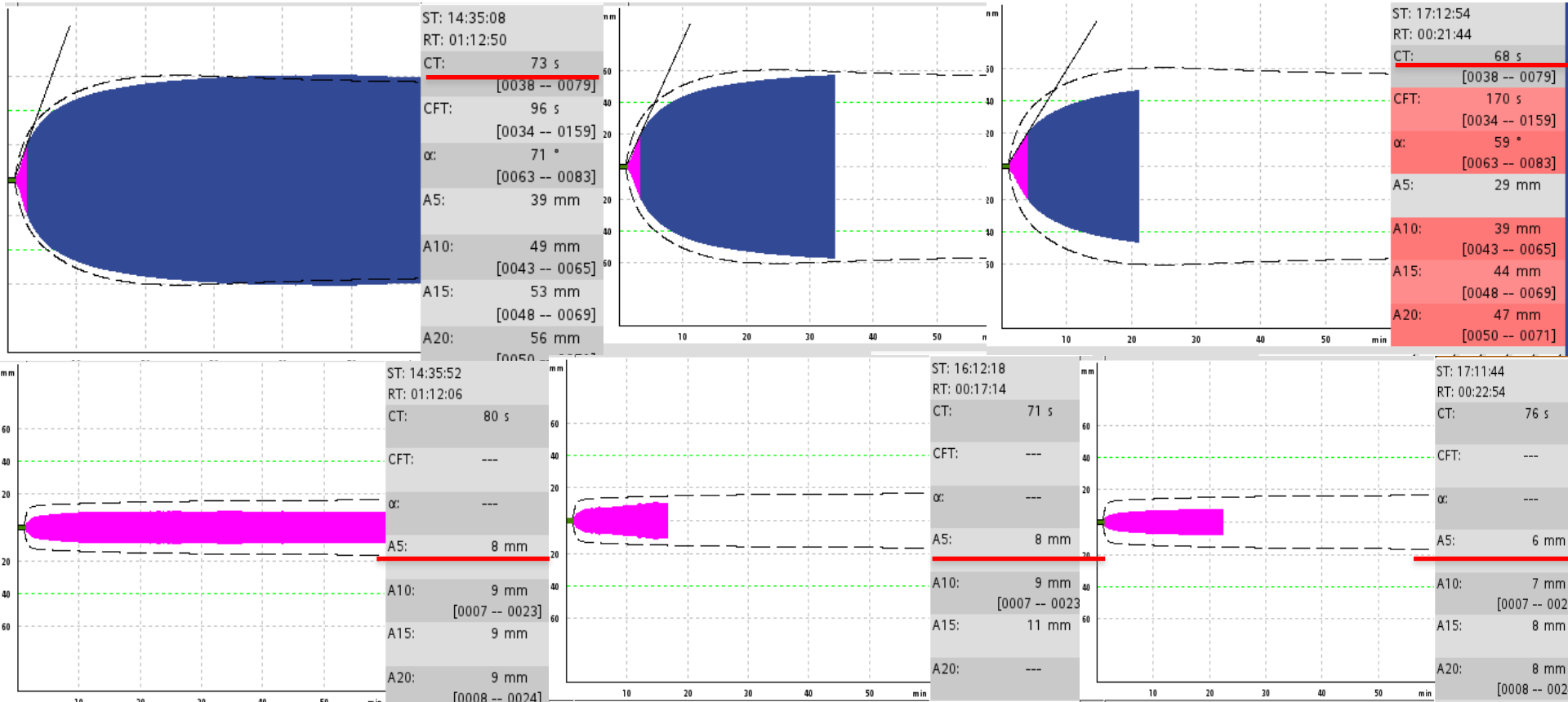
DÉCHOCAGE :

Catastrophe …
Exsangue,
PA non mesurable / Fc > 150
Hemocue : 4,1 g
Bras non garroté
GCS < 8 / Désaturation …



G

	Heure	Hgb	TP	FIB	PLT	AL	CGR	FIB	CP	PFC
DCA	14:34	53	57	0.75	-	16	4	4.5	0	0
SCAN	15:40	94	35	1.58	119	10	0	0	0	0
BLOC	17:07	65	23	0.90	83	7	2	1.5	0	0
	18:05	86	-	-	77		0	0	0	0
SSPI	20:40	106	27	1.44	112	5	0	0	0	0



CONCLUSION

- **Agir vite en cas de Coagulopathie : !!**
- **Diagnostic Rapide = Biologie Déportée = Examen Répété**
- **Ratio = Choc Hémorragique !!**
  - Ratio 1:1 = Risque de sur-transfusion / sous compensation
  - Ratio adapté ++
  - Coagulopathie = TT Ciblé guidé par biologie (VTE +++)
- **Algorithme de PEC ++ / Règle de TM**
- **Association <u>Fibrinogène /</u> CGR puis PFC / CP**