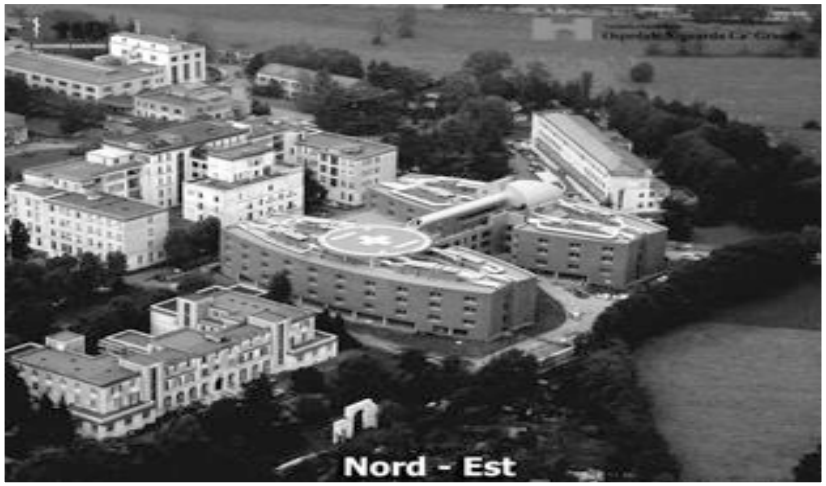
08 Giugno 2009
H. Vimercate

LA COAGULOPATIA NELLE FRATTURE DELLA PELVI

Dr.ssa Terzi Valeria
I.C.U. Bozza
A.O. Niguarda, Milano



Azienda Ospedaliera
Ospedale Niguarda Ca' Granda

GABRIELLA, 37 AA, PRECIPITATA:
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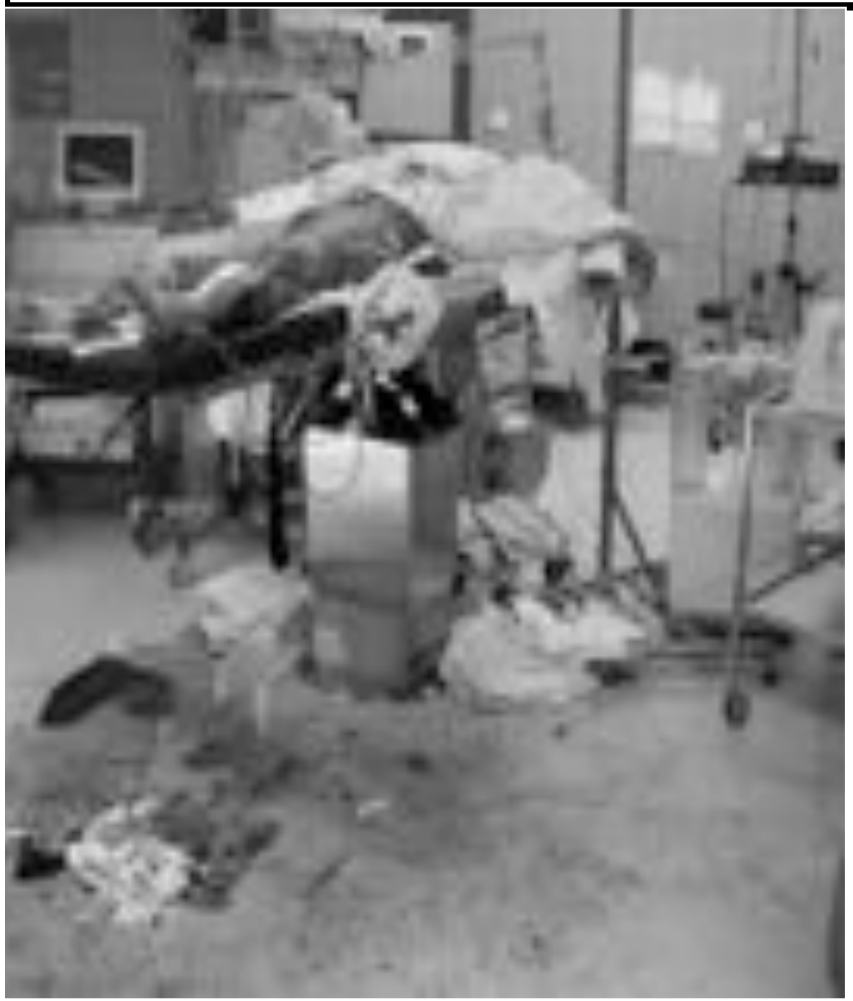
FR BACINO
LACERAZ MILZA E FEGATO
CONTUSIONE RENALE



SPLENECTOMIA
EPATECTOMIA DX
PACKING ADDOMINOPELVICO
ANGIOEMBOLIZZAZIONE
37 GRC 37 PFC 9 CRIO 12 PST 4
FATTVIIa 80 gamma/kg

VIVA

AGENDA DELLA COAGULOPATIA

1) DEFINIZIONE

2) EPIDEMIOLOGIA

3) FISIOPATOLOGIA
   - CAUSE
   - CONSEGUENZE

4) DIAGNOSI

5) TRATTAMENTO

DEFINIZIONE

The Coagulopathy of Trauma versus Disseminated Intravascular Coagulation

John R. Hess, MD, MPH and Jeffrey H. Lawson, MD, PhD

J Trauma. 2006;60:S12–S19.

The coagulopathy of trauma is a syndrome of non-surgical bleeding from mucosal lesions, serosal surfaces, and wound and vascular access sites, the tissue oozing that continues after identifiable vascular bleeding has been controlled. It occurs in the presence of profoundly depressed concentrations of blood coagulation proteins and platelets but also in situations where the normal clotting factors are present but do not work. Recent clinical and laboratory studies now permit a comprehensive view of the coagulopathy associated with severe injury.

Treating Coagulopathy in Trauma Patients

Ray Armand and John R. Hess

Transfusion Medicine Reviews, Vol 17, No 3 (July), 2003: pp 223-231

most injured patients, this works well. For a few, with injuries not amenable to immediate hemorrhage control such as high-grade liver injury or open pelvic fractures, ongoing bleeding and resuscitation can lead to hemodilution, hypothermia, acidosis, and coagulopathy.[5] Coagulopathy also occurs when brain or fat embolism leads to disseminated intravascular coagulation (DIC), hepatic

In Vivo Bleeding Time and In Vitro Thrombelastography Measurements are Better Indicators of Dilutional Hypothermic Coagulopathy Than Prothrombin Time

Bijan S. Kheirabadi, PhD, Jacqueline M. Crissey, BS, Rodolfo Deguzman, BS, and John B. Holcomb, MD

Background: The coagulopathy of trauma is generally confirmed by prothrombin time (PT) ≥3 seconds or an international normalized ratio ≥1.5. However, the utility of these values as a screening test is unknown. We examined different coagulation tests to determine the best predictor of coagulopathic bleeding and mortality in a small animal hemorrhage model.

Methods: Coagulopathy was induced in male New Zealand White rabbits by warfarin (W; 2 mg/kg for 2 days; n = 7), or hemodilution and hypothermia (HH; 50% blood exchange with Hextend, 34.5 ± 0.3°C; n = 7). Normal (N) rabbits without pretreatment served as the control (n = 7). Blood samples collected after coagulopathy induction and analyzed by prothrombin time (PT), activated partial thromboplastin time (aPTT), and thromboelastography (TEG) tests. Liver bleeding time (BT) was also measured before injury. An uncontrolled hemorrhage was created by a longitudinal splenic incision and the abdomen was closed. Rabbits were resuscitated with Hextend solution (25 mL/kg) to return blood pressure to baseline and monitored for 2 hours or until death at which time blood loss was measured.

Results: Warfarin-induced coagulopathy increased BT, PT, and aPTT. TEG showed increased reaction (R) and clot formation (K) times and marked decrease in clotting rate (α angle and Vmax). Hemodilution hypothermia coagulopathy increased only BT and aPTT, and decreased the clotting rate (α angle and Vmax) and strength of the clot. After injury, blood losses were higher in coagulopathic rabbits (W = 54.6 ± 4.2 and HH = 51.1 ± 8.9 mL/kg) than in normal rabbits (30.6 ± 12.4 mL/kg) and resulted in 86%, 100%, and 0% death, respectively. BT and Vmax consistently predicted coagulopathic bleeding and death in all animals.

Conclusion: Although satisfactory in warfarin-induced coagulopathy, PT was not a valid screening test for dilutional and hypothermic coagulopathy. BT and TEG measurements of blood clotting rate are better indicators of coagulopathic bleeding and mortality in this lethal hemorrhage model.

Key Words: Coagulopathy, Warfarin, Hemodilution, Hypothermia, Hemorrhage model.

J Trauma 2007;62:1352–1361.

J Trauma [0022-5282] 1997 May;42(5) Pages: 857-61

Predicting life-threatening coagulopathy in the massively transfused trauma patient: hypothermia and acidoses revisited.

Cosgriff N, Moore EE, Sauaia A, Kenny-Moynihan M, Burch JM, Galloway B
Department of Surgery, Denver Health Medical Center, Colorado 80204, USA.

BACKGROUND: Recalcitrant coagulopathy "the bloody vicious cycle," produces the majority of deaths after torso trauma. A model predicting this life-threatening complication may facilitate clinical decision-making. METHODS: We prospectively analyzed patients > 15 years old who received a massive transfusion (> 10 units of packed red blood cells (PRBC)/24 h) over a 2-year period. Excluding massive head injuries and pre-existing disease, the 58 study patients had a mean age = 35.4 years, Injury Severity Score (ISS) = 30.6, and PRBC = 24.2 units/24 h. RESULTS: Defined as prothrombin time of two times that of normal laboratory controls and partial thromboplastin time as two times that of normal laboratory controls, 27 patients (47%) developed life-threatening coagulopathy. Using a multiple logistic regression model, the four significant risk factors (with odds ratio) were (1) pH < 7.10 (12.3), (2) temperature < 34 degrees C (8.7), (3) ISS > 25 (7.7), and (4) systolic blood pressure < 70 mm Hg (5.8). The conditional probability of developing coagulopathy was ISS > 25 + systolic blood pressure < 70 mm Hg = 39%, ISS > 25 + temperature < 34 degrees C = 49%, ISS > 25 + pH < 7.10 = 49%; with all four risk factors the incidence was 98%. CONCLUSION: Postinjury life-threatening coagulopathy in the seriously injured requiring massive transfusion is predicted by persistent hypothermia and progressive metabolic acidosis.

Damage Control Resuscitation: Directly Addressing the Early Coagulopathy of Trauma

John B. Holcomb, MD, FACS, Don Jenkins, MD, FACS, Peter Rhee, MD, FACS, Jay Johannigman, MD, FS, FACS, Peter Mahoney, FRCA, RAMC, Sameru Mehta, MD, E. Darrin Cox, MD, FACS, Michael J. Gehrke, MD, Greg J. Beilman, MD, FACS, Martin Schreiber, MD, FACS, Stephen F. Flaherty, MD, FACS, Kurt W. Grathwohl, MD, Phillip C. Spinella, MD, Jeremy G. Perkins, MD, Alec C. Beekley, MD, FACS, Neal R. McMullin, MD, Myung S. Park, MD, FACS, Ernest A. Gonzalez, MD, FACS, Charles E. Wade, PhD, Michael A. Dubick, PhD, C. William Schwab, MD, FACS, Fred A. Moore, MD, FACS, Howard R. Champion, FRCS, David B. Hoyt, MD, FACS, and John R. Hess, MD, MPH, FACP

J Trauma. 2007;62:307-310.

specifically to their needs. However, even in the largest civilian academic trauma centers, patients with injuries at the outer limits of survivability, such as those massively transfused with more than 10 units of RBCs in the first 24 hours, are uncommon and constitute only 1% to 2% of the patient population, making it difficult to develop and test new resuscitation concepts.[21] Because 7% of combat casualties require massive transfusion, we have had just such an opportunity to observe the effects of new resuscitation strategies in the combat hospitals of Iraq and Afghanistan.

Blood transfusion rates in the care of acute trauma

Volume 44, June 2004 **TRANSFUSION** 809

John J. Como, Richard P. Dutton, Thomas M. Scalea, Bennett B. Edelman, and John R. Hess

BACKGROUND: Ten to 15 percent of all RBCs are used in the care of injury. Understanding patterns of RBC use is important. Routine resource allocation, planning for mass casualty situations, designing research, and optimizing triage all can be usefully informed.
STUDY DESIGN AND METHODS: Blood Bank and Trauma Registry records were linked to produce a transfused blood product list for each patient directly admitted from the scene of injury to a large Level 1 trauma center in calendar year 2000. Categorical associations between demographic data, Injury Severity Score, transfused products, and outcome were sought. Special attention was paid to the groups receiving uncross-matched RBCs and more than 10 units of RBCs.
RESULTS: Eight percent (479/5645) of acute trauma patients received RBCs, using 5219 units and sustaining an overall mortality of 27 percent. Sixty-two percent of RBCs were given in the first 24 hours of care. Three percent of patients (147 injured) received more than 10 units and received 71 percent of all RBCs given. Mortality in this cohort was 39 percent. Ninety percent of the patients who received more than 10 units of RBCs received plasma, and 71 percent received PLTs.
CONCLUSIONS: A small number of patients receives most of the blood products used in the treatment of injury. Transfusion of more than 10 units of RBCs identifies a subgroup where most patients received plasma and PLTs to treat actual or anticipated dilutional coagulopathy. There is no clear threshold beyond which blood use is futile.

CAUSE

Coagulopathy: Its Pathophysiology and Treatment in the Injured Patient

World J Surg (2007) 31: 1055–1064

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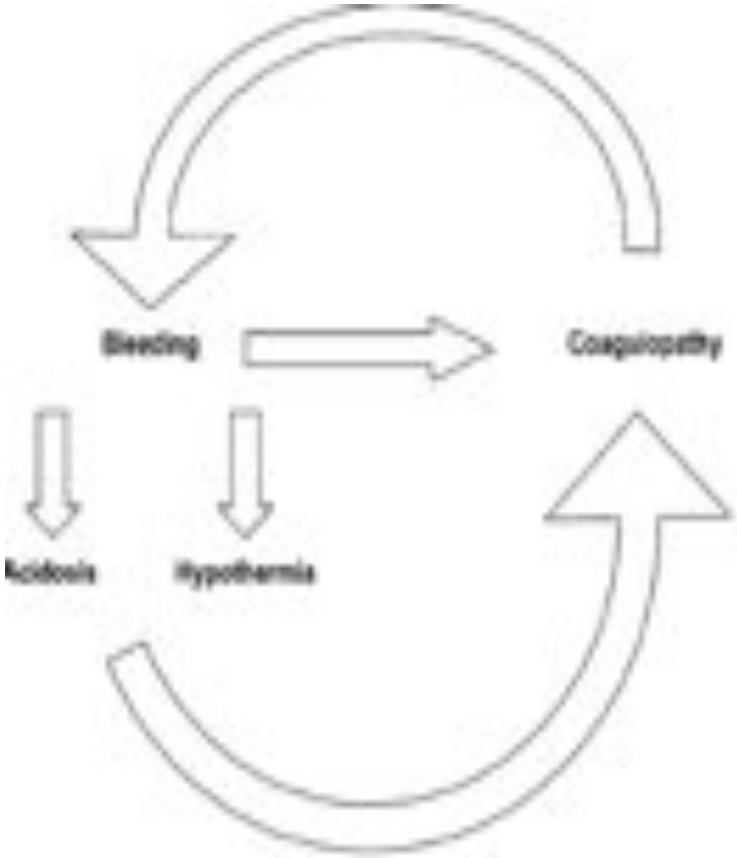


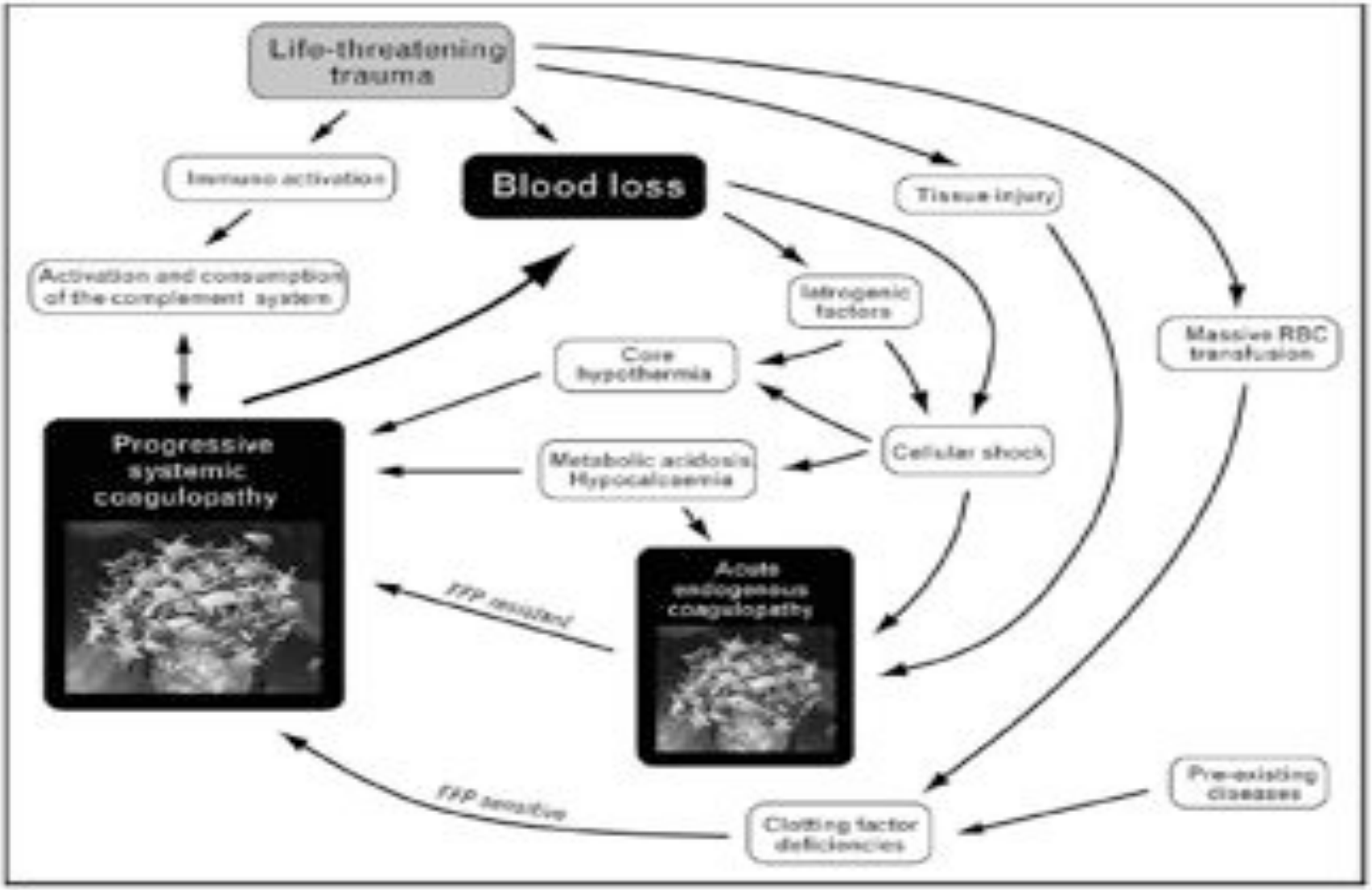
Figure 2. Severely injured patients can present with coagulopathy at the time of hospital admission. This soldier arrived in hemorrhagic shock and required massive transfusion with packed red blood cells (pRBC), coagulation products, and whole blood. Tourniquets were placed on the patient's thighs in the field to minimize blood loss.

Transfusion strategies in postinjury coagulopathy

Philip F. Stahel[a], Ernest E. Moore[b], Star L. Schreier[a], Michael A. Flierl[a] and Jeffry L. Kashuk[b]

Current Opinion in Anaesthesiology 2009, 22:289–298

Figure 2 Presumed mechanisms of posttraumatic coagulopathy



Hypothermia

Hypothermia has been a well-described cause of trauma-related coagulopathy. Hypothermia, defined by a core body temperature < 35°C, can occur from numerous sources. The patient can lose heat by convection and radiation with exposure in the field or trauma bay or by evaporative losses when wearing wet clothing. Reduced heat production occurs from decreased oxygen consumption during hemorrhagic shock. Operative intervention results in further heat loss from peritoneal and pleural surfaces. Fluid resuscitation results in a large potential for heat loss.[13] This can be quantified by the equation

Hypothermia acts primarily on platelet activation and adhesion by inhibiting the interaction between von Willebrand factor with platelet glycoprotein Ib-IX-V complex,[14] but it also slows the metabolic rate of coagulation factor enzymes.[15] Ferrara *et al.* studied 45 trauma patients and found that hypothermia (T ≤ 34°C) occurred in 80% of non-survivors and 36% of survivors. Clinically significant bleeding occurred in hypothermic and acidotic patients despite adequate blood, platelet, and plasma replacement.[16] Johnston *et al.* found that at 35°C, without dilution, there was a decrease in all coagulation factors. Factors XI and XII were only functioning at 65% of normal at this temperature, and at 32°C their activity was reduced to 17% and 32%, respectively.[17]

Acidosis

Metabolic acidosis is commonly seen in patients following trauma. The development of acidosis mainly affects coagulopathy by inhibiting the activities of the enzyme complexes on lipid surfaces. Meng *et al.* noted when the pH is reduced from 7.4 to 7.0, the activity level of FVIIa was reduced by 90%; FVIIa/TF complex, by 55%; and the rate of prothrombin activation by FXa/FVa complex, by 70%.[18] The activity of these coagulation factor complexes depends on their interaction with the negatively charged exposed phospholipids on the surface of activated platelets that are affected by increasing concentrations of hydrogen ions.[19] Temperature had a lesser effect on the enzymes, only reducing their activity by 10% for each 1°C decrease in temperature.[18] In a swine study, Martini *et al.* showed that acidosis alone (pH 7.1) and when combined with hypothermia (T = 32°C) increased splenic bleeding time by 41% and 72%, respectively. Similar findings were noted when they examined the affects of acidosis and hypothermia on thrombin generation. Thrombin plays a central role in activating cofactors, platelets, and enzymes, and in cleaving fibrinogen to fibrin. Acidosis was found to have a profound inhibitory affect on the thrombin generation rate that was increased when combined with hypothermia (Fig. 3).[20]

Resuscitation with crystalloid fluid has also been associated with the development of worsening acidosis. Following the Stewart model of acid base equilibrium, the administration of solutions with supraphysiologic levels of chloride relative to sodium results in a decreased strong ion difference (SID) (Na + K + Ca + Mg – Cl – lactate). This decreased SID causes further dissociation of H^+ from H_2O to maintain charge neutrality and therefore a decreased pH. Because of its supraphysiologic levels of chloride (154 mEq/l), normal saline (NS) has been associated with hyperchloremic acidosis. Waters *et al.* found that the use of NS in patients undergoing abdominal aortic aneurysm repair resulted in the use of significantly more blood products, suggesting that it may have a harmful effect on the coagulation system.[21]

Hypothermia and Acidosis Synergistically Impair Coagulation in Human Whole Blood

Daniel Dirkmann, MD

Alexander A. Hanke, MD

Klaus Görlinger, MD

Jürgen Peters, MD

BACKGROUND: Hypothermia and acidosis were reported to influence coagulopathy in different clinical settings. We evaluated whole blood coagulation to determine the effects of hypothermia and/or acidosis on hemostasis.

METHODS: Whole blood samples (3,000 μL) from 10 healthy volunteers (2 female, 8 male) were acidified by adding 40 μL of hydrochloric acid of increasing molarity to achieve a blood pH (α-stat) between 7.0 and 7.37, and coagulation was analyzed by rotational thromboelastometry after an incubation period of 30 min using both intrinsically (InTEM™) and extrinsically (ExTEM™) activated assays. To assess temperature-dependent effects, all tests were performed at blood/thromboelastometer temperatures of 30, 33, 36, and 39°C, respectively. An additional extrinsically activated test with addition of cytochalasin D was performed to examine clot formation without platelet contribution.

RESULTS: Hypothermia at a normal pH produced an increased coagulation time [ExTEM: 65 s ± 3.6 (36°C) vs 85 ± 4 (30°C), $P < 0.001$; coagulation time, InTEM: 181 s ± 10 (36°C) vs 226 ± 9, $P < 0.001$] and clot formation time [ExTEM: 105 s ± 5 (36°C) vs 187 ± 6 (30°C), $P < 0.001$]; clot formation time [InTEM: 101 s ± 5 (36°C) vs 175 ± 7, $P < 0.001$], as well as decreased α angle [ExTEM: 65.6 ± 1.8 (36°C) vs 58 ± 1.1, $P < 0.01$, $P < 0.01$; InTEM: 70.5 ± 1.8 (36°C) vs 60.2 ± 1.5, $P < 0.001$]. Maximum clot firmness was significantly impaired only in InTEM assays [56.9 mm ± 0.9 (36°C) vs 52.7 ± 0.9, $P < 0.05$]. In contrast, acidosis *per se* had no significant effects during normothermia. Acidosis amplified the effects of hypothermia, and synergistically impaired clotting times, α angle, and decreased maximum clot firmness, again in both extrinsically and intrinsically activated assays. Formation of a fibrin clot tested after abolition of platelet function by cytochalasin D was not impaired. Clot lysis decreased under hypothermic and/or acidotic conditions, but increased with hyperthermia.

CONCLUSIONS: In this *in vitro* study, hypothermia produced coagulation changes that were worsened by acidosis whereas acidosis without hypothermia has no significant effect on coagulation, as studied by thromboelastometry. This effect was mediated by the inhibition of coagulation factors and platelet function. Thus, thromboelastometry performed at 37°C overestimated integrity of coagulation during hypothermia in particular in combination with acidosis.

(Anesth Analg 2008;106:1627–32)

Hemodilution

Hemodilution of coagulation products can have a profound effect on the development of coagulopathy. Several factors can lead to the dilution of the body's coagulation factors. Direct loss of coagulation factors through hemorrhage can quickly reduce the body's small stores of fibrinogen (10 g) and platelets (15 ml).[23] Dilutional coagulopathy can then develop when these losses are replaced with fluids that do not contain clotting factors. Dilution often starts in the pre-hospital setting when crystalloids are given en route to the trauma center, followed by pRBCs in the trauma bay before laboratory test results become available. Abnormal results trigger the request for Fresh frozen plasma (FFP), which takes another 20–30 min to thaw resulting in a further delay to correct the ongoing coagulopathy. This cycle perpetuates itself with delays in diagnosis followed by treatments that only assist in further development of dysfunctional clotting capabilities.

The use of artificial colloids like hetastarch and dextran solutions has also been associated with the development of coagulopathy. Hetastarch solutions with high mean molecular weights, a large degree of substitution of hydroxyethyl groups per glucose unit, and a high C2/C6 ratio suppress coagulation more than solutions with more rapidly degradable low molecular weight colloids in vivo.[34–36] Various mechanisms including a reduction in von Willebrand factor, platelet dysfunction, reduced factor VIII levels, and interaction with fibrinogen have been hypothesized to produce this coagulopathy.[37]

COLLOIDI

1) Entholzner EK, Mielke LL, Calatzis AN, *et al*. Coagulation effects of a recently developed hydroxyethyl starch (HES 130/0.4) compared to hydroxyethyl starches with higher molecular weight. Act Anesth Scand 2000; 44:1116–1121.

2) Jamnicki M, Zollinger A, Seifert B, *et al*. Compromised blood coagulation: an in vitro comparison of hydroxyethyl starch 130/0.4 and hydroxyethyl starch 200/0.5 using thrombelastography. Anesth Analg 1998;87:989–993.

3) Langeron O, Doelberg M, Ang ET, *et al*. Voluven, a lower substituted novel hydroxyethyl starch (HES 130/0.4), causes fewer effects on coagulation in major orthopedic surgery than HES 200/0.5. Anesth Analg 2001;92:855–862.

TABLE I Characteristics of the available colloids and their effects on coagulation

Product	*Commercial name*	*Concentration %*	*Oncotic pressure mmHg*	*Initial volume expansion %*	*Persistance in the body (days)*	*Maximal dose/24 hr*	*Effect on hemostasis*
Albumin		4	20–29	80			0
			20	100–120	200–400		
Dextran 70	Macrodex	6	56–68	120	28–42	1.5 g·kg^{-1}	+++
Dextran 40	Rheomacrodex	10	168–191	200	6	1.5 g·kg^{-1}	+++
Fluid gelatin	Gelofusine, Plasmion	3–4	42	70–90	7		0 to +
Urea linked gelatin	Hemacel	3.5	25–29	70–80	2–7		0 to +
HES 450/0.7	Plasmasteril	6	24–30	100	120–182	20 mL·kg^{-1}	+++
HES 200/0.62/10	Elohes	6	25–30	110	6–7	20 mL·kg^{-1}	++
HES 200/0.5/5	Hesteril	6	30–37	100	3–4	33 mL·kg^{-1}	+
HES 200/0.5/5	Lomol, Hesteril	10	59–82	145	3–4	20 mL·kg^{-1}	+
HES 130/0.4/11	Voluven	6	36	100–110		50 mL·kg^{-1}	0 to +

Effect on hemostasis: 0 = none; + = weak; ++ = moderate; +++ = important. Commercial names are European. Some data are not available. In the "product" column, the first number is the molecular weight in Daltons, the second is the degree of substitution and the third is the C2/C6 ratio of hydroxyethylstarch (HES) substitution. The higher the molecular weight and the degree of substitution, the longer the plasma half-life and the effects on hemostasis. Adapted from Ickx, BE and Van der Linden P. Interactions entre solutés colloïdes et l'hémostase. Sang Thrombose Vaisseaux 2002; 7: 408–16 [article in French] Hetastarch (480/0.7), used in the USA, has important effects on hemostasis. Pentastarch (260/0.45), available in Canada, is similar to Hesteril 10% and has weak effects on hemostasis at the maximal dose (28 mL·kg^{-1}) recommended by the manufacturer.

Preconditions of hemostasis in trauma: a review. The influence of acidosis, hypocalcemia, anemia, and hypothermia on functional hemostasis in trauma.

Lier H, Krep H, chroeder S, Stuber F.
Department of Anaesthesiology and Intensive Care Medicine, University of Cologne,Germany.

BACKGROUND: Beside the often discussed topics of consumption and dilution coagulopathy, additional perioperative impairments of coagulation are caused by acidosis, hypocalcemia, anemia, hypothermia, and combinations. METHODS: Reviewing current literature, cutoff values of these parameters become obvious at which therapy should commence. RESULTS: A notable impairment of hemostasis arises at a pH < or = 7.1. Similar effects are caused by a BE of -12.5 or less. Thus, in case of severe bleeding, buffering toward physiologic pH values is recommended, especially with massive transfusions of older RBCCs displaying exhausted red blood cell buffer systems. It completes the optimization of the volume homeostasis to ensure an adequate tissue perfusion. Combining beneficial cardiovascular and coagulation effects, the level for ionized calcium concentration should be held > or = 0.9 mmol/L. From the hemostatic point of view, the optimal Hct is higher than the one required for oxygenation. Even without a "classical" transfusion trigger, the therapy of acute, persistent bleeding should aim at reaching an Hct > or = 30%. A core temperature of < or = 34 degrees C causes a decisive impairment of hemostasis. A controlled hypotensive fluid resuscitation should aim at reaching a mean arterial pressure of > or = 65 mm Hg (possibly higher for cerebral trauma). Prevention and later aggressive therapy of hypothermia by exclusive infusion of warmed fluids and the use of warming devices are prerequisites for the cure of traumatic coagulopathy. Combined appearance of single preconditions cause additive impairments of the coagulation system. CONCLUSIONS: The prevention and timely correction, especially of the combination acidosis plus hypothermia, is crucial for the treatment of hemorrhagic coagulopathy.

NUOVE TEORIE

1) Acute Traumatic Coagulopathy: Initiated by Hypoperfusion *Modulated Through the Protein C Pathway?*

(*Ann Surg* 2007;245: 812–818)

Karim Brohi, FRCS, FRCA, Mitchell J. Cohen, MD,* Michael T. Ganter, MD,† Michael A. Matthay, MD,‡ Robert C. Mackersie, MD,* and Jean-François Pittet, MD†‡*

2) **Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients**

British Journal of Anaesthesia 100 (6): 792–7 (2008)

A. Levrat[2], A. Gros[2], L. Rugeri[2], K. Inaba[2], B. Floccard[2], C. Negrier[3] and J.-S. David[1]*

3) **Coagulopathy in trauma patients: importance of thrombocyte function?**

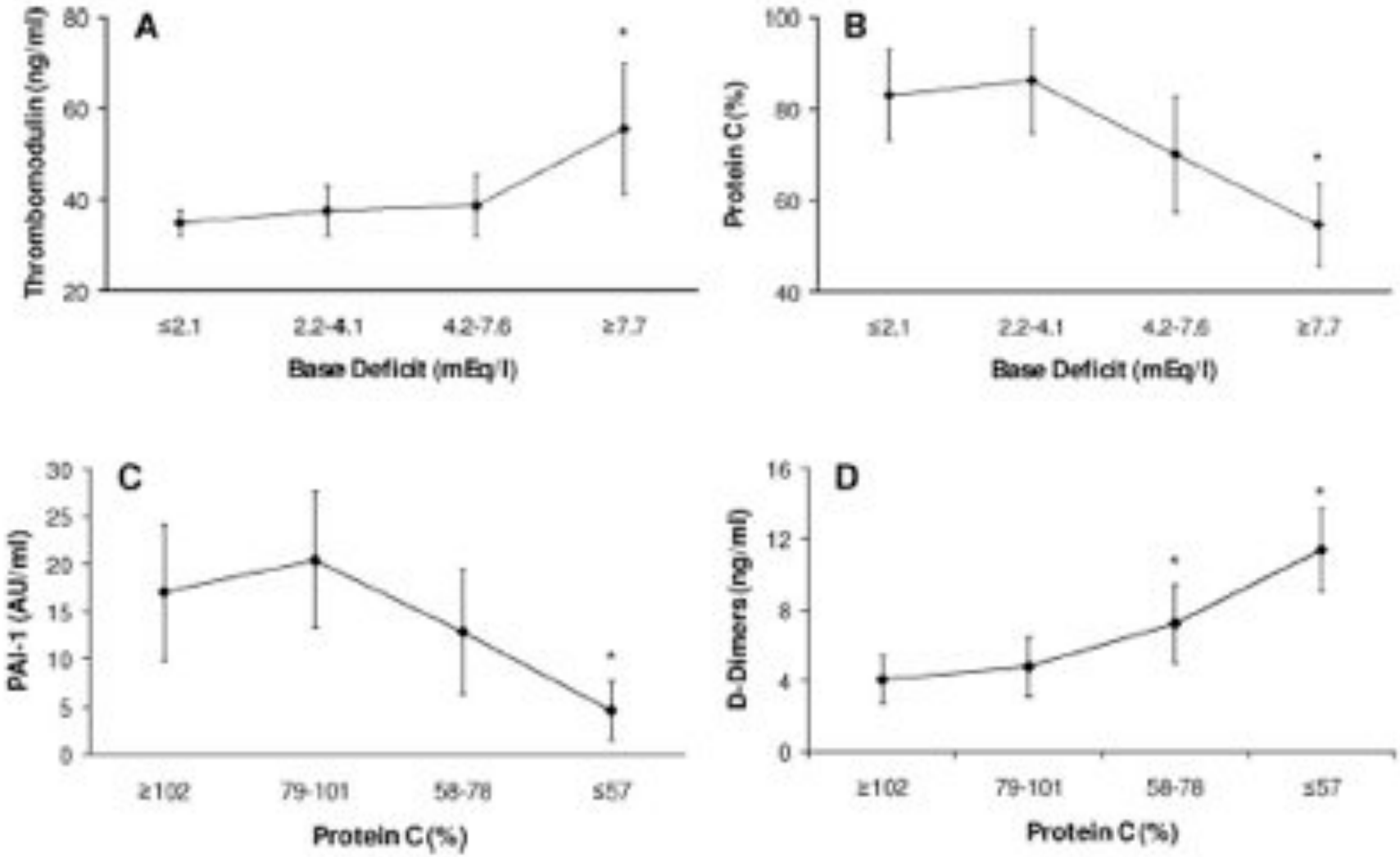
Current Opinion in Anaesthesiology 2009, 22:261–266

Ross A. Davenport and Karim Brohi

(*Ann Surg* 2007;245: 812–818)

Acute Traumatic Coagulopathy: Initiated by Hypoperfusion

Modulated Through the Protein C Pathway?



British Journal of Anaesthesia 100 (6): 792–7 (2008)

Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients

Background. Blood loss and uncontrollable bleeding are major factors affecting survival in trauma patients. Because treatment with antifibrinolytic drugs may be effective, early detection of hyperfibrinolysis with rotation thrombelastography (ROTEM®) may be beneficial.

Methods. Eighty-seven trauma patients were included in this prospective observational study. Blood samples were collected at admission. After *in vitro* activation with tissue factor (EXTEM) and inhibition with aprotinin (APTEM), ROTEM® parameters including maximal clot firmness (MCF) and clot lysis index at 30 min (CLI_{30}) were determined. Hyperfibrinolysis was defined as a euglobulin lysis time (ELT) <90 min. Threshold for ROTEM® parameters were determined with receiver-operating characteristic curves (ROC) analysis according to the ELT results.

Results. ELT was determined in a subgroup of 23 patients. In this group of patients, ROC analysis showed that for a threshold of 18 mm (MCF-EXTEM), 71% (CLI_{30}) and 7% (increase of MCF-APTEM), sensitivity was, respectively 100%, 75%, and 80% with a specificity of 100%. With the application of these thresholds to the whole trauma cohort, ROTEM® analysis detected hyperfibrinolysis in five patients (6%; 95% confidence interval (CI): 2–13%). As expected, patients with hyperfibrinolysis were more severely injured (median Injury Severity Score: 75 vs 29, $P<0.05$), had greater coagulation abnormalities (international normalized ratio (INR): 8.2 vs 1.3, $P<0.05$; fibrinogen: 0.0 vs 2.2 g $litre^{-1}$, $P<0.05$), and a higher mortality rate (100% CI: 48–100% vs 11% CI: 5–20%, $P<0.05$).

Conclusions. ROTEM® provided rapid and accurate detection of hyperfibrinolysis in severely injured trauma patients.

Current Opinion in Anaesthesiology 2009, 22:261–266

Coagulopathy in trauma patients: importance of thrombocyte function?

Purpose of review

Trauma-induced coagulopathy results from a complex interplay between shock resuscitation and impaired clotting protease function. A pathophysiological role of platelets in this condition remains as yet undefined. This review examines our current knowledge of platelet function in haemostasis, possible mechanisms for aberrant activity in trauma and the role of platelet transfusions in exsanguinating haemorrhage.

Recent findings

Platelet adhesion and aggregation enable a haemostatic plug to form at the site of vessel injury. As described within cell-based models of thrombin generation, platelet membranes provide a platform to amplify clot formation. There is evidence to suggest platelet activity may be of greater importance than platelet number for clot integrity. Analysis of platelet function is limited by currently available devices. Therefore, the precise role and triggers for platelet transfusion in trauma have yet to be fully characterized. Retrospective studies show that early high-volume platelet transfusion in trauma may be associated with similar outcome benefits observed in high ratio plasma : red blood cell replacement.

Summary

Platelets undoubtedly play a pivotal role in haemostasis and trauma-induced coagulopathy. However, their specific dysfunction in trauma remains to be elucidated. Further research to characterize the dysfunctional pathways of the platelet response is required, together with clinical trials of the optimal timing and dose of platelet transfusions.

Current Opinion in Anaesthesiology 2009, 22:261–266

Coagulopathy in trauma patients: importance of thrombocyte function?

It would appear from this study that severe injury results in increased platelet activation and hyperfunctional platelets, which have faster rates of adhesion and aggregation. Platelet function in trauma returns to normal within 24–48 h, although platelets appear to remain in a state of activation up to 72 h following injury. This prolonged period of activation may represent a process of downregulation in platelet function to reduce disseminated clot formation. Platelet mapping in viscoelastic tests of clot strength has shown similar transiently impaired platelet responses in TBI and to a lesser degree in general trauma [45]. The authors hypothesized that a degree of platelet hyperactivation in trauma may result in the depletion of intracellular mediators and, therefore, shift platelets into a refractory state.

CONSEGUENZE

Clinical Review

The Journal of Emergency Medicine,

ARTICLE IN PRESS

TRANSFUSION OF BLOOD PRODUCTS IN TRAUMA: AN UPDATE

Gustavo P. Fraga, MD, PHD,*† Vishal Bansal, MD,* and Raul Coimbra, MD, PHD, FACS*

*Department of Surgery, Division of Trauma, Surgical Critical Care, and Burns, University of California San Diego, San Diego, California and †Division of Trauma Surgery, State University of Campinas, Campinas, Brazil

Table 1. Definitions of Massive Hemorrhage

Loss of an entire blood volume equivalent within 24 h; or
Loss of 50% of blood volume within 3 h; or
Continuing blood loss of 150 mL/min; or
Continuing blood loss of 1.5 mL/kg/min over 20 min; or
Rapid blood loss leading to decompensation and circulatory failure despite volume replacement and interventional treatment

Trauma Associated Severe Hemorrhage (TASH)-Score: Probability of Mass Transfusion as Surrogate for Life Threatening Hemorrhage after Multiple Trauma

Nedim Yücel, MD, Rolf Lefering, PhD, Marc Maegele, MD, Matthias Vorweg, MD, Thorsten Tjardes, MD, Steffen Ruchholtz, MD, Edmund A. M. Neugebauer, PhD, Frank Wappler, MD, Bertil Bouillon, MD, Dieter Rixen, MD, and the "Polytrauma Study Group" of the German Trauma Society

Background: To develop a simple scoring system that allows an early and reliable estimation for the probability of mass transfusion (MT) as a surrogate for life threatening hemorrhage following multiple trauma.

Methods: Potential clinical and laboratory variables documented in the Trauma Registry of the German Trauma Society (DGU) (1993–2003; n = 17,200) were subjected to univariate and multivariate logistic regression analysis to predict the probability for MT.

Results: Clinical and laboratory variables available from data sets were screened for their association with mass transfusion. MT was defined by transfusion requirement of ≥10 units of packed red blood cells from emergency room (ER) to intensive care unit admission. Seven independent variables were identified to be significantly correlated with an increased probability for MT: systolic blood pressure (<100 mm Hg = 4 pts, <120 mm Hg = 1 pt), hemoglobin (<7 g/dL = 8 pts, <9 g/dL = 6 pts, <10 g/dL = 4 pts, <11 g/dL = 3 pts, and <12 g/dL = 2 pts), intra-abdominal fluid (3 pts), complex long bone and/or pelvic fractures (AIS 3/4 = 3 pts and AIS 5 = 6 pts), heart rate (>120 = 2 pts), base excess (<−10 mmol/L = 4 pts, <−6 mmol/L = 3 pts, and <−2 mmol/L = 1 pt), and gender (male = 1 pt). These variables were incorporated into a risk score, the Trauma Associated Severe Hemorrhage Score (TASH-Score, 0–28 points). Performance of the score was tested with respect to discrimination, precision, and calibration. Increasing TASH-Score points were associated with an increasing probability for MT.

Conclusion: The TASH-Score is an easy-to-use scoring system that reliably predicts the probability for MT after multiple trauma. Taken as a surrogate for life threatening bleeding calculation may focus attention on relevant variables indicative for risk and impact strategies to stop bleeding and stabilize coagulation in acute trauma care.

Key Words: Multiple trauma, Hemorrhage, TASH-Score, Outcome, Multivariate analysis.

J Trauma. 2006;60:1228–1237.

Trauma Associated Severe Hemorrhage (TASH)-Score: Probability of Mass Transfusion as Surrogate for Life Threatening Hemorrhage after Multiple Trauma

J Trauma. 2006;60:1228–1237.

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: Probability of Mass Transfusion as Surrogate for Life Threatening Hemorrhage after Multiple Trauma

J Trauma. 2006;60:1228–1237.

Clinical Review

The Journal of Emergency Medicine,

ARTICLE IN PRESS

TRANSFUSION OF BLOOD PRODUCTS IN TRAUMA: AN UPDATE

Gustavo P. Fraga, MD, PHD,*† Vishal Bansal, MD,* and Raul Coimbra, MD, PHD, FACS*

*Department of Surgery, Division of Trauma, Surgical Critical Care, and Burns, University of California San Diego, San Diego, California and †Division of Trauma Surgery, State University of Campinas, Campinas, Brazil

□ Abstract—Background: Blood transfusion in the management of severely injured patients can be lifesaving. These patients are susceptible to developing early coagulopathy, thus perpetuating bleeding. Objectives: This article presents recent advances in both the civilian and military clinical arena to improve the treatment of trauma patients with severe hemorrhage, the use of agents to support coagulation, perspectives on restrictive transfusion strategies, and transfusion-related risks. Discussion: Massive blood transfusion is an adjunct to surgical care. The volume of blood products transfused and the ratio of blood components have been associated with increased morbidity and mortality rates. The adverse clinical effects of transfusion and the limited supply of blood products have resulted in modern resuscitation protocols to limit the volume of blood transfused. Conclusion: A restrictive blood transfusion strategy and the use of hemostatic agents may decrease morbidity and mortality in trauma patients, but insufficient data are available for their use in trauma patients. Massive transfusion should reflect an equal ratio of packed red cells and plasma to limit coagulopathy. Prospective randomized trials are needed to standardize an effective protocol. © 2009 Elsevier Inc.

J Trauma [0022-5282] 2003 Jun;54(6) Pages: 1127-30.
Acute traumatic coagulopathy.
Brohi K, Singh J, Heron M, Coats T
Trauma and Critical Care Unit, Royal London Hospital, United Kingdom.

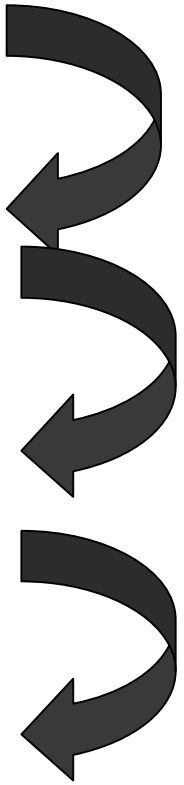
J Trauma [0022-5282] 2003 Jul;55(1) Pages: 39-44.
Early coagulopathy predicts mortality in trauma.
MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M
Jackson Memorial Hospital and Department of Surgery,
University of Miami school of Medicine, Miami, Florida 33101, USA.

COAGULOPATIA

EMORRAGIA MASSIVA

TRASFUSIONE MASSIVA

AUMENTATA MORTALITA'



DIAGNOSI

SEMINARS IN THROMBOSIS AND HEMOSTASIS/VOLUME 34, NUMBER 5 2008

Point of Care Coagulation Tests in Critically Ill Patients

Carl-Erik Dempfle, M.D.,[1] and Martin Borggrefe, M.D.[1]

ABSTRACT

Point of care assays for various analytes have been established in critical care, including blood gas analysis, glucose, electrolytes, and markers for cardiac ischemia. Coagulation assays can also be adapted to the critical care environment by using whole blood as sample material and instruments optimized for point of care analysis. Available assays include the conventional coagulation assays, such as prothrombin time and activated partial thromboplastin time, fibrinogen, assays for monitoring of anticoagulant drugs, global coagulation assays based on thrombelastography and viscosimetry, platelet function assays, and D-dimer assays. The main problem in point of care coagulation diagnostics is quality control. Point of care coagulation assays help in rapidly establishing a diagnosis, clarifying causes of bleeding, and monitoring therapy. Thrombelastography and similar assays extend the scope of coagulation diagnostics by visualizing the process of clot formation and extending the observation period to provide an estimate of clot stability versus mechanical and proteolytic attack.

Clin. Lab. Haem.
2005, 27, 81–90

REVIEW

Thrombelastography/thromboelastometry

R. J. LUDDINGTON *Haematology Department, Addenbrooke's Hospital, Cambridge, UK*

Summary The term thrombelastograph (TEG) was used to describe the trace produced from the measurement of the viscoelastic changes associated with fibrin polymerization. Recently the term rotational thromboelastometry has been applied to the output of the ROTEM® instrument. Since its first description in 1948, the TEG®/ROTEM® has been successfully used in the near patient assessment of haemostasis. The greatest use has been the application of TEG®-guided transfusion of blood components in hepatic and more widely in cardiac surgery. Recent years have seen a renewed interest in the technology with applications for both pharmaceutical monitoring and patient screening being described. The present review gives a broad overview of the developments and applications related to thrombelastography/thromboelastometry.

Keywords Thrombelastography, thromboelastometry, haemostasis, global screening, blood transfusion

Clin. Lab. Haem.
2005, **27**, 81–90

REVIEW

Thrombelastography/thromboelastometry

Introduction

Thrombelastography was first described by Hartert (1948). The viscoelastic changes that occur during coagulation were recorded, providing a graphical representation of the fibrin polymerisation process. The rate of fibrin polymerisation as well as the overall clot strength is assessed. Thus, the thrombelastograph® (TEG®; Haemoscope Corporation, IL, USA) or thromboelastogram® (ROTEM®; Symex, Milton Keynes, UK) enable a complete evaluation of the process of clot initiation, formation and stability, using whole blood or plasma.

The main uses of the TEG®/ROTEM® have been to monitor blood component therapy during surgery. Its use was first documented in the field of liver transplantation (Kang *et al.*, 1985). The use of the TEG® was later described in cardiac surgery (Spiess *et al.*, 1995; Shore-Lesserson *et al.*, 1999). Hepatic and cardiac surgery are both associated with the potential for massive blood loss as multiple insults can result in the haemostatic system being overwhelmed. In trauma patients, who share the same pattern of multiple insult, the TEG® has been shown to predict early transfusion requirements (Kaufmann *et al.*, 1997).

The advantage that the TEG®/ROTEM® offers is its bedside capability to deliver within 30 min a representation of the sum of platelet function, coagulation proteases and inhibitors, and the fibrinolytic system. The elements of the TEG®/ROTEM® trace have been dissected to assess the need for blood component therapy. The time to clot formation is used as a guide for fresh frozen plasma (FFP), the clot strength to judge platelet infusion, addition of heparinase to assess protamine dosage and the degree of lysis used to indicate the need for antifibrinolytic therapy.

It is only recently that the TEG®/ROTEM® has been used within haemostasis laboratories. The poor acceptance of the technology stems largely from the lack of agreement with standard laboratory variables (Zuckerman *et al.*, 1981).

The use of the TEG®/ROTEM® in the laboratory setting represents a significant change of use for the instrument. It was originally designed as a bedside monitor using native whole blood. To perform tests within the laboratory

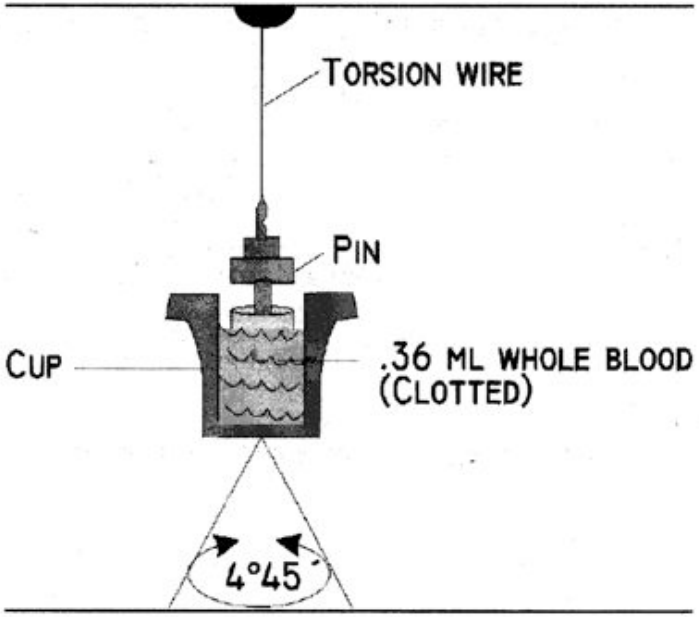


Figure 1.
The TEG® analyzer measures the clot's physical properties by the use of a special stationary cylindrical cup that holds a 360-µl sample of whole blood and is oscillated through an angle of 4° 45'. Each rotation cycle lasts ten seconds. A pin is suspended in the blood by a torsion wire and is monitored for motion. Thus, the magnitude of the output is directly related to the kinetics and the strength of the formed clot. As the clot retracts or lyses, these bonds are broker and the transfer of cup motion is diminished.

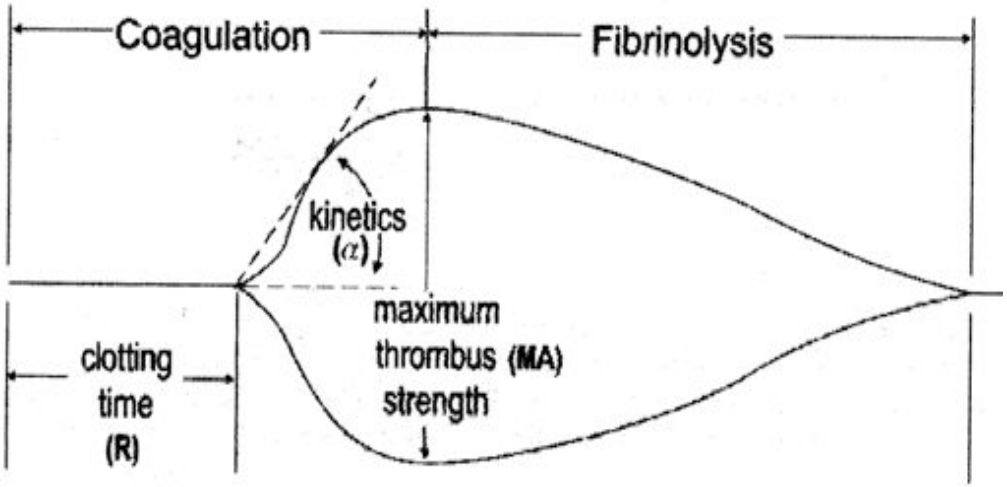


Figure 2.
Schematic representation of TEG® tracing with its principal parameters.

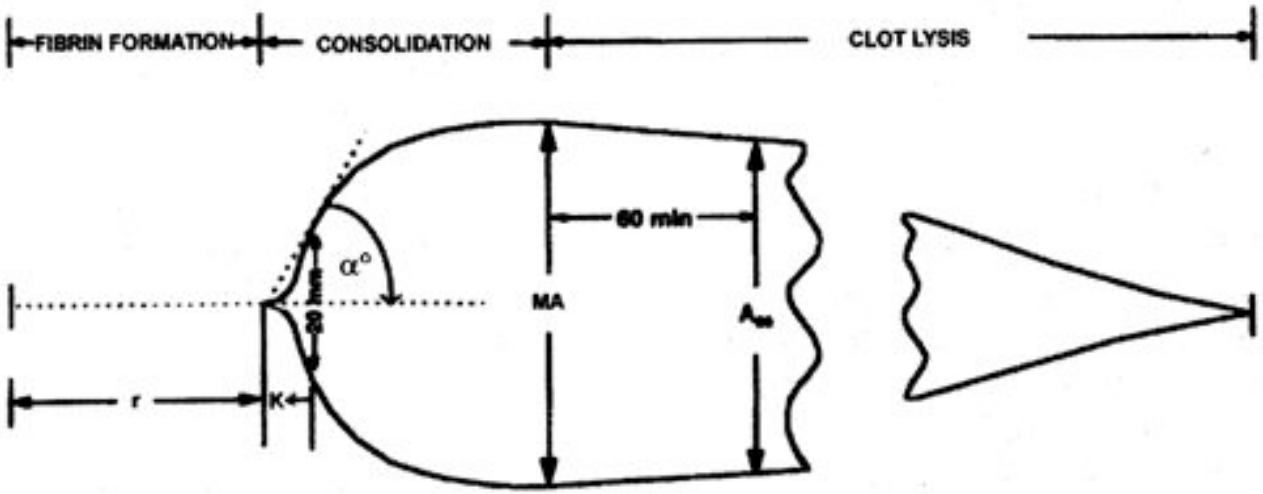


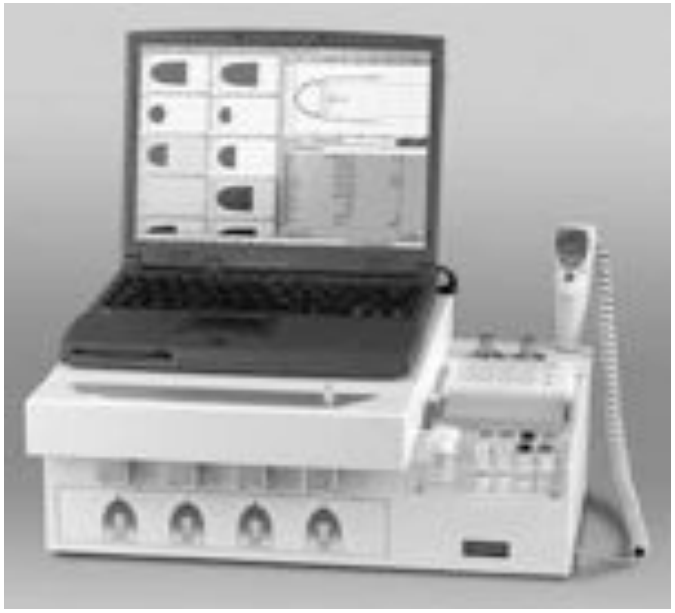
Fig. 3. – Tromboelastogramma.

TABELLA 1. – *Principali parametri tromboelastografici.*

R	Il tempo R è l'intervallo di tempo che trascorre dal momento in cui il campione di sangue viene posto nella cuvetta sino alla formazione iniziale di fibrina
K	Il tempo K è l'intervallo di tempo per raggiungere un determinato livello di consistenza del coagulo.
α	L'angolo alpha misura la velocità di formazione e cross-linking della fibrina (*clot strengthening*)
MA	La massima ampiezza MA è una funzione diretta delle proprietà dinamiche del legame fibrina piastrine tramite recettore GPIIb/IIIa e rappresenta la consistenza finale del coagulo di fibrina.
LY30	LY30 misura la percentuale di riduzione 30 minuti dopo MA.

LE MACCHINE

TEG SYSTEM (HAEMOSCOPE, USA)



ROTEM THROMBOELASTOMETER (PENTAPHARM, GERMANY)

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

Anaesthesia, 2009, 64, pages 212–215 doi:10.1111/j.1365-2044.2008.05752.x

HEAD-TO-HEAD

The TEG® vs the ROTEM® thromboelastography/ thromboelastometry systems

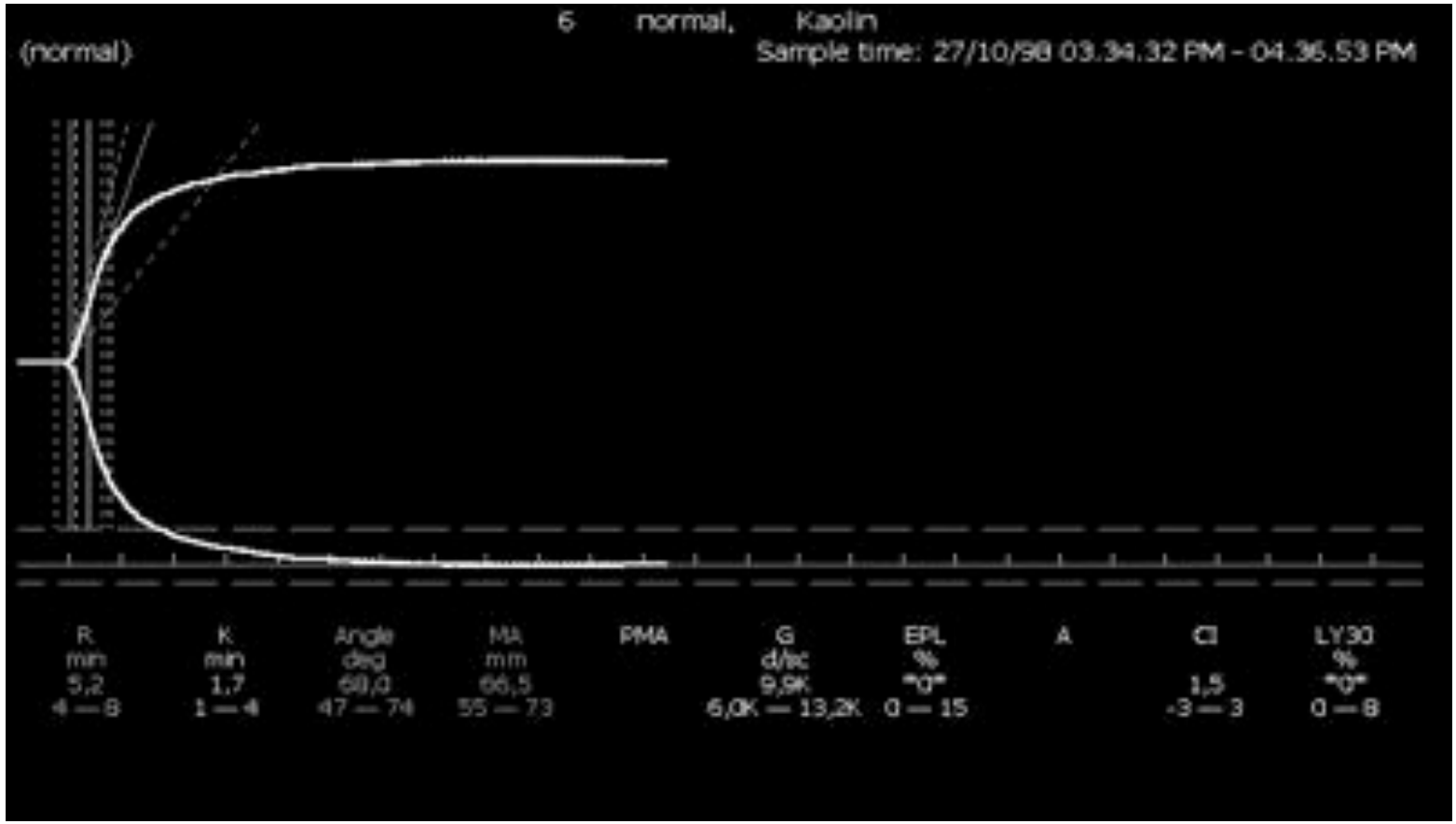
G. N. B. Jackson,[1] K. J. Ashpole[2] and S. M. Yentis[3]

VS

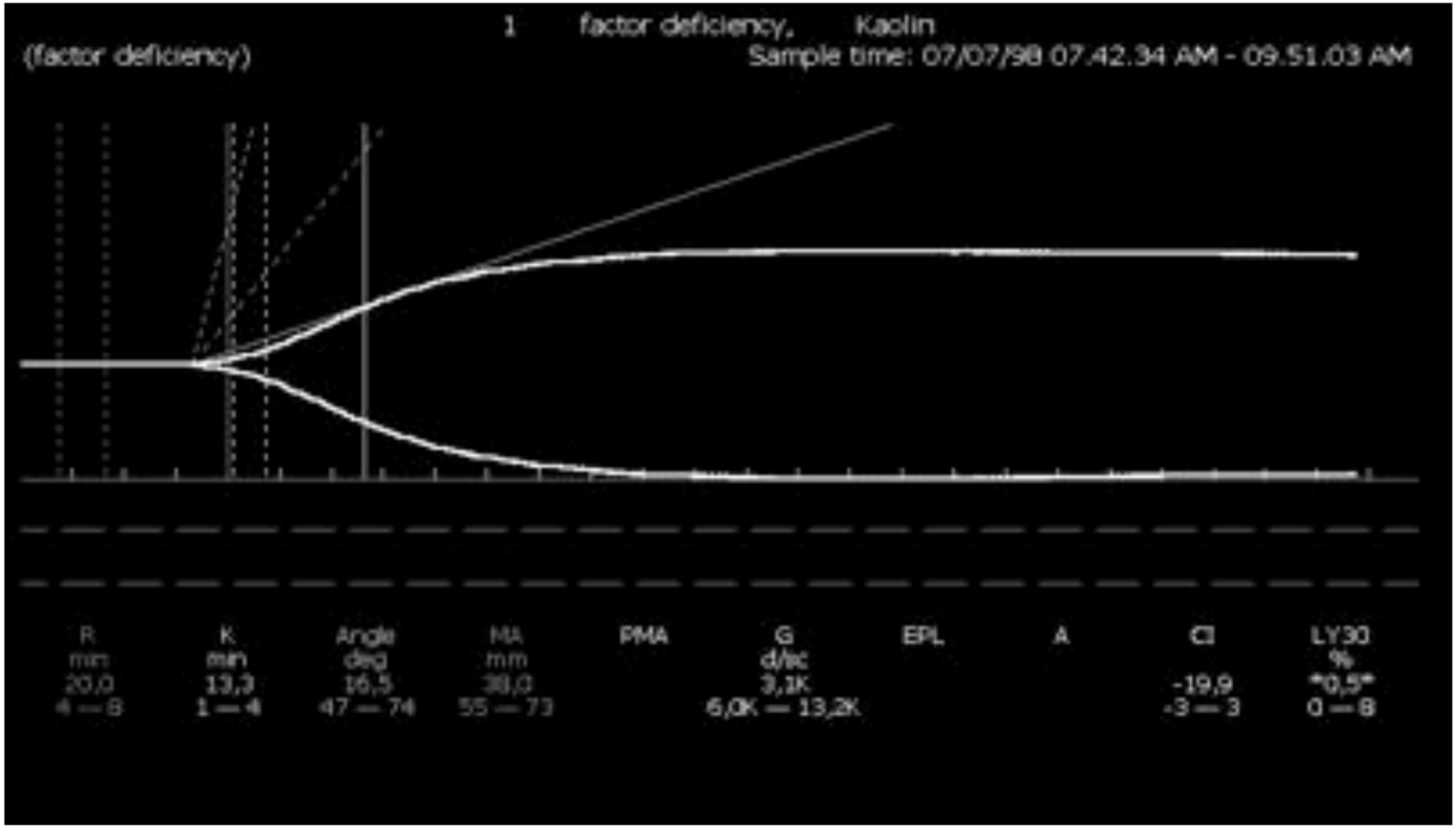
TEG SYSTEM (HAEMOSCOPE, USA)

ROTEM THROMBOELASTOMETER (PENTAPHARM, GERMANY)

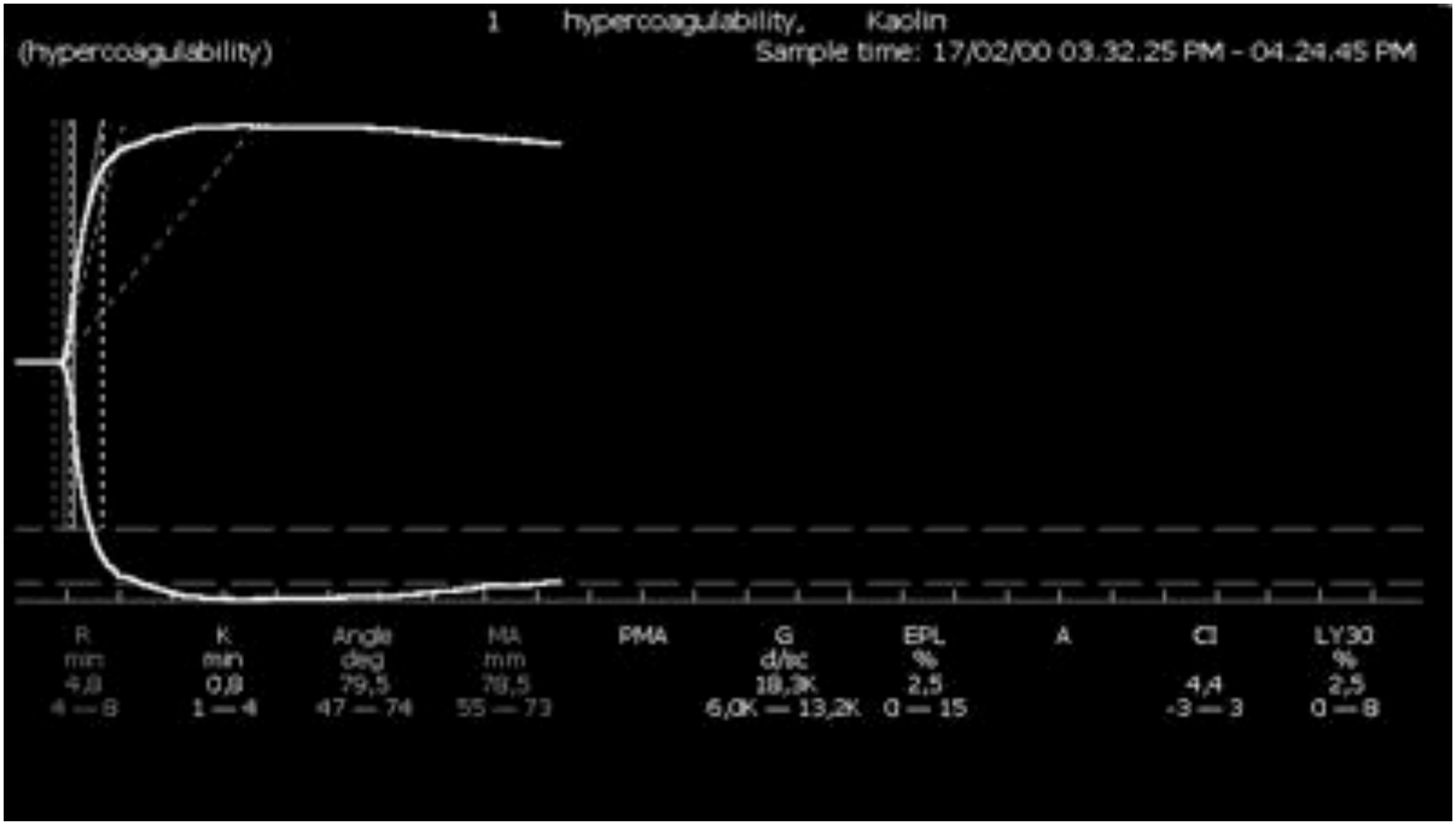
SANO


6 normal, Kaolin
(normal)
Sample time: 27/10/98 03.34.32 PM - 04.36.53 PM
R min 5,2 4 — 8
K min 1,7 1 — 4
Angle deg 68,0 47 — 74
MA mm 66,5 55 — 73
PMA
G d/sc 9,9K 6,0K — 13,2K
EPL % "0" 0 — 15
A
CI 1,5 -3 — 3
LY30 % "0" 0 — 8

DEFICIT DI FATTORI



IPERCOAGULABILITA’



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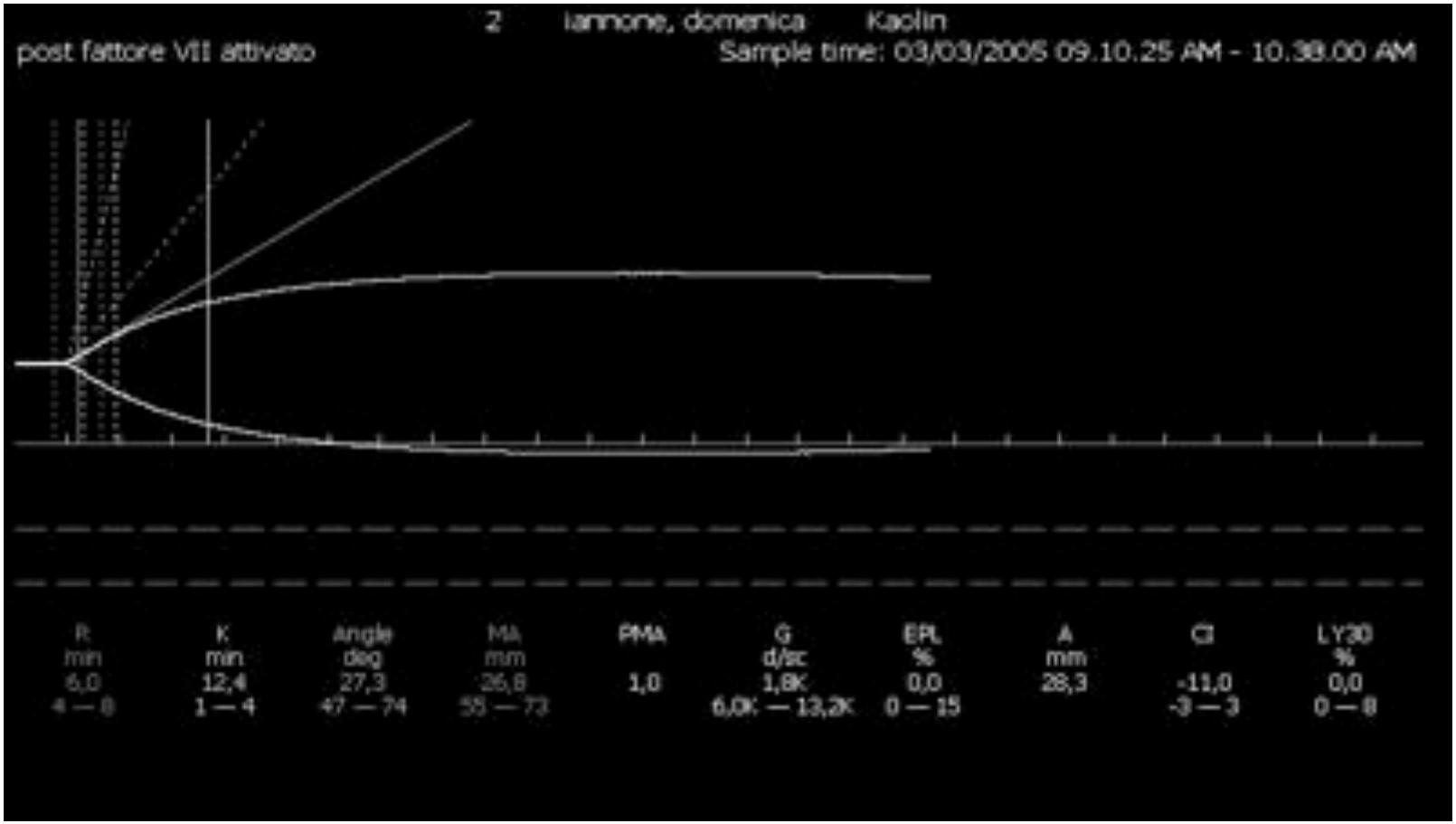
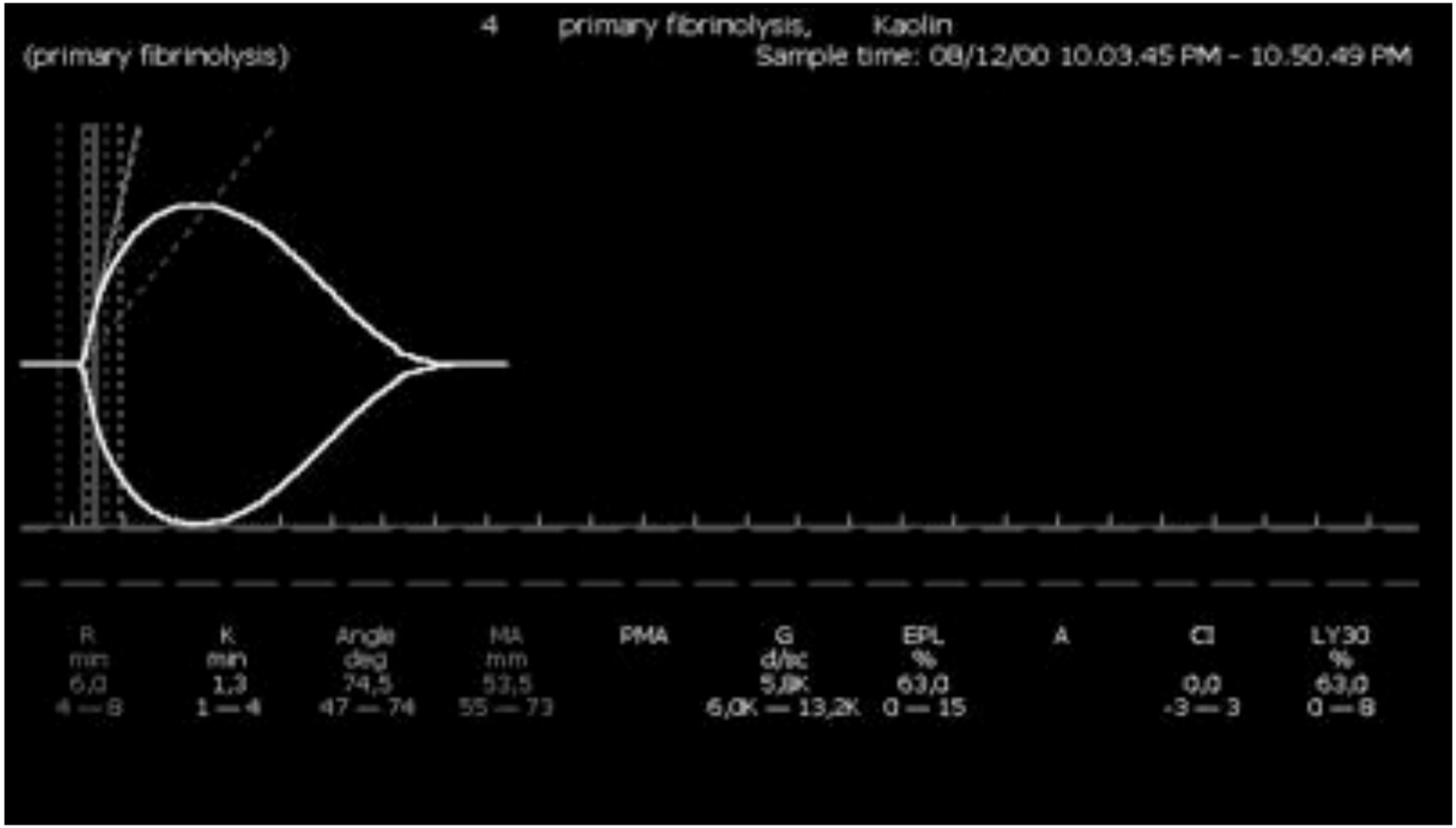


IPERFIBRINOLISI



ECCESSO DI EPARINA

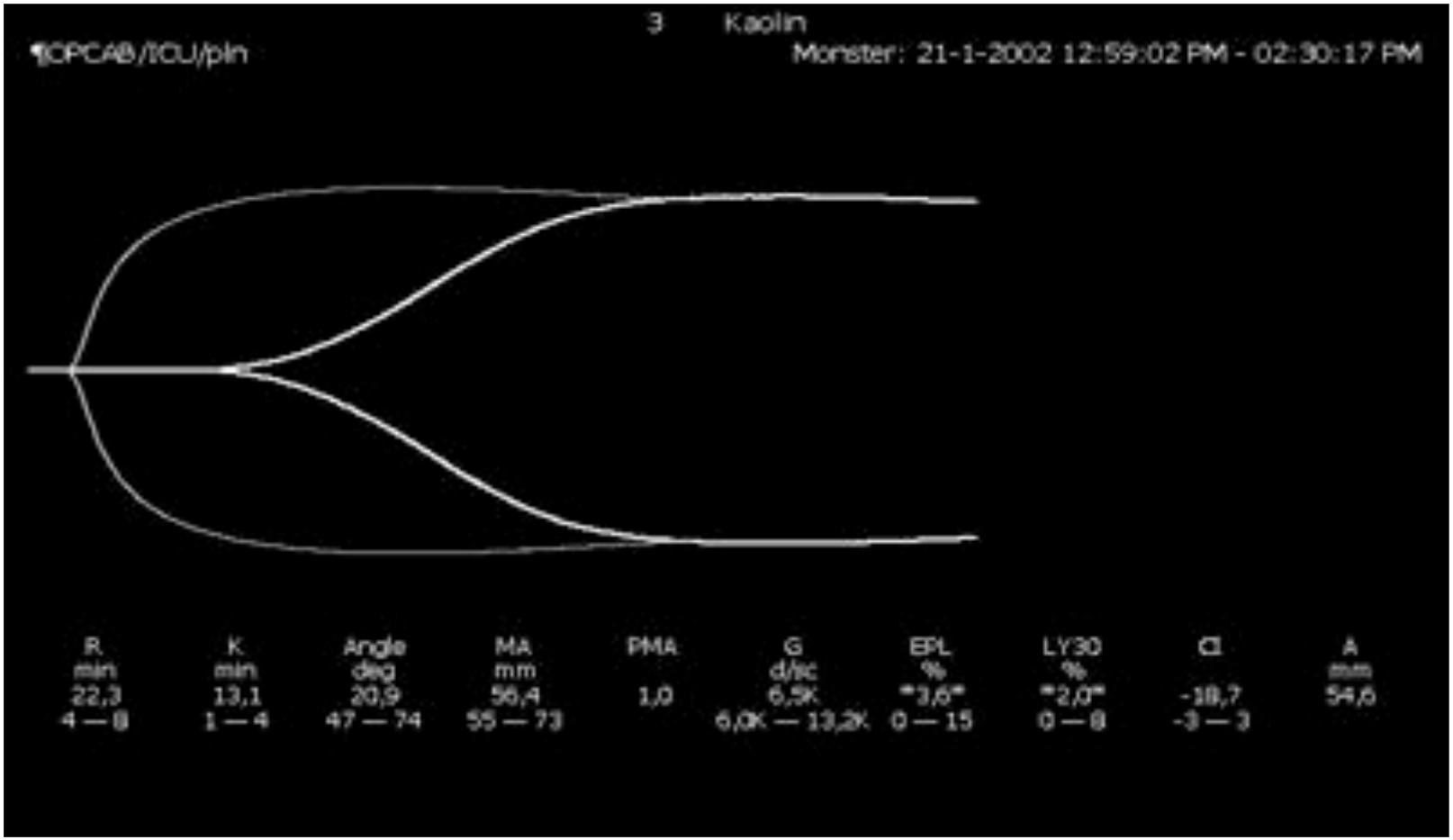


Tabella 1 – possibilità di intervento con farmaci ed emoderivati sulle variabili TEG (modificato da Kang, Anesthesiology, 1985)

TEG	problema	terapia
r lunga; α ed MA normali	deficit di fattori	PFC (10 - 15 ml / kg)
r lunga; a piccolo; Ma normale	ipofibrinogenemia	CRYO (400 - 600 UI)
r normale ; α normale ; MA ridotto	ipopiastrinemia	PLT (1 U da aferesi / 6 U random)
r normale; α ridotto ; MA ridotto	ipoPLT / ipoFBG	PLT / CRYO
r molto lungo; α ridotto; MA ridotto	effetto eparinico	protamina solfato *
r normale, α normale; MA con CLI 40 - 70%	lisi moderata	tranexamico bolo + infusione** aprotinina bolo + infusione**
r normale, α normale; MA con CLI < 40%	lisi severa	tranexamico bolo + infusione** aprotinina bolo + infusione **
r lunga; α piccolo; MA ridotto CLI < 60%	lisi in DIC	PFC / PLT / ATIII / CRYO

l'effetto eparinico dipendente da eparina esogena è presente praticamente solo dopo la riperfusione: la correzione con solfato di protamina di r lungo, α stretto, MA stretto deve essere prevista solo per contrastare eparine esogenee e pertanto solo dopo la riperfusione . La correzione prevede la somministrazione di 50 - 100 mg di solfato di protamina per via endovenosa lenta (pericolo di reazioni anafilattiche con ipotensione severa e vasocostrizione polmonare). L'uso di cuvetta "normale" e con eparinasi (blu) consente una diagnosi eziologica precisa (vedi testo)

** *Ac tranexamico - bolo di 15 mg / kg + infusione continua di 2 mg / kg / ora*

** *Aprotinina - bolo di 2 000 000 UI in 20minuti seguito da infusione continua di 500 000 UI /ora per la durata dell'intervento (non più disponibile)*

VANTAGGI TEG:

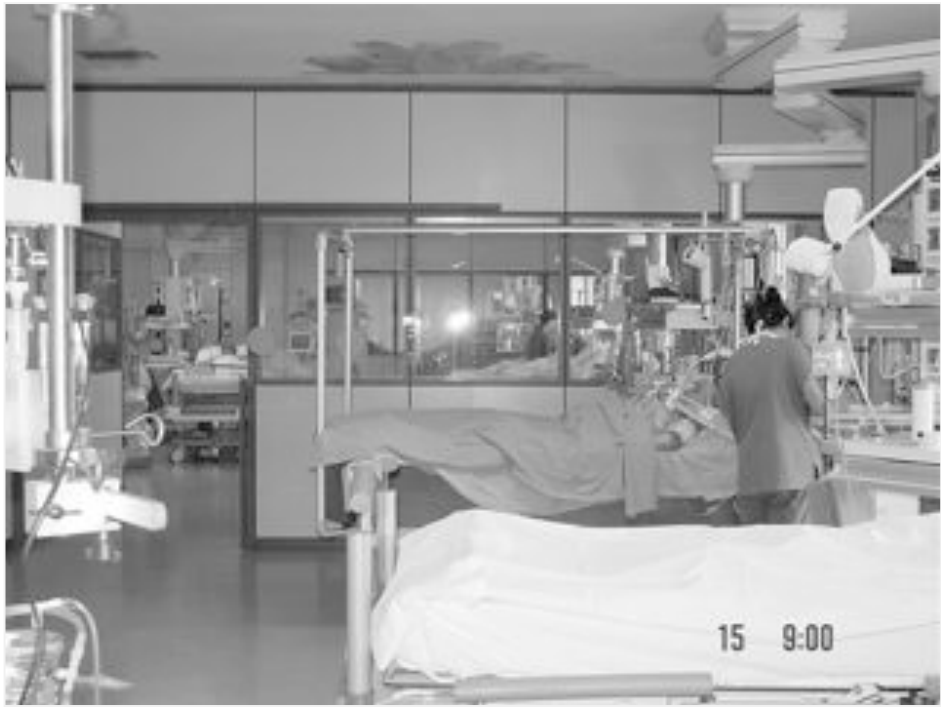
1) INDAGA TUTTA LA COAGULAZIONE (UMORALE E CELL)

2) MOSTRA IPERCOAG

3) MOSTRA IPERFIBRINO

4) SCOPRE EF EPARINICO

5) TEMP REALE, 15 MIN



6) GUIDA IL PROTOCOLLO TRASFUSIONALE

In Vivo Bleeding Time and In Vitro Thrombelastography Measurements are Better Indicators of Dilutional Hypothermic Coagulopathy Than Prothrombin Time

Bijan S. Kheirabadi, PhD, Jacqueline M. Crissey, BS, Rodolfo Deguzman, BS, and John B. Holcomb, MD

Background: The coagulopathy of trauma is generally confirmed by prothrombin time (PT) ≥16 seconds or an international normalized ratio ≥1.5. However, the utility of these values as a screening test is unknown. We examined different coagulation tests to determine the best predictor of coagulopathic bleeding and mortality in a small animal hemorrhage model.

Methods: Coagulopathy was induced in male New Zealand White rabbits by warfarin (W; 2 mg/kg for 2 days; n = 7), or hemodilution and hypothermia (HH; 50% blood exchange with Hextend, 34.5 ± 0.3°C; n = 7). Normal (N) rabbits without pretreatment served as the control (n = 7). Blood samples collected after coagulopathy induction and analyzed by prothrombin time (PT), activated partial thromboplastin time (aPTT), and thrombelastography (TEG) tests. Liver bleeding time (BT) was also measured before injury. An uncontrolled hemorrhage was created by a longitudinal splenic incision and the abdomen was closed. Rabbits were resuscitated with Hextend solution (25 mL/kg) to return blood pressure to baseline and monitored for 2 hours or until death at which time blood loss was measured.

Results: Warfarin-induced coagulopathy increased BT, PT, and aPTT. TEG showed increased reaction (R) and clot formation (K) times and marked decrease in clotting rate (α angle and Vmax). Hemodilution hypothermia coagulopathy increased only BT and aPTT, and decreased the clotting rate (α angle and Vmax) and strength of the clot. After injury, blood losses were higher in coagulopathic rabbits (W = 54.6 ± 4.2 and HH = 51.1 ± 8.9 mL/kg) than in normal rabbits (30.6 ± 12.4 mL/kg) and resulted in 86%, 100%, and 0% death, respectively. BT and Vmax consistently predicted coagulopathic bleeding and death in all animals.

Conclusion: Although satisfactory in warfarin-induced coagulopathy, PT was not a valid screening test for dilutional and hypothermic coagulopathy. BT and TEG measurements of blood clotting rate are better indicators of coagulopathic bleeding and mortality in this lethal hemorrhage model.

Key Words: Coagulopathy, Warfarin, Hemodilution, Hypothermia, Hemorrhage model.

J Trauma 2007;62:1352–1361.

J Trauma [1529-8809] 2008 Sep;65(3), 535-43. Martini WZ, Cortez DS, Dubick MA, Park MS, Holcomb JB
The US Army Institute of Surgical Research, Houston, USA

Thrombelastography is better than PT, aPTT, and activated clotting time in detecting clinically relevant clotting abnormalities after hypothermia, hemorrhagic shock and resuscitation in pigs.

***BACKGROUND:** Hypothermia and hemorrhagic shock contribute to coagulopathy after trauma. In this study, we investigated the independent and combined effects of hypothermia and hemorrhage with resuscitation on coagulation in swine and evaluated clinically relevant tests of coagulation. **METHODS:** Pigs (n = 24) were randomized into four groups of six animals each: sham control, hypothermia, hemorrhage with resuscitation, and hypothermia, hemorrhage with resuscitation combined. Hypothermia to 32 degrees C was induced with a cold blanket. Hemorrhage was induced by bleeding 35% of total blood volume followed by resuscitation with lactated Ringer's solution. Coagulation was assessed by thrombin generation, prothrombin time (PT), activated partial thromboplastin time (aPTT), activated clotting time (ACT), and thrombelastography (TEG) from blood samples taken at baseline and 4 hour after hypothermia and/or hemorrhage with resuscitation. Data were compared with analysis of variance. **RESULTS:** Baseline values were similar among groups. There were no changes in any measurements in the control group. Compared with baseline values, hemorrhage with resuscitation increased lactate to 140% +/- 15% ($p < 0.05$). Hypothermia decreased platelets to 73% +/- 3% ($p < 0.05$) with no effect on fibrinogen. Hemorrhage with resuscitation reduced platelets to 72% +/- 4% and fibrinogen to 71% +/- 3% (both $p < 0.05$), with similar decreases in platelets and fibrinogen observed in the combined group. Thrombin generation was decreased to 75% +/- 4% in hypothermia, 67% +/- 6% in hemorrhage with resuscitation, and 75% +/- 10% in the combined group (all $p < 0.05$). There were no significant changes in PT or aPTT by hemorrhage or hypothermia. ACT was prolonged to 122% +/- 1% in hypothermia, 111% +/- 4% in hemorrhage with resuscitation, and 127% +/- 3% in the combined group (all $p < 0.05$). Hypothermia prolonged the initial clotting time (R) and clot formation time (K), and decreased clotting rapidity (alpha) (all $p < 0.05$). Hemorrhage with resuscitation only decreased clot strength (maximum amplitude [MA], $p < 0.05$). TEG parameters in the combined group reflected the abnormal R, K, MA, and alpha observed in the other groups. **CONCLUSION:** Hypothermia inhibited clotting times and clotting rate, whereas hemorrhage impaired clot strength. Combining hypothermia with hemorrhage impaired all these clotting parameters. PT, aPTT were not sensitive whereas ACT was not specific in detecting these coagulation defects. Only TEG differentiated mechanism related to clotting abnormalities, and thus may allow focused treatment of clotting alterations associated with hypothermia and hemorrhagic shock.*

Journal of Thrombosis and Haemostasis, 5: 289–295

ORIGINAL ARTICLE

Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography

L. RUGERI,* A. LEVRAT,† J. S. DAVID,† E. DELECROIX,* B. FLOCCARD,† A. GROS,† B. ALLAOUCHICHE† and C. NEGRIER*

*Laboratory of Haemostasis; and †Department of Anaesthesia, Intensive Care and EMS, Edouard Herriot Hospital, Hospices Civils de Lyon and Claude Bernard University, Lyon, France

Summary. *Background:* Reagent-supported thromboelastometry with the rotation thrombelastography (e.g. ROTEM®) is a whole blood assay that evaluates the visco-elastic properties during blood clot formation and clot lysis. A hemostatic monitor capable of rapid and accurate detection of clinical coagulopathy within the resuscitation room could improve management of bleeding after trauma. *Objectives:* The goals of this study were to establish whether ROTEM correlated with standard coagulation parameters to rapidly detect bleeding disorders and whether it can help to guide transfusion. *Methods:* Ninety trauma patients were included in the study. At admission, standard coagulation assays were performed and ROTEM parameters such as clot formation time (CFT) and clot amplitude (CA) were obtained at 15 min (CA_{15}) with two activated tests (INTEM, EXTEM) and at 10 min (CA_{10}) with a test analyzing specifically the fibrin component of coagulation (FIBTEM). *Results:* Trauma induced significant modifications of coagulation as assayed by standard assays and ROTEM. A significant correlation was found between prothrombin time (PT) and CA_{15}-EXTEM ($r = 0.66$, $P < 0.0001$), between activated partial thromboplastin time and CFT-EXTEM ($r = 0.91$, $P < 0.0001$), between fibrinogen level and CA_{10}-FIBTEM ($r = 0.85$, $P < 0.0001$), and between platelet count and CA_{15}-INTEM ($r = 0.57$, $P < 0.0001$). A cutoff value of CA_{15}-EXTEM at 32 mm and CA_{10}-FIBTEM at 5 mm presented a good sensitivity (87% and 91%) and specificity (100% and 85%) to detect a PT > 1.5 of control value and a fibrinogen less than 1 g L^{-1}, respectively. *Conclusion:* ROTEM is a point-of-care device that rapidly detects systemic changes of *in vivo* coagulation in trauma patients, and it might be a helpful device in guiding transfusion.

J Trauma ,1997 Apr;42(4):716-20

Usefulness of Thrombelastography in Assessment of Trauma Patient Coagulation

Christoph R. Kaufmann, MD, MPH, Kevin M. Dwyer, MD, John D. Crews, BS, Sheila J. Dols, MT, and Arthur L. Trask, MD

Objective: Thrombelastography (TEG) is used to rapidly assess coagulation abnormalities in cardiac and transplant surgery. The purpose of this study was to investigate TEG in the initial assessment of trauma patient coagulation.

Methods: TEG was performed on 69 adult blunt trauma patients during their initial evaluation. Demographics, history of inherited coagulopathies, medications, TEG parameters, platelet count, prothrombin time/partial thromboplastin time, Revised Trauma Score (RTS), Injury Severity Score (ISS), use of blood products, and outcome were recorded.

Results: Mortality was 4.3%. Fifty-two patients demonstrated coagulation abnormalities by TEG; of these, 45 were hypercoagulable (mean ISS 13.1), and seven were hypocoagulable (mean ISS 28.6). Six of the seven hypocoagulable patients received blood transfusions within the first 24 hours. Mean ISS of the 17 patients with normal TEG parameters was 3.7. Logistic regression of ISS, Revised Trauma Score, prothrombin time/partial thromboplastin time, and TEG on use/nonuse of blood products within the first 24 hours demonstrates that only ISS ($p < 0.001$) and TEG ($p < 0.05$) are predictive of early transfusion.

Conclusions: The majority of blunt trauma patients in this series were hypercoagulable. TEG is a rapid, simple test that can broadly determine coagulation abnormalities. TEG is an early predictor of transfusion in blunt injury patients.

Key Words: Thrombelastography, Trauma, Coagulation, Transfusion.

PIU' GRAVI = IPOCOAGULATI

TABLE 1. Thrombelastography results

Result	N	Injury Severity Score	Transfusion (24 hours)
Hypocoagulable	7	28.6	6
Normal	17	3.7	0
Hypercoagulable	45	13.1	2
Total	69	12.3	8

TRATTAMENTO

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

Massive Transfusion Practices Around the Globe and a Suggestion for a Common Massive Transfusion Protocol

Debra L. Malone, MD, LTC USAF, SGRS, John R. Hess, MD, MPH, and Abe Fingerhut, MD

Background: Massive transfusion, the administration of 10 to more than 100 units of red blood cells (RBC) in less than 24 hours, can be a life saving therapy in the treatment of severe injury. The rapid administration of large numbers of RBC, along with sufficient plasma and platelets to treat or prevent coagulopathy, is frequently a disorderly process. Patient care and collaborative research might be aided with a common protocol.

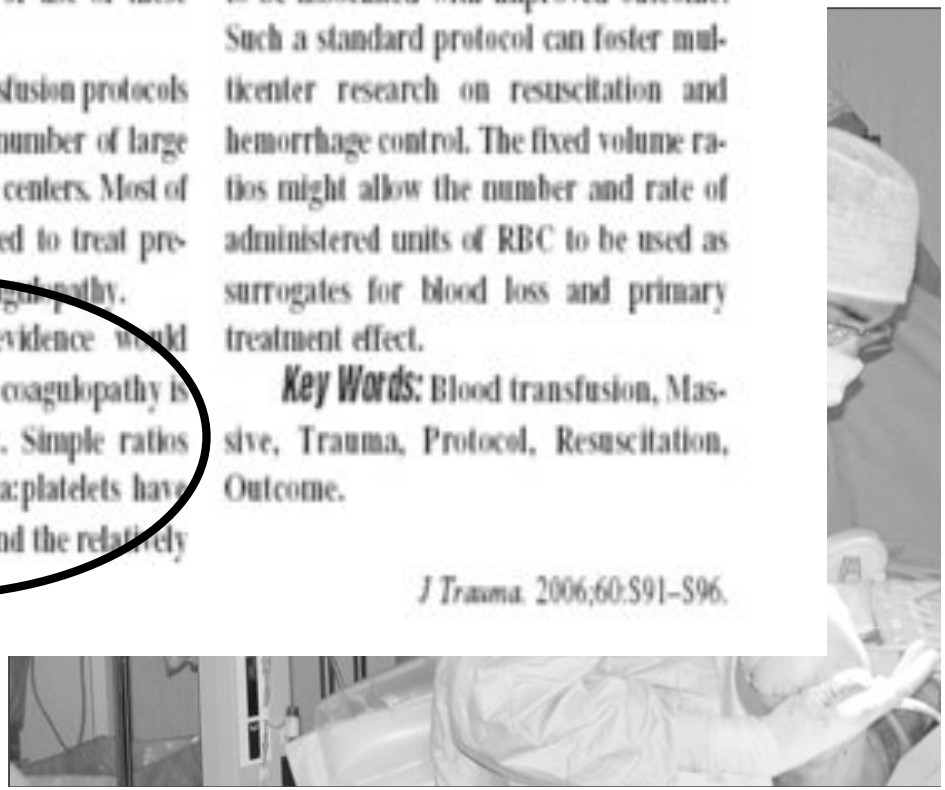
Methods: The authors polled trauma organizations and trauma centers to find examples of massive transfusion protocols. The goals and ease of use of these protocols were evaluated.

Results: Massive transfusion protocols exist at a relatively small number of large and well-organized trauma centers. Most of these protocols are designed to treat preexisting and/or ongoing coagulopathy.

Conclusions: The evidence would suggest that prevention of coagulopathy is superior to its treatment. Simple ratios such as 1:1:1 RBC:plasma:platelets have the benefit of ease of use and the relatively higher plasma and platelet doses appear to be associated with improved outcome. Such a standard protocol can foster multicenter research on resuscitation and hemorrhage control. The fixed volume ratios might allow the number and rate of administered units of RBC to be used as surrogates for blood loss and primary treatment effect.

Key Words: Blood transfusion, Massive, Trauma, Protocol, Resuscitation, Outcome.

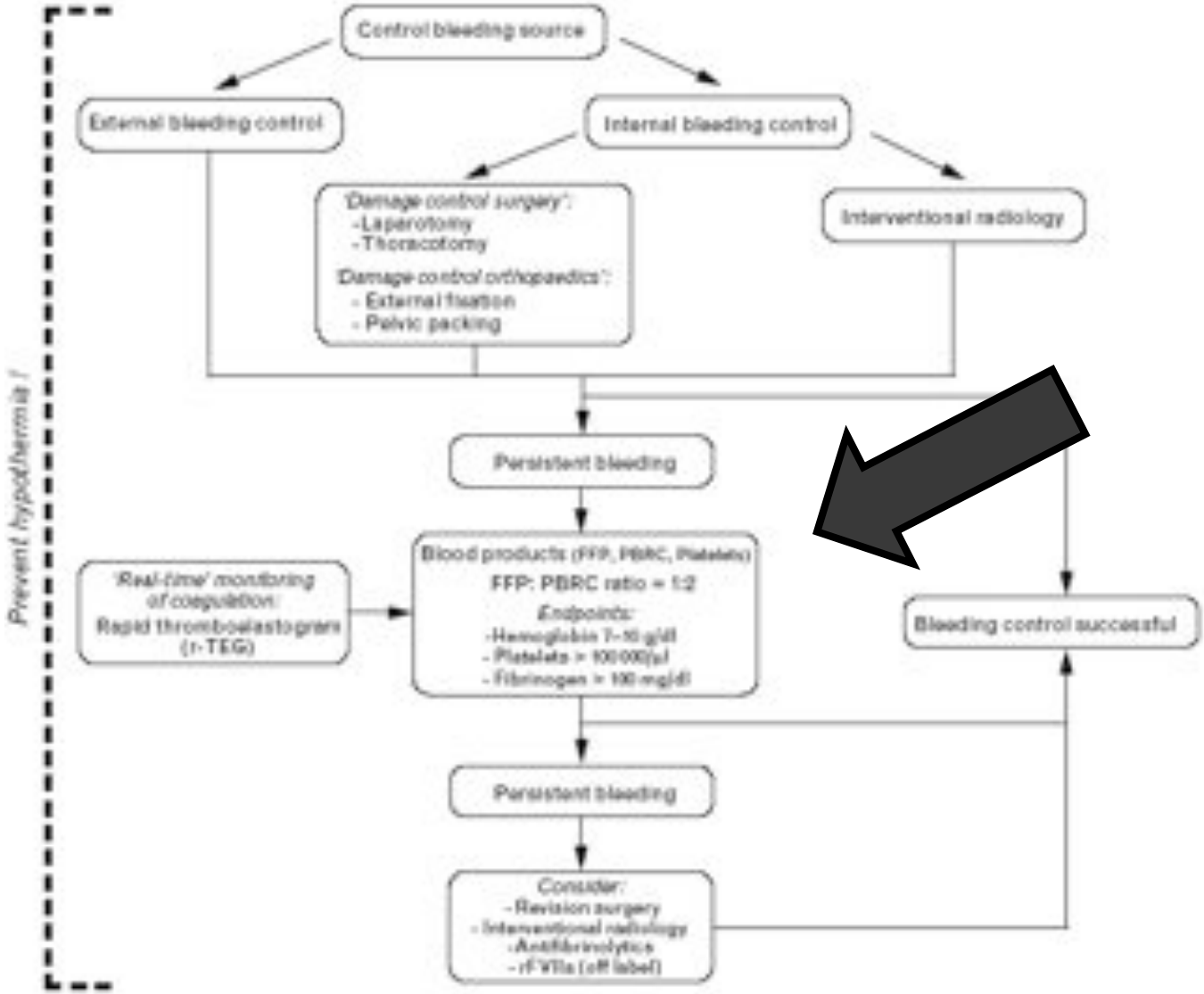
J Trauma. 2006;60:S91–S96.



Transfusion strategies in postinjury coagulopathy

Philip F. Stahel[a], Ernest E. Moore[b], Star L. Schreier[a], Michael A. Flierl[a] and Jeffry L. Kashuk[b]

Current Opinion in Anaesthesiology 2009, 22:289–298



Current Opinion in Anaesthesiology 2009, 22:289–298

Transfusion strategies in postinjury coagulopathy

Citation	Patient cohort	Study center, study period	Investigated FFP concentration/ FFP:RBC ratio	Recommended FFP concentration/ FFP:RBC ratio	Pitfalls and limitations
Kashuk *et al.* [21]	*n* = 133 trauma patients, >10 RBCs/6 h	Level 1 trauma center, 2001–2006	1 : 1, 1 : 2, 1 : 3, 1 : 4, <1 : 5	1 : 2	Retrospective study; no mechanisms
Sperry *et al.* [43]	*n* = 415 trauma patients, ≥8 RBCs/12 h	Multicenter study (*n* = 7), 2003–2005	1 : 1, 1 : 2, 1 : 3, 1 : 4, <1 : 5	≥1 : 1.5	Retrospective study; no mechanisms
Duchesne *et al.* [44]	*n* = 135 trauma patients, >10 RBCs/24 h; *n* = 250 trauma patients, ≤10 RBCs/24 h	Level 1 trauma center, 2002–2006	1 : 1, 1 : 4	1 : 1	Retrospective study; no mechanisms
Maegele *et al.* [45]	*n* = 713 trauma patients, >10 RBCs between ED and ICU admission	German Trauma Registry (DGU), 2002–2006	>1 : 1, 1 : 1, <1 : 1	1 : 1 (?)	Retrospective analysis of a prospective database; no mechanisms
Holcomb *et al.* [46]	*n* = 467 trauma patients, ≥10 RBCs/24 h	Multicenter study (*n* = 16), 2005–2006	≥1 : 2, <1 : 2	1 : 1	Retrospective study; no mechanisms
Gonzalez *et al.* [17]	*n* = 97 trauma patients, ≥10 RBCs/24 h	Level 1 trauma center, 1998–2003	1 : 1	1 : 1	Retrospective study; no mechanisms
Spahn *et al.* [12••]	Systematic review of the literature	European guidelines by the Multidisciplinary Task Force for Advanced Bleeding Care in Trauma	Systematic review of the literature	10–15 ml/kg (initial FFP dose) for PT or aPTT > 1.5 × control	Review of the literature; recommendations based on limited available science
Spinella *et al.* [47]	*n* = 708 combat trauma patients, ≥1 RBCs overall	Combat support hospital, 2003–2004	0–4 : 2–7	Each FFP unit increased survival; each RBC unit decreased survival	Retrospective study; no mechanisms
Borgman *et al.* [48]	*n* = 246 combat trauma patients, ≥10 RBCs/24 h	Combat support hospital, 2003–2005	1 : 1.4, 1 : 2.5, 1 : 8	1 : 1.4	Retrospective study; no mechanisms
Gunter *et al.* [49]	*n* = 269 trauma patients, ≥10 RBCs/24 h	Level 1 trauma center, 2004–2006	0 : 1–1 : 2.9, 1 : 3–1 : 1.49, 1 : 1.5–0.9 : 1, ≥1 : 1	2 : 3	Retrospective study; no mechanisms
Scalea *et al.* [50••]	*n* = 260 trauma patients, ≥1 RBC and FFP/24 h	Level 1 trauma center, prospective study, 2004–2006	1 : 1 versus any other ratios	1 : 1 does not improve outcome	Small group of patients (*n* = 51) in 1 : 1 cohort

AFGHANISTAN

Holcomb JB, Jenkins D, Rhee P, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. J Trauma 2007; 62:307–10.

BOSNIA

Kauvar DS, Holcomb JB, Norris GC, Hess JR. Fresh whole blood transfusion: a controversial military practice. J Trauma 2006;61: 181–4.

BOSNIA

Repine TB, Perkins JG, Kauvar DS, Blackborne L. The use of fresh whole blood in massive transfusion. J Trauma 2006;60(6 Suppl):S59–69.

IRAQ

Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma 2007;63:805–13.

…MA…I MILITARI:

1) TRAUMA PENETRANTE

2) DA SCOPPIO

3) LUNGHI TEMPI DI TRASPORTO

4) USO DI FATTORE VII ATTIVATO

Transfusion and Apheresis Science 39 (2008) 3–8

Transfusion packages for massively bleeding patients: The effect on clot formation and stability as evaluated by Thrombelastograph (TEG®)

Vox Sanguinis (2009) **96**, 111–118

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

Vox Sanguinis (2009) **96**, 111–118

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

Appendix 1 Thrombelastography (TEG) treatment algorithm for patients with ongoing bleeding

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

R, R-time, minutes; MA, maximum amplitude; Ly30, lysis in percent 30 min after MA is reached; FFP, fresh-frozen plasma.

rFATTVIIa = OFF LABEL

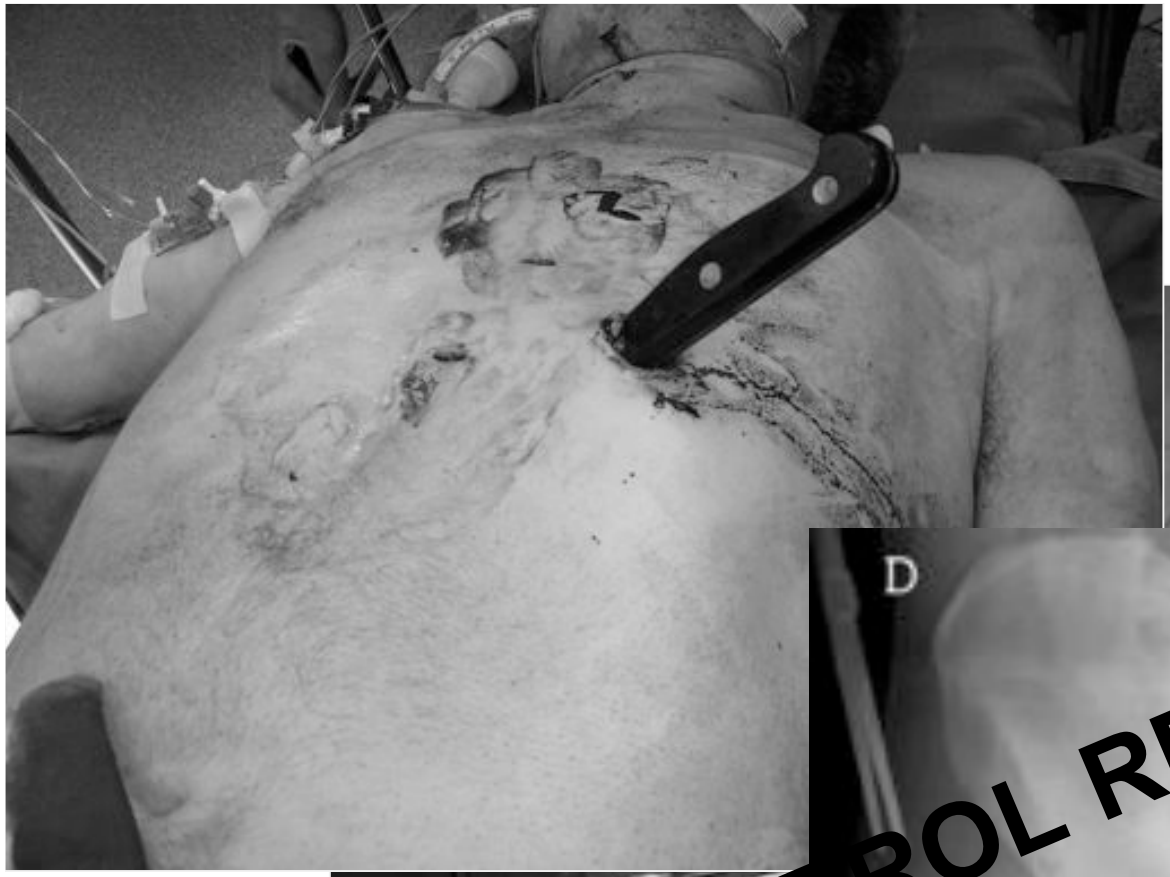
Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia (Review)
The Cochrane Library 2009, Issue 2

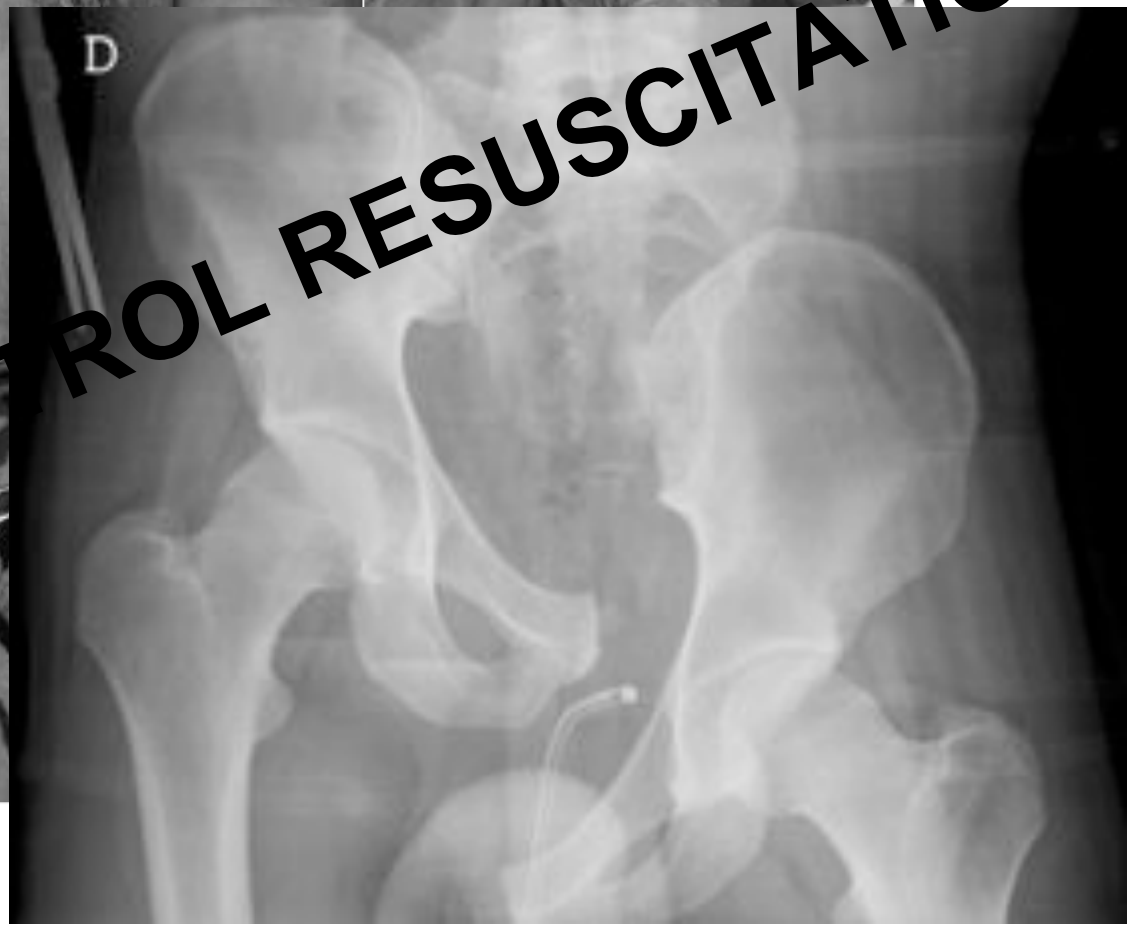
Evidence for the Use of Recombinant Factor VIIa in the Prevention and Treatment of Bleeding in Patients Without Hemophilia
Transfusion Medicine Reviews, Vol 22, No 3 (July), 2008: pp 177-187

1) PFC replacement regimens are inadeguate to manage the coagulopaty
2) rFVIIa has become an accepted part of the therapeutic armamentarium for the treatment of refractory hemorrhage
3) the results (17 RCT) for both prophylactic and therapeutic use of rFVIIa are not indicative for universal efficacy
4) in intracerebral hemorrhage limits growth of hematoma
5) no obvious correlation between response and dose size or frequency
6) selected positive studies have methodological limitations
7) about tromboembolic event, there is no statistical difference between rFVIIa and placebo (except for ICH)

Recombinant FVIIa in the management of uncontrolled hemorrhage
Volume 43, December 2003 **TRANSFUSION** 1711

Off-label use of recombinant factor VIIa for treatment of haemorrhage: results from randomized clinical trials
Vox Sanguinis (2008) 95, 1–7





DAMAGE CONTROL RESUSCITATION

Damage Control Resuscitation: Directly Addressing the Early Coagulopathy of Trauma

John B. Holcomb, MD, FACS, Don Jenkins, MD, FACS, Peter Rhee, MD, FACS, Jay Johannigman, MD, FS, FACS, Peter Mahoney, FRCA, RAMC, Sumeru Mehta, MD, E. Darrin Cox, MD, FACS, Michael J. Gehrke, MD, Greg J. Beilman, MD, FACS, Martin Schreiber, MD, FACS, Stephen F. Flaherty, MD, FACS, Kurt W. Grathwohl, MD, Phillip C. Spinella, MD, Jeremy G. Perkins, MD, Alec C. Beekley, MD, FACS, Neil R. McMullin, MD, Myung S. Park, MD, FACS, Ernest A. Gonzalez, MD, FACS, Charles E. Wade, PhD, Michael A. Dubick, PhD, C. William Schwab, MD, FACS, Fred A. Moore, MD, FACS, Howard R. Champion, FRCS, David B. Hoyt, MD, FACS, and John R. Hess, MD, MPH, FACP

J Trauma. 2007;62:307–310.

In the severely injured casualty, damage control resuscitation consists of two parts and is initiated within minutes of arrival in the ED. First, resuscitation is limited to keep blood pressure at approximately 90 mm Hg, preventing renewed bleeding from recently clotted vessels.[15,17,39,57–62] Second, intravascular volume restoration is accomplished by using thawed plasma as a primary resuscitation fluid in at least a 1:1 or 1:2 ratio with PRBCs.[8,10,48–50] Our initial clinical experi-

Damage control resuscitation: A sensible approach to the exsanguinating surgical patient

MAJ (P) Alec C. Beekley, MD, FACS

Crit Care Med 2008 Vol. 36, No. 7 (Suppl.)

BLUNT : 90 mmHg
(radial pulse)
PENETRATING : 70 mmHg
(carotid pulse)
BLUNT + HEAD : 110 mmHg

Revell M, Greaves I, Porter K: Endpoints for fluid resuscitation in hemorrhagic shock. J Trauma 2003; 54: S63-S67

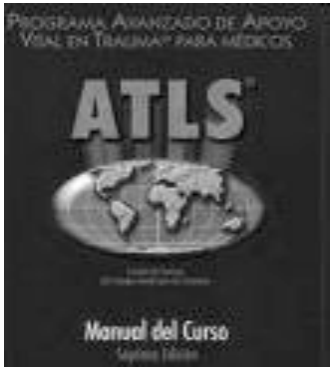
CON LA DAMAGE CONTROL RESUSCITATION: LE COSE CAMBIANO

Management of bleeding following major trauma: a European guideline

Critical Care 2007, 11:R17 doi:10.1186/cc5686

Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies



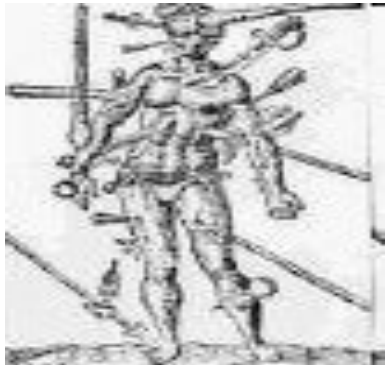


Table 2

American College of Surgeons Advanced Trauma Life Support classification of haemorrhage severity

Haemorrhage severity according to ACS/ATLS classification[a]	Class I	Class II	Class III	Class IV
Blood loss (ml)	<750	750–1,500	1,500–2,000	>2,000
Pulse rate (per minute)	<100	>100	>120	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal	Decreased	Decreased	Decreased
Respiratory rate (per minute)	14–20	20–30	30–40	>40
Urine output (ml/hour)	>30	20–30	5–15	Negligible
Central nervous system (mental status)	Slightly anxious	Mildly anxious	Anxious, confused	Lethargic

[a]Values are estimated for a 70-kg adult. Table reprinted with permission from the American College of Surgeons [26]. ACS/ATLS, American College of Surgeons/Advanced Trauma Life Support.

IL SANGUE INVECCHIA

Naotaka Hamasaki[a] Masaaki Yamamoto[b]
Vox Sang 2000;79:191–197

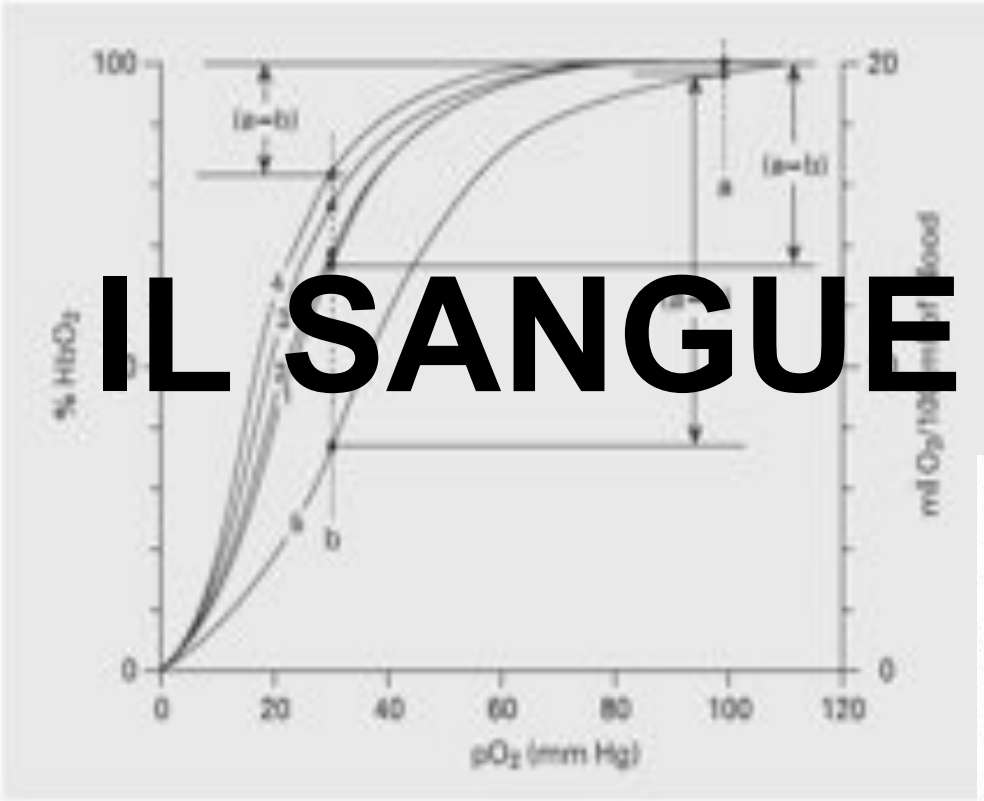
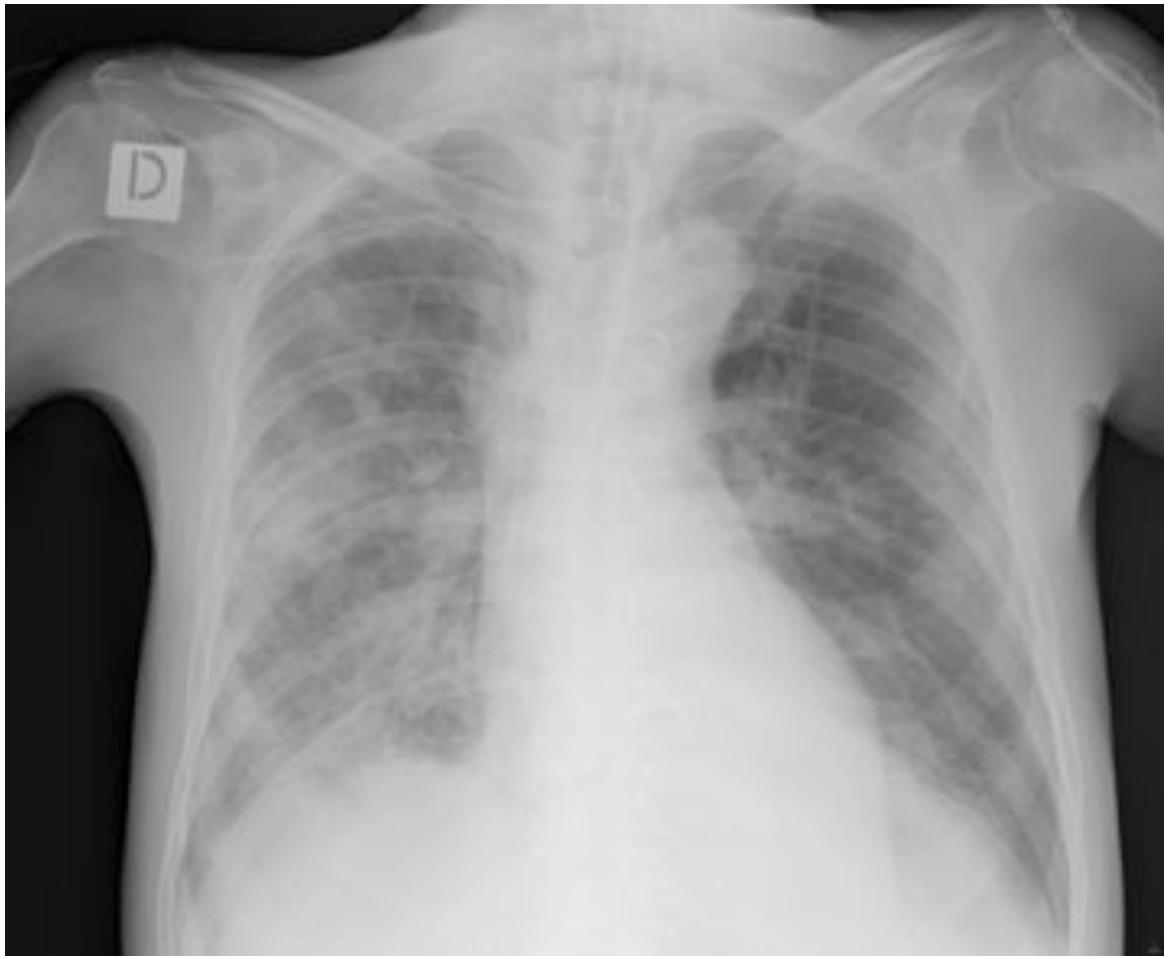


Fig. 2. Oxygen dissociation curves of preserved red blood cells. Curve 1: oxygen dissociation curve of fresh blood; curve 2: oxygen dissociation curve of 1-week-old CPD blood; curve 3: oxygen dissociation curve of 2-week-old CPD blood; curve 4: oxygen dissociation curve of 3-week-old CPD blood; curve 5: oxygen dissociation curve of 3-week-old CPD blood after treatment with PEP. (a–b) is the oxygen-delivering capacity of red blood cells.

TRALI



Transfusion-related acute lung injury surveillance (2003-2005) and the potential impact of the selective use of plasma from male donors in the American Red Cross

Anne F. Eder, Ross Herron, Annie Strupp, Beth Dy, Edward P. Notari, Linda A. Chambers, Roger Y. Dodd, and Richard J. Benjamin

TAKE AT HOME:

1) LA COAGULOPATIA E LA TRASFUSIONE MASSIVA UCCIDONO

2) IL TEG E' MEGLIO DI AP E PTT

3) FARE DAMAGE CONTROL RESUSCITATION

* IPOTENSIONE PERMISSIVA

* ATTENZIONE AI LIQ

* RISCALDARE, EVITARE ACIDOSI

5) PENSARE AD UN PROTOCOLLO…MAGARI GRC:PFC 1:1

6) rFATTVIIa RESTA OFF LABEL