SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

APPROCCIO AL TRAUMA MAGGIORE
ATLS E ETC: DUE FILOSOFIE COMPLEMENTARI?

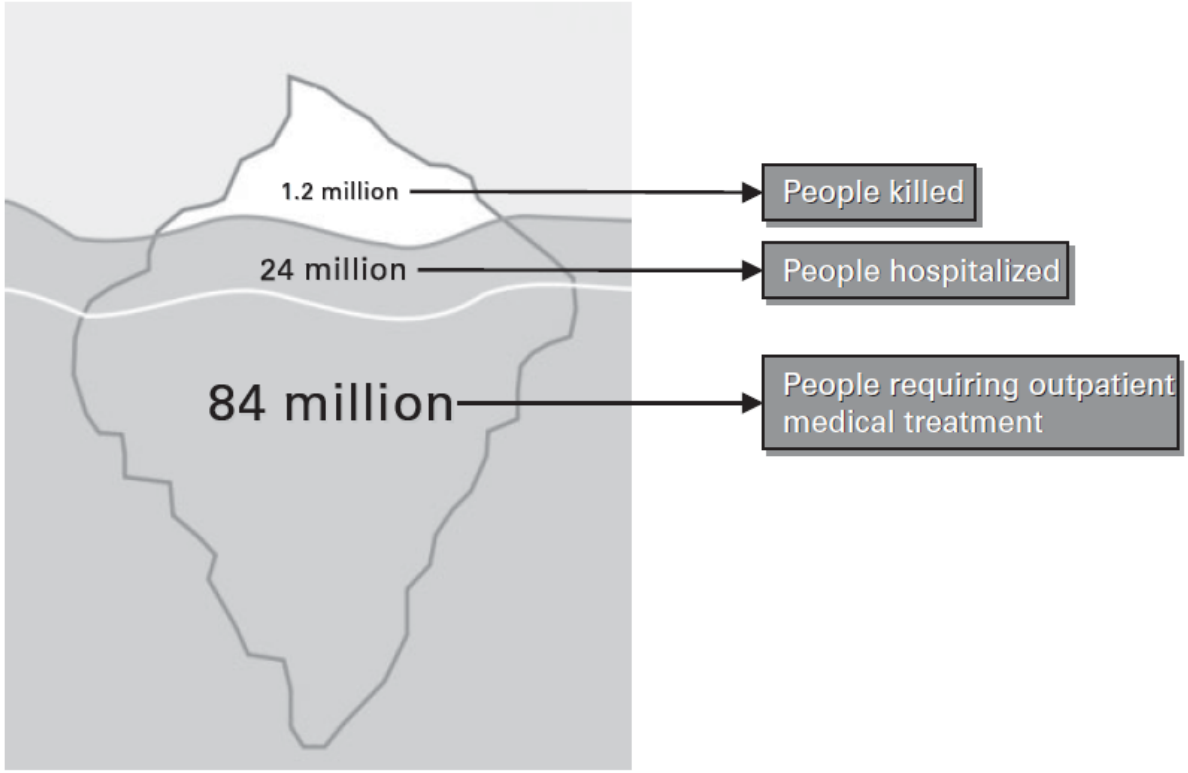
23 GENNAIO 2013
ore 9.30 - 17.00

15.00 - 15.30 G. Lippi

Il ruolo del laboratorio
nella diagnostica e terapia
della coagulopatia del trauma

Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]



Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]

- Trauma patients are susceptible to early development of coagulopathy.
- Most severely injured patients are already coagulopathic on hospital admission.
- The zenith of the problem is typically seen in patients with severe head injuries and in those who are massively injured and transfused.

J Trauma. 2006;60:S12–S19.

The Coagulopathy of Trauma versus Disseminated Intravascular Coagulation

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

- DIC in patients with severe trauma and systemic inflammatory response syndrome can be as high as 70%.
- Hemorrhage is the second leading cause of death following severe injury.
- The coagulopathy is characterized by nonsurgical bleeding from mucosal lesions, serosal surfaces, wound and vascular access sites.
- 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.

Disseminated Intravascular Coagulation in Trauma Injuries

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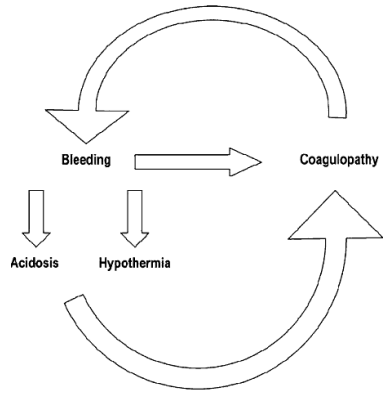


Clinicians have identified the "**triad of death**," acidosis, hypothermia, and coagulopathy, and described their important place in the "bloody vicious cycle" of hemorrhage, resuscitation, hemodilution, coagulopathy, and continued bleeding.

Probability of Life-Threatening Coagulopathy Increases with Shock, Hypothermia and Acidosis

Clinical Status	Conditional Probability of developing Coagulopathy
No risk factor	1%
ISS > 25	10%
ISS > 25 + SBP < 70 mmHg	39%
ISS > 25 + pH < 7,1	58%
ISS > 25 + temperature < 34°C	49%
ISS > 25 + SBP < 70 mmHg + temperature < 34°C	85%
ISS > 25 + SBP < 70 mmHg + temperature < 34°C + pH < 7,1	98%

ISS = Injury Severity Score

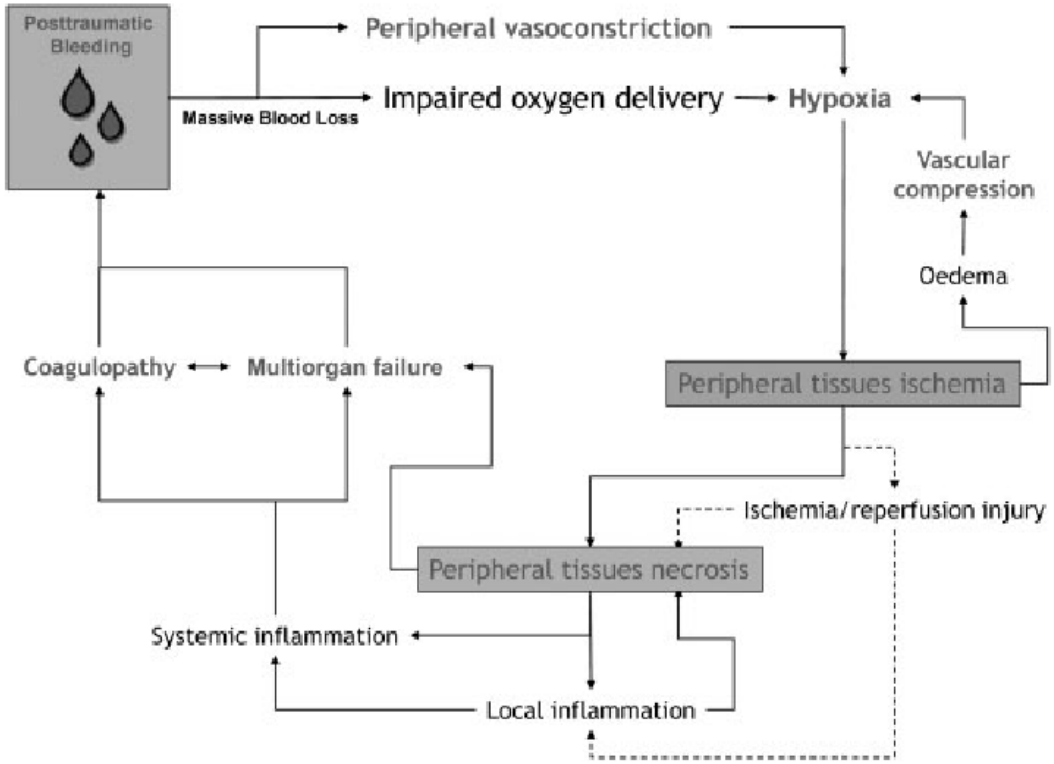
SBP = Systolic Blood Pressure

Cosgriff et al., J Trauma 1997; 42: 857-861

Seminars in Thrombosis & Hemostasis

Massive Posttraumatic Bleeding: Epidemiology, Causes, Clinical Features, and Therapeutic Management

Giuseppe Lippi, MD[1] Emmanuel J. Favaloro, PhD, FFSc (RCPA),[2] Gianfranco Cervellin, MD[3]



Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]

- A combination of mechanisms may promote the systemic activation of coagulation, including:
  - Cell injury
  - Release of procoagulant substances into the blood
  - Hemolysis
  - Systemic hypoperfusion
  - Production and release of inflammatory cytokines

Disseminated Intravascular Coagulation in Trauma Injuries

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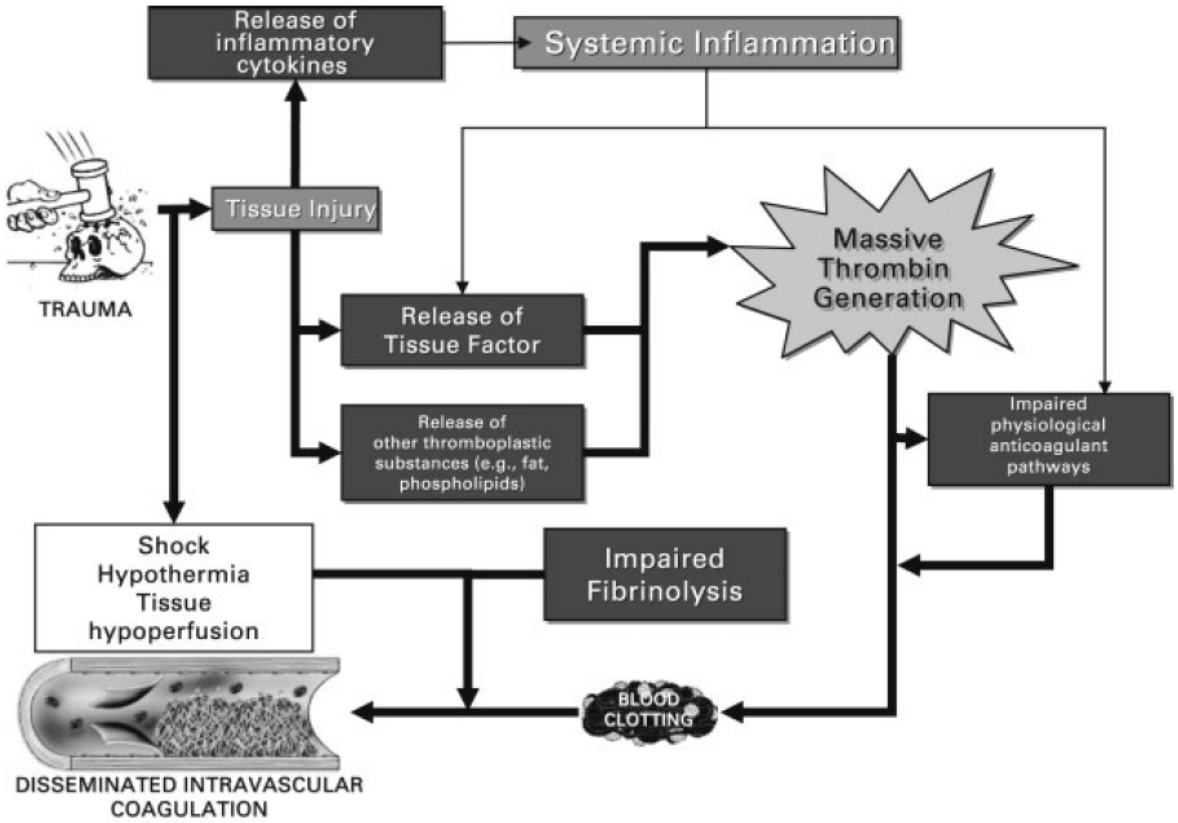


Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]

Kushimoto et al compared the clinical course and outcome of DIC between patients with underlying sepsis and those with trauma:

- The 28-day mortality rate was significantly higher in sepsis than in trauma patients (**34.7% versus 10.5%**; p<0.0001).

Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]

Niles et al performed a retrospective study of combat casualties admitted to a combat support hospital in 15 months.

- The prevalence of acute coagulopathy was **38%**.
- Mortality in those presenting some forms of coagulopathies at ED arrival was **24% versus 4%** in those not presenting with coagulopathy ($p<0.001$).
- Coagulopathy was strongly associated with mortality (**OR 5.38**; 95% CI, 1.55-11.37).

Disseminated Intravascular Coagulation in Trauma Injuries

Giuseppe Lippi, M.D.,[1] and Gianfranco Cervellin, M.D.[2]

In a prospective cohort study by Brohi et al on 208 major trauma patients admitted to a single trauma center:

- The mortality rate was **12%**
- Coagulation was found to be activated, and thrombin generation was related to injury severity
- Although patients without concurrent hypoperfusion did not develop early coagulopathy after trauma, patients with concomitant hypoperfusion were coagulopathic early after trauma, displaying higher PT, APTT, D-dimer, and lower protein C and PAI-1 values.

World J Emerg Med, Vol 1, No 1, 2010

Original Article

Acute traumatic coagulopathy: Incidence, risk stratification and therapeutic options

Marc Maegele

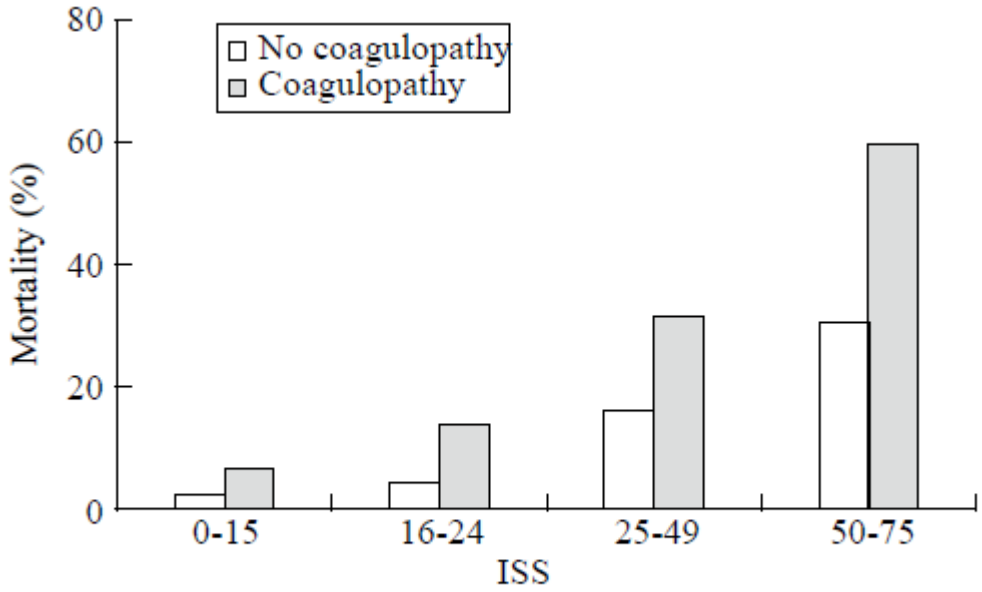


Figure 3. The mortality of patients with and without ATC on ER arrival according to the severity of injury as reflected by ISS.

Seminars in Thrombosis & Hemostasis

Massive Posttraumatic Bleeding: Epidemiology, Causes, Clinical Features, and Therapeutic Management

Giuseppe Lippi, MD [1] Emmanuel J. Favaloro, PhD, FFSc (RCPA), [2] Gianfranco Cervellin, MD [3]

* As regards laboratory diagnostics, the relative contribution is limited in the early triage of patients with trauma, whereby clinics and imaging techniques should guide the clinical management.
* However, since trauma and hemorrhagic shock impair the function of most - if not all - organs and tissues, **patients should be tightly monitored with a large number of vital laboratory parameters**, including:

- Blood gases (ABG)
- Lactic acid
- Complete blood count (CBC)
- Calcium and electrolytes
- Blood glucose
- Aminotransferases (for liver injury)
- Lipase (for assessing pancreatic involvement),
- Cardiospecific troponins (for identifying myocardial injury),
- Serum creatinine or neutrophil gelatinase-associated lipocalin (NGAL) (for early identification of AKI)
- Procalcitonin (for identifying superimposed infections and sepsis)
- Protein S100B (for assessing brain and myocardium damage)

Seminars in Thrombosis & Hemostasis

Massive Posttraumatic Bleeding: Epidemiology, Causes, Clinical Features, and Therapeutic Management

Giuseppe Lippi, MD [1] Emmanuel J. Favaloro, PhD, FFSc (RCPA), [2] Gianfranco Cervellin, MD [3]

Arterial blood gas is essential to identify the degree of metabolic imbalance.

- The leading laboratory abnormalities that can be detected include:
  - Decreased pH (i.e., acidosis);
  - Abnormal base deficit
  - Elevated lactate along with increased osmolarity.
- The concentration of blood lactate is usually between 1 and 2 mmol/L at rest, and its increased production in severe trauma is an adaptive mechanism by which oxidation of lactate rather than glucose is promoted in tissues where oxygen deprivation is more tolerated.
- The degree of hyperlactatemia is strongly correlated with oxygen debt, hypoperfusion, and severity of shock
- Serial lactate assessment is crucial for monitoring:
  - Blood lactate **>2.5 mmol/L** is associated with a worse prognosis and increased mortality.
  - Blood lactate **>5.0 mmol/L** with a pH <7.35 is associated with a 75% mortality rate.

Thrombosis Journal

BioMed Central

Review

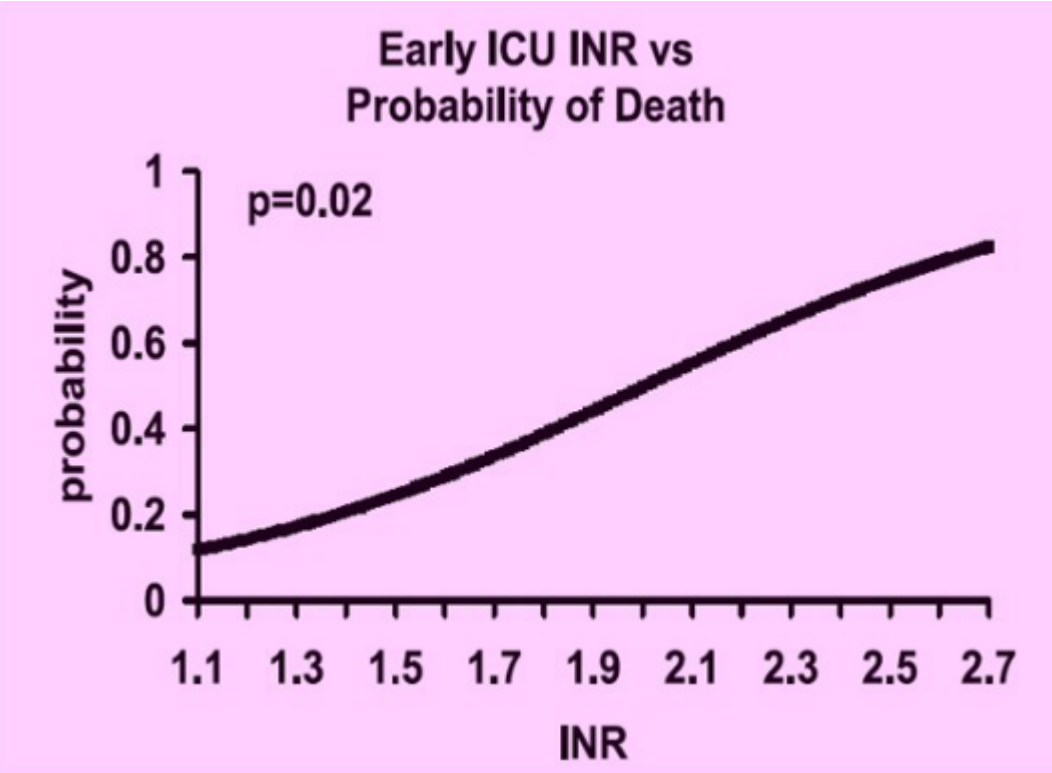
Open Access

Recent acquisitions in the pathophysiology, diagnosis and treatment of disseminated intravascular coagulation

Massimo Franchini*[1], Giuseppe Lippi[2] and Franco Manzato[3]

The classical laboratory findings of **coagulopathy** (and DIC) in trauma include:

- Prolonged clotting times of PT, APTT (and TT).
- Increased levels of fibrin-related markers (fibrin degradation products [FDP] and D-dimer)
- Low platelet count
- Decreased fibrinogen levels
- Low plasma levels of coagulation factors (i.e., FV and FVII)
- Low plasma levels of coagulation inhibitors (i.e., antithrombin, PC)


Early ICU INR vs
Probability of Death
p=0.02
probability
1
0.8
0.6
0.4
0.2
0
1.1
1.3
1.5
1.7
1.9
2.1
2.3
2.5
2.7
INR

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Recent acquisitions in the pathophysiology, diagnosis and treatment of disseminated intravascular coagulation

Massimo Franchini*[1], Giuseppe Lippi[2] and Franco Manzato[3]

DIAGNOSTIC challenges:

- PT and APTT: Low sensitivity
- Fibrinogen: Acute phase protein, large interindividual variability
- D-dimer: Low specificity
- Platelet count: Large interindividual variability

Thereby...

The **scoring system** issued by Scientific Subcommittee on DIC of the International Society on Thrombosis and Haemostasis (ISTH) is highly recommended.

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Recent acquisitions in the pathophysiology, diagnosis and treatment of disseminated intravascular coagulation

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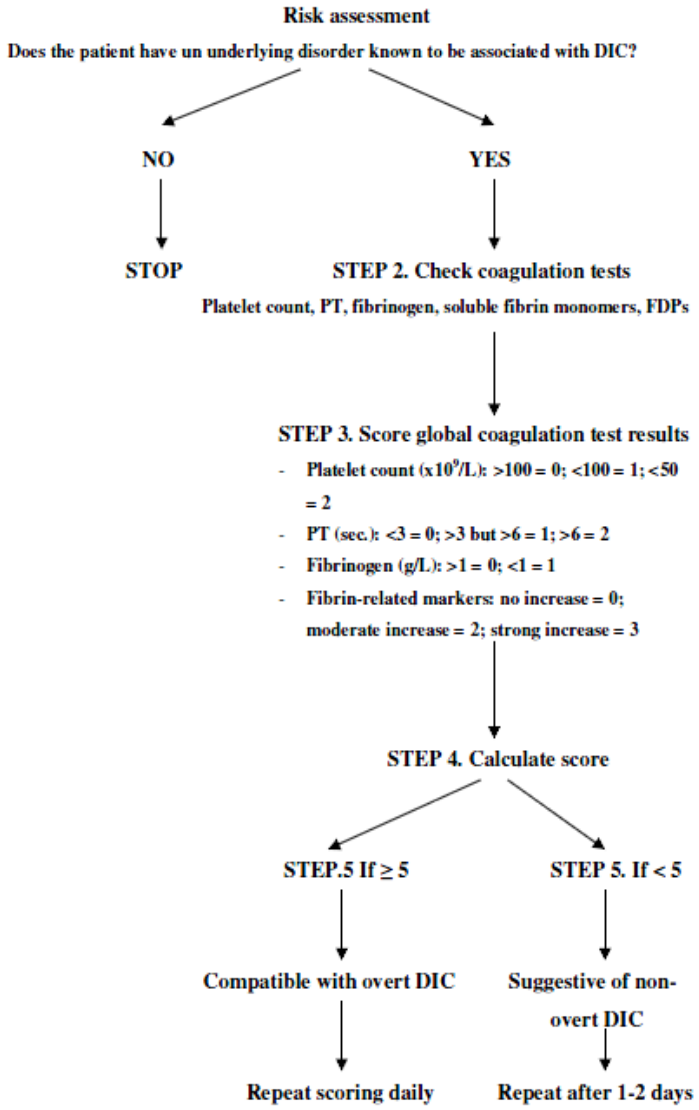
- Other, more specialized tests, unavailable in all laboratories, include soluble fibrin and assays of thrombin generation.
- Serial coagulation tests is essential and more helpful than single laboratory results in establishing a diagnosis of DIC.



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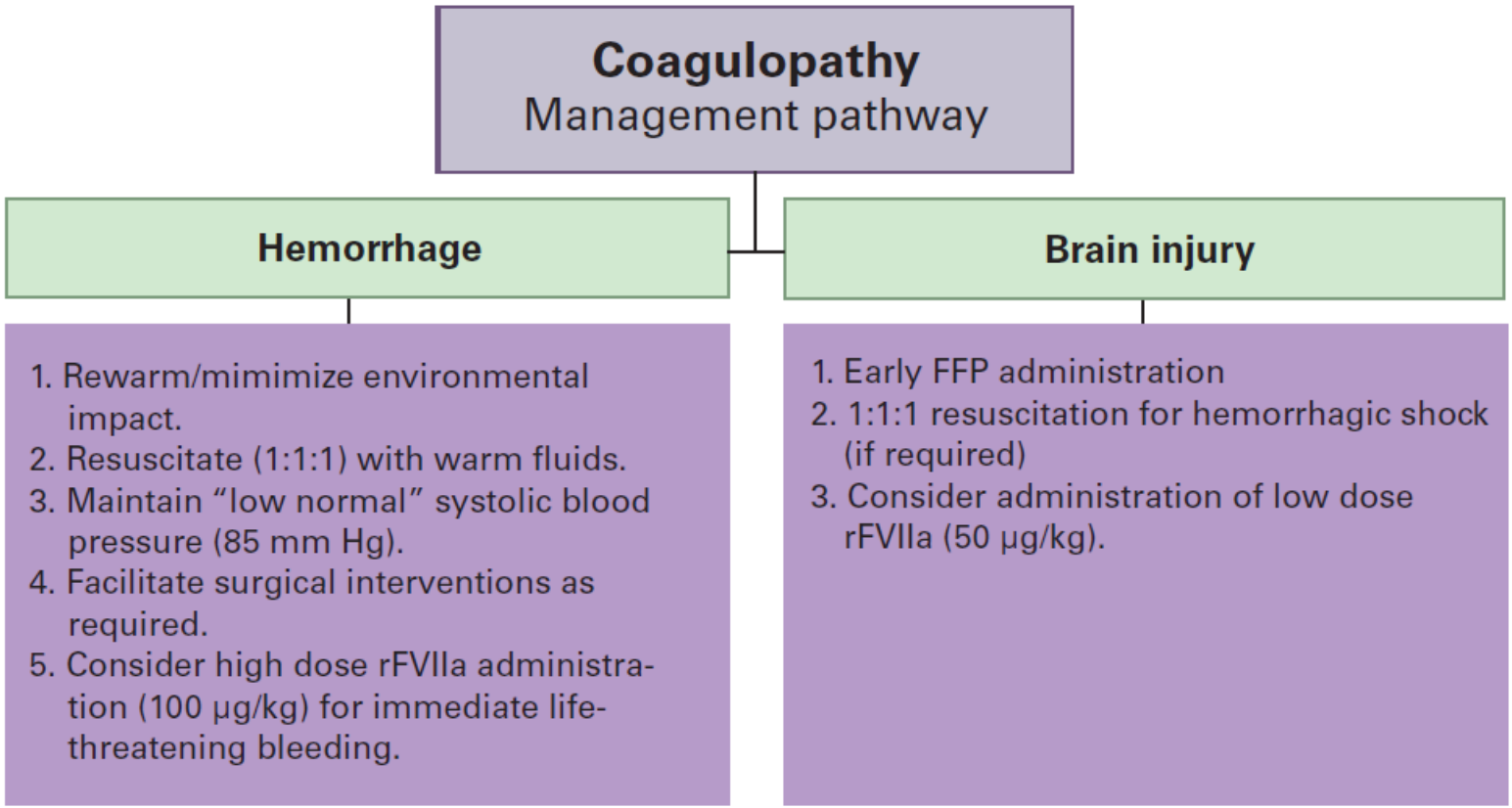
Management of Trauma-Induced Coagulopathy: Trends and Practices

Matthew R. D'Angelo, CRNA, DNP
Richard P. Dutton, MD, MBA



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Management of Trauma-Induced Coagulopathy: Trends and Practices

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Source (country of study)	No. of individuals	Outcome
Kenet,[34] 1999 (Israel)	1	Gunshot wound, 19-year-old man survived
Martinowitz,[35] 2001 (Israel)	7	Multitrauma; uncontrolled hemorrhage; 57% survival
O'Neill,[36] 2002 (United States)	1	Multistab wounds to chest; survived
Vlot,[37] 2001 (The Netherlands)	1	Gastrointestinal bleed; 59-year-old man survived
Dutton,[38] 2003 (United States)	5	Retrospective study; blunt and penetrating trauma; 60% survival
Dutton,[39] 2004 (United States)	46	Hypothesized that patients who are already in irreversible shock will not respond despite rFVIIa administration
Stein,[5] 2004 (United States; review study)	*	Authors conclude that data are promising, but no prior study has demonstrated significant clinical or economic benefit to using rFVIIa in trauma

Table. Selected Publications With Anecdotal Use of Recombinant Factor VIIa (rFVIIa) for Trauma-Induced Coagulopathy

* In this review article, more than 300 cases were evaluated, but they were not clearly described.

In 2007,the European Task Force for Advanced Bleeding Care in Trauma

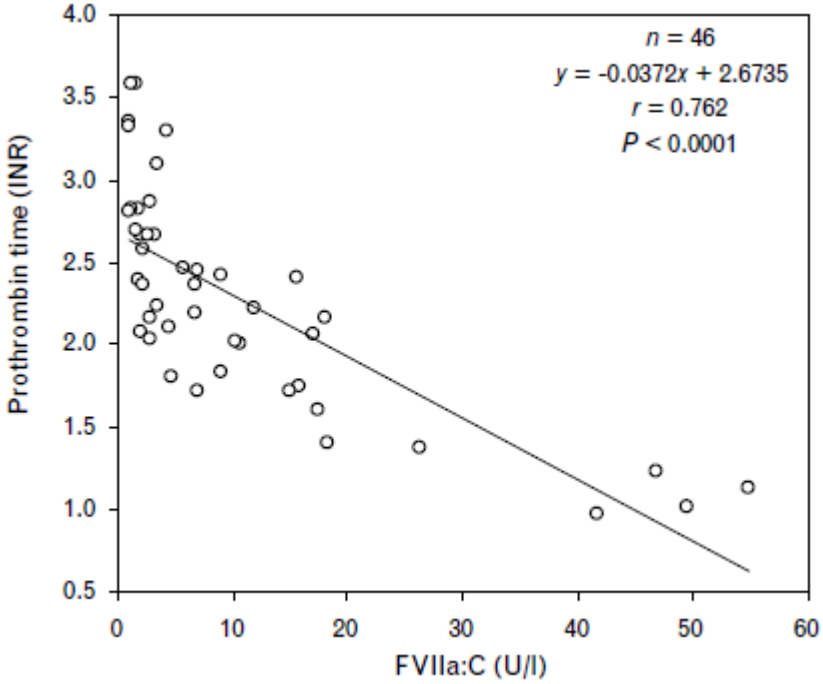
(Spahn et al., Crit Care 2007; 11:R17)

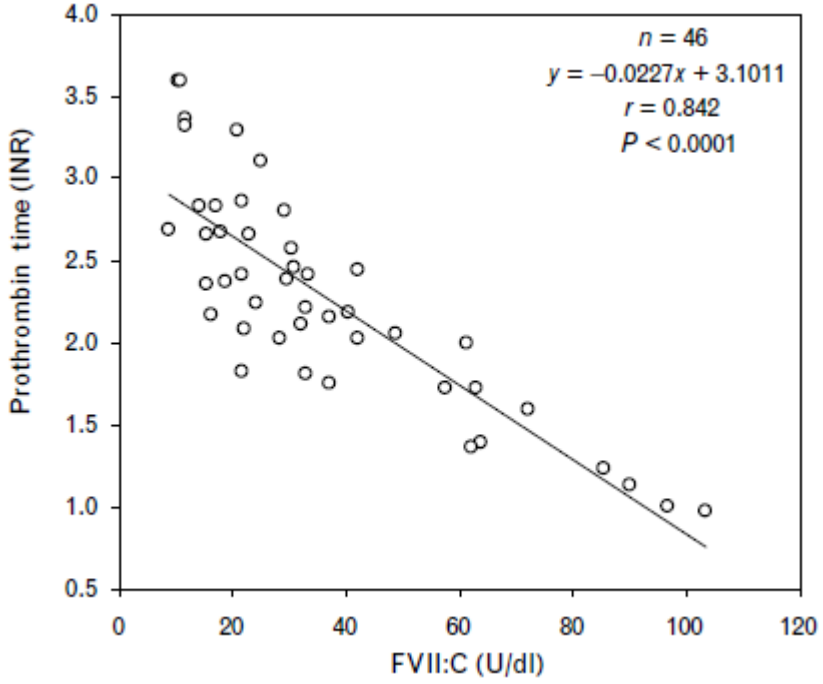
- We suggest that the use of rFVIIa be considered if major bleeding in blunt trauma persists despite standard attempts to control bleeding an best practice use of blood components.
- We suggest an initial dose of 200 microgramm/kg followed by two 100 microgramm/kg doses administered at 1 and 3 hours following the first dose. (Grade 2C)

Blood Coagulation and Fibrinolysis 2006, 17:221–224

Influence of warfarin therapy on activated factor VII clotting activity

Giuseppe Lippi[a], Martina Montagnana[a], Gian Luca Salvagno[a], Giovanni Poli[a], Massimo Franchini[b] and Gian Cesare Guidi[a]





Owing to the good correlation with FVIIa:C, we hypothesized that PT and/or FVII:C might be employed for monitoring rFVIIa therapy.

British Journal of Surgery September 2009

Trauma Induced Coagulopathy

K Brohi

There is renewed interest in the use of near-patient functional tests of coagulation such as thromboelastometry for the diagnosis of coagulopathy. These devices (Rotational Thromboelastometry - ROTEM, Thromboelastography - TEG) have become robust, reliable tools which may be suitable for the emergency department. These tools are in routine use in some elective surgery settings such as cardiac and liver transplant surgery. Very early work in trauma suggests that they may be able to diagnose TIC and guide therapy, but much is yet to be learnt about thromboelastometric definitions of ATC/TIC and what the appropriate therapeutic response to abnormal traces should be.