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

MODENA MICU INTENSIVE CARE UNIT 2

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

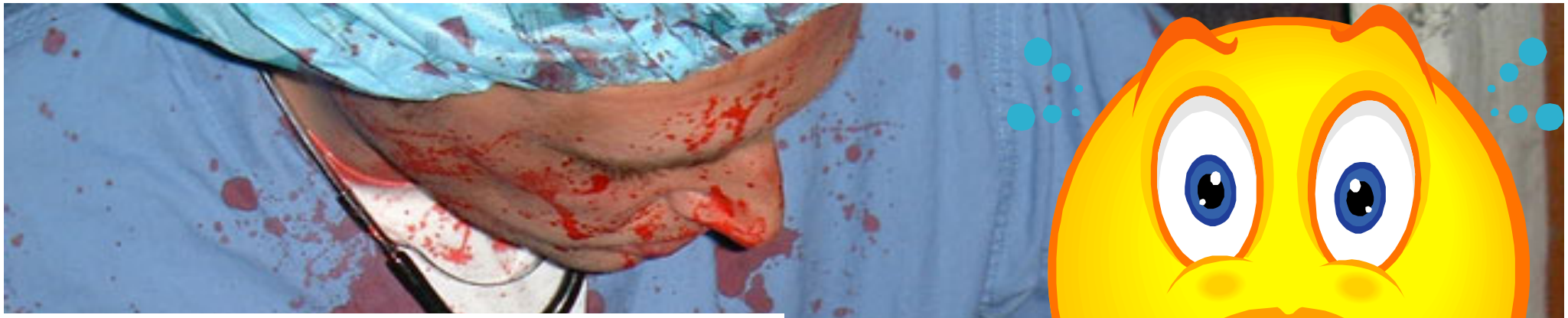
Il trattamento dell'emorragia critica visto da un intensivista

slides and discussion
girardis.massimo@unimo.it

Disclosures

None conflict of interest
related to this lecture/issue

I trust in PHYSIOLOGY & EBM,
but the latter is more ‘voluble’, particularly in these days



Matera, muore dopo cesareo gemellare Sospesi due medici, arrivano gli ispettori

Dopo il parto, la 32enne è stata portata in rianimazione per complicanze post operatorie. Avviate tre inchieste

L'ospedale di Policoro (Milestone Media)

MATERA - Nuovo episodio drammatico legato a un semplice parto in ospedale, dopo il caso della lite nel policlinico di Messina. A Policoro (Matera) una donna di 32 anni è morta mercoledì mattina dopo aver subito un intervento cesareo gemellare, quattro ore prima. Tre le inchieste per accertare le cause del decesso: una congiunta del ministero della Salute e della Regione, una della Procura di Matera che ha fatto sequestrare la cartella clinica e una dell'Asl locale. Ma una decisione è stata presa ancor prima di avere in mano i risultati delle verifiche: i due ginecologi che hanno eseguito l'intervento e assistito al parto sono stati sospesi in via cautelare. «Da giovedì nel reparto ci sarà la presenza del capodipartimento per verificarne il corretto funzionamento» spiega un comunicato della Regione Basilicata.

NOTIZIE CORRELATE

Fazio: legge su intramoenia poco limpida (8 settembre 2010)

Lite in sala parto a Messina. «Ischemia cerebrale per il bimbo» (7 settembre 2010)

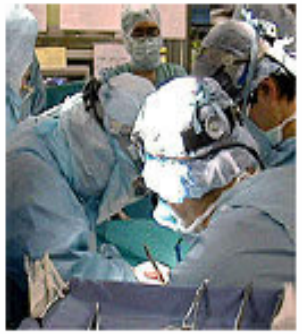
MORTA IN RIANIMAZIONE - Rosalba Pascucci, 32enne di Bernalda (Matera), era ricoverata nel reparto di Ostetricia e ginecologia dell'ospedale civile di Policoro intitolato a Giovanni Paolo II, dove ha dato alla luce i due gemelli. Subito dopo, a causa di complicanze seguite all'intervento, è stata trasferita in rianimazione. Lì è morta rapidamente, nonostante i febbrili tentativi dei sanitari di ripristinare le sue funzioni vitali. La causa del decesso, secondo quanto riferito dal direttore dell'Azienda sanitaria di Matera Vito Gaudiano, è stata «uno choc emorragico».

la Repubblica BARI.it
Mercoledì 17.11.2010 Ore 17.41

Muore durante il parto cesareo

Dieci sanitari indagati all´ospedale di Altamura. Viva la bambina

di Gabriella De Matteis



Domenica prossima avrebbe compiuto 40 anni. E avrebbe festeggiato con la sua quarta figlia. Ma Caterina Lomurno di Altamura è morta durante il parto cesareo, dando alla luce una bambina di tre chili e otto. E ora sul caso il sostituto procuratore Ciro Angelillis ha aperto un´inchiesta. «Mia moglie stava bene. In sala operatoria è entrata reggendo la flebo con la mano destra. Era serena, felice. Mi ha detto di andare a prendere i vestiti per la piccola. Sono state le sue ultime parole. Non posso credere a quello che è accaduto» dice Vito Indrio, 44 anni, marito della donna.

La brutta storia di Caterina comincia alle dieci di giovedì sera. Il parto, nel reparto di ginecologia dell´ospedale di Altamura, è programmato. Per la signora è il quarto taglio cesareo. La quarta bambina. «Dopo mezz´ora un medico è uscito dalla sala operatoria. Ha detto che mia figlia stava bene, ma c´erano state alcune complicazioni per Caterina». L´intervento non va come previsto. La bambina nasce, sta bene, ma le condizioni della madre precipitano quasi subito. Perde sangue, ha un´emorragia, due trasfusioni non sono sufficienti. L´equipè chirurgica chiede altre sei sacche che arrivano dall´ospedale di Acquaviva. La giovane madre è sempre più grave. In sala operatoria arriva anche il primario che decide di asportare l´utero. Un tentativo inutile: Caterina muore nella notte.

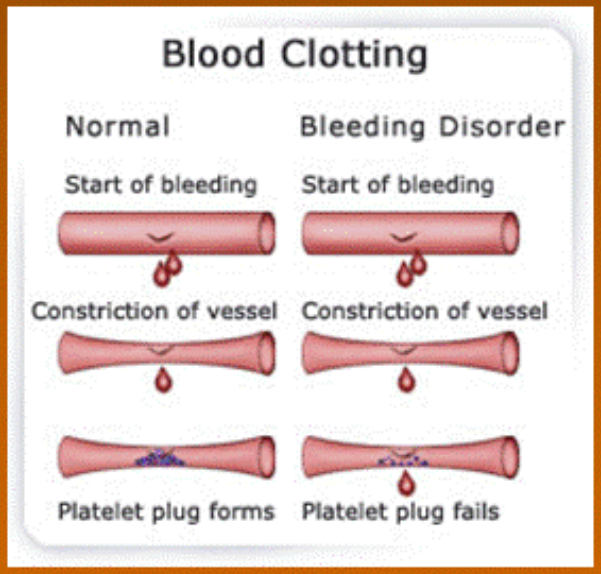
Paziente letto # A

EMORRAGIA POST-PARTUM

- ✓ Donna di 65 kg con atonia uterina dopo Parto Spontaneo.
- ✓ Condotta in sala operatoria dove viene eseguita isterectomia dopo circa 1 h dal parto con grave sanguinamento diffuso e shock
- ✓ Trasfusi 10 UEC + 7 PFC + 2000 ATIII + 1500 colloidi + 4500 cristalloidi
- ✓ All'arrivo in TIPO sanguinamento in atto dai drenaggi. Hb 6, Plts 30, INR 2,0, aPTT > 120 sec, D-dimero 10000, fibrinogeno 105 mg/dl
- ✓ Sedata e intubata con sub-edema polmonare, PaO2/FiO2 150, ipotesa (PAM 50 mmHg); pH 7.31, pCO_2 28, BE -12; Oliguria, Temperatura °C 35,7

COSA VOGLIO
NEL SANGUINAMENTO CRITICO ?

CONTROLLO SORGENTE



EMOSTASI

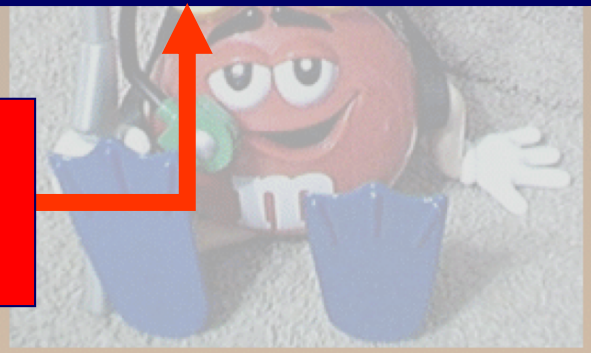
O_2 TISSUTALE

SOURCE CONTROL

- ✓ **Tourniquet, dressing**
(e.g. pre-H penetrating trauma)
- ✓ **Surgery**
(e.g. 'damage control' in trauma)
- ✓ **Radiology**
(e.g. retroperitoneal bleeding)
- ✓ **Endoscopy**
(e.g. esophageal/gastric bleeding
- ✓ **Medical Therapy**
(e.g. reversal anticoag; uterotonic)

VOLUME RESUSCITATION/O2 TRANSPORT

- ✓ **Evaluation**
- Cardiovascular parameters
- Organ perfusion parameters
- ✓ **Therapy**
- Red Blood Cell if Hb < 8-9 g/dl
- FLUIDS : if PAS < 80 mmHg
  Traumatic Brain Injury: fluids if PAM < 90 mmHg



CRITICAL BLEEDING

1. **Evaluate Patient, Setting**
2. **Activate available resources**

HEMOSTASIS

- ✓ **AVOID HYPOTHERMIA / CORRECT ACIDOSIS if pH < 7,2**
- ✓ **FRESH FROZEN PLASMA (15-20 ml/Kg) if INR > 1,5 or if the PT and aPTT cannot be obtained within a reasonable period.**
- ✓ **PLATELETS (1-2 U/10 Kg) if count < 75.000/µl or platelet dysfunction**
- ✓ **PROTHROMBIN CONCENTRATE (35-50 U/Kg) if oral anticoagulant**
- ✓ **DESMOPRESSIN (0,3 µg/Kg) if platelet dysfunction**
- ✓ **FIBRINOGEN (1-2 g) if fibrinogen < 100mg/ml**
- ✓ **TRANEXAMIC ACID (1 g i.v. in 10 min) if TEG evidence of hyperfibrinolysis**
- ✓ **rFVIIa (90-120µg/Kg) if standard therapy failed**

90's

00's

"It is better to cure in more phases than to kill in one ..."

COSA VOGLIO
NEL SANGUINAMENTO CRITICO ?

RIANIMAZIONE VOLEMICA

TRASPORTO O2

QUANDO RESUSCITARE ?

QUANTO RESUSCITARE ?

COME RESUSCITARE ?

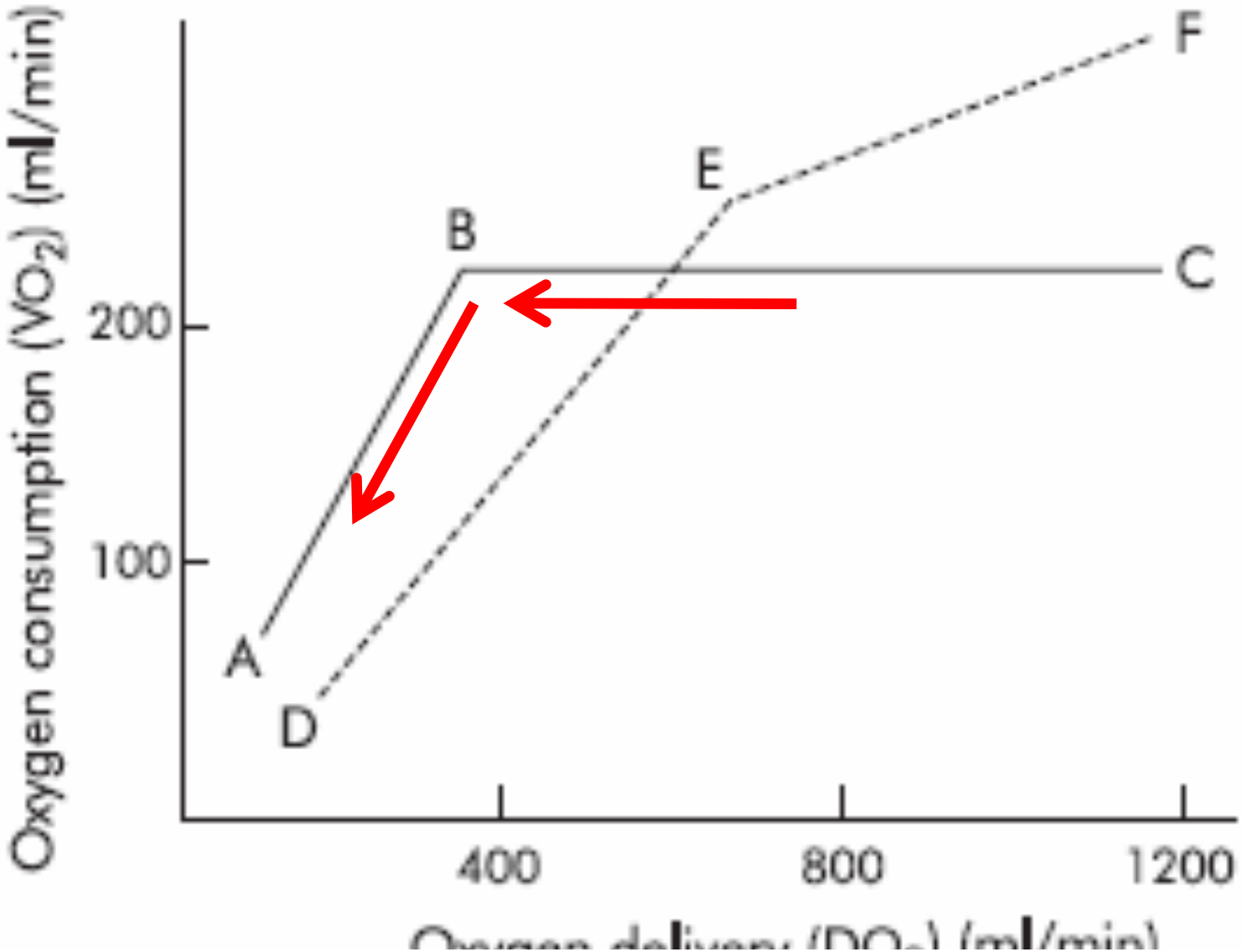
EMAZIE CONCENTRATE ?

O_2 TISSUTALE

Today Scenario

Shocked patients

EQUILIBRIO SISTEMI CARDIOCIRCOLATORIO E TISSUTALE: VO2/DO2 (O2ext)



O_2 Delivery (DO_2)

DO_2

CO

CaO_2

Increase O_2
CPAP
MV

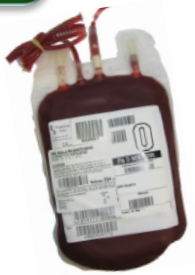
HR

SV

SaO_2

Hb

Transfusion



Preload

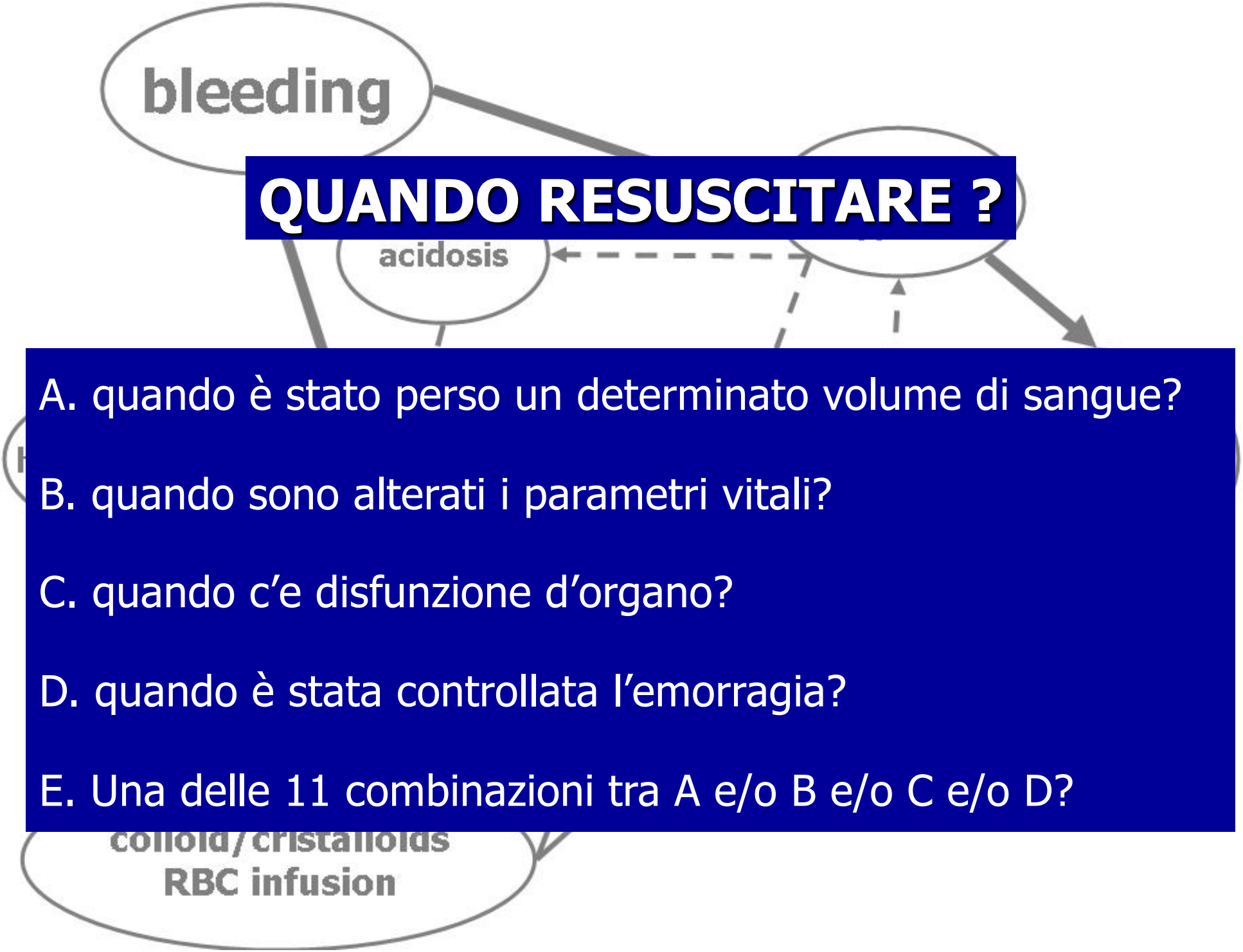
Contractility

Afterload

Fluids

Inotropes

- Vasopressors
- Vasodilators



QUANDO RESUSCITARE ?

A. quando è stato perso un determinato volume di sangue?

B. quando sono alterati i parametri vitali?

C. quando c'e disfunzione d'organo?

D. quando è stata controllata l'emorragia?

E. Una delle 11 combinazioni tra A e/o B e/o C e/o D?

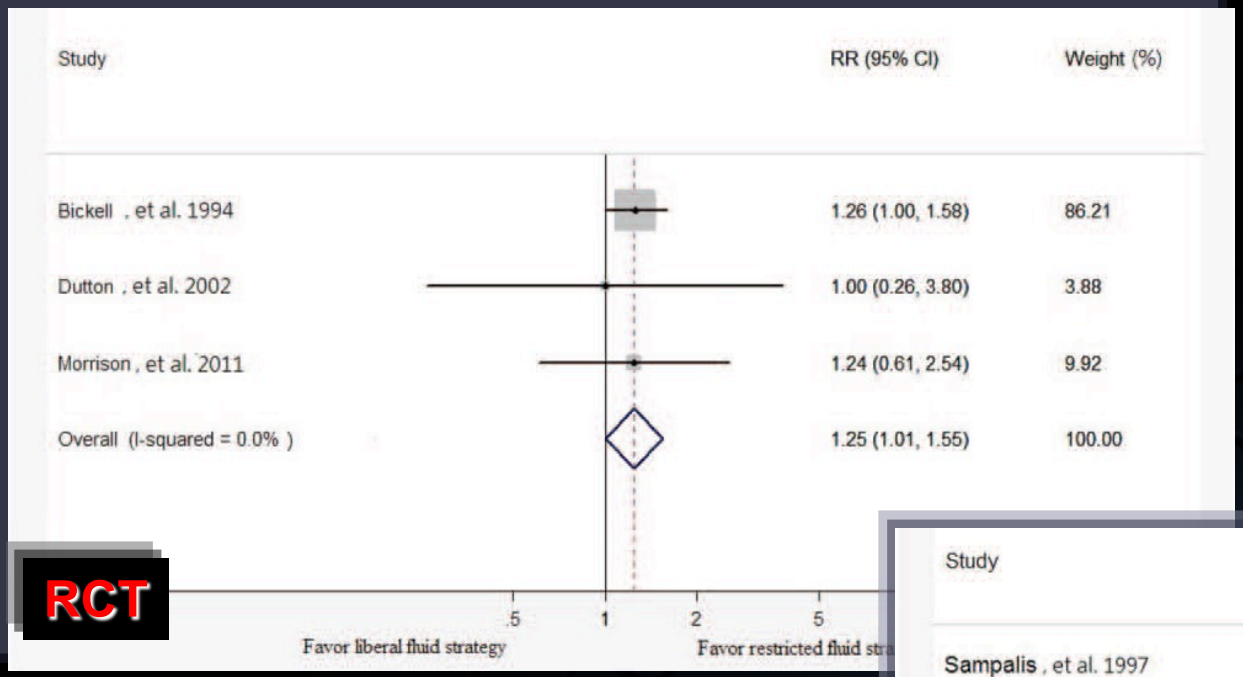
QUANDO RESUSCITARE ?

QUANTO RESUSCITARE ?

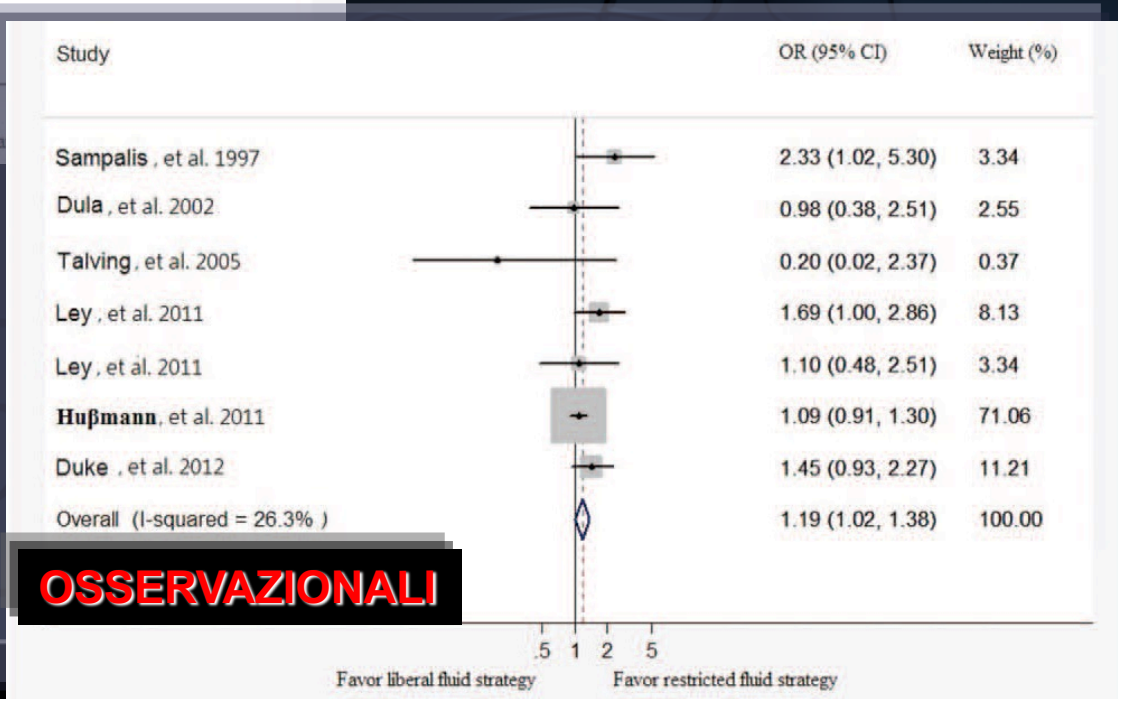
Liberal Versus Restricted Fluid Resuscitation Strategies in Trauma Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies

Chih-Hung Wang, MD[1]; Wen-Han Hsieh, MS[2]; Hao-Chang Chou, MD[1]; Yu-Sheng Huang, MD[1]; Jen-Hsiang Shen, MS[3]; Yee Hui Yeo, MS[4]; Huai-En Chang, MS[5]; Shyr-Chyr Chen, MD, MBA[1]; Chien-Chang Lee, MD, MSc[6,7]

Critical Care Medicine | April 2014 • Volume 42 • Number 4



RCT



OSSERVAZIONALI

Timing and volume of fluid administration for patients with bleeding

Editorial group: Cochrane Injuries Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 3, 2014.
Review content assessed as up-to-date: 5 February 2014.

Irene Kwan[1], Frances Bunn[2], Paul Chinnock[3], Ian Roberts[3]

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

Early versus delayed fluid administration

Three trials reported mortality and two reported coagulation data.

In the first trial (n = 598) the relative risk (RR) for death with early fluid administration was 1.26 (95% confidence interval (CI) 1.00 to 1.58). The weighted mean differences (WMD) for prothrombin time and partial thromboplastin time were 2.7 (95% CI 0.9 to 4.5) and 4.3 (95% CI 1.74 to 6.9) seconds, respectively.

In the second trial (n = 50) the RR for death with early blood transfusion was 5.4 (95% CI 0.3 to 107.1). The WMD for partial thromboplastin time was 7.0 (95% CI 6.0 to 8.0) seconds. In the third trial (n = 1309) the RR for death with early fluid administration was 1.06 (95% CI 0.77 to 1.47).

Larger versus smaller volume of fluid administration

Three trials reported mortality and one reported coagulation data.

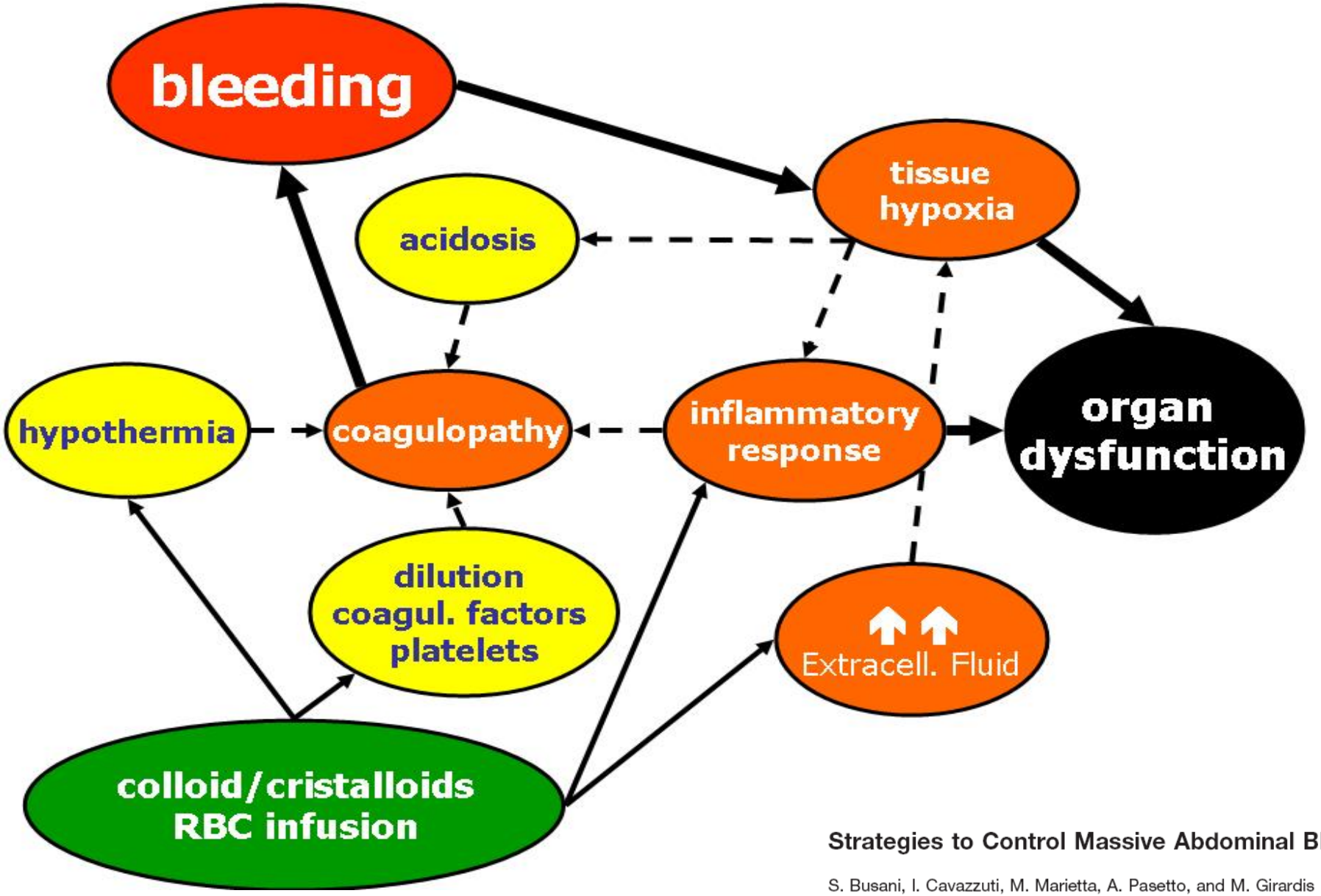
In the first trial (n = 36) the RR for death with a larger volume of fluid resuscitation was 0.80 (95% CI 0.28 to 22.29). Prothrombin time and partial thromboplastin time were 14.8 and 47.3 seconds in those who received a larger volume of fluid, as compared to 13.9 and 35.1 seconds in the comparison group.

In the second trial (n = 110) the RR for death with a high systolic blood pressure resuscitation target (100 mm Hg) maintained with a larger volume of fluid as compared to a low systolic blood pressure resuscitation target (70 mm Hg) maintained with a smaller volume of fluid was 1.00 (95% CI 0.26 to 3.81). In the third trial (n = 25) there were no deaths.

Authors' conclusions

We found no evidence from randomised controlled trials for or against early or larger volume of intravenous fluid administration in uncontrolled haemorrhage. There is continuing uncertainty about the best fluid administration strategy in bleeding trauma patients. Further randomised controlled trials are needed to establish the most effective fluid resuscitation strategy.

Come possiamo mantenere un buon bilancio tra resuscitazione e sanguinamento?



Strategies to Control Massive Abdominal Bleeding

S. Busani, I. Cavazzuti, M. Marietta, A. Pasetto, and M. Girardis

Transplantation Proceedings, 40, 1212–1215 (2008)

QUANDO RESUSCITARE ?

QUANTO RESUSCITARE ?

Visione tradizionale

Resuscitazione aggressiva con fluidi al fine di ristabilire una gittata cardiaca e una pressione arteriosa simile a valori di normalità

- ✓ Diluzione dei coaguli
- ✓ Ipotermia
- ✓ Rimozione del coagulo
- ✓ Aumento della pressione idrostatica
- ✓ Ipertensione addominale

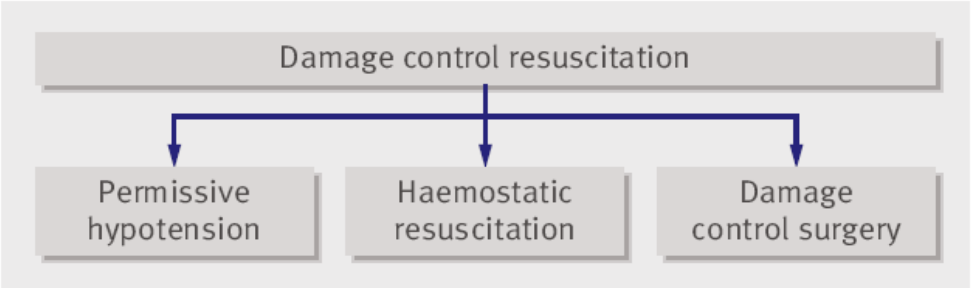


Fig 2 | The components of damage control resuscitation

Low-volume fluid resuscitation

We suggest a target systolic blood pressure of 80 to 100 mm Hg until major bleeding has been stopped in the initial phase following trauma without brain injury (grade 2C).

undesirable cooling of the patient. The concept of low-volume fluid resuscitation, so-called 'permissive hypotension,' avoids the adverse effects of early aggressive resuscitation while maintaining a level of tissue perfusion that, although lower than normal, is adequate for short periods [108]. Its general effec-

Research Open Access

Management of bleeding following major trauma: a European guideline

Donat R Spahn[1], Vladimir Cerny[2], Timothy J Coats[3], Jacques Duranteau[4], Enrique Fernández-Mondéjar[5], Giovanni Gordini[6], Philip F Stahel[7], Beverley J Hunt[8], Radko Komadina[9], Edmund Neugebauer[10], Yves Ozier[11], Louis Riddez[12], Arthur Schultz[13], Jean-Louis Vincent[14] and Rolf Rossaint[15]

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?

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

Spahn *et al. Critical Care* (2019) 23:98

III. Tissue oxygenation, volume, fluids and temperature

Tissue oxygenation

Recommendation 12 We recommend permissive hypotension with a target systolic blood pressure of 80–90 mmHg (mean arterial pressure 50–60 mmHg) until major bleeding has been stopped in the initial phase following trauma without brain injury. (Grade 1C)

In patients with severe TBI (GCS ≤ 8), we recommend that a mean arterial pressure ≥ 80 mmHg be maintained. (Grade 1C)

COME RESUSCITARE ?

Combat Fluid Resuscitation: Introduction and Overview of Conferences

J Trauma. 2003;54:S7–S12.

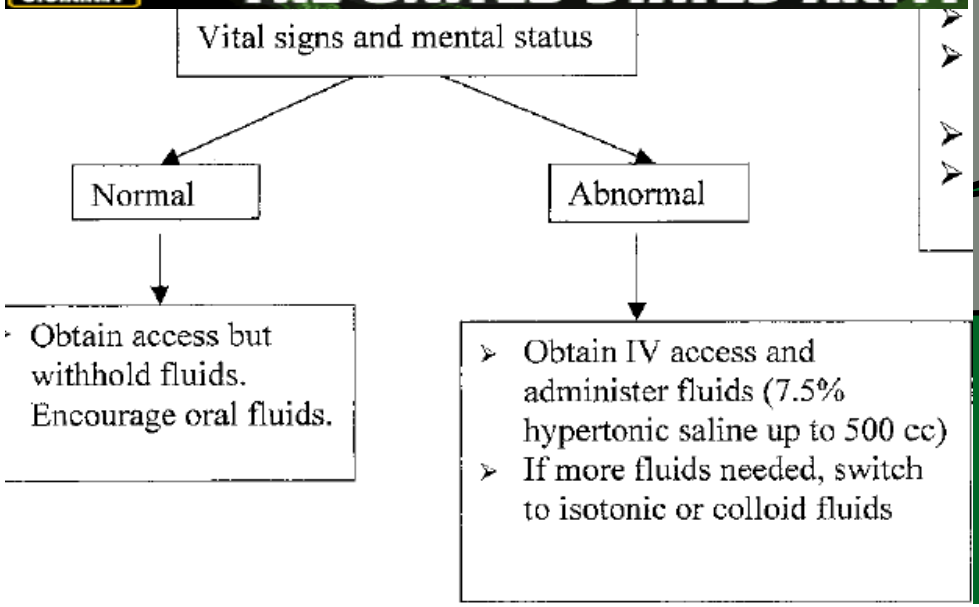
Howard R. Champion FRCS (Edin), FACS

cols do not address. Over a period of a year, four conferences on combat fluid resuscitation were held. The purpose of these conferences was to develop a consensus regarding contemporary practice and to identify and energize a research agenda.

CLINICAL RECOMMENDATIONS

- The primary recommendation was that fluid resuscitation should be instituted for a systolic blood pressure of <80–85 mm Hg, a falling blood pressure, or decreasing ability to mentate without evidence of head injury.

U.S.ARMY **THE UNITED STATES ARMY**



NATO OTAN *North Atlantic Treaty Organisation*

2. Fluid resuscitation of controlled hemorrhage in the battlefield, where indicated, should be an initial 250-mL infusion of 7.5 percent hypertonic saline (HTS) combined with 6 percent dextran (HSD), administered slowly over at least 10 to 15 minutes. This initial volume of HSD may be followed by a second 250-mL dose of HSD only in those patients who fail to stabilize. The

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

COME RESUSCITARE ?

NO FLUIDI?!

CRISTALLOIDI?!

COLLOIDI?!

Alcuni fattori da considerare:

1. Volume di distribuzione ed effetti emodinamici precoci: vantaggio a ripristinare una normale portata cardiaca in sanguinamento in atto ?
2. Effetti emostasi: diluizione fattori coagulazione, vasodilatazione, ipotermia
3. Risposta infiammatoria: ipertonica e colloidi hanno minor effetto di attivazione neutrofili
4. Sicurezza
5. Costo

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

$V_{Cristalloidi} / V_{Colloidi}$

3:1 (?)

A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

N Engl J Med 2004;350:2247-56.

The SAFE Study Investigators*

Variable	VCristalloidi / VColloidi	Albumin Group		Saline Group		P Value†
		No. of Patients	Value	No. of Patients	Value	
Study fluid (ml)						
Day 1	1,3	3410	1183.9±973.6	3418	1565.3±1536.1	<0.001
Day 2	1,6	3059	602.7±892.7	3068	954.0±1484.4	<0.001
Day 3	1,3	2210	268.0±554.5	2202	348.3±753.5	0.03
Day 4	1,2	1686	192.3±427.0	1664	228.6±642.6	0.57

A Systematic Review of Third-Generation Hydroxyethyl Starch (HES 130/0.4) in Resuscitation: Safety Not Adequately Addressed

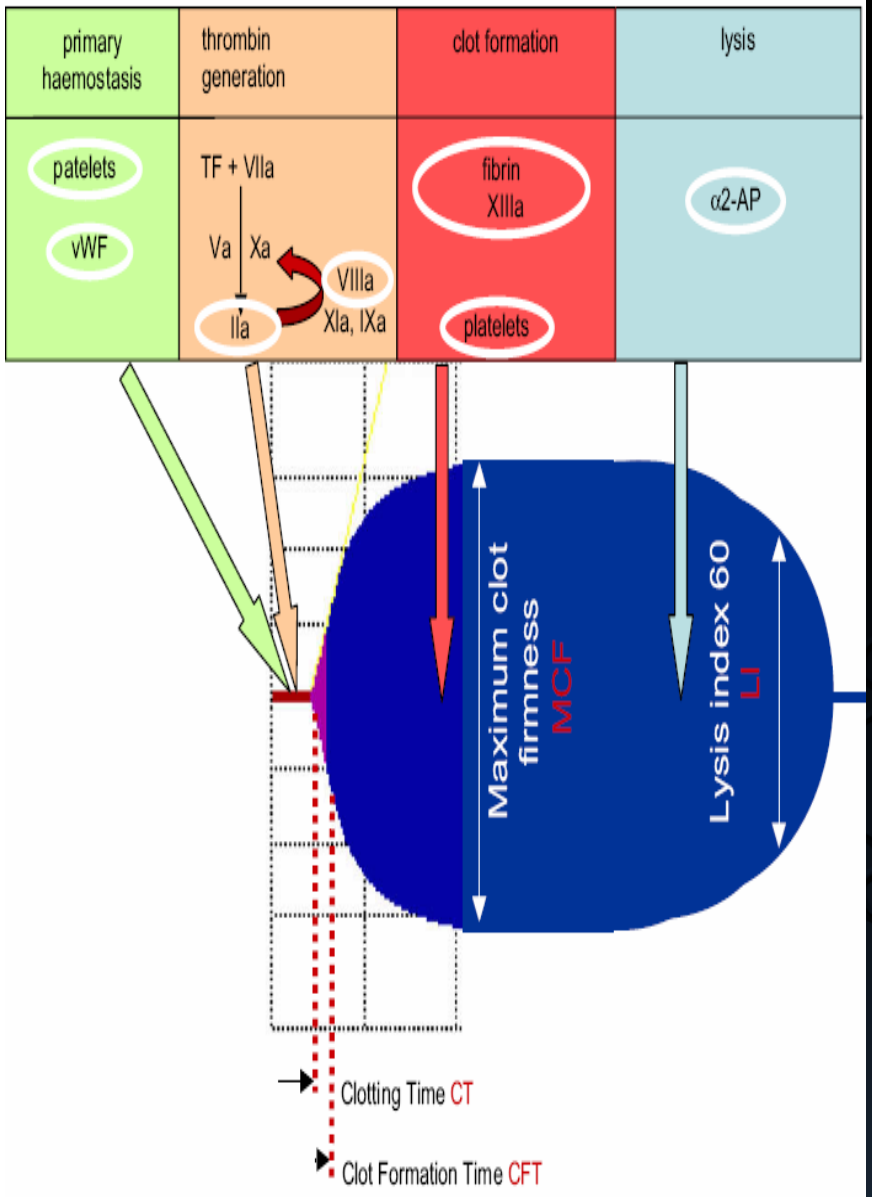
(Anesth Analg 2011;112:635–45)

Christiane S. Hartog, MD, Matthias Kohl, PhD, and Konrad Reinhart, MD

Table 5. Crystalloid to Colloid Volume Ratios in Surgical Randomized Controlled Trials (RCTs) with a Goal-Directed Fluid Regimen

Study	Condition	Crystalloid: Patients, N	Crystalloid: Total volume,[a] mL	Crystalloid: Type of fluid	Colloid: Patients, N	Colloid: Total volume,[a] mL	Study design: Fluid regimen	Study design: Hours[b]	Crystalloid-to-colloid volume ratio
Boldt 2001[89]	Abdominal surgery	25	11,150	RL	25	7210	Goal directed	24	1.6
Boldt 2002[60]	Abdominal surgery	21	18,750	RL	21	10,820	Goal directed	48	1.7
Lang 2003[90]	Abdominal surgery	18	14,310	RL	18	8610	Goal directed	24	1.7
Boldt 2004[76c]	Abdominal surgery, patients >65 years	22	10,150	RL	22	5660	Goal directed	24	1.8
Boldt 2004[76]	Abdominal surgery, patients >65 years	22	10,220	NS	22	5660	Goal directed	24	1.8
Lang 2001[88]	Abdominal surgery	21	11,740	RL	21	5970	Goal directed	24	2.0

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?



	Piastrine Aggrega	vWF + FVIII	Trombina + Coagulo	Lisi coagulo
Cristallodi	↔ ↑(?)	↔	↔↑	↔
Albumina	↔	↔	↔ ↑	↔
Destrani	↓↓	↓↓	↓↓	↑
HES lenti	↓↓	↓↓	↓↓	↑ (?)
HES rapidi	↔	↔ ↓ (?)	↓ emodil > 30 -40%	↑ (?)
Gelatine	↓↓	↓	↓	↑ (?)

Influence of fluid therapy on the haemostatic system of intensive care patients

S.A. Kozek-Langenecker / Best Practice & Research Clinical Anaesthesiology 23 (2009) 225–236

ORIGINAL ARTICLE

N ENGL J MED 367;20 NEJM.ORG NOVEMBER 15, 2012

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D.,

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

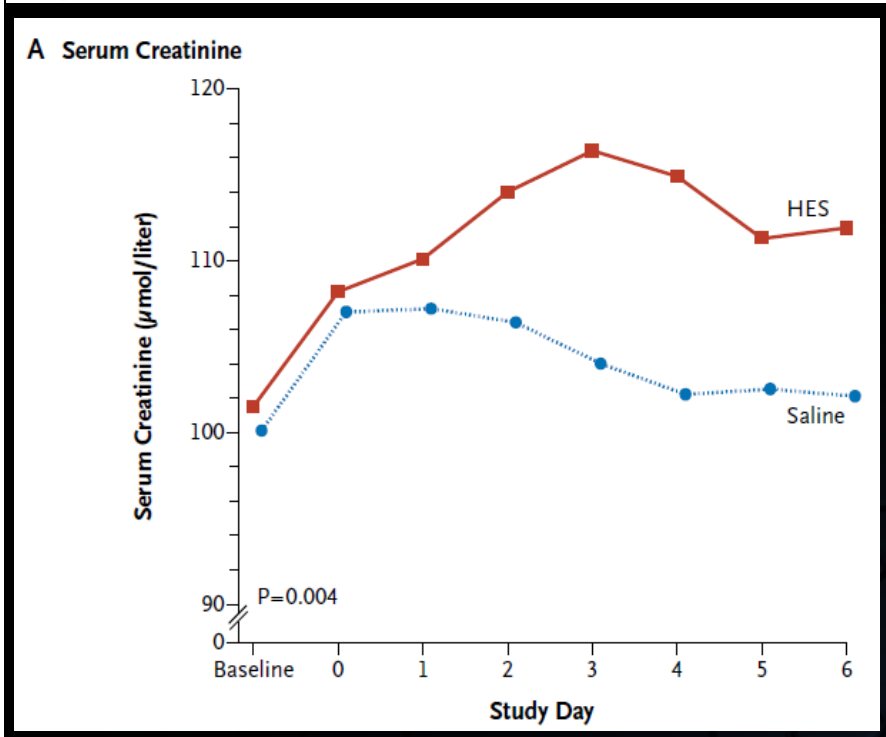


Table 2. Outcomes and Adverse Events.*

Variable	HES	Saline	Relative Risk (95% CI)	P Value
Outcome				
Primary outcome of death at day 90 — no./total no. (%)	597/3315 (18.0)	566/3336 (17.0)	1.06 (0.96 to 1.18)	0.26
Secondary outcomes — no./total no. (%)				
Renal outcomes				
RIFLE-R	1788/3309 (54.0)	1912/3335 (57.3)	0.94 (0.90 to 0.98)	0.007
RIFLE-I	1130/3265 (34.6)	1253/3300 (38.0)	0.91 (0.85 to 0.97)	0.005
RIFLE-F	336/3243 (10.4)	301/3263 (9.2)	1.12 (0.97 to 1.30)	0.12
Use of renal-replacement therapy	235/3352 (7.0)	196/3375 (5.8)	1.21 (1.00 to 1.45)	0.04
New organ failure†				
Respiratory	540/2062 (26.2)	524/2094 (25.0)	1.05 (0.94 to 1.16)	0.39
Cardiovascular	663/1815 (36.5)	722/1808 (39.9)	0.91 (0.84 to 0.99)	0.03
Coagulation	142/2987 (4.8)	119/3010 (4.0)	1.20 (0.95 to 1.53)	0.13
Hepatic	55/2830 (1.9)	36/2887 (1.2)	1.56 (1.03 to 2.36)	0.03

CONCLUSIONS

In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy.

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

HES 2014

Nota Informativa importante AIFA su restrizione d'uso di HES (medicinali contenenti amido idrossietilico).

AIFA, in accordo con EMA informa dei risultati della valutazione eseguita sui benefici e sui rischi dei prodotti contenenti amido idrossietilico (HES).
AIFA, in data 28 giugno 2013, aveva già disposto a scopo cautelativo il **"divieto di utilizzo"** per tutti i medicinali per uso infusionale contenente amido idrossietitico (con esclusione delle soluzioni per la conservazione degli organi) in attesa della decisione della Commissione Europea, legalmente vincolante in tutta EU.

La CE ha concluso che il rapporto beneficio-rischio per medicinali contenenti amido idrossielitico (HES) rimane favorevole nel trattamento dell'ipovolemia causata da emorragia acuta, quando I cristalloidi da soli non sono considerati sufficenti, a condizione che siano implementate restrizioni delle indicazioni, controindicazioni, avvertenze ed altre modifiche alle informazioni contenute nel riassunto delle caratteristiche del prodotto, quail misure di minimizzazione dei rischi.

Riassunto

- I prodotti contenenti HES devono essere utilizzati solo per il trattamento dell'ipovolemia causata da emorragia acuta quando I cristalloidi da soli non sono considerati sufficenti.
- I prodotti contenenti HES devono essere utilizzati alla più bassa dose efficace per il più breve periodo di tempo. Il trattamento deve essere guidato da un monitoraggio emodinamico continuo, in modo da poter interrompere l'infusione non appena siano stati raggiunti adeguati valori emodinamici.

Colloids versus crystalloids for fluid resuscitation in critically ill patients (Review)

Perel P, Roberts I, Ker K

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

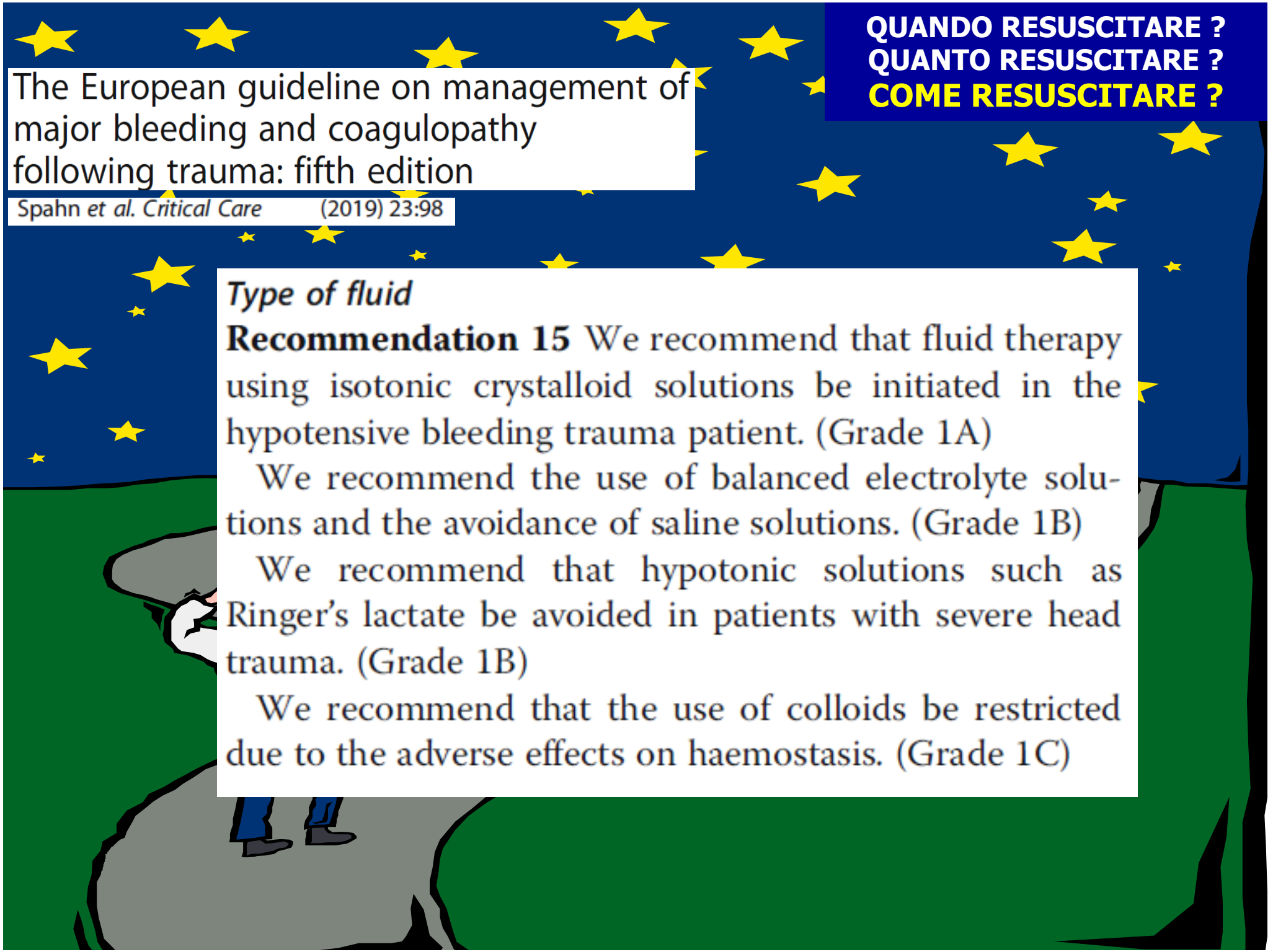
This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 3

Comparison 1. Colloid versus crystalloid (add-on colloid)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Deaths	56		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Albumin or plasma protein fraction	24	9920	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.93, 1.10]
1.2 Hydroxyethyl starch	25	9147	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [1.02, 1.19]
1.3 Modified gelatin	11	506	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.49, 1.72]
1.4 Dextran	9	834	Risk Ratio (M-H, Fixed, 95% CI)	1.24 [0.94, 1.65]

Authors' conclusions

There is no evidence from randomised controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. Furthermore, the use of hydroxyethyl starch might increase mortality. As colloids are not associated with an improvement in survival and are considerably more expensive than crystalloids, it is hard to see how their continued use in clinical practice can be justified.



QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

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

Spahn *et al. Critical Care* (2019) 23:98

Type of fluid

Recommendation 15 We recommend that fluid therapy using isotonic crystalloid solutions be initiated in the hypotensive bleeding trauma patient. (Grade 1A)

We recommend the use of balanced electrolyte solutions and the avoidance of saline solutions. (Grade 1B)

We recommend that hypotonic solutions such as Ringer's lactate be avoided in patients with severe head trauma. (Grade 1B)

We recommend that the use of colloids be restricted due to the adverse effects on haemostasis. (Grade 1C)

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santullano, Edoardo De Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juul Wikkelsø, Patrick Wouters and Piet Wyffels

Eur J Anaesthesiol 2013; **30**:270–382

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

6.2.4.2 Crystalloids versus colloids

Recommendation

We suggest the replacement of extracellular fluid losses with isotonic crystalloids in a timely and protocol based manner. **2C**

Compared with crystalloids, haemodynamic stabilisation with iso-oncotic colloids, such as human albumin and hydroxyethyl starch, causes less tissue oedema. **C**

Recommendation

We suggest the use of balanced solutions for crystalloids and as a basic solute for iso-oncotic preparations. **2C**

QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

EMAZIE CONCENTRATE ?

Vox Sanguinis (2006) **91**, 214–220

REVIEW

DOI: 10.1111/j.1423-0410.2006.00793.x

Evidence-based decision making in transfusion medicine

N. M. Heddle

McMaster Transfusion Research Program, McMaster University, and Canadian Blood Services, Hamilton, Ontario, Canada

transfusion decisions. If blood transfusion were considered by drug regulatory authorities for approval as a new drug there is no doubt it would be rejected because there is no randomized evidence that documents improved outcome. Despite this lack of evidence, few clinicians doubt that blood transfusion can save lives when used in severely anaemic patients. Most clinicians use a haemoglobin trigger to make

ACUTE ANEMIA (& normo-volemia)

Physiological Adaptive Response

Adaptive Response: Which is the critical Hb level ?

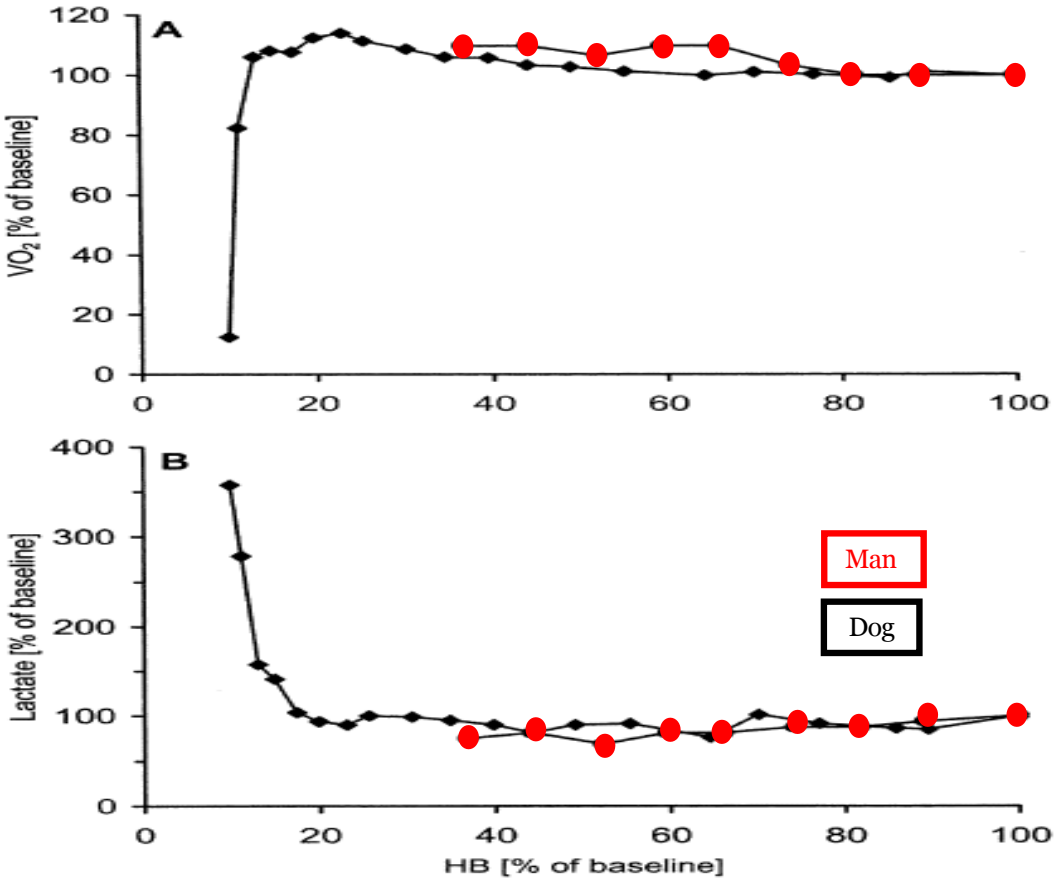


Fig 2. Relative changes of (A) O_2 consumption ($\dot{V}O_2$, % of baseline) and (B) lactate levels (Lactate, % of baseline) during progressive ANH in dogs (◆) and man (●). Note that $\dot{V}O_2$ is maintained even at very low hemoglobin levels. Only at extremely low hemoglobin values $\dot{V}O_2$ decreases and blood lactate levels increase indicating insufficient oxygenation of the organism because of extreme ANH. (Modified according to Weiskopf et al[13] and van der Linden et al.[24])

	DO_2 (ml/Kg*min)	Hb (g/dl)
Dog	4-10	2,5-4,0
Pig	9-13	3,0-4,5
Man*	< 7,5	< 4,0

*Healthy , no drugs, O2 room air

Acute Normovolemic Hemodilution: Physiology, Limitations, and Clinical Use

Marina Jamnicki, MD,* Roman Kocian, MD,† Philippe van der Linden, MD,‡ Michael Zaugg, MD,* and

Linee Guida (alcune……)

QUALE TRIGGER ?
(in pazienti critici)

Guidelines on the management of massive blood loss

l, *British Journal of Haematology*, **135**, 634–641

British Committee for Standards in Haematology: Writing Group: D. Stainsby,[1] S. MacLennan,[1] D. Thomas,[2] J. Isaac[3] and P. J. Hamilton[4]

Maintain Hb >8 g/dl

are rarely indicated when the haemoglobin concentration is >10 g/dl but almost always indicated when it is <6 g/dl. (British Committee for Standards in Haematology Blood Transfusion Task Force, 2001) *(Grade C recommendation, Level IV evidence)*. Decisions on red cell transfusion at intermediate haemoglobin concentrations should be based on the patient's risk factors for complications of inadequate oxygenation, such as rate of blood loss, cardiorespiratory reserve, oxygen consumption and atherosclerotic disease. Measured physiolo-

EJA

Eur J Anaesthesiol 2013; **30**:270–382

GUIDELINES

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Transfusion triggers
We recommend a target haemoglobin concentration of 7–9 g dl^{-1} during active bleeding. **1C**

It has been demonstrated that acute anaemia (Hb < 5 g dl^{-1}) can be tolerated in healthy individuals, because compensatory mechanisms (predominantly an increase of cardiac output) can ensure sufficient tissue oxygenation.[296]

During bleeding, patients may be less able to tolerate anaemia because the compensatory mechanisms may be impaired. However, it is not known whether the lowest tolerable haemoglobin concentration is determined

Spahn *et al. Critical Care* 2013, **17**:R76
http://ccforum.com/content/17/2/R76

CRITICAL CARE

RESEARCH Open Access

Management of bleeding and coagulopathy following major trauma: an updated European guideline

Treatment should aim to achieve a target Hb of 7–9 g/dl.

No prospective RCT has compared restrictive and liberal transfusion regimens in trauma, but 203 trauma patients from the Transfusion Requirements in Critical Care trial [228] were re-analysed [229]. A restrictive transfusion regimen (Hb transfusion trigger <7.0 g/dl) resulted in fewer transfusions as compared with the liberal transfusion regimen (Hb transfusion trigger <10 g/dl) and appeared to be safe. However, no statistically significant benefit in terms of multiple organ failure or post-traumatic infections was observed. It should be emphasised that this study was neither designed nor powered to answer these questions

One Size Fits all ???

QUALE TRIGGER ?

Appropriateness of Allogeneic Red Blood Cell Transfusion: The International Consensus Conference on Transfusion Outcomes

Transfusion Medicine Reviews, Vol 25, No 3 (July), 2011:

Aryeh Shander, Arlene Fink, Mazyar Javidroozi, Jochen Erhard, Shannon L. Farmer, Howard Corwin, Lawrence Tim Goodnough, Axel Hofmann, James Isbister, Sherri Ozawa, and Donat R. Spahn, for the International Consensus Conference on Transfusion Outcomes Group

An international multidisciplinary panel of 15 experts reviewed 494 published articles and used the RAND/UCLA Appropriateness Method to determine the appropriateness of allogeneic red blood cell (RBC) transfusion based on its expected impact on outcomes of stable nonbleeding patients in 450 typical inpatient medical, surgical, or trauma scenarios. Panelists rated allogeneic

For each setting 12 scenarios: a(1,2) x b (1,2) x c (1,2,3))

a. ≥ 65; < 65 anni
b. Comorbidities yes; Comorbidities no
c. Hb < 8,0; 8,0-9,9; >10 g/dl

Table 2. Clinical Settings for Allogeneic RBC Transfusion Considered in This Study

Settings	Scenarios
Medical	Patient is admitted to the cardiac unit with suspected acute coronary syndrome
	Patient is admitted to the ICU with noncardiogenic shock
	Patient is admitted to the ICU with sepsis
	Patient is admitted to the ICU with multiple organ failure
	Patient is admitted to the ICU with respiratory failure requiring the use of ventilatory support
	Patient has been on mechanical ventilation and is due to be weaned
	Patient has been diagnosed with a high-prevalence cancer and is undergoing radiotherapy (in- or outpatient)
	Patient with cancer-related and/or chemotherapy-induced anemia is admitted with fever
	Patient with myelodysplastic syndrome is admitted with fever
	Patient with sickle cell disease is admitted for elective surgery
	Patient is admitted with acute brain attack (stroke)
	Patient is admitted with subarachnoid/intracranial bleeding with potential for vasospasm
	Patient is admitted to the ED with upper GI bleeding
	Patient is admitted to the ED with lower GI bleeding
	Patient is admitted with acute pancreatitis

SOURCE CONTROL

- ✓ **Tourniquet, dressing**
(e.g. pre-H penetrating trauma)
- ✓ **Surgery**
(e.g. 'damage control' in trauma)
- ✓ **Radiology**
(e.g. retroperitoneal bleeding)
- ✓ **Endoscopy**
(e.g. esophageal/gastric bleeding
- ✓ **Medical Therapy**
(e.g. reversal anticoag; uterotonic)

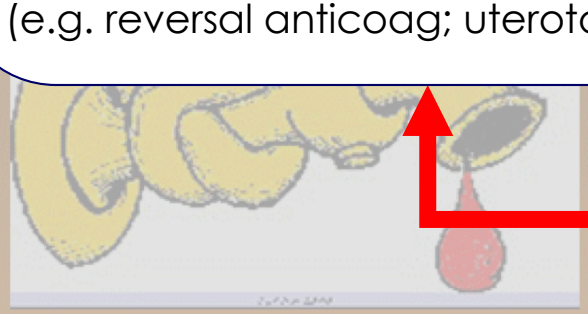
VOLUME RESUSCITATION/O2 TRANSPORT

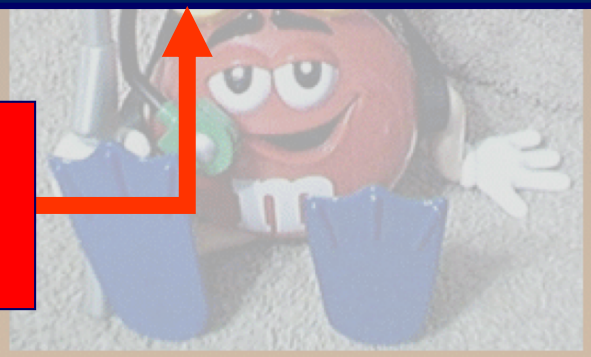
✓ **Evaluation**

- Cardiovascular parameters
- Organ perfusion parameters

✓ **Therapy**

- Red Blood Cell if Hb < 8-9 g/dl
- FLUIDS : if PAS < 80 mmHg
  Traumatic Brain Injury: fluids if PAM < 90 mmHg





CRITICAL BLEEDING

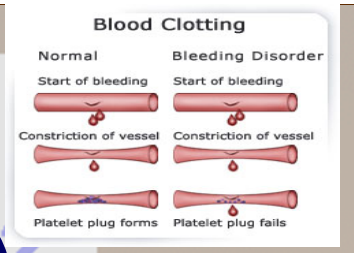
1. **Evaluate Patient, Setting**
2. **Activate available resources**

HEMOSTASIS

- ✓ **AVOID HYPOTHERMIA / CORRECT ACIDOSIS if pH < 7,2**
- ✓ **FRESH FROZEN PLASMA (15-20 ml/Kg) if INR > 1,5 or if the PT and aPTT cannot be obtained within a reasonable period.**
- ✓ **PLATELETS (1-2 U/10 Kg) if count < 75.000/µl or platelet dysfunction**
- ✓ **PROTHROMBIN CONCENTRATE (35-50 U/Kg) if oral anticoagulant**
- ✓ **DESMOPRESSIN (0,3 µg/Kg) if platelet dysfunction**
- ✓ **FIBRINOGEN (1-2 g) if fibrinogen < 100mg/ml**
- ✓ **TRANEXAMIC ACID (1 g i.v. in 10 min) if TEG evidence of hyperfibrinolysis**
- ✓ **rFVIIa (90-120µg/Kg) if standard therapy failed**

COSA VOGLIO

NEL SANGUINAMENTO CRITICO ?



EMOSTASI

HEMOSTASIS

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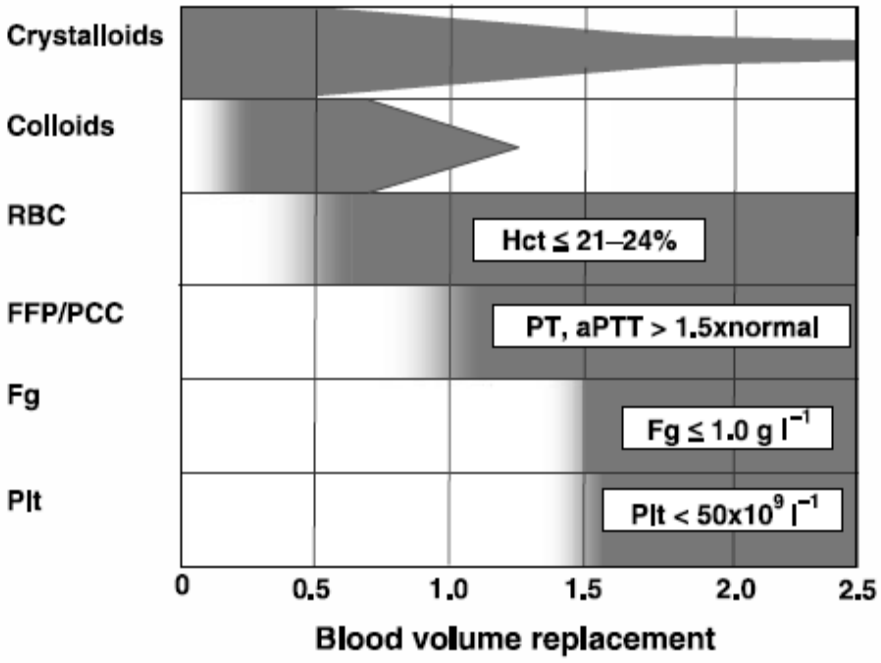
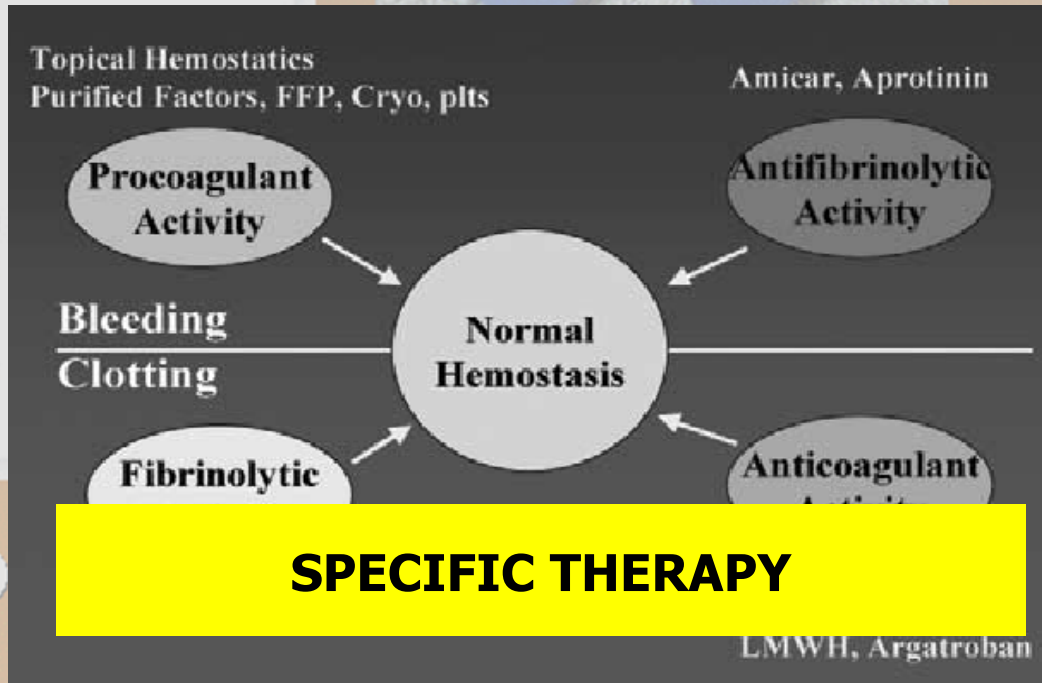




SPECIFIC THERAPY

Setting	Recommendation	GoR	Source
TRAUMA PTS	In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies: •Plasma (FFP or pathogen-inactivated plasma) in a plasma–RBC ratio of at least 1:2 as needed •Fibrinogen concentrate and RBC according to Hb level.	1B 1C	Trauma European Guidelines 2016
	If a plasma-based coagulation resuscitation strategy is used, we recommend that plasma (FFP or pathogen-inactivated plasma) be administered to maintain **PT and APTT <1.5 times the normal control**	1C	
	We recommend that plasma transfusion be avoided in patients without substantial bleeding.	1B	
	Provided that fibrinogen levels are normal, we suggest that PCC or plasma be administered in the bleeding patient based on evidence of delayed coagulation initiation using viscoelastic monitoring.	2C	

Setting	Recommendation	GoR	Source
Severe perioperative bleeding	We recommend **against** the use of plasma transfusion for preprocedural correction of mild-to-moderately elevated INR.	1C	ESA Guidelines, 2017
	In the treatment of acquired coagulation factor deficiency, we suggest the consideration of a ratio-driven protocol (RBC:plasma:platelet concentrates) early in uncontrolled massive bleeding outside the trauma setting followed by a goal-directed approach as soon as possible.	2C	
	We recommend against indiscriminate use of plasma transfusion in perioperative bleeding management.	1C	
	Plasma transfusion alone is not sufficient to correct hypo-fibrinogenaemia.	C	

JAMA. 2015;313(5):471-482.

Original Investigation

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

The PROPPR Randomized Clinical Trial

Table 2. Trial Outcomes by Treatment Group

	1:1:1 Group (n = 338)	1:1:2 Group (n = 342)	Difference (95% CI), %	Adjusted RR (95% CI)	*P* Value[a]
24-h Mortality, No. (%)[b]	43 (12.7)	58 (17.0)	−4.2 (−9.6 to 1.1)	0.75 (0.52 to 1.08)	.12
30-d Mortality, No. (%)[b]	75 (22.4)	89 (26.1)	−3.7 (−10.2 to 2.7)	0.86 (0.65 to 1.12)	.26
Achieved hemostasis					
No. (%)	291 (86.1)	267 (78.1)			.006

Table 3. Adjudicated Cause of Death by Treatment Group and Period From Randomization

	First 24 Hours		
	No. (%)		
	1:1:1 Group (n = 338)	1:1:2 Group (n = 342)	Difference (95% CI),%[a]
Total No. of deaths	43	58	
Cause of death[b]			
Exsanguination	31 (9.2)	50 (14.6)	−5.4 (−10.4 to −0.5)

Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial

Lancet 2018; 392: 283–91

Hunter B Moore, Ernest E Moore, Michael P Chapman, Kevin McVaney, Gary Bryskiewicz, Robert Blechar, Theresa Chin, Clay Cothren Burlew,

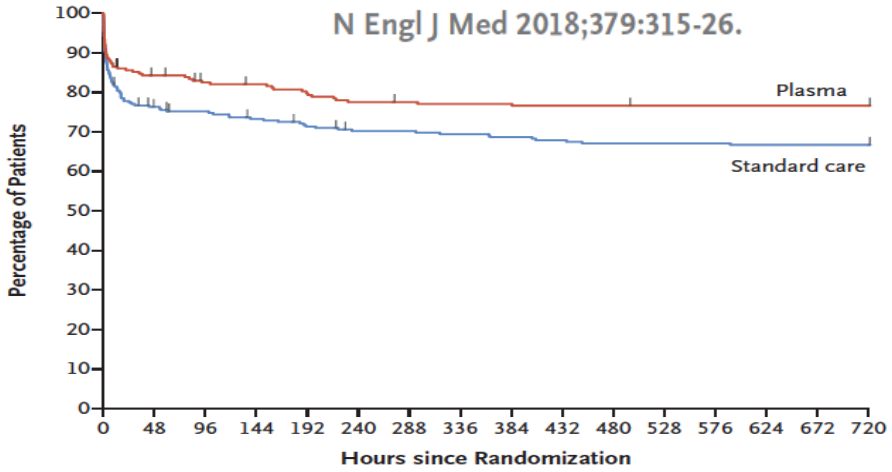
WHEN Plasma pre-hospital trauma

	Plasma group (n=65)	Control group (n=60)	Effect size (95% CI)*	p value
Clinical outcome				
Mortality at 28 days†	10 (15%)	6 (10%)	1·54 (0·60 to 3·98)	0·37
Mortality at 24 h	8 (12%)	6 (10%)	1·23 (0·45 to 3·34)	0·68
Acute lung injury within 28 days	28 (43%)	30 (50%)	0·86 (0·59 to 1·26)	0·44
Multiple organ failure within 28 days (Denver score >3)	4 (6%)	1 (2%)	3·69 (0·42 to 32·11)	0·37
Composite outcome (multiple organ failure or death) at 28 days‡	14 (21%)	7 (12%)	1·85 (0·80 to 4·26)	0·14
Ventilator-free days	26 (11 to 28)	26 (18 to 28)	0 (–1·00 to 0)	0·35
Intensive-care-free days	23 (7 to 26)	24 (17 to 26)	0 (–3·00 to 1·00)	0·49

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

J.L. Sperry, F.X. Guyette, J.B. Brown, M.H. Yazer, D.J. Triulzi, B.J. Early-Young, P.W. Adams, B.J. Daley, R.S. Miller, B.G. Harbrecht, J.A. Claridge, H.A. Phelan, W.R. Witham, A.T. Putnam, T.M. Duane, L.H. Alarcon, C.W. Callaway,

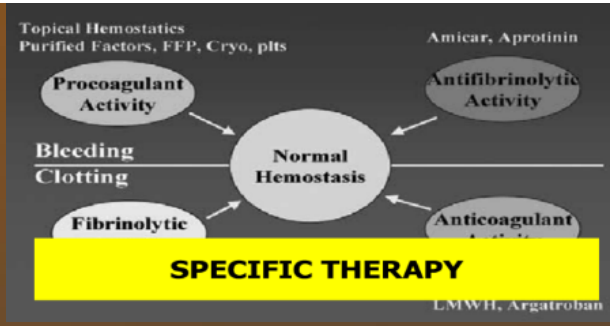
N Engl J Med 2018;379:315-26.



Same Inclusion Criteria
- SAP <70
- SAP 70- 90 and HR> 108

Mortality at 30 days:
23.2% plasma vs. 33.0% standard care
(95% CI −18.6 to −1.0%)
P = 0.03

COSA VOGLIO NEL SANGUINAMENTO CRITICO ?



TERAPIA SPECIFICA IN EMORRAGIA MASSIVA ?

Scelta 'Obbligata'

Scelta 'Possibile'

Evidenza (o quasi) dell'utilità

- ✓ *Coagul. primarie: SPECIFICHE*
- ✓ *TAO: PCC*
- ✓ *Piastrinopatie : DESMO*
- ✓ *Trauma precoce: AC. TRANEX.*

Emorragia non controllata/bile

Trauma, PPH: rVIIa

Approcci alternativi

Trauma e chirurgici : FIBRINOGENO-PCC (guida TEG/ROTEM)

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

HEMORRHAGIC BUNDLES

Patients in hemorrhagic shock (class II-III)

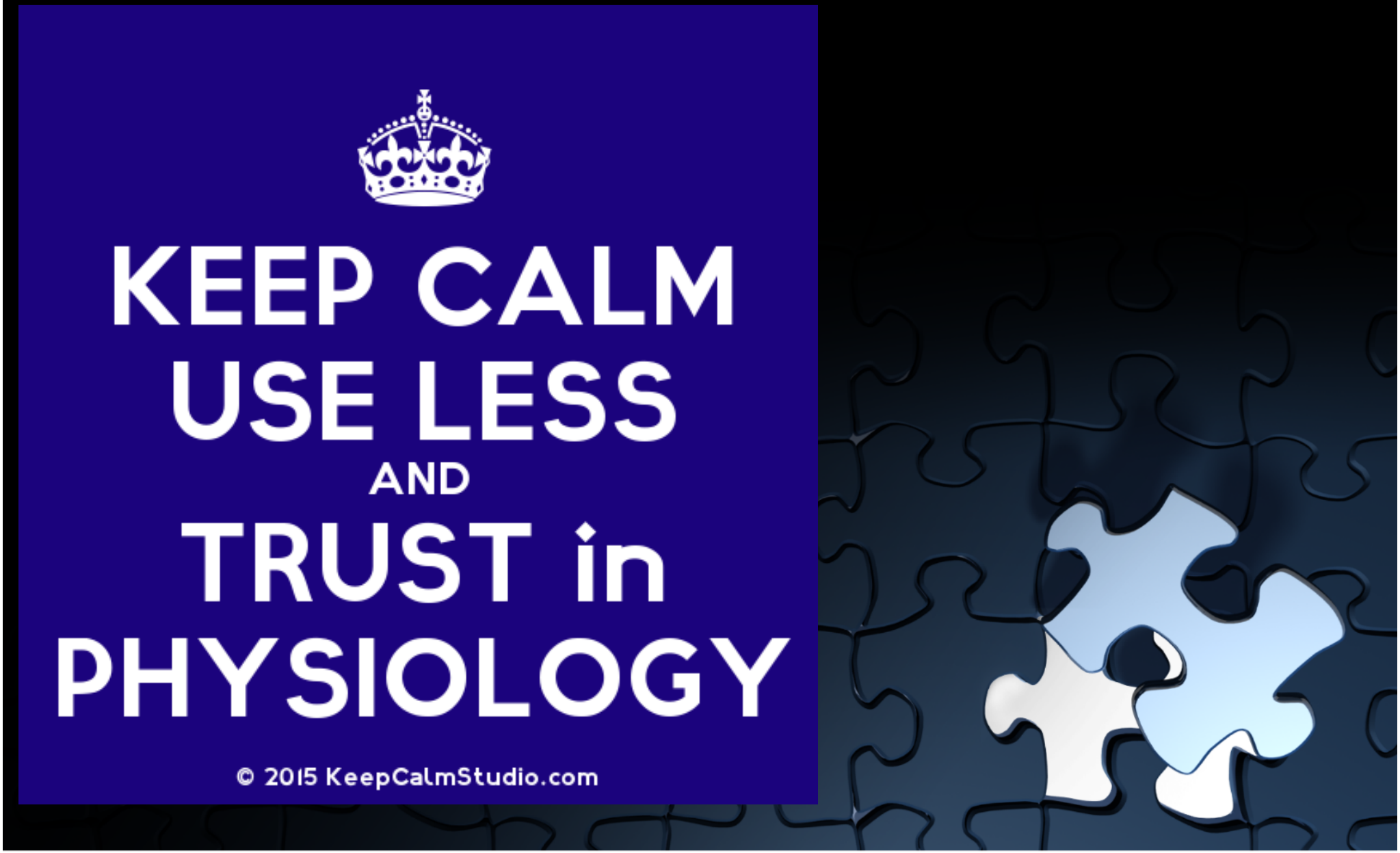
Bundle: Source and Volume (1 h)

- ❑ source diagnosis and control (caveat: 30 min in OR)
- ❑ monitoring : hemoglobin + serum lactate (or BE)
- ❑ fluid resuscitation: SAP >80 mmHg (<100 mmHg if ongoing bleeding) (caveat : NA in TBI)
- ❑ RBC if hemoglobin <8g/dl

Bundle: Hemostasis (2 h)

- ❑ monitoring PT/APTT/Fibri/Platel. (or TEG/ROTEM) (at least 2 times in 6-hours)
- ❑ preconditions of hemostasis: pH>7.3 ; body temperature >35 °C
- ❑ fresh frozen plasma (10-15 ml/kg)
- ❑ if OAT: prothrombin complex concentrate (30-50 U/kg) + Vitamin K (10 mg)
- ❑ if platelets <50.000 /μl and/or dysfunction: platelets concentrates (1-2 units/10 kg)
- ❑ if trauma or hyperfibrinolysis: tranexamic acid (1g/bolus + 1g/8h)
- ❑ If inherited bleeding disorders: specific substitution therapy.

TAKE HOME PICTURE



QUANDO RESUSCITARE ?
QUANTO RESUSCITARE ?
COME RESUSCITARE ?

ORIGINAL ARTICLE

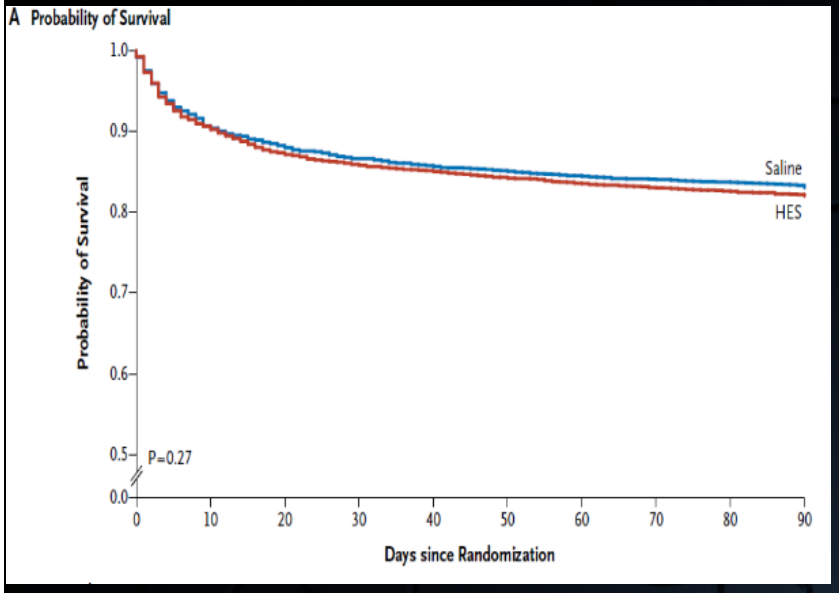
N ENGL J MED 367;20 NEJM.ORG NOVEMBER 15, 2012

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D.,

METHODS

We randomly assigned 7000 patients who had been admitted to an intensive care unit (ICU) in a 1:1 ratio to receive either 6% HES with a molecular weight of 130 kD and a molar substitution ratio of 0.4 (130/0.4, Voluven) in 0.9% sodium chloride or 0.9% sodium chloride (saline) for all fluid resuscitation until ICU discharge, death, or 90 days after randomization. The primary outcome was death within 90 days. Secondary outcomes included acute kidney injury and failure and treatment with renal-replacement therapy.



B Subgroup Analyses

Subgroup	HES	Saline	Risk Ratio (95% CI)	P Value
	no. of events/total no. (%)			
Death from any cause at 90 days	597/3315 (18.0)	566/3336 (17.0)	1.06 (0.96–1.18)	0.26
RIFLE criteria at randomization				0.66
Presence of acute renal injury	99/519 (19.1)	95/503 (18.9)	1.01 (0.78–1.30)	0.94
Absence of acute renal injury	132/919 (14.4)	118/896 (13.2)	1.09 (0.87–1.37)	0.46
Sepsis at randomization				0.78
Diagnosis on admission	248/976 (25.4)	224/945 (23.7)	1.07 (0.92–1.25)	0.38
No diagnosis on admission	349/2337 (14.9)	342/2383 (14.4)	1.04 (0.91–1.19)	0.57
Trauma				0.90
Yes	18/258 (7.0)	18/263 (6.8)	1.02 (0.54–1.91)	0.95
No	579/3057 (18.9)	548/3073 (17.8)	1.06 (0.96–1.18)	0.26
Traumatic brain injury				0.31
Yes	1/27 (3.7)	3/30 (10.0)	0.37 (0.04–3.35)	0.35
No	594/3269 (18.2)	560/3287 (17.0)	1.07 (0.96–1.18)	0.23
APACHE II score before randomization				0.60
≥25	217/590 (36.8)	221/616 (35.9)	1.03 (0.88–1.19)	0.74
<25	372/2702 (13.8)	342/2690 (12.7)	1.08 (0.94–1.24)	0.25
Receipt of HES before randomization				0.78
Yes	48/508 (9.4)	42/499 (8.4)	1.12 (0.76–1.67)	0.57
No	547/2798 (19.5)	522/2825 (18.5)	1.06 (0.95–1.18)	0.31

EBM and INTENSIVE CARE

American Thoracic Society Documents

Am J Respir Crit Care Med Vol 185, Iss. 10, pp 1117–1124, May 15, 2012

An Official Multi-Society Statement: The Role of Clinical Research Results in the Practice of Critical Care Medicine

THIS OFFICIAL STATEMENT OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS (ACCP), THE AMERICAN THORACIC SOCIETY (ATS), AND THE SOCIETY OF CRITICAL CARE MEDICINE (SCCM) WAS APPROVED BY THE ACCP BOARD OF REGENTS, JUNE 2011, BY THE ATS BOARD OF DIRECTORS, NOVEMBER 2011, AND BY THE SCCM COUNCIL, SEPTEMBER 2011

- The results of clinical research, pathophysiologic reasoning, and clinical experience represent different kinds of medical knowledge crucial for effective clinical decision making.
- Each kind of medical knowledge has various strengths and weaknesses when utilized in the care of individual patients.
- No single source of medical knowledge is sufficient to guide clinical decisions.
- No kind of medical knowledge always takes precedence over the others.