Remplissage :
Physiologie, Qui je remplis? Comment je remplis?

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RENAU, Juin 2018

Pas de conflit d'intérèt

Des raisons pour remplir…

- Static evaluation
  - Signs of dehydration
    - Diminished skin turgor
    - Thirst
    - Dry mouth
    - Dry axillae
    - Hypernatremia, hyperproteinemia, elevated hemoglobin/hematocrit
  - Circulatory signs of hypovolemia
    - Tachycardia
    - Arterial hypotension (severe cases)
    - Increased serum lactate (severe cases)
    - Decreased toe temperature
  - Decreased renal perfusion
    - Concentrated urine (low urine sodium concentration, high urine osmolarity)
    - Increased blood urea nitrogen relative to creatinine concentration
    - Persistent metabolic alkalosis
- Dynamic evaluation
  - Orthostatic hypotension
  - Respiratory variations in arterial pressure or stroke volume (during mechanical ventilation, in the absence of ventilatory dyssynchrony or arrhythmias)
  - Passive leg raising
  - Positive response to fluid challenge

Crit Care Med 2006 Vol. 34, No. 5

Critères cliniques : dans 80% des cas

2213 patients- 211 services – 36 pays

Indication	n (%)
Hypotension	1211 (58.7 [56.7–60.8])
Weaning vasopressor	146 (7.1 [6.0–8.2])
Cardiac output	62 (3.0) [2.3–3.7]
Oliguria	372 (18.0 [16.4–19.6])
Skin mottling	36 (1.7 [1.2–2.2])
Lactate	128 (6.2 [5.2–7.2])
$SvO_2/ScvO_2$	10 (0.5 [0.2–0.8])
SVV/PPV	37 (1.8 [1.3–2.4])
CVP/PAOP	60 (2.9 [2.2–3.6])

Fluid challenges in intensive care: the FENICE study

A global inception cohort study

500 ml (500-1000)
24 min (40 – 60)
1000ml/h (500-1333)

Intensive Care Med (2015) 41:1529–1537
DOI 10.1007/s00134-015-3850-x

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D., Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S., Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D., Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SALT-ED Investigators*

Table 2. Crystalloids Received in the Emergency Department According to Assigned Treatment Group.*

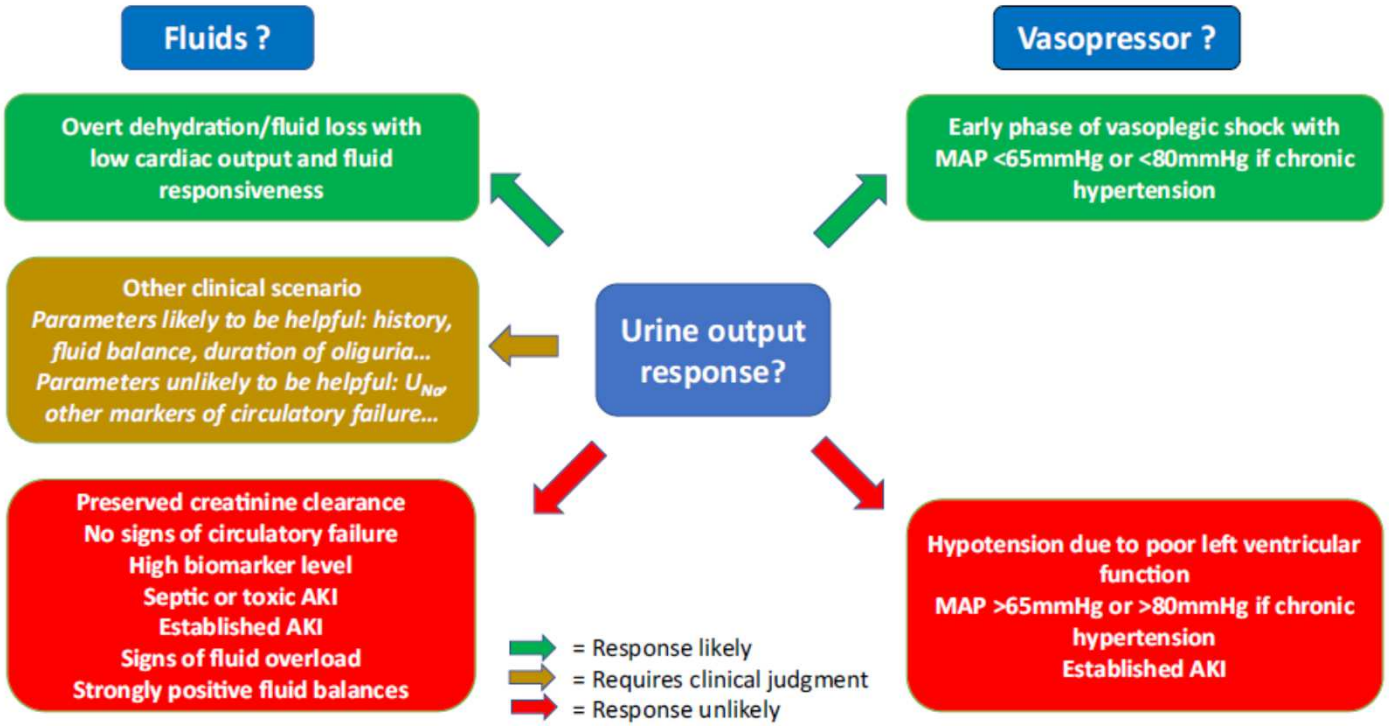
Variable	Balanced Crystalloids (N=6708)	Saline (N=6639)
Total crystalloid volume		
Mean — ml	1608±1095	1597±1105
Median (IQR) — ml	1089 (1000–2000)	1071 (1000–2000)
≥2000 ml — no. (%)	2207 (32.9)	2150 (32.4)

N Engl J Med 2018;378:819-28.

Un remplissage pas anodin

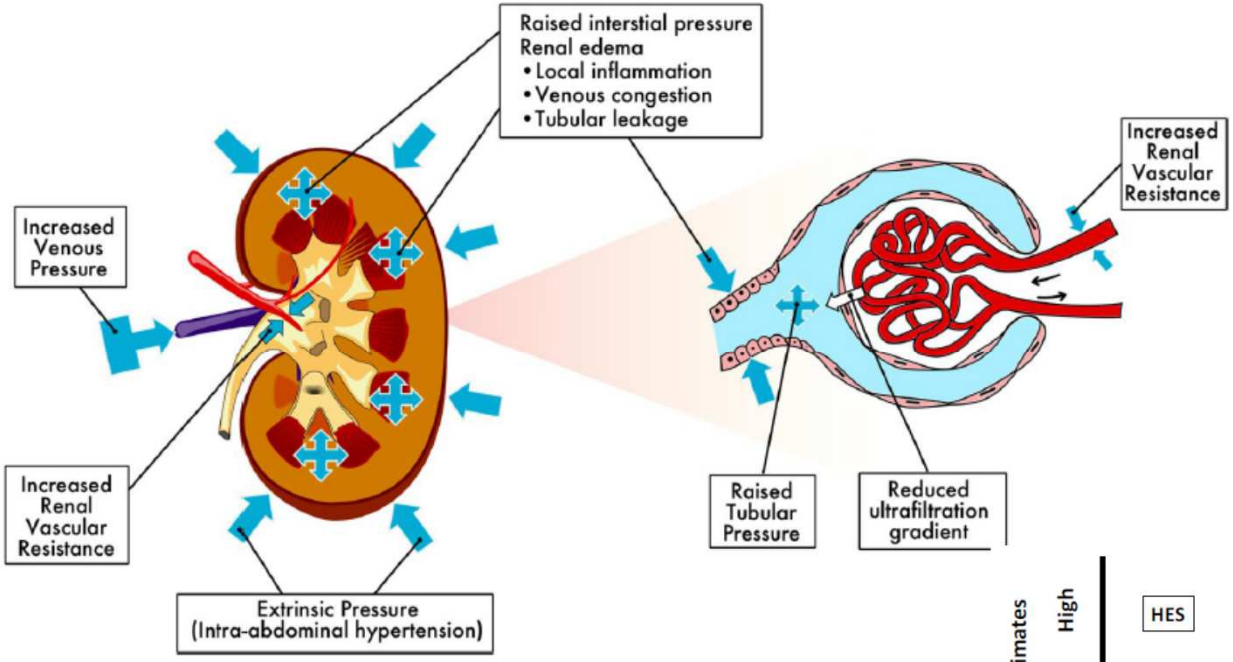
Body System	Effect of Fluid Overload	Clinical Manifestation
Central Nervous System	Cerebral edema	Impaired cognition Delirium
Respiratory System	Pulmonary edema Pleural effusions	Increased work of breathing Impaired gas exchange Decreased lung compliance Increased extravascular lung water
Cardiovascular System	Myocardial edema Pericardial effusions	Impaired contractility Diastolic dysfunction Conduction abnormalities
Gastrointestinal System	Gut wall edema Ascites	Malabsorption Ileus Bacterial translocation Intra-abdominal hypertension
Hepatobiliary System	Hepatic congestion	Cholestasis Impaired synthetic function
Renal System	Renal interstitial edema Elevated renal venous pressure	Acute Kidney Injury Uremia Salt and water retention
Skin and Musculoskeletal System	Tissue edema Impaired lymphatic drainage Deranged microcirculation	Poor wound healing Pressure ulcers Wound infection

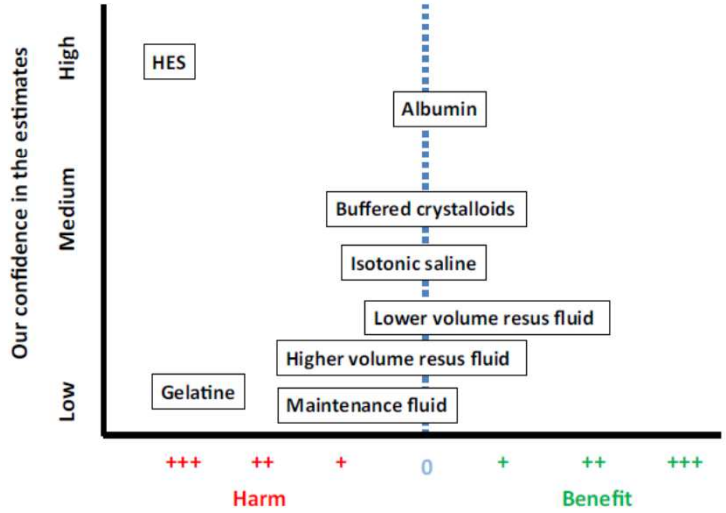
Does this critically ill patient with oliguria need more fluids, a vasopressor, or neither?



Intensive Care Med (2017) 43:907–910

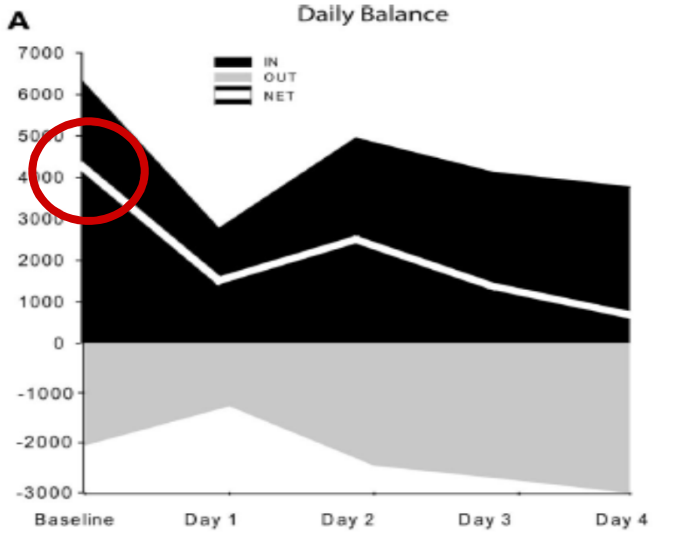
Remplissage : vigilance rénale

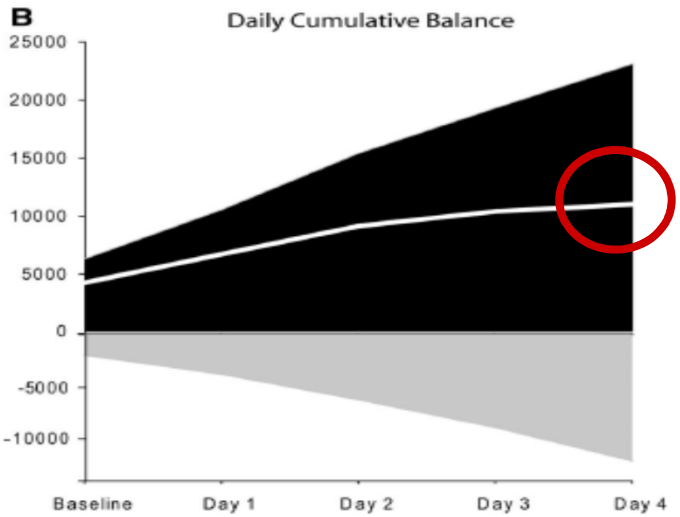


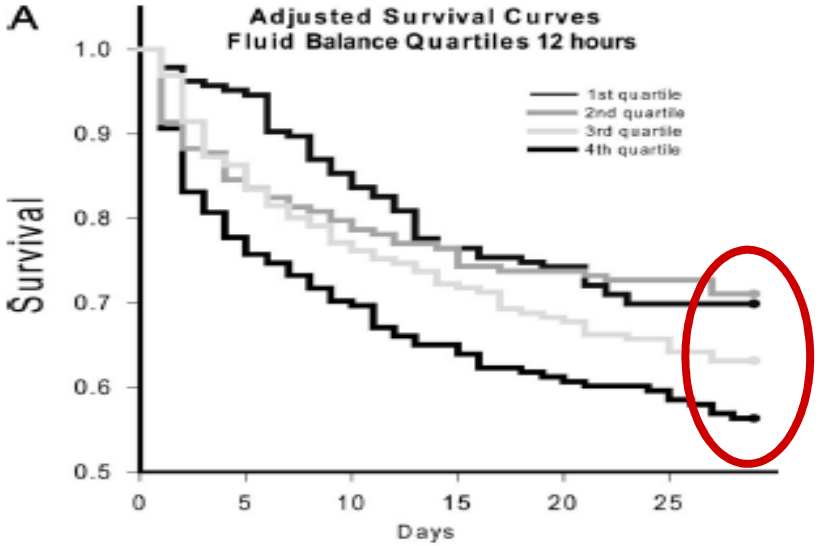


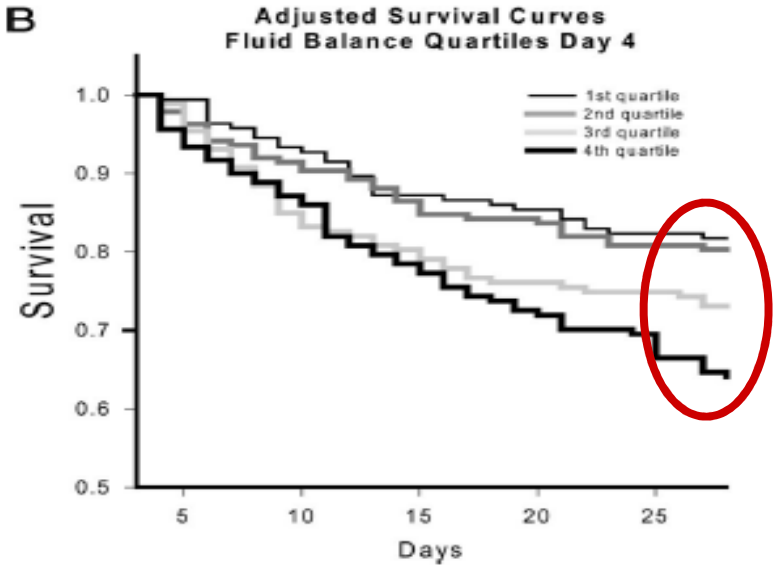
Intensive Care Med
DOI 10.1007/s00134-017-4817-x

La surcharge impacte la survie





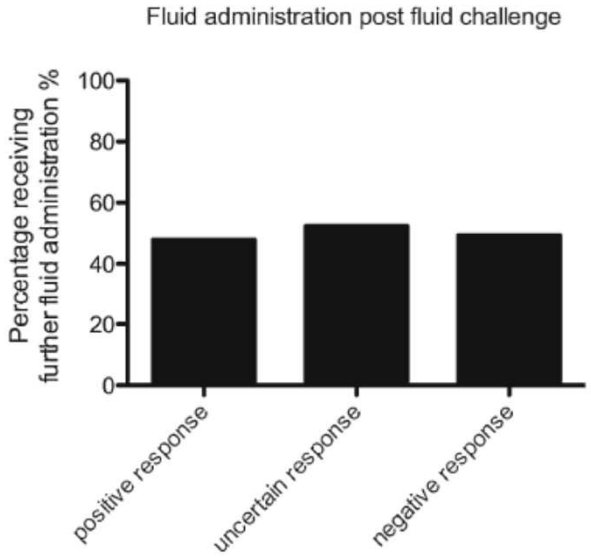




Crit Care Med 2011 Vol. 39, No. 2

Évaluation du remplissage

Hemodynamic variable used to predict fluid responsiveness	*n*	% Of category
No variable used	945	
Any variable used	1268	
Static	785	
CVP	572	89.9 [87.8–92.0]
PAOP	31	4.9 [3.4–6.4]
GEDVI	33	5.2 [3.6–6.8]
Other	149	23.4 [20.4–26.4]
Dynamic	483	
PPV	88	18.2 [14.8–21.6]
SVV	88	18.2 [14.8–21.6]
PPV + SVV	24	5.0 [3.1–6.9]
PLR	238	49.3 [44.8–53.8]
Echo variables	45	9.3 [6.7–11.9]



Intensive Care Med (2015) 41:1529–1537
DOI 10.1007/s00134-015-3850-x

Remplissage:

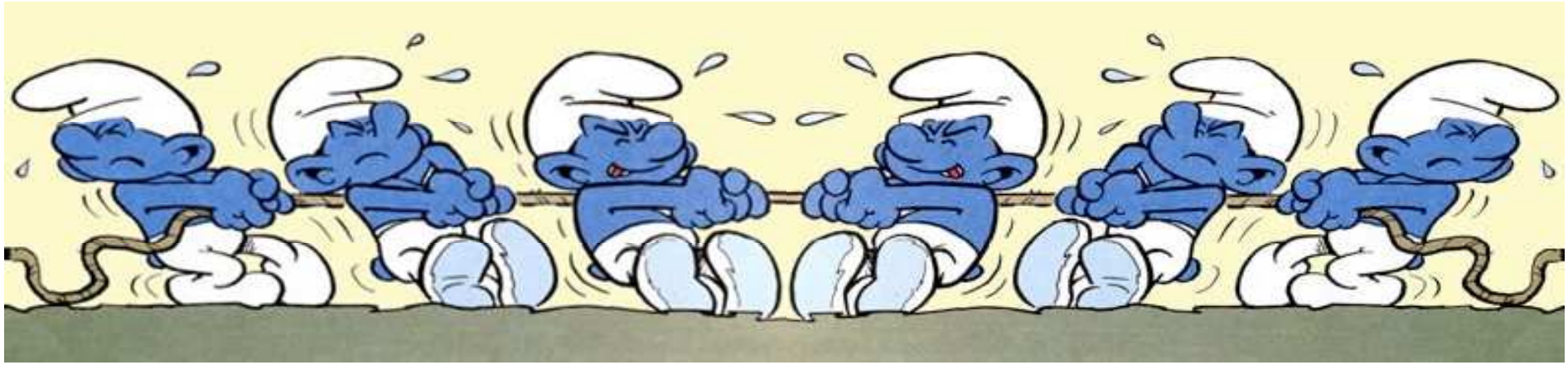
Qui?
Indication(s)?
Quelle(s) précaution(s)?

Pourquoi?
Quel(s) objectif(s)?
Quel(s) risque(s)?

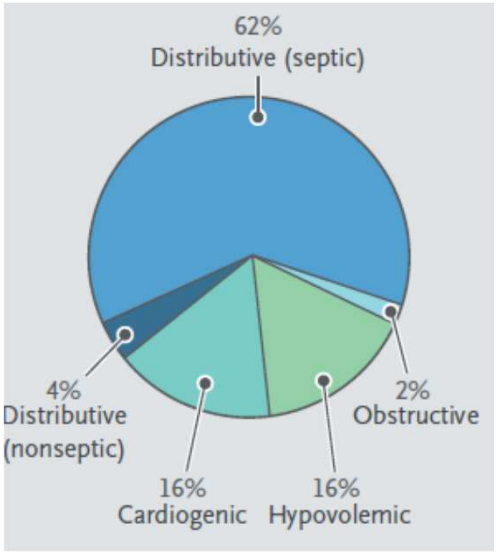
Comment?
Fluid-challenge?
Mini-fluid challenge?
IV challenge ?

Avec quoi?
Cristalloides? Balancés ou pas?
Colloides? Albumine ou pas?
Combien?
Quantité?
De sous?

Maintenir l'équilibre entre les apports et les besoins en oxygène

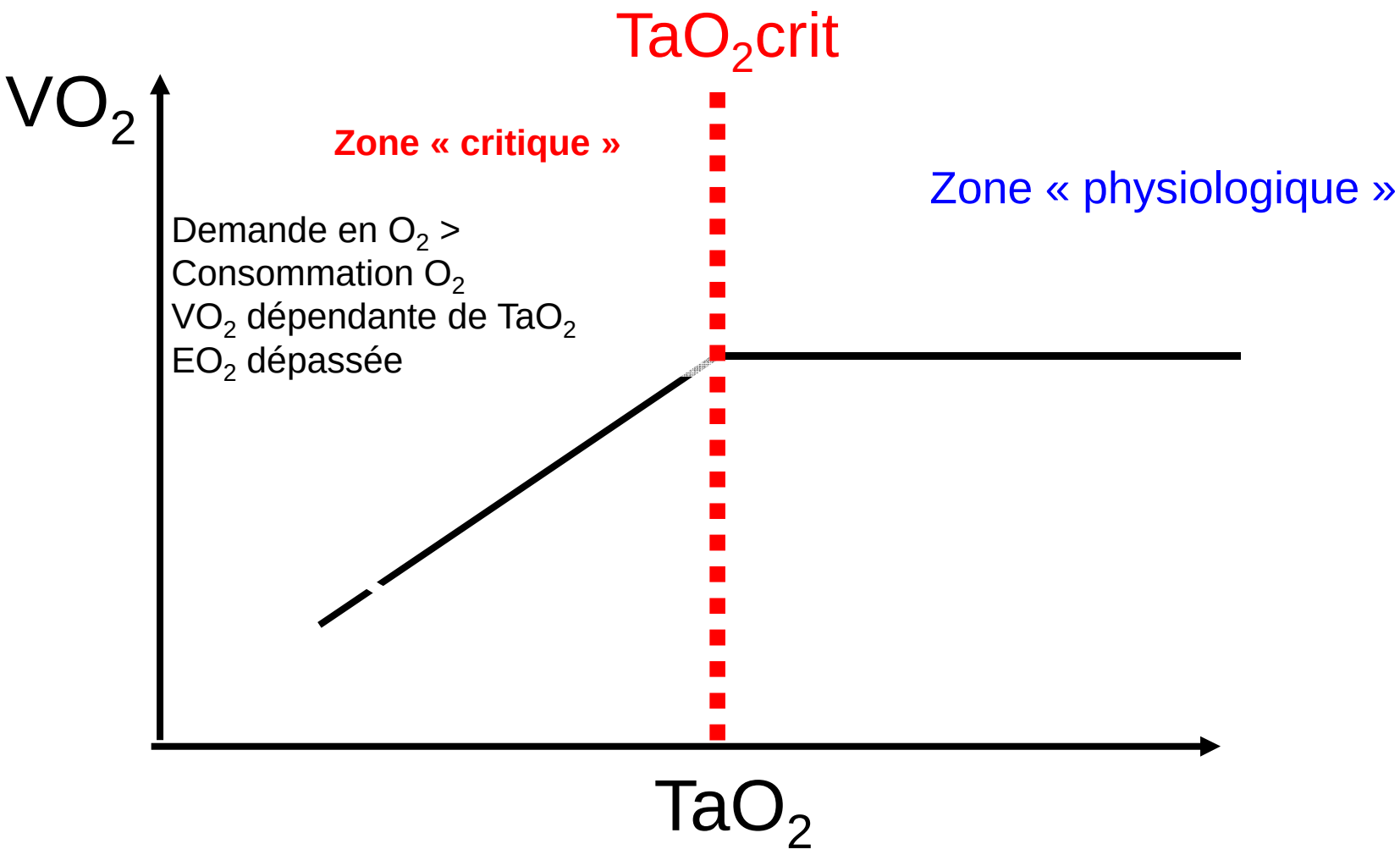


Apports
Transport O_2

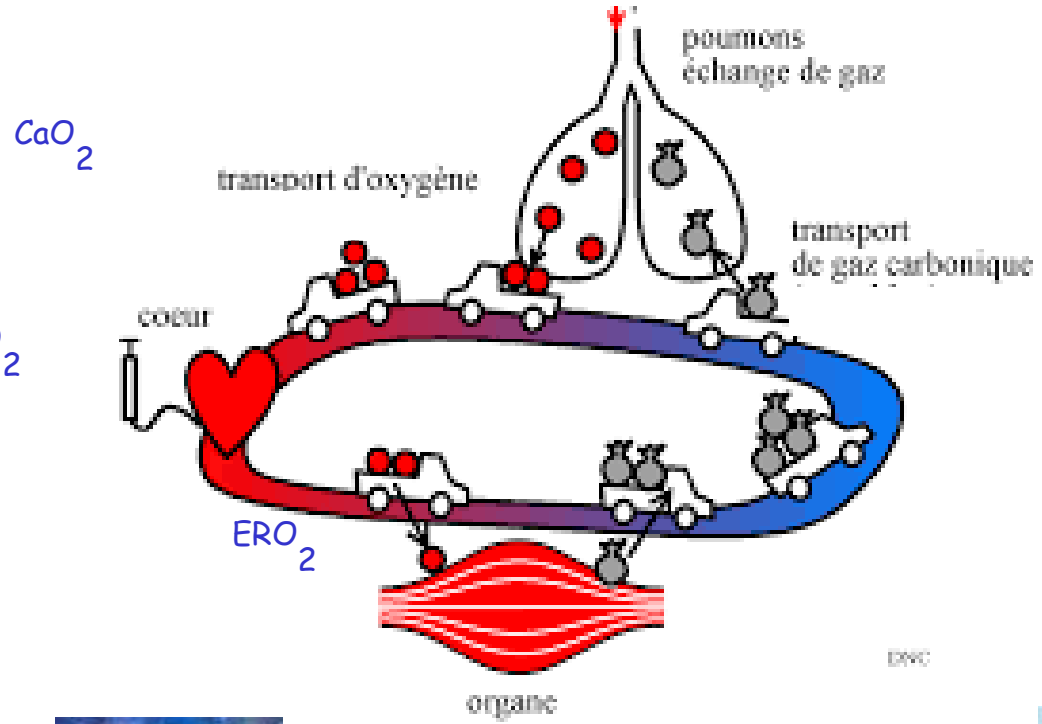


Besoins
Consommation O_2

TaO_2 vs VO_2


TaO2crit
VO2
Zone « critique »
Zone « physiologique »
Demande en O2 >
Consommation O2
VO2 dépendante de TaO2
EO2 dépassée
TaO2

Cibler la délivrance en oxygène et oxygénation tissulaire



CaO_2

DO_2

ERO_2

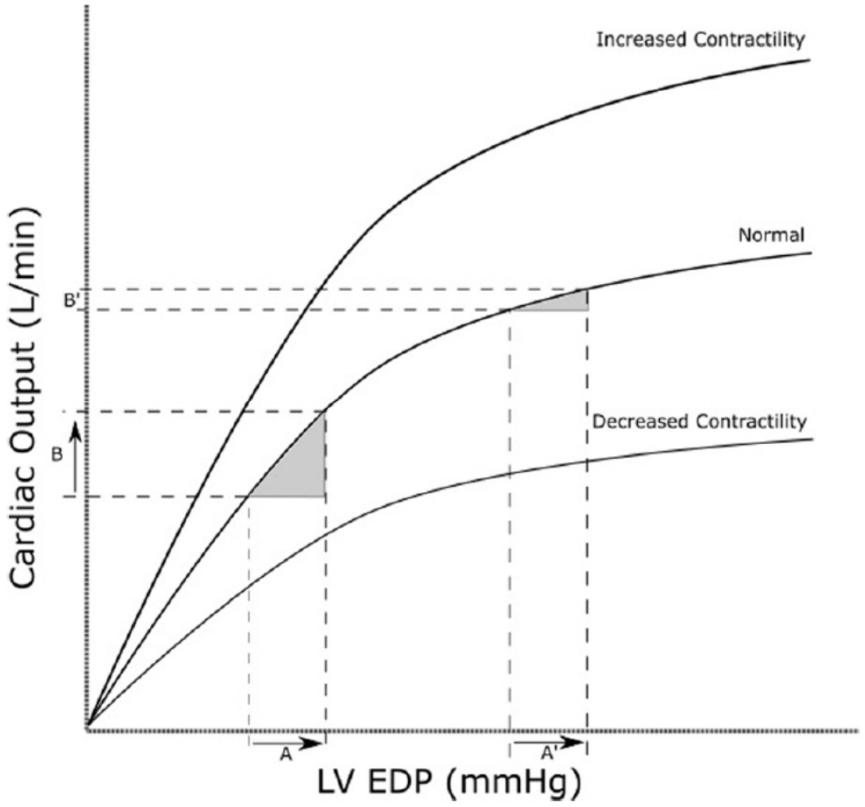
VO_2

Hypoxie hypoxémique
Hypoxie ischémique
Hypoxie anémique
Hypoxie cytopathique

Utilisation de l'O_2

Bioénergétique cellulaire

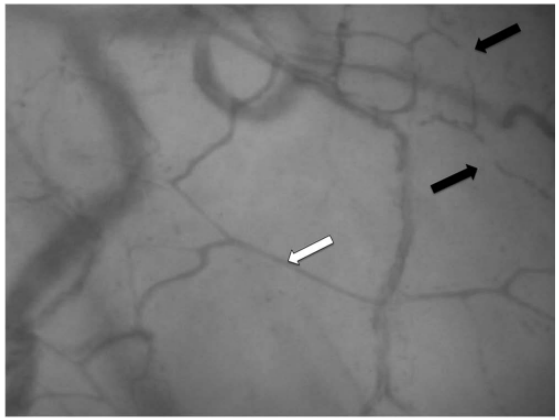
Se rappeler la non linéarité entre remplissage et débit cardiaque



Focus sur microcirculation et choc hétérogénéité microvasculaire

- Indépendamment anomalies macrocirculatoires

- Réduction de la densité capillaire
- Hétérogénéité des flux
  - juxtaposition Capillaires perfusés-non perfusés
- Hétérogénéité de l'oxygénation



- Dysfonction endothéliale
  - Régulation flux

- Impact pronostique

- Cible thérapeutique?

Virulence 5:1, 73–79; January 1, 2014;

Critical Care (2016) 20:319

Les propriétés des solutés disponibles

- 2 types de solutés
  - Cristalloides vs colloides

- Expansion plasmatique

- Durée d'action
- Impact intégrité vasculaire
- Équilibre acido-basique
- Réponse infammatoire
- Rhéologie
- hémostase

Les cristalloides disponibles

Solutions/characteristics	Osmolality (mOsm/L)	pH	Sodium (mEq/L)	Chloride (mEq/L)	Potassium (mEq/L)	Calcium (mEq/L)	Magnesium (mEq/L)	Buffers (mEq/L)
Plasma	290	7.4	140	103	4	4	2	Bicarbonate (24)
Normal saline (0.9% NaCl)	308	5.7	154	154	0	0	0	0
Ringer's injection	309	5.8	147	156	4	4	0	0
Ringer lactate	273	6.5	130	109	4	3	0	Lactate (28)
Ringer acetate	275	6.7	131	109	4	3	0	Acetate (28)
Plasma-Lyte	295	7.4	140	98	5	0	3	Acetate (28) Gluconate (23)

Un contenu et osmolarité variables :

Solutions de glucose ou serum physiologique

Eau – électrolytes – petites molécules- avec ou sans tampon

Tampon bicarbonate ou non bicarbonate

Hypo – iso ou hypertonique

Les colloides disponibles

Solutions/characteristics	Albumin		Hydroxyethyl starch		Dextran		Gelatins
Solution concentration	4%, 5%	20%, 25%	6%, 10% pentastarch	6% hetastarch	10% Dextran 40	3% Dextran 60 6% Dextran 70	
Molecular weight	69		100-450		40-70		30-35
Osmolality (mOsm/L)	300	1.500	300-326		280-324		300-350
Oncotic pressure (mmHg)	19-30	74-120	23-82		20-60		25-42
Plasmatic expansion (%)	70-100	200-300	100-160		100-200	80-140	70-100
Duration of plasmatic expansion (h)	≤24		≤12	≤4-36	≤4-6	≤8-24	≤4-6
Plasma half-life (h)	16-24		2-12		2	~24	~2-9
Possible adverse effects	High cost, risk of infection and anaphylactic reactions		Impairment coagulation, pruritus, acute kidney failure, and anaphylactic reactions		Changes in blood viscosity, coagulopathy, renal dysfunction, and anaphylactic reactions		Hypercalcemia and anaphylactic reactions

Naturels ou semi-synthétiques

3 groupes de molecules

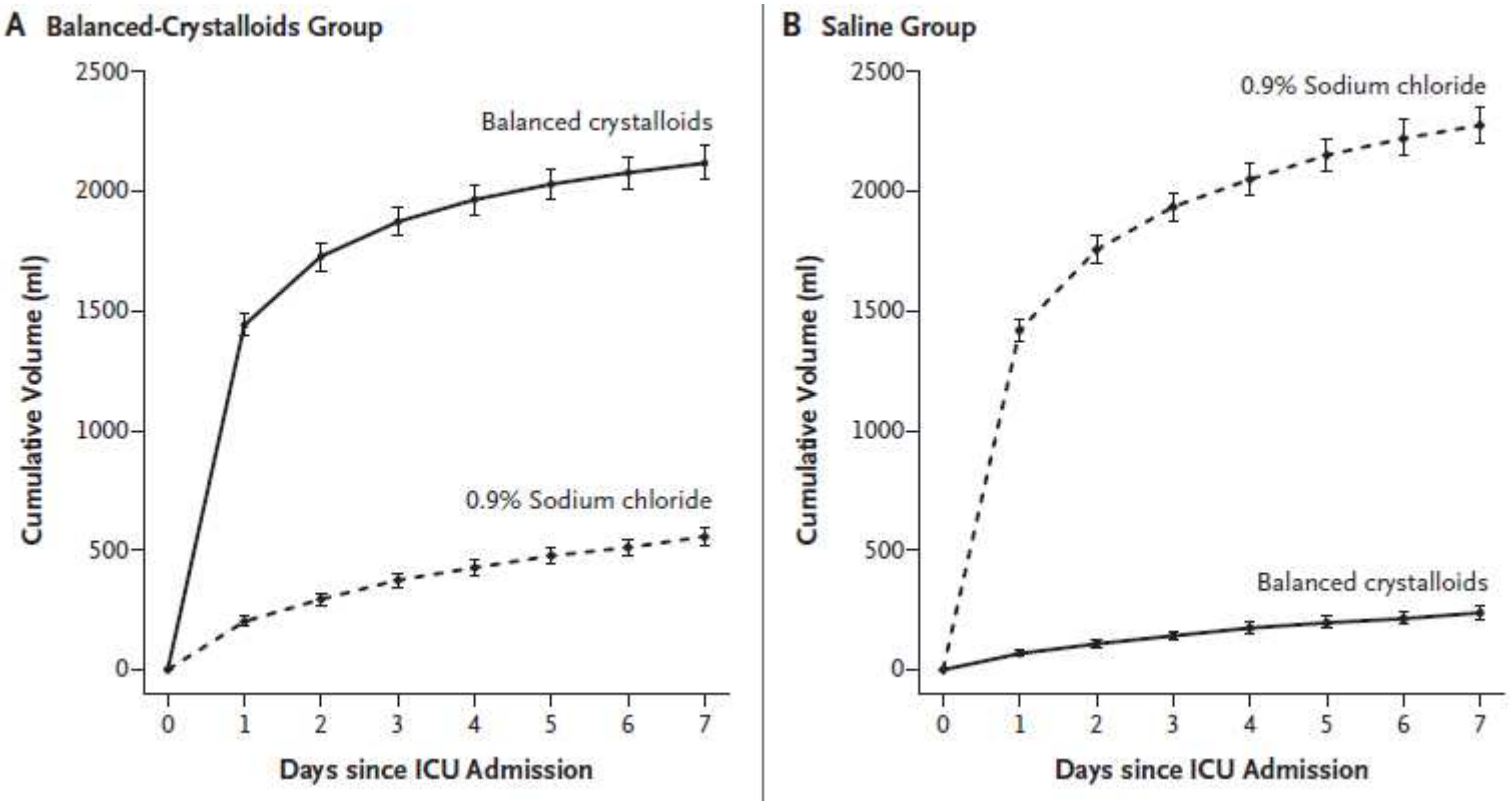
Solvant sel, sucre ou solution balancée, iso ou hypertonique

The NEW ENGLAND JOURNAL of MEDICINE

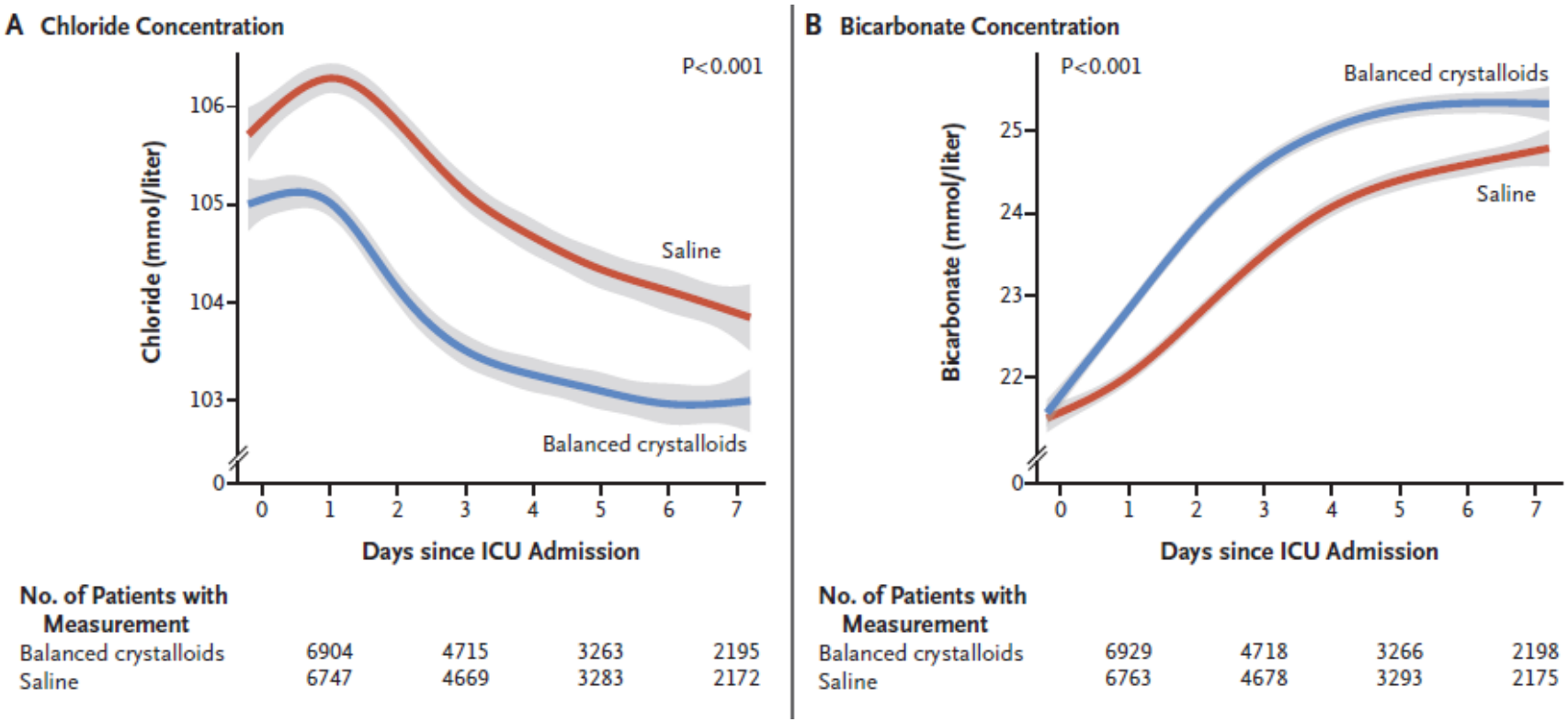
N Engl J Med 2018;378:829-39.

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults



Chlore et bicarbonate



Clinical outcomes

Outcome	Balanced Crystalloids (N=7942)	Saline (N=7860)	Adjusted Odds Ratio (95% CI)†	P Value†
Primary outcome				
Major adverse kidney event within 30 days — no. (%)‡	1139 (14.3)	1211 (15.4)	0.90 (0.82 to 0.99)	0.04
Components of primary outcome				
In-hospital death before 30 days — no. (%)	818 (10.3)	875 (11.1)	0.90 (0.80 to 1.01)	0.06
Receipt of new renal-replacement therapy — no./total no. (%)§	189/7558 (2.5)	220/7458 (2.9)	0.84 (0.68 to 1.02)	0.08
Among survivors	106/6787 (1.6)	117/6657 (1.8)		
Final creatinine level ≥200% of baseline — no./total no. (%)§	487/7558 (6.4)	494/7458 (6.6)	0.96 (0.84 to 1.11)	0.60
Among survivors	259/6787 (3.8)	273/6657 (4.1)		
Among survivors without new renal-replacement therapy	215/6681 (3.2)	219/6540 (3.3)		

Secondary outcomes				
In-hospital death — no. (%)				
Before ICU discharge	528 (6.6)	572 (7.3)	0.89 (0.78 to 1.02)	0.08
Before 60 days	928 (11.7)	975 (12.4)	0.92 (0.83 to 1.02)	0.13
ICU-free days¶				0.94
Median	25.3	25.3	1.00 (0.89 to 1.13)	
Interquartile range	22.1 to 26.6	22.2 to 26.6		
Mean	21.8±8.3	21.7±8.6		
Ventilator-free days¶			1.06 (0.97 to 1.16)	0.22
Median	28.0	28.0		
Interquartile range	26.0 to 28.0	26.0 to 28.0		
Mean	24.2±8.6	23.9±8.9		
Vasopressor-free days¶			1.05 (0.97 to 1.14)	0.26
Median	28.0	28.0		
Interquartile range	27.0 to 28.0	27.0 to 28.0		
Mean	24.7±8.5	24.4±8.8		
Renal-replacement therapy–free days¶			1.11 (1.02 to 1.20)	0.01
Median	28.0	28.0		
Interquartile range	28.0 to 28.0	28.0 to 28.0		
Mean	25.0±8.6	24.8±8.9		

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Balanced Crystalloids versus Saline in Noncritically Ill Adults

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Table 3. Clinical Outcomes According to Assigned Treatment Group in the Intention-to-Treat Analysis.

Outcome	Balanced Crystalloids (N=6708)	Saline (N=6639)	Adjusted Odds Ratio (95% CI)*	Adjusted P Value
Median hospital-free days to day 28 (IQR)	25 (22–26)	25 (22–26)	0.98 (0.92–1.04)	0.41
Major adverse kidney event within 30 days — no. (%)	315 (4.7)	370 (5.6)	0.82 (0.70–0.95)	0.01
Death — no. (%)	94 (1.4)	102 (1.5)	0.89	
New renal-replacement therapy — no./total no. (%)†	18/6582 (0.3)	31/6530 (0.5)	0.56	
Final serum creatinine ≥200% of baseline — no./total no. (%)†	253/6582 (3.8)	293/6530 (4.5)	0.84	
Stage 2 or higher acute kidney injury — no./total no. (%)†	528/6582 (8.0)	560/6530 (8.6)	0.91 (0.80–1.03)	0.14
In-hospital death — no. (%)	95 (1.4)	105 (1.6)	0.88 (0.66–1.16)	0.36

ORIGINAL ARTICLE

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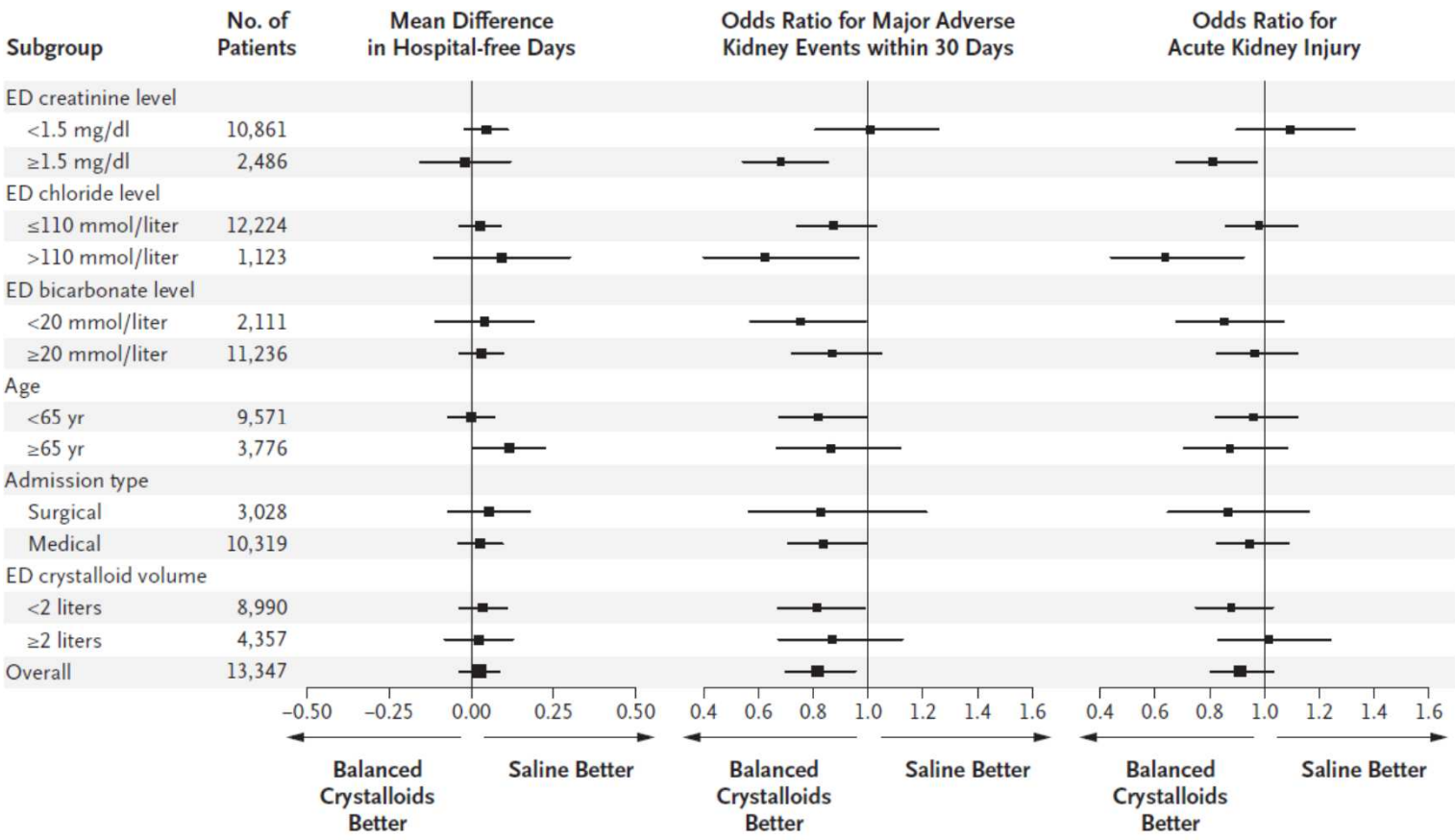


N Engl J Med 2018;378:819-28.

The NEW ENGLAND JOURNAL of MEDICINE
N ENGL J MED 367;2 NEJM.ORG JULY 12, 2012

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D.,

6S

Table 3. Primary and Secondary Outcomes.*

Outcome	HES 130/0.42 (N = 398)	Ringer's Acetate (N = 400)	Relative Risk (95% CI)	P Value
Primary outcome				
Dead or dependent on dialysis at day 90 — no. (%)	202 (51)	173 (43)	1.17 (1.01–1.36)	0.03
Dead at day 90 — no. (%)	201 (51)	172 (43)	1.17 (1.01–1.36)	0.03
Dependent on dialysis at day 90 — no. (%)	1 (0.25)	1 (0.25)	—	1.00
Secondary outcome measures				
Dead at day 28 — no. (%)	154 (39)	144 (36)	1.08 (0.90–1.28)	0.43
Severe bleeding — no. (%)†	38 (10)	25 (6)	1.52 (0.94–2.48)	0.09
Severe allergic reaction — no. (%)†	1 (0.25)	0	—	0.32
SOFA score at day 5 — median (interquartile range)	6 (2–11)	6 (0–10)	—	0.64
Use of renal-replacement therapy — no. (%)‡	87 (22)	65 (16)	1.35 (1.01–1.80)	0.04
Use of renal-replacement therapy or renal SOFA score ≥3 — no. (%)§	129 (32)	108 (27)	1.20 (0.97–1.48)	0.10
Doubling of plasma creatinine level — no. (%)†	148 (41)	127 (35)	1.18 (0.98–1.43)	0.08

The NEW ENGLAND JOURNAL of MEDICINE

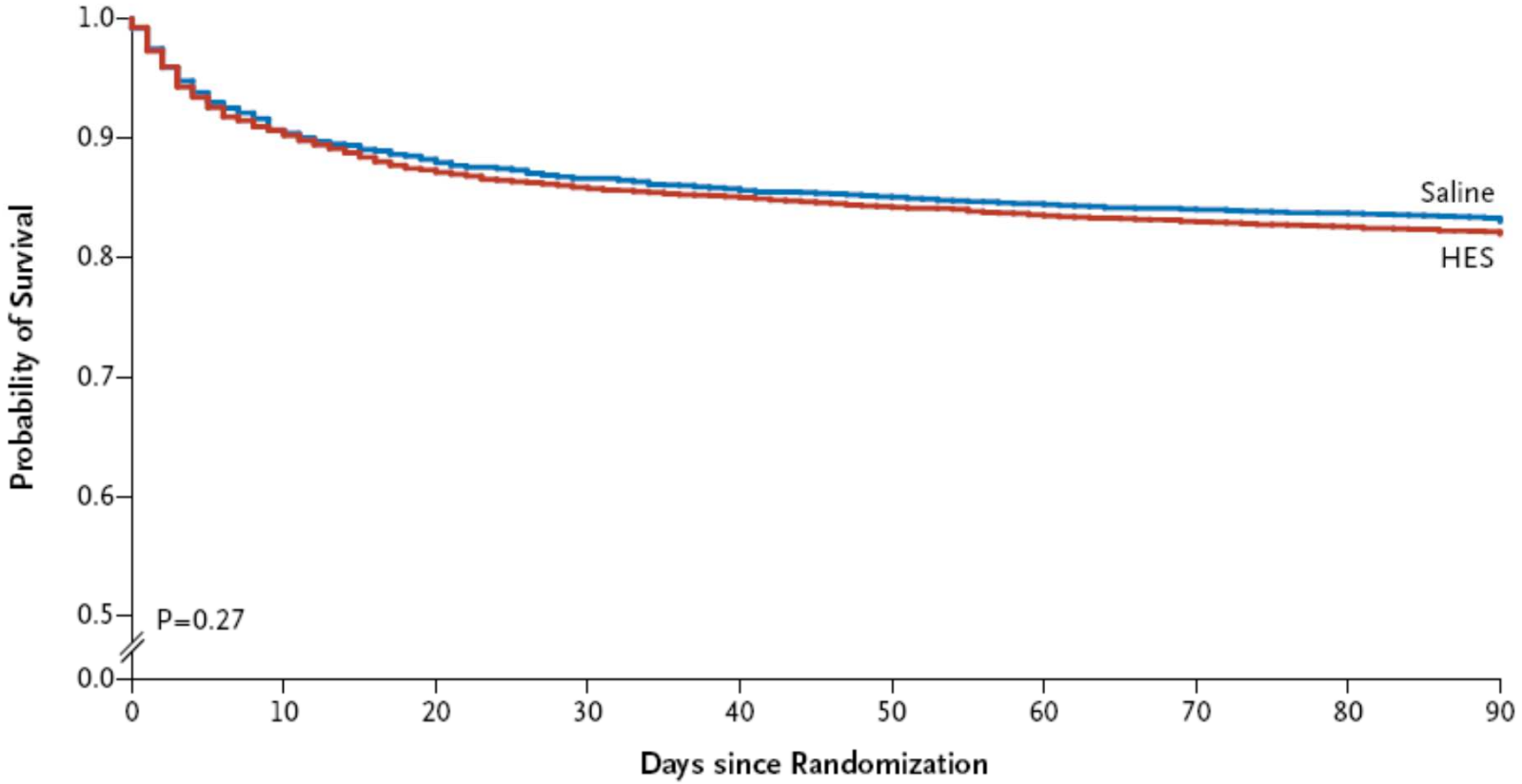
ORIGINAL ARTICLE

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., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

This article was published on October 17, 2012, at NEJM.org.

A Probability of Survival



No. at Risk

Saline	3336	3024	2943	2889	2860	2837	2816	2801	2788	2752
HES	3315	3004	2895	2846	2819	2791	2766	2747	2731	2695

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

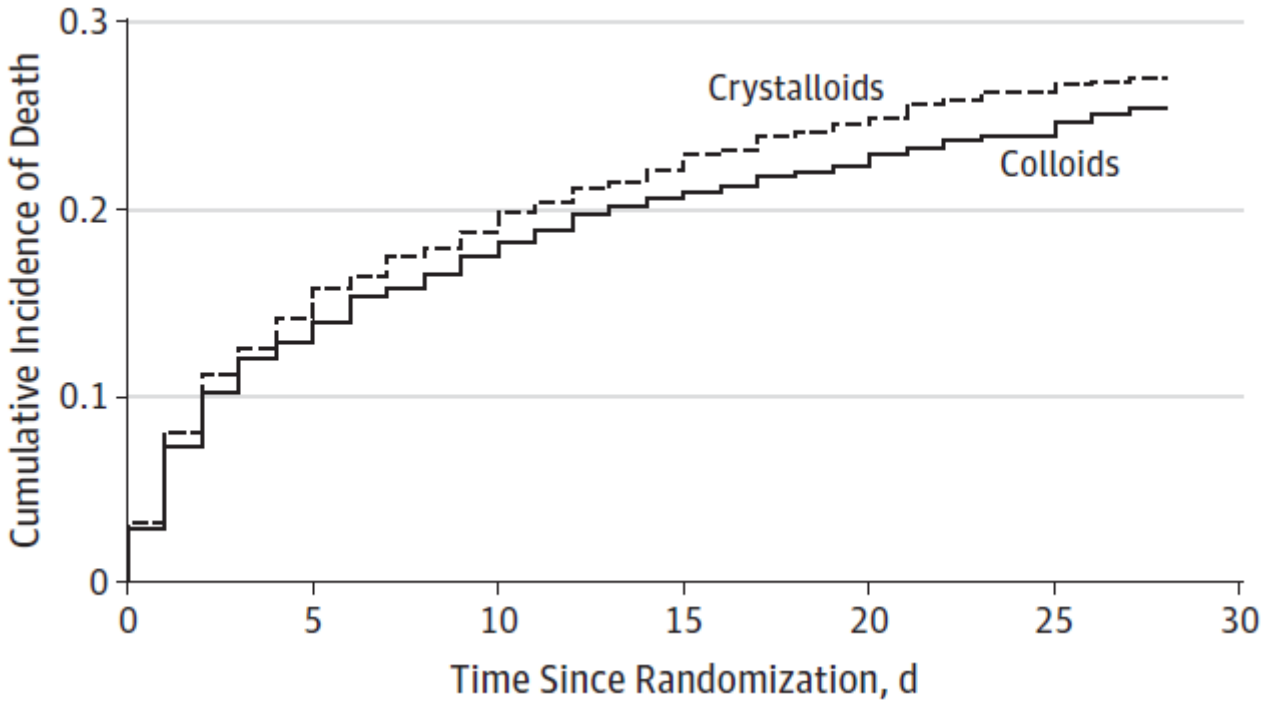
The CRISTAL Randomized Trial

Djillali Annane, MD, PhD; Shidasp Siami, MD; Samir Jaber, MD, PhD; Claude Martin, MD, PhD; Souheil Elatrous, MD; Adrien Descorps Declère, MD; Jean Charles Preiser, MD; Hervé Outin, MD; Gilles Troché, MD; Claire Charpentier, MD; Jean Louis Trouillet, MD; Antoine Kimmoun, MD; Xavier Forceville, MD, PhD; Michael Darmon, MD; Olivier Lesur, MD, PhD; Jean Régnier, MD; Fékri Abroug, MD; Philippe Berger, MD; Christophe Clec'h, MD, PhD; Joël Cousson, MD; Laure Thibault, MD; Sylvie Chevret, MD, PhD; for the CRISTAL Investigators

CRISTAL

JAMA. 2013;310(17):1809-1817. doi:10.1001/jama.2013.280502
Published online October 9, 2013.

Cumulative death within first 28d



JAMA. 2013;310(17):1809-1817. doi:10.1001/jama.2013.280502
Published online October 9, 2013.

Patients with severe sepsis

	colloids	crystalloids
n	774	779
d28 mortality	27.7	29
d90 mortality	32.5	36.7

JAMA. 2013;310(17):1809-1817. doi:10.1001/jama.2013.280502
Published online October 9, 2013.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

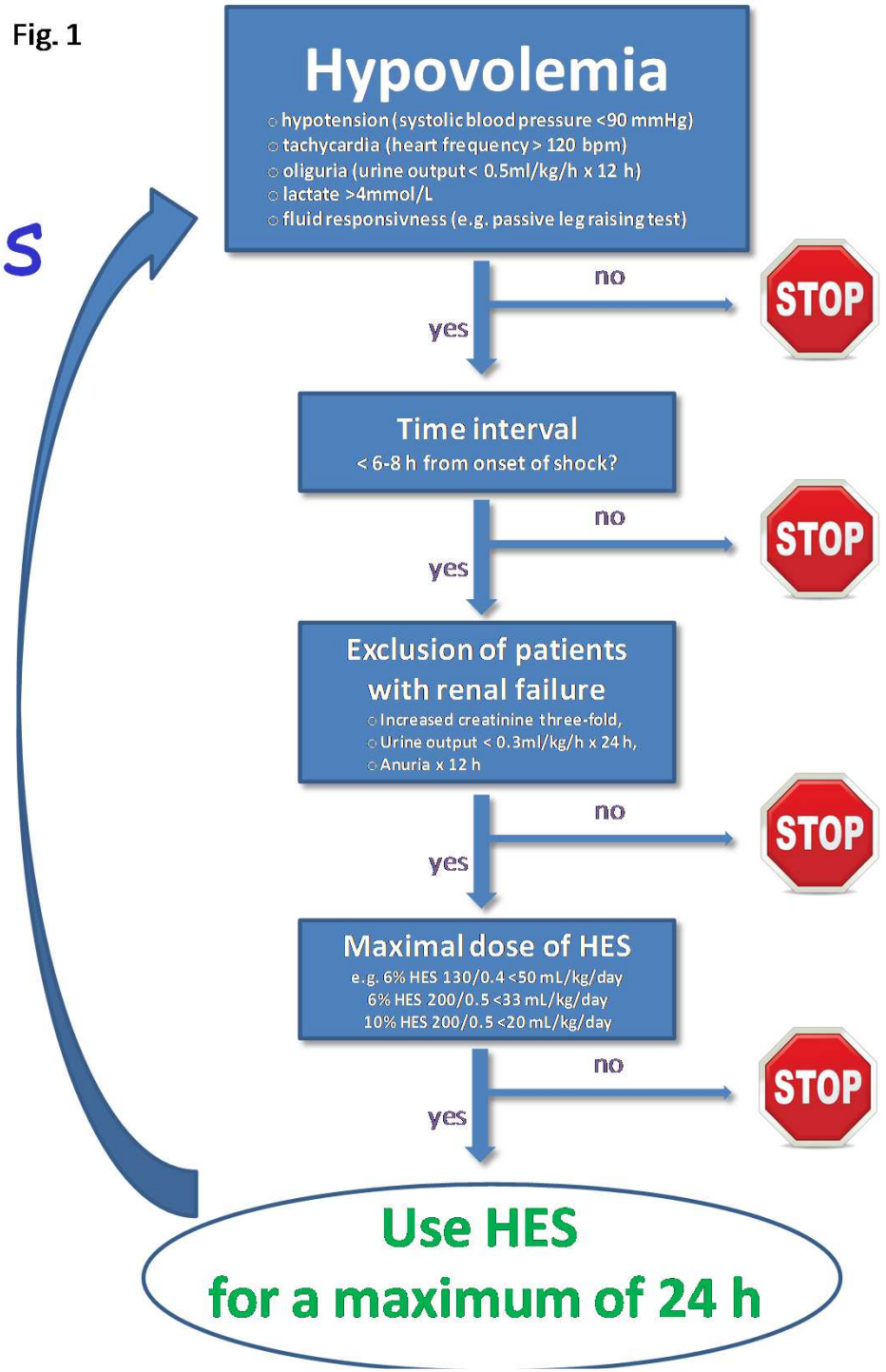
19 December 2013
EMA/809470/2013

Hydroxyethyl-starch solutions (HES) no longer to be used in patients with sepsis or burn injuries or in critically ill patients

HES will be available in restricted patient populations

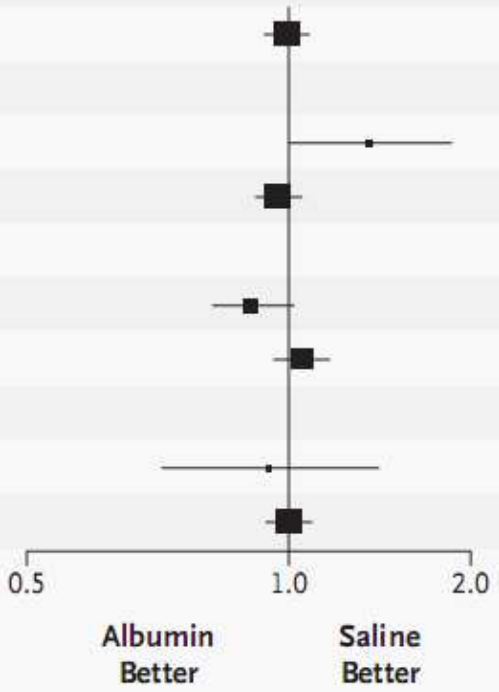
Algorithm strict pour l'indication des HES et autres colloides ?

Fig. 1



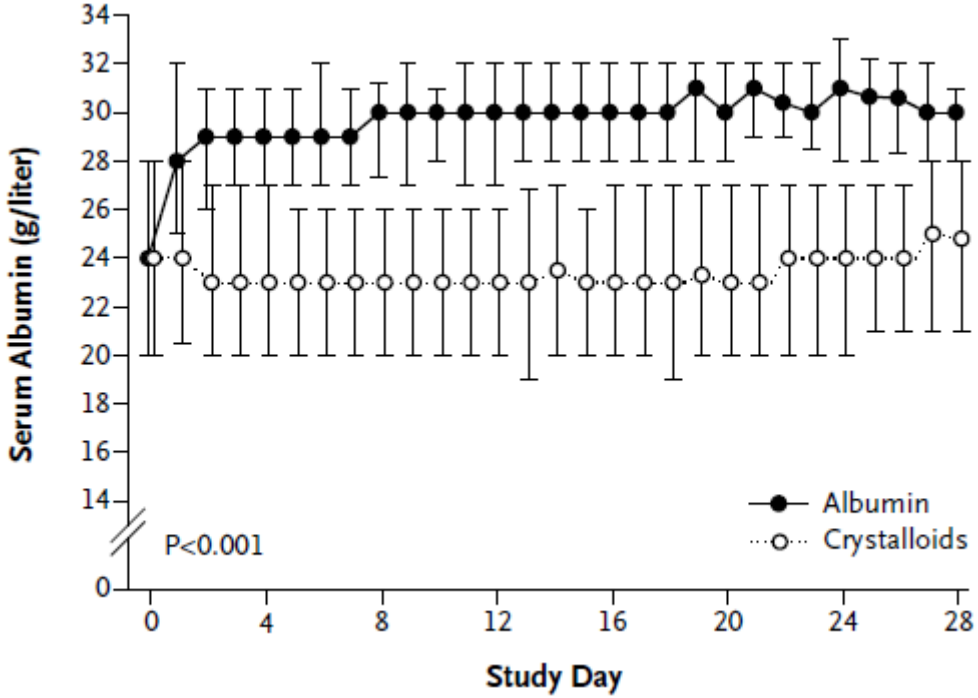
4% Albumin vs Isotonic saline

Patients	Albumin Group	Saline Group	Relative Risk (95% CI)
	no. of deaths/total no.		
Overall	726/3473	729/3460	0.99 (0.91–1.09)
Trauma			
Yes	81/596	59/590	1.36 (0.99–1.86)
No	641/2831	666/2830	0.96 (0.88–1.06)
Severe sepsis			
Yes	185/603	217/615	0.87 (0.74–1.02)
No	518/2734	492/2720	1.05 (0.94–1.17)
ARDS			
Yes	24/61	28/66	0.93 (0.61–1.41)
No	697/3365	697/3354	1.00 (0.91–1.09)



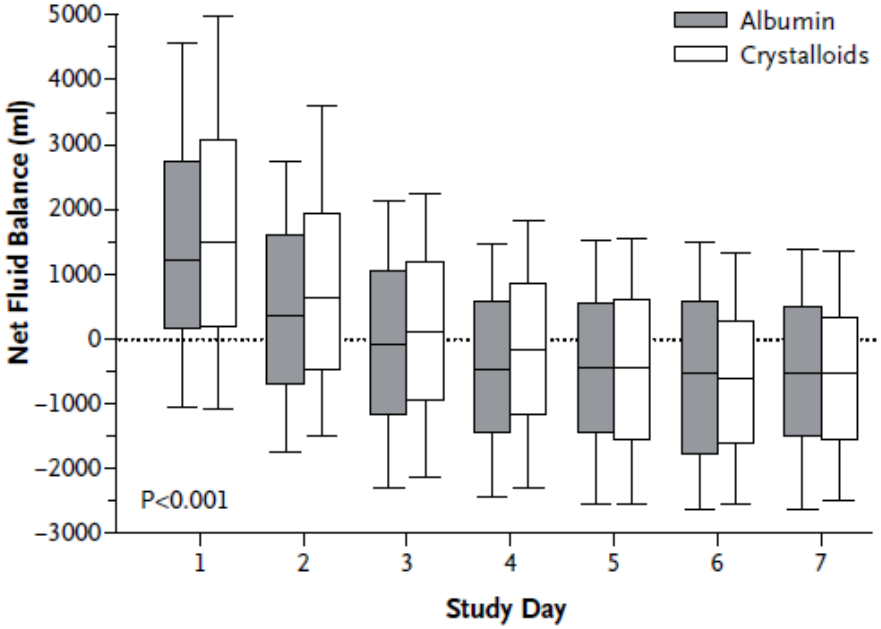
The Safe Study Investigators. N Engl J Med 2004 ; 350:2247-56

Albuminemia & fluid balance

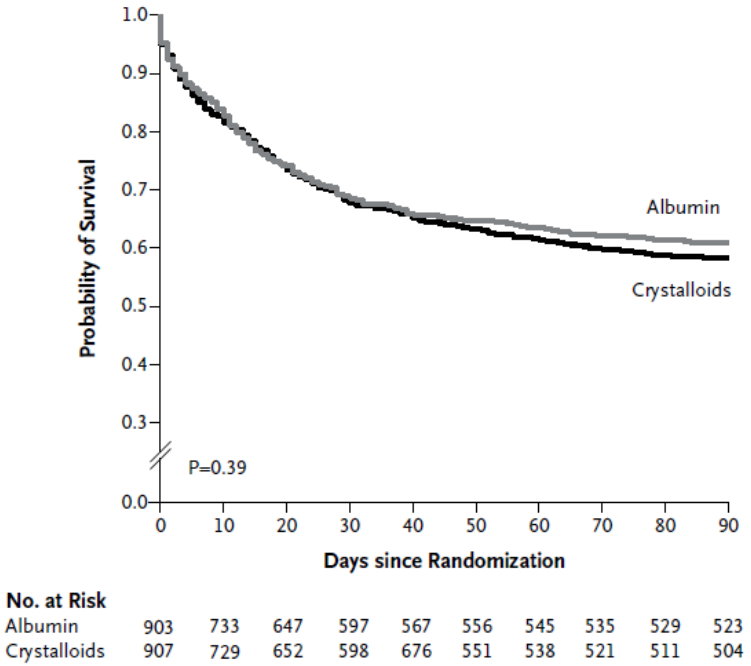


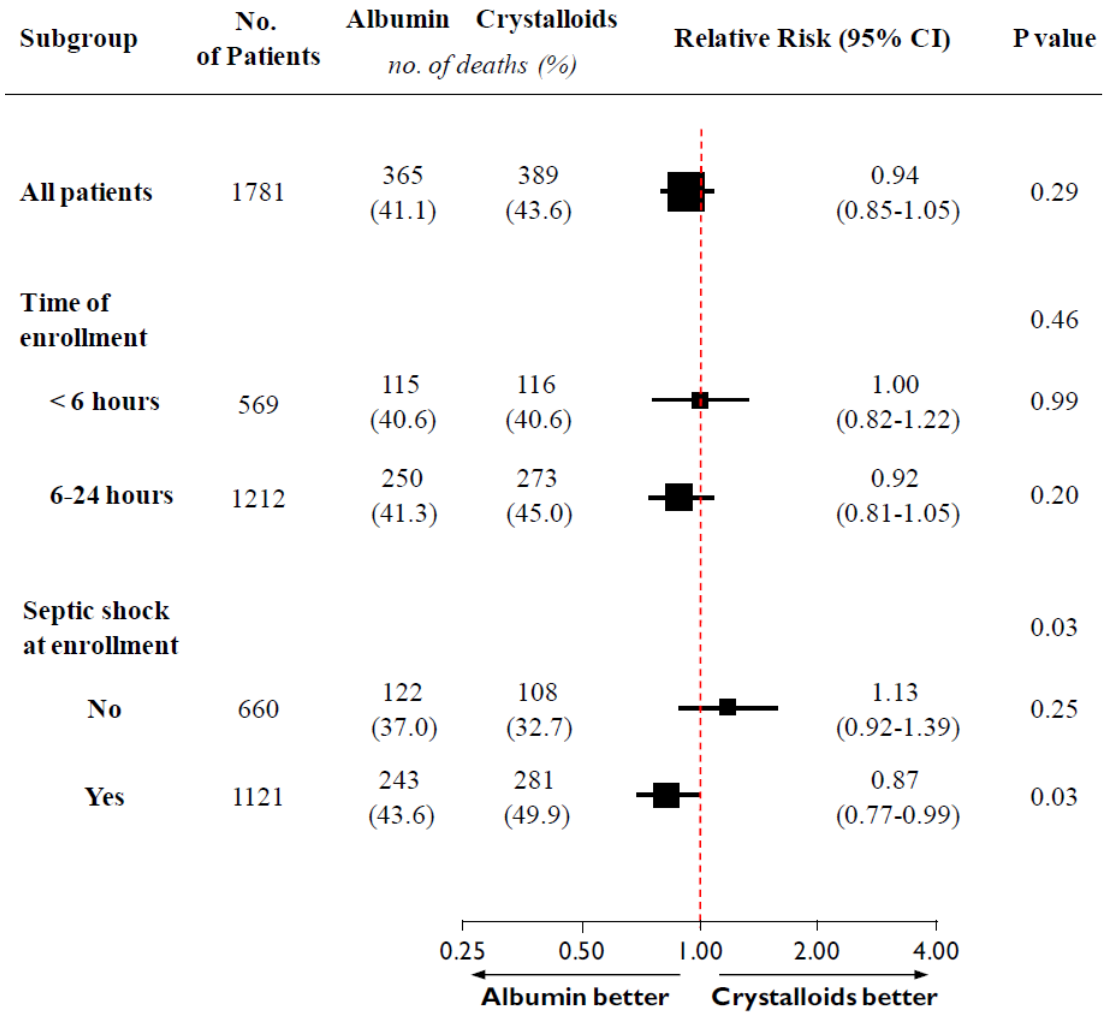
ALBIOS

N ENGL J MED 370;15 NEJM.ORG APRIL 10, 2014

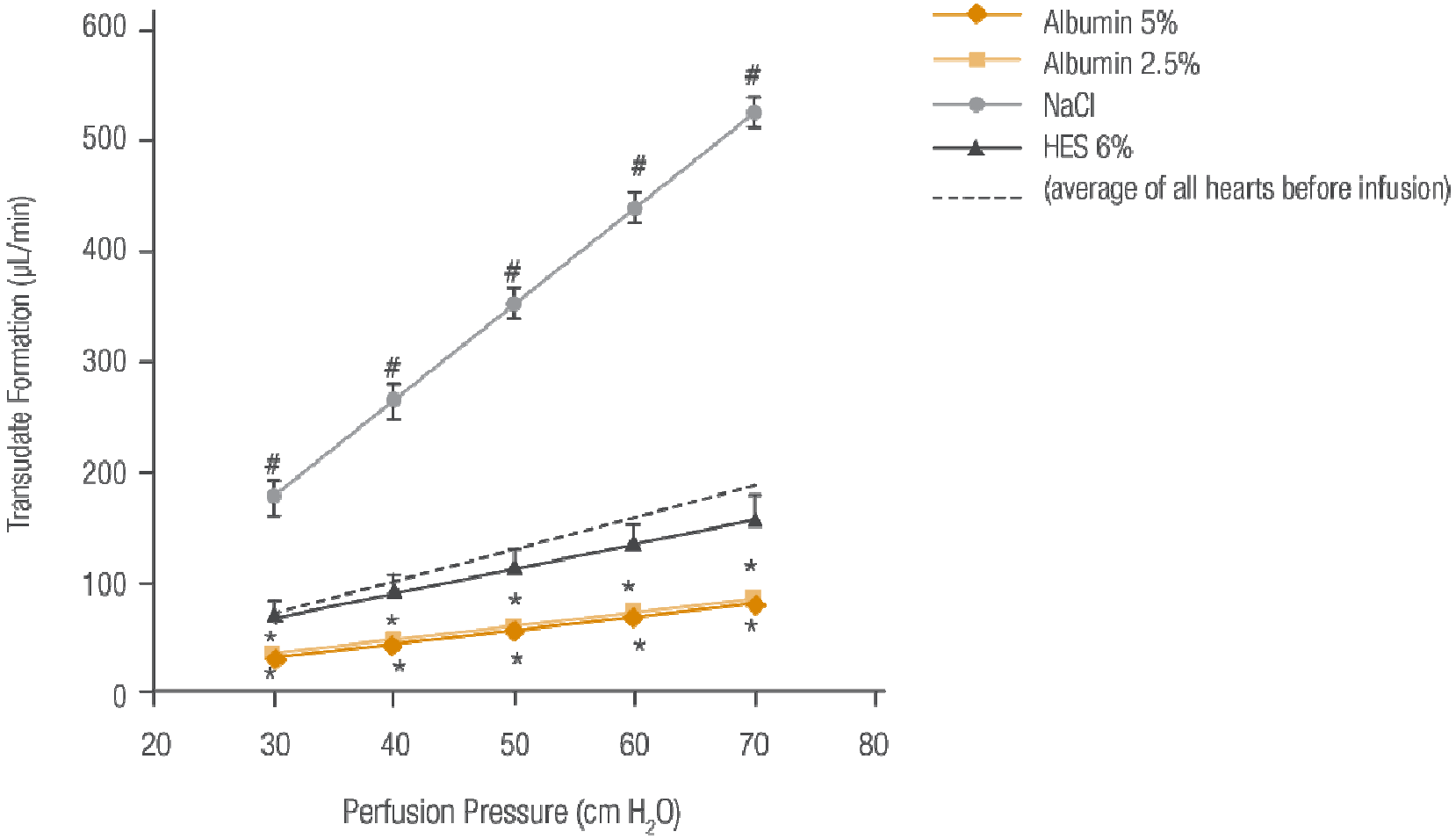


Probability of survival





Albumine versus autres solutés



Moret E. *et al.* Semin Cardiothorac Vasc Anesth. 2014;18(3):252-9. 2. Jacob M. *et al.* Anesthesiology. 2006;104(6):1223-31.

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http://ccforum.com/content/18/4/231

CRITICAL CARE

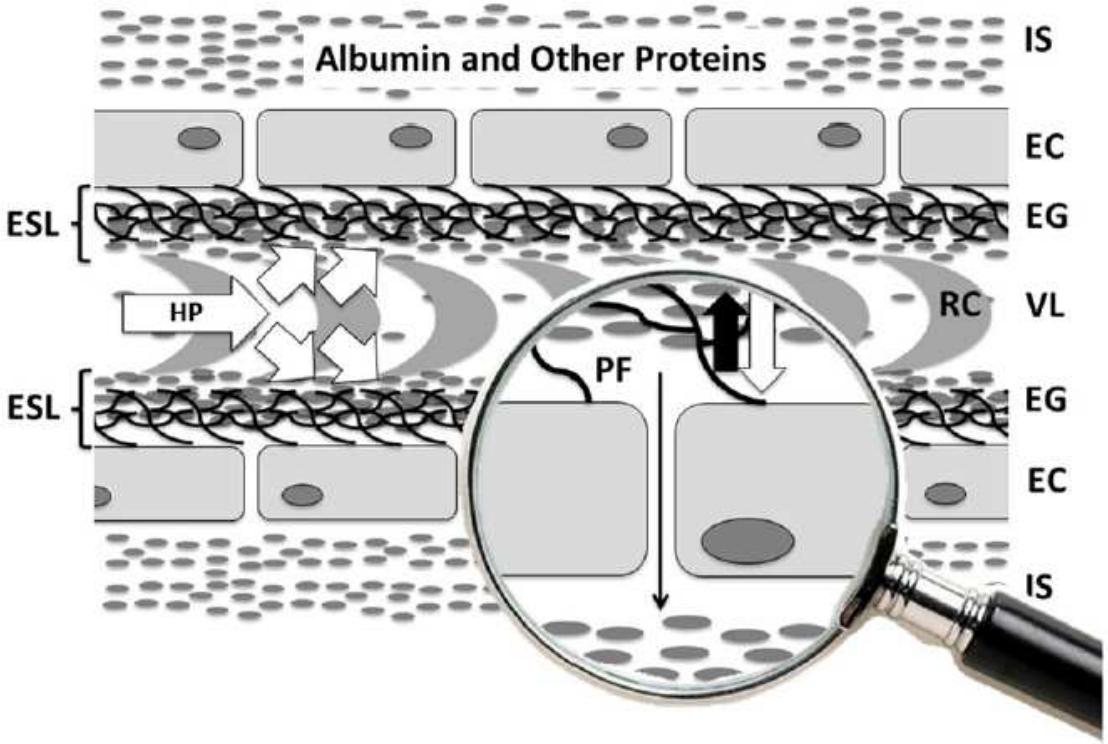
REVIEW

Albumin administration in the acutely ill: what is new and where next?

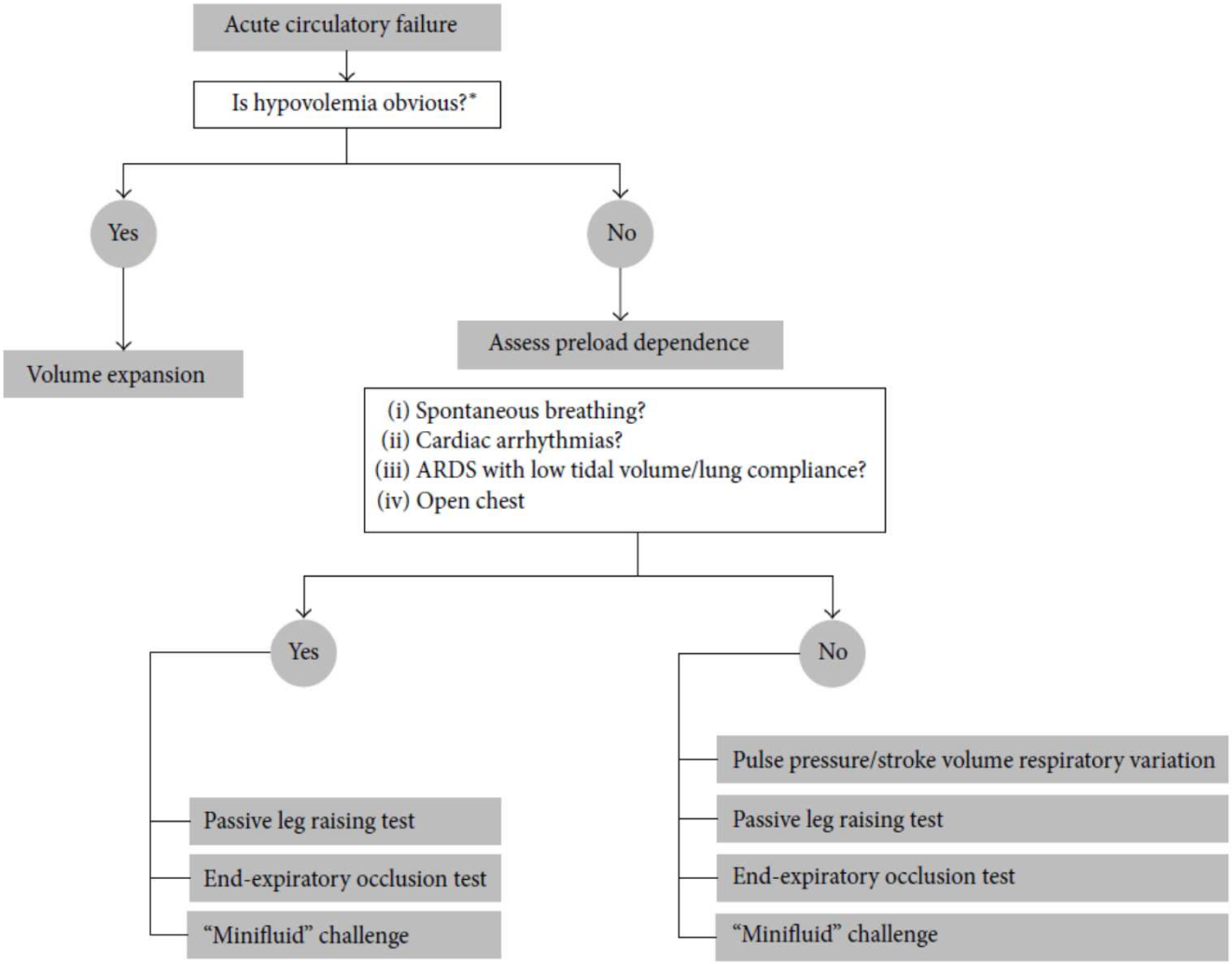
Jean-Louis Vincent[1*], James A Russell[2], Matthias Jacob[3], Greg Martin[4], Bertrand Guidet[5,6], Jan Wernerman[7], Ricard Ferrer Roca[8], Stuart A McCluskey[9] and Luciano Gattinoni[10]

Propriétés oncotiques

Propriétés non oncotiques
anti-oxydant
Immunomodulateur
Anti-inflammatoire
Stabilisation endothéliale
Perméabilité vasculaire
Transport coagulation

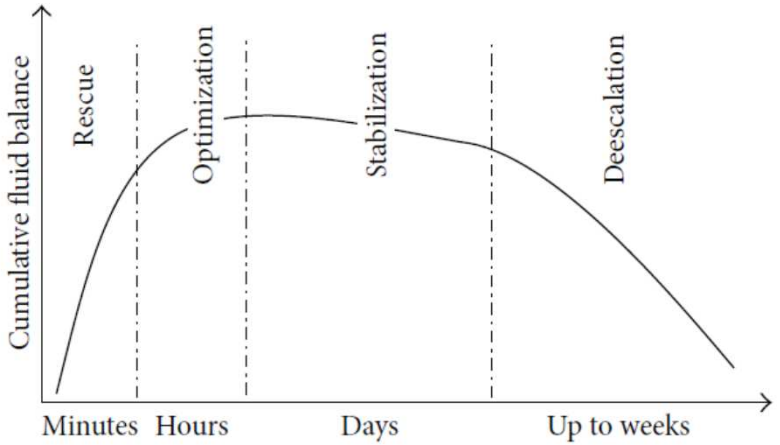


Remplissage raisonné



Remplissage : la temporalité

	Rescue	Optimization	Stabilization	Deescalation
Treatment goal	Shock reversal/Life salvage	Adequate tissue perfusion	Zero-to-negative daily fluid balance	Fluid accumulation reversal/edema resolution
Time course	Minutes	Hours	Days	Up to weeks
Hemodynamic targets	Autoregulatory thresholds of perfusion pressure	Micro/macrocirculatory blood flow parameters	Weaning of vasopressors with stable hemodynamic conditions	Return to premorbid/chronic values of pressure and flow
Treatment options	Rapid fluid boluses + vasopressors	Repeated fluid challenges + vasopressors + Inotropes	Maintenance fluids + decreasing/chronic vasoactive agents	Diuretics or other means of fluid removal



BioMed Research International
Volume 2015, Article ID 729075, 14 pages

Recommandations sur la réanimation du choc hémorragique☆

Jacques Duranteau [1], Karim Asehnoune [2], Sébastien Pierre [3], Yves Ozier [4], Marc Leone [5], Jean-Yves Lefrant [6], le groupe de travail de la Société française d'anesthésie et de réanimation (Sfar), de la Société de réanimation de langue française (SRLF), de la Société française de médecine d'urgence (SFMU), du Groupe d'études sur l'hémostase et la thrombose (GEHT)

- Hypotension « permissive »
  - PAS 80- 90 mmHg – PAM 60-65 mmHg
  - Sujet âgé – hypertendu chronique?

- Cas particulier traumatisé cranien
  - PAM>80 mmHg

- Cristalloides en 1ere intention

- Pas de soluté hypotonique si TC grave
- HEA si cristalloides insuffisants
- Albumine non recommandée

Intensive Care Med
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

1. We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve (BPS).
2. We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).

3. We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock (weak recommendation, low quality of evidence).
4. We suggest using albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock, when patients require substantial amounts of crystalloids (weak recommendation, low quality of evidence).
5. We recommend against using hydroxyethyl starches for intravascular volume replacement in patients with sepsis or septic shock (strong recommendation, high quality of evidence).
6. We suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock (weak recommendation, low quality of evidence).

Sepsis : update 2018

- Measure lactate level. Remeasure if initial lactate is >2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate ≥4 mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg.

**"Time zero" or "time of presentation" is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of sepsis (formerly severe sepsis) or septic shock ascertained through chart review.*

Fig. 1 Hour-1 Surviving Sepsis Campaign Bundle of Care

Intensive Care Med , 2017: 43:3014677

Ce qu'il faut retenir

- Les cristalloides ont moins effets secondaires
- Le sérum salé induit une acidose hyperchlorémique
  - La pertinence clinique de cette AHC n'est pas démontrée
- Les marqueurs –cliniques, biochimiques et hémodynamiques – de perfusion tissulaire adéquate sont à définir
- Faut –il traiter une hypotension sans hypoperfusion?
- La(s) stratégie(s) pour améliorer le pronostic reste(nt) à définir
- Quel est le critère d' »outcome » à atteindre?

Remplissage mode d'emploi

- Je dois remplir précocément
- Je remplis avec des cristalloides en 1ère intention
- Je remplis avec des objectifs individualisés
- Je monitore mon remplissage avec les outils appropriés
  - Ceux dont je dispose- ceux que je maîtrise