

Albumine traitement de l'hypoprotidémie en réanimation

karim.asehnoune@chu-nantes.fr
Service d'Anesthésie-Réanimation, CHU Nantes, F-44000
France

Conflicts of interests

Baxter

LFB

Fisher and Paykel

Edwards

Physiologie

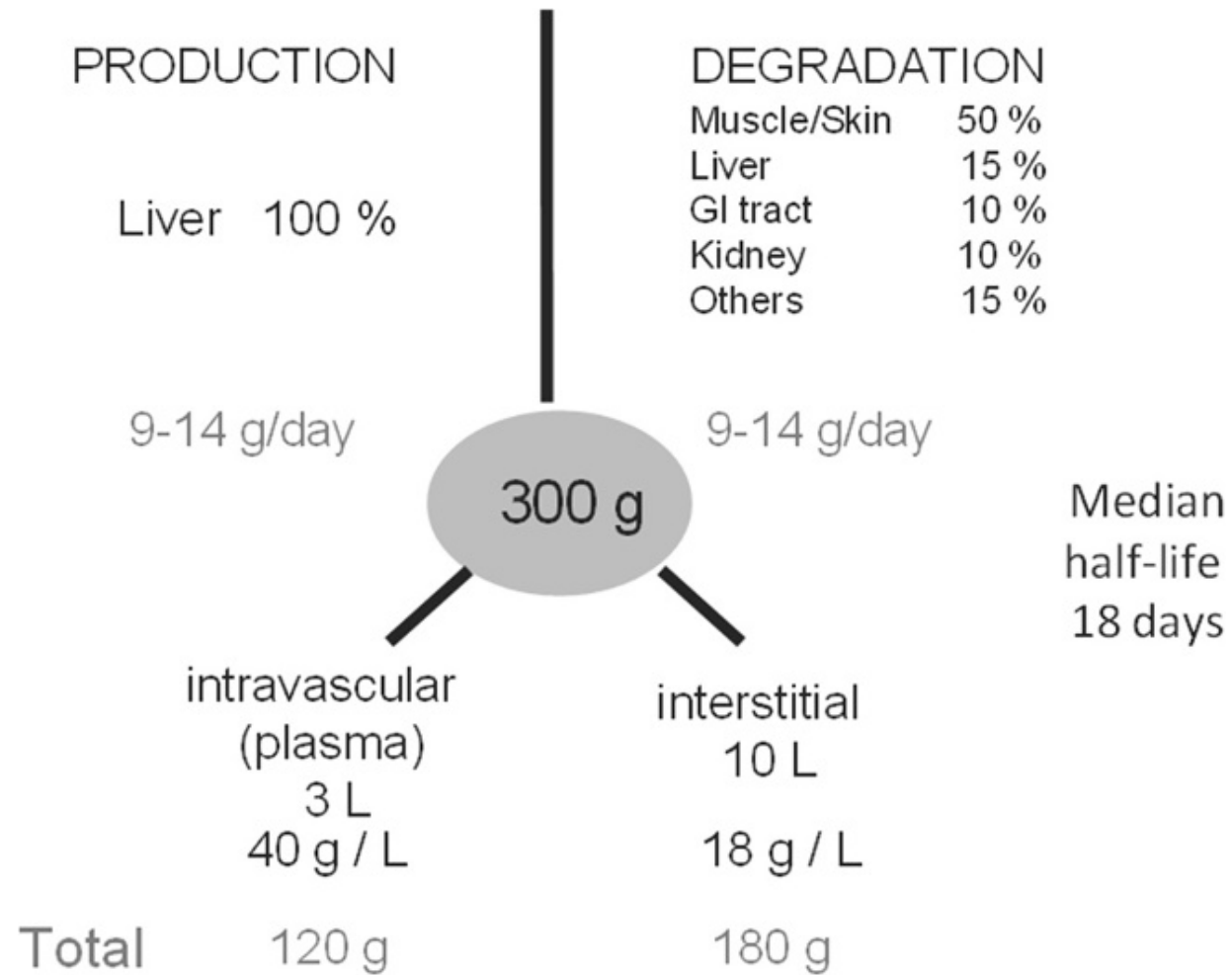
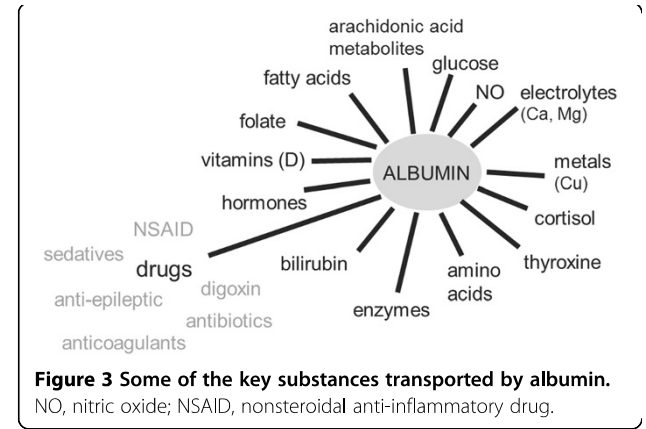


Figure 1 Schematic illustration of metabolism of albumin in healthy adults. GI, gastrointestinal.

albumin has multiple physiological effects

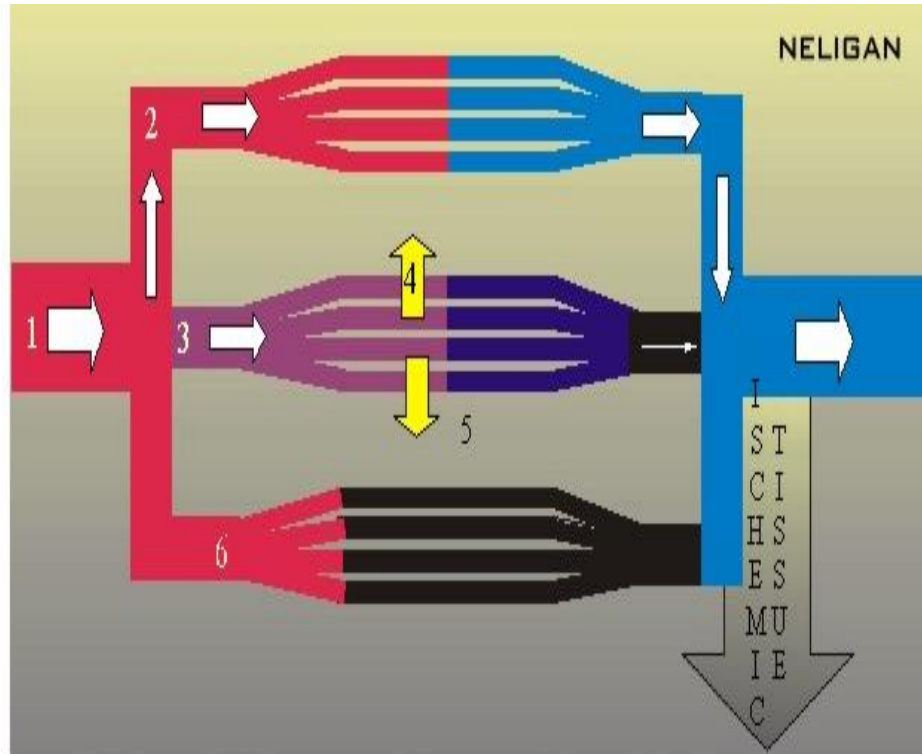
- regulation of colloid osmotic pressure (COP),
 - binding and transportation of various substances (for example, drugs, hormones),
 - antioxidant properties, nitric oxide modulation and buffer capabilities,
- low serum albumin levels, a common occurrence in critically ill patients, are associated with worse outcomes**

there is evidence to support its use in some patient populations

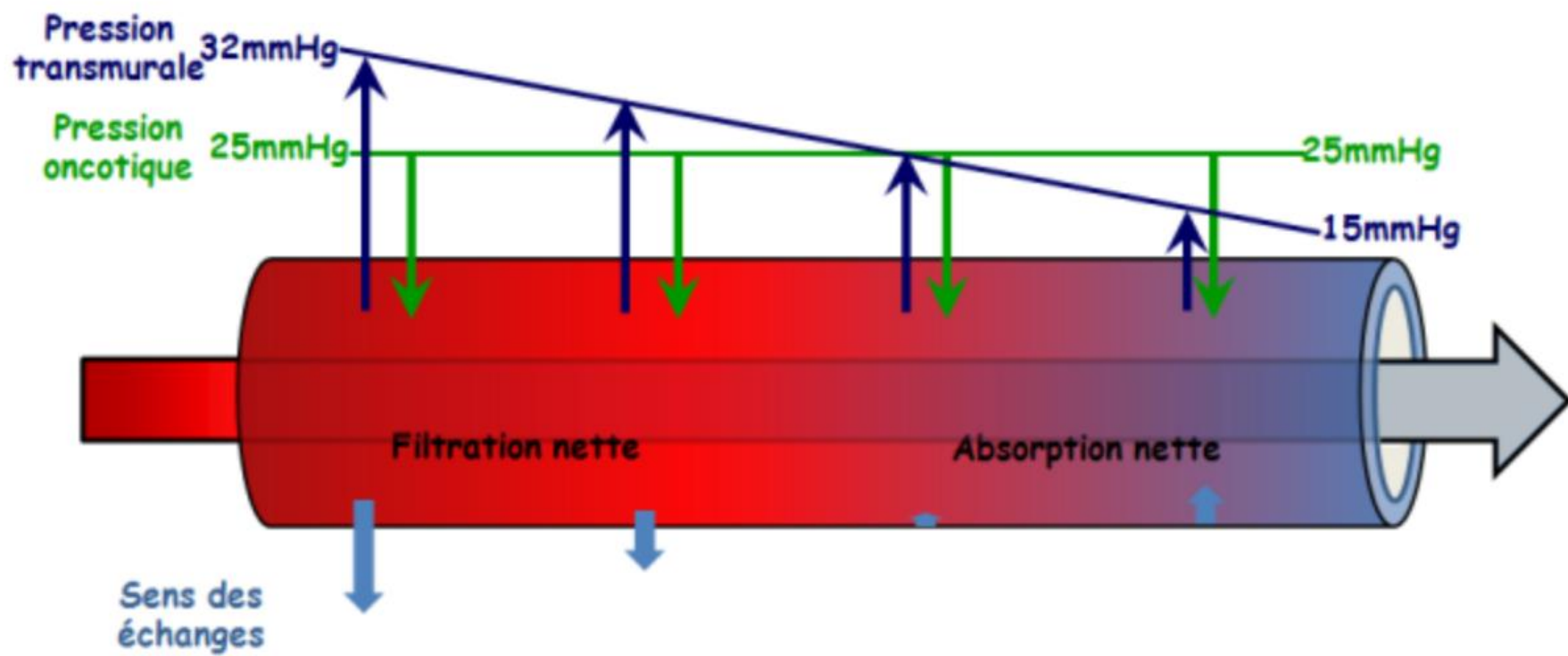


- Albumin decreases neutrophil activation induced by fluid infusion, crystalloids and synthetic colloids increase it. Rhee P, et al. *Crit Care Med* 2000; 28(1): 74-78.
- Albumin reduces TNF induced endothelial activation. Nohe et al *Intensive Care Med* 1999; 25: 1381-1385; Zhang et al *Cardiovasc Res*. 2002 Sep;55(4):820-9
- Albumin solution reverses the LPS induced albumin leakage across vessel walls. Powers KA, et al. *Crit Care Med* 2003; 31: 2355-63 ;Anning PB et *Intensive Care Med*. 2004 Oct;30(10):1944-9
- Albumin infusion results in sustained thiol levels in septic patients. Quinlan G, et al. *Clin Sci* 1998; 95: 459-65.

Effet oncotique



1. Vasodilation leads to slow organ perfusion pressure
2. capillary leak, resulting in
3. edematous tissues, tissue compression and prevention of oxygen exchange
4. Due to venous stasis and activation of coagulation, small vessels become obstructed and blood flow stops



Pression oncotique et pression transmurale

RESEARCH

Open Access

The intravascular volume effect of Ringer's lactate is below 20%: a prospective study in humans

Matthias Jacob^{1*}, Daniel Chappell^{1†}, Klaus Hofmann-Kiefer¹, Tobias Helfen¹, Anna Schuelke¹, Barbara Jacob¹, Alexander Burges², Peter Conzen¹ and Markus Rehm¹

- 10 volontaires sains

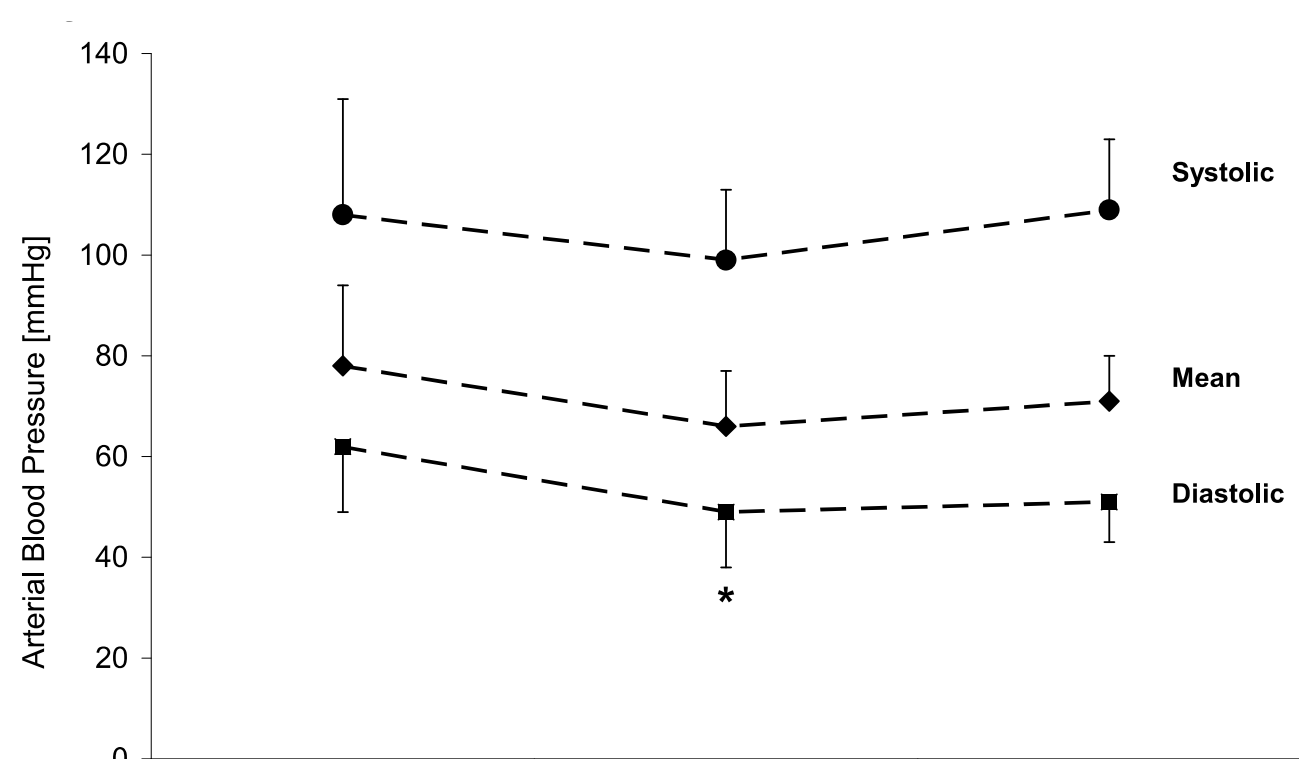
Hemodilution normovolémique

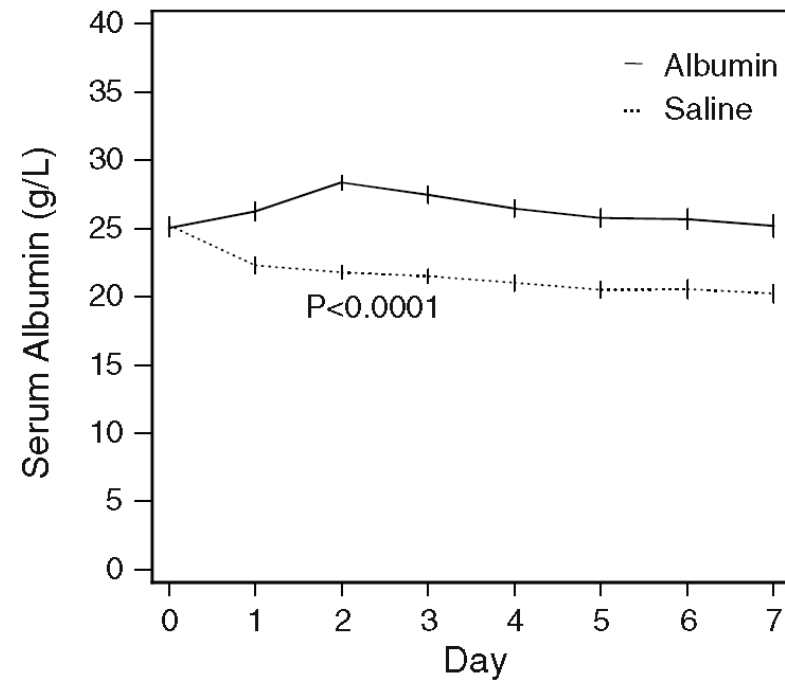
Restauration volumique

- 3000 RL : - 460 ml BV
- 250 ml Alb (20%) restauration BV

Effet volume

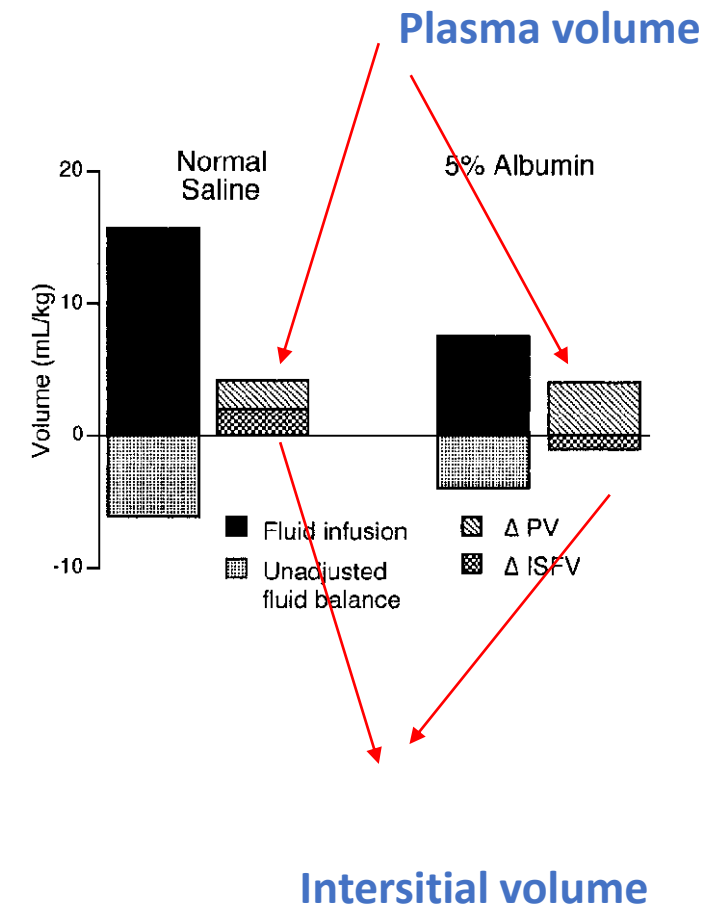
- RL 17%
- Alb 184%





SAFE investigators Int Care Med 2011, 37 (1), 86-96

- 40 patients post CEC
- Cible hémodynamique



Hypoalbuminémie

- Serum albumine concentration < 30 g/l
- Pertes
 - Hémorragie
 - Perte digestives
 - Défaillance d'organe
- ATCD
 - Dénutrition
 - Âge
 - Pathologie hépatiques

Traiter l'hypoalbuminémie
ou pas?

Risk Factors for Hospital-acquired Bacteremia

Takuhiro YOSHIDA, Kenji TSUSHIMA, Ayako TSUCHIYA, Noriko NISHIKAWA,
Kumiko SHIRAHATA, Kazuma KANEKO, Ken-ichi ITO, Hirotaka KAWAKAMI,
Shin-ichi NAKAGAWA, Toshiro SUZUKI*, Keishi KUBO** and Shu-ichi IKEDA***

406 patients dont 176 ICU

Table 3. Comparison of Laboratory Data between Blood Culture-positives and -negative cases

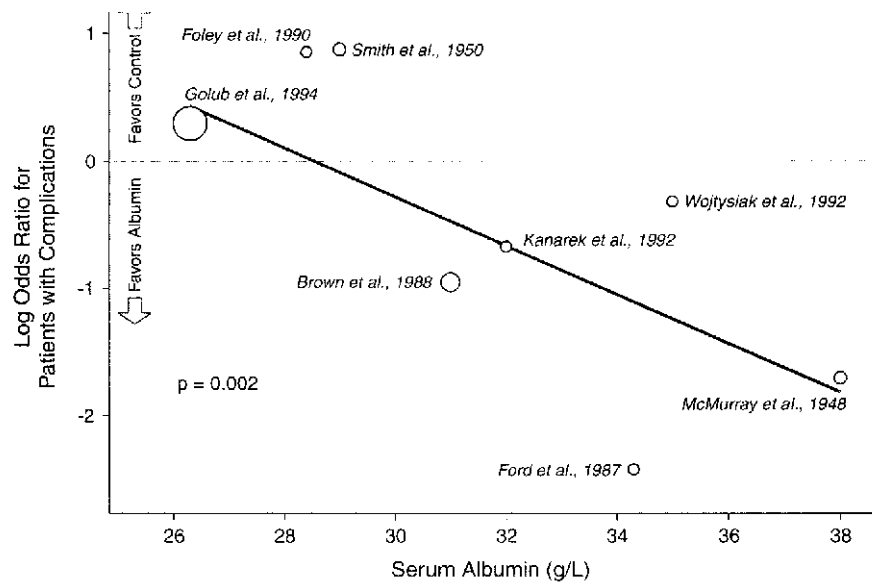
Variable	Culture-positive	Culture-negative	P-value (Univariate)	P-value (Multivariate)	AUC
Age	75.8±2.1	71.0±1.1	0.019		
Neutrophil (/mm ³)	10,784±866	8,519±434	0.01		
C-reactive protein (mg/dl)	11.6±9.1	11.1±11.3	0.358		
Platelet (×10 ⁴ /mm ³)	19.7±11.5	23.8±11.8	0.006	0.04	0.574
Total cholesterol (mg/dl)	157±49	155±39	0.396		
Total protein (g/dl)	6.3±1.0	6.6±0.8	0.009		
Albumin (g/dl)	3.2±0.6	3.5±0.6	<0.001	<0.001	0.644
Cholinesterase (U/dl)	161±71	192±81	0.003		

Hypoalbuminemia in Acute Illness: Is There a Rationale for Intervention?

A Meta-Analysis of Cohort Studies and Controlled Trials

Jean-Louis Vincent, MD, PhD, FCCM,* Marc-Jacques Dubois, MD,* Roberta J. Navickis, PhD,† and Mahlon M. Wilkes, PhD†

90 études
>290 000 patients



Cut-off morbidité >30g/l

safe

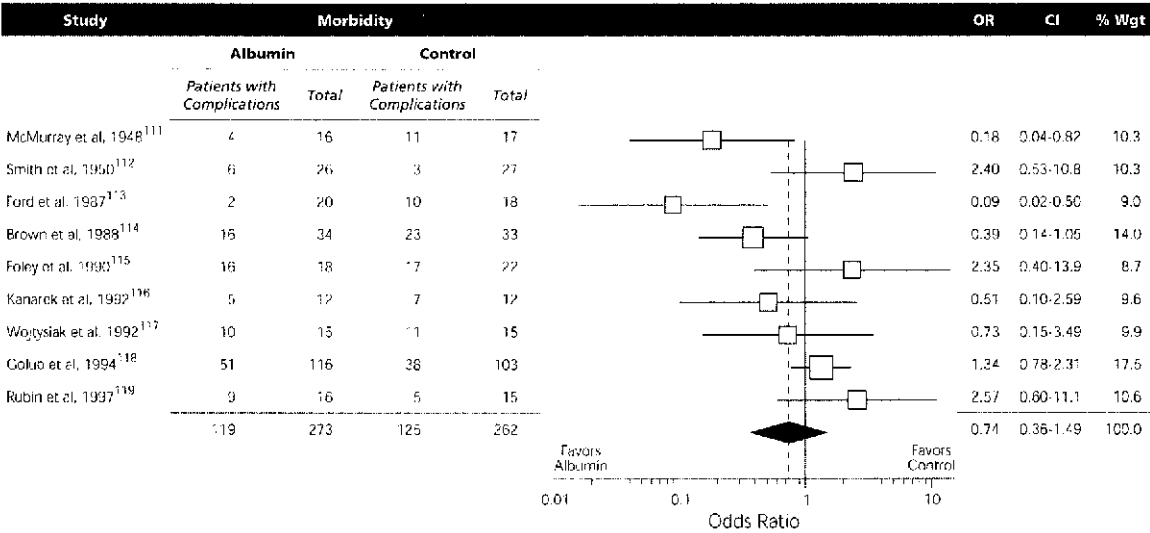


Figure 3. Morbidity in controlled trials evaluating the correction of hypoalbuminemia.

Par 10g de diminution
137% OR of death
89% morbidity
71% durée de séjour

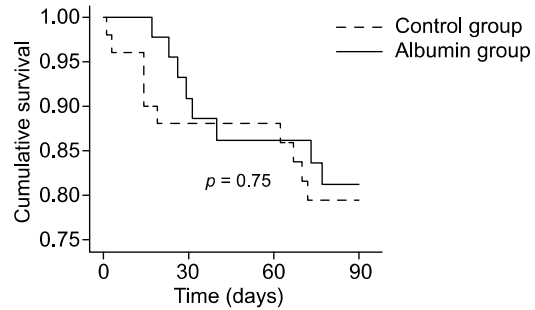
EFFECT OF INTRAVENOUS ALBUMIN ON RENAL IMPAIRMENT AND MORTALITY
IN PATIENTS WITH CIRRHOSIS AND SPONTANEOUS BACTERIAL PERITONITIS

PAU SORT, M.D., MIQUEL NAVASA, M.D., VICENTE ARROYO, M.D., XAVIER ALDEGUER, M.D., RAMON PLANAS, M.D.,
LUIS RUIZ-DEL-ARBOL, M.D., LLUIS CASTELLS, M.D., VICTOR VARGAS, M.D., GERMÁN SORIANO, M.D.,
MÓNICA GUEVARA, M.D., PERE GINÉS, M.D., AND JOAN RODÉS, M.D.

OUTCOME VARIABLE	CEFOTAXIME (N=63)	CEFOTAXIME PLUS ALBUMIN (N=63)	P VALUE
Resolution of infection — no. (%)†	59 (94)	62 (98)	0.36
Duration of antibiotic therapy — days	6±1	5±1	0.48
Paracentesis for ascites after resolution of infection — no. (%)‡	16 (25)	14 (22)	0.83
Hospital stay — days	13±1	14±1	0.48
Renal impairment — no. (%)	21 (33)	6 (10)	0.002
Death — no. (%)			
In hospital§	18 (29)	6 (10)	0.01
At three months¶	26 (41)	14 (22)	0.03

- 126 patients
- Alb 20% 1.5 g/kg D1 and D3
- IR et mortalité

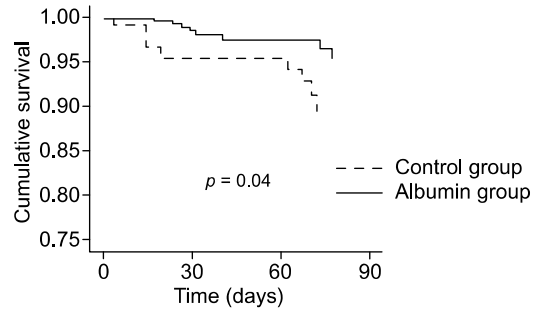
Non ajustée



Ajustée

Patients at risk

Control group	51	45	42	38
Albumin group	46	40	35	32



Albumin for bacterial infections other than spontaneous bacterial peritonitis in cirrhosis. A randomized, controlled study[☆]

Mónica Guevara^{1,2,3,4,†}, Carlos Terra^{1,2,3,4,†}, André Nazar^{1,2,3,4}, Elsa Solà^{1,2,3,4}, Javier Fernández^{1,2,3}, Marco Pavesi^{1,2,3}, Vicente Arroyo^{1,2,3}, Pere Ginès^{1,2,3,4,*}



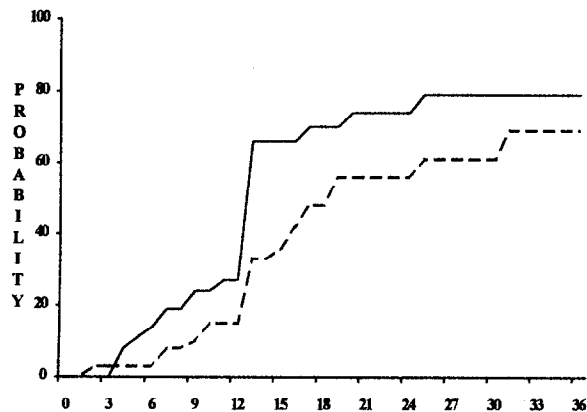
- 110 patients
- Alb 20% 1.5 g/kg D1 and D3
- Mortalité à 3 mois

Albumin improves the response to diuretics in patients with cirrhosis and ascites: results of a randomized, controlled trial

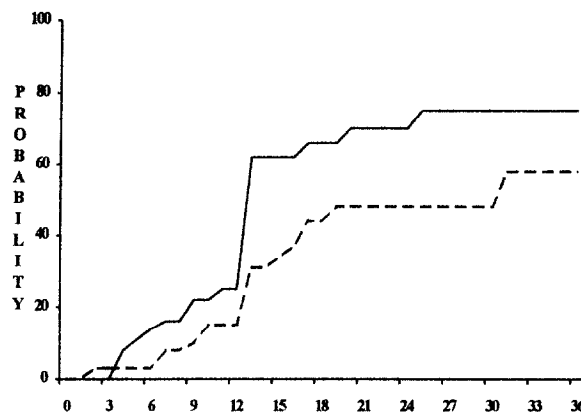
Paolo Gentilini, Vincenzo Casini-Raggi, Giuseppe Di Fiore, Roberto Giulio Romanelli,
Giampiero Buzzelli, Massimo Pinzani, Giorgio La Villa and Giacomo Laffi
Institute of Internal Medicine, University of Florence School of Medicine, Florence, Italy

- >1000 patients
- Ascite refractaire repos lit/restriction sodique

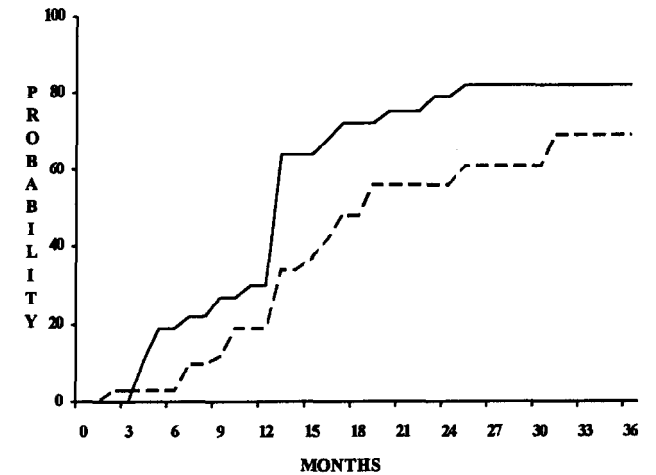
Toutes causes



Cause ascite



Re hospitalisation



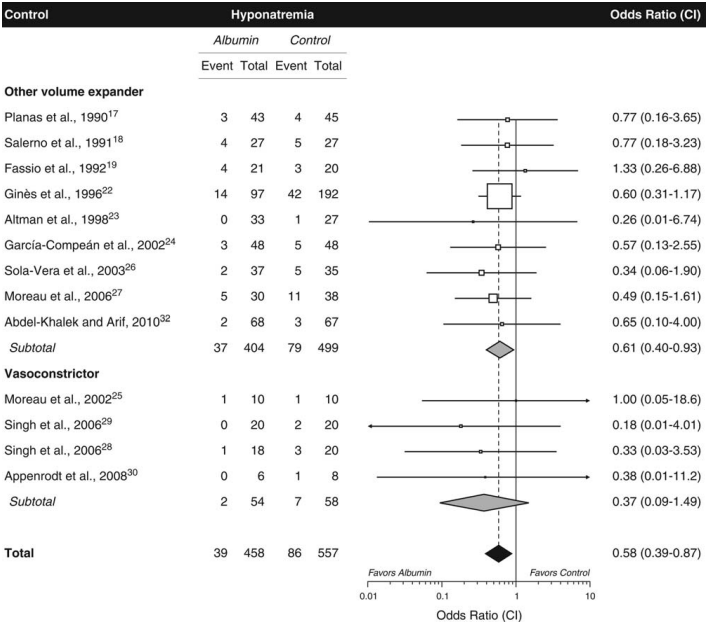
Recurrence ascite

— Furosémide
- - - Furosemide+Alb 20%

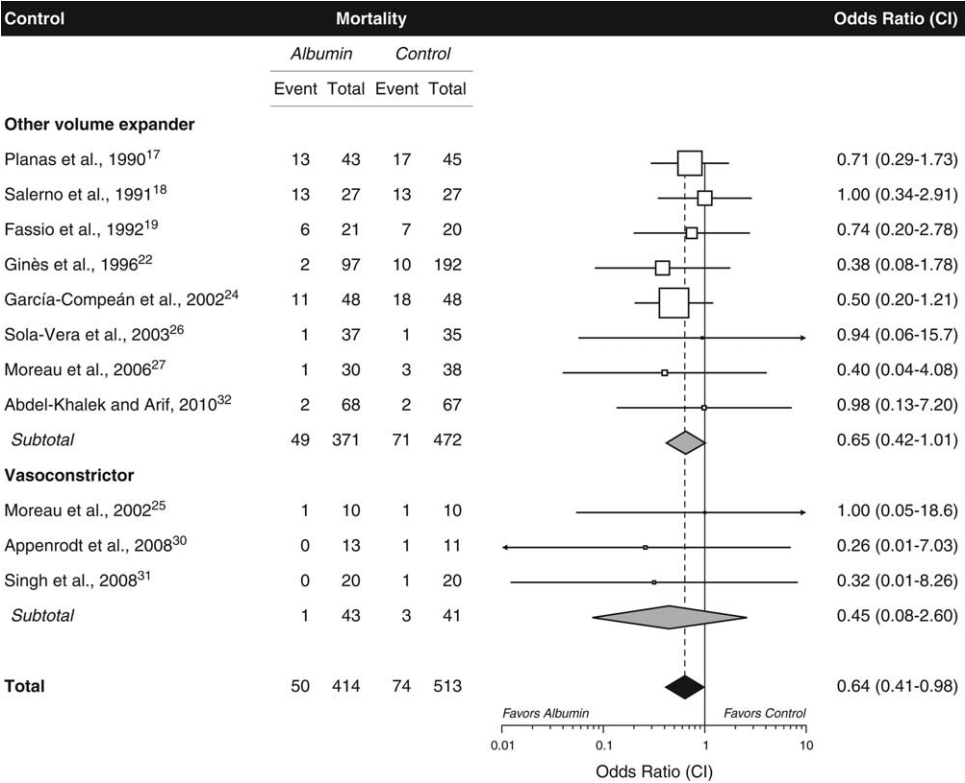
Albumin Infusion in Patients Undergoing Large-Volume Paracentesis: A Meta-Analysis of Randomized Trials

Mauro Bernardi,¹ Paolo Caraceni,¹ Roberta J. Navickis,² and Mahlon M. Wilkes²

Hyponatrémie



Mortalité



- 17 études 1225 patients
- Pas d'hétérogénéité ou de biais
- Objectif principal hypoNa, mortalité



Guidelines

Management of liver failure in general intensive care unit☆☆☆☆

C. Paugam-Burtz^{1,2}, E. Levesque^{3,4}, A. Louvet⁵, D. Thabut⁶, R. Amathieu^{7,8},
C. Bureau^{9,10,11}, C. Camus¹², G. Chanques¹³, S. Faure¹⁴, M. Ferrandière¹⁵, C. Francoz^{16,17},
A. Galbois¹⁸, T. Gustot^{19,20}, C. Ichai²¹, P. Ichai^{22,23,24}, S. Jaber²⁵, T. Lescot²⁶,
R. Moreau^{27,28,29,30}, S. Roullet^{31,32}, F. Saliba³³, T. Thévenot³⁴, L. Velly^{35,36}, E. Weiss^{37,38,*}



R5.2 – In patients with cirrhosis hospitalised in the ICU, we suggest treating hepatorenal syndrome with a vasoconstrictor agent (terlipressin as first-line therapy) and concentrated albumin

GRADE 2+, STRONG AGREEMENT

R7.1 – In cirrhotic patients hospitalised in the ICU, we recommend the use of a concentrated albumin infusion after high-volume paracentesis (more than 4 to 5 litres of ascites fluid removed)

GRADE 1+, STRONG AGREEMENT

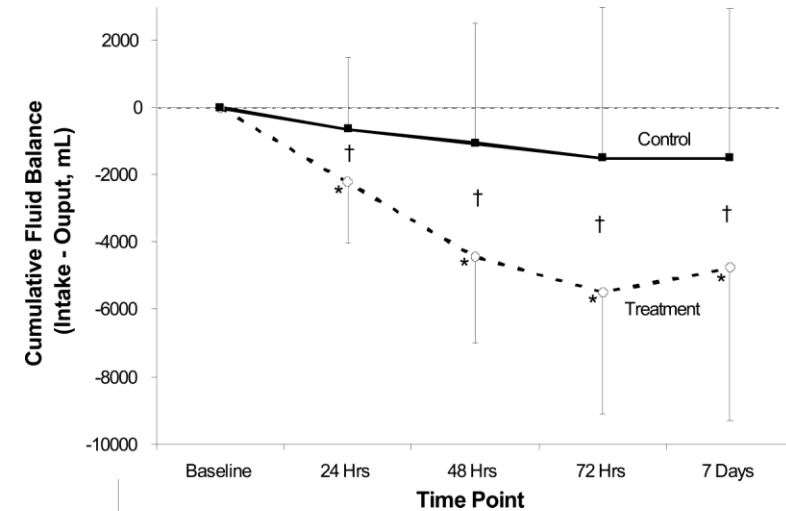
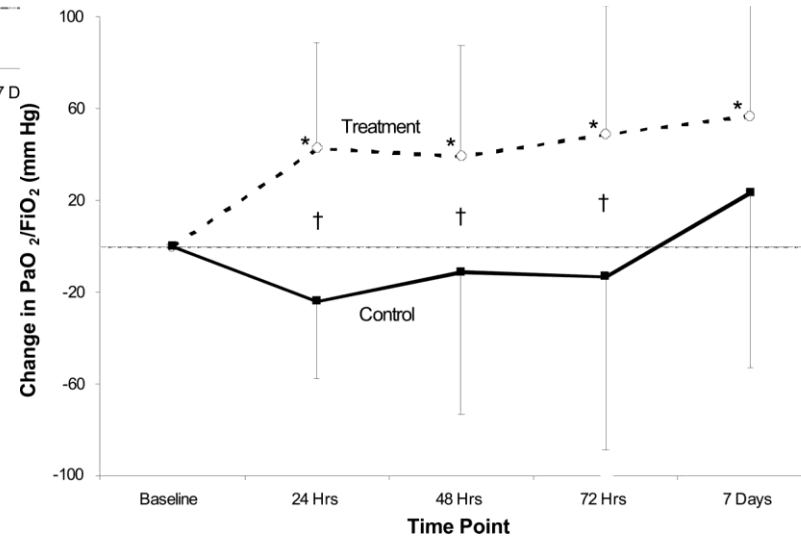
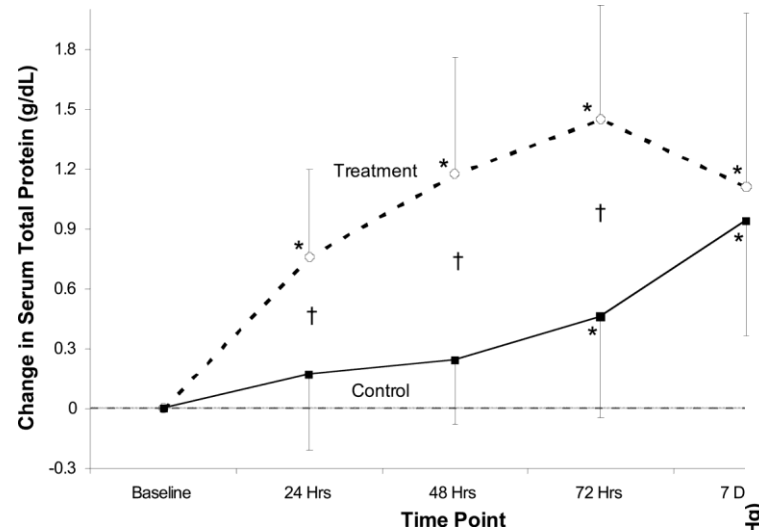
R7.2 – In patients with cirrhosis hospitalised in the ICU, we suggest that concentrated albumin infusions should be used in the event of spontaneous bacterial peritonitis (SBP)

GRADE 2+, STRONG AGREEMENT

A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury*

Greg S. Martin, MD, MSc; Marc Moss, MD; Arthur P. Wheeler, MD; Meredith Mealer, RN;
John A. Morris, MD; Gordon R. Bernard, MD

40 patients hypoprotidémiques
Furosemide versus
furosemide + Alb 20% (dose titrée sur protidémie)

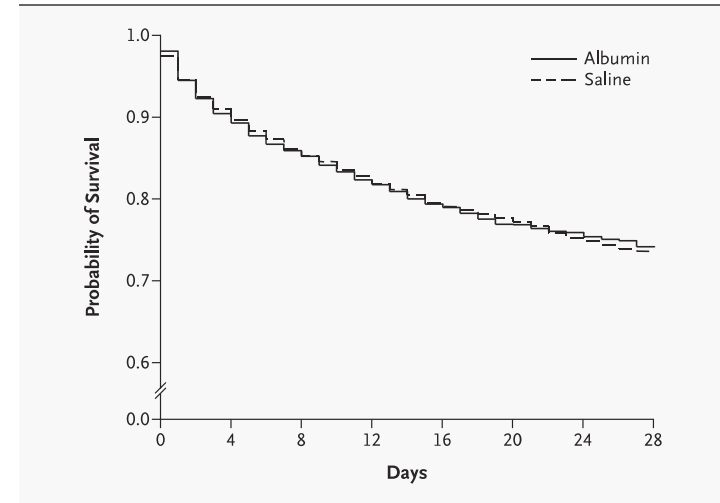


Les « grandes » études

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

The SAFE Study Investigators*

- 7000 patients
- Alb 4% vs Isotonique
- ICU patients
- Meilleure survie Sepsis sévère



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)

0.5 1.0 2.0

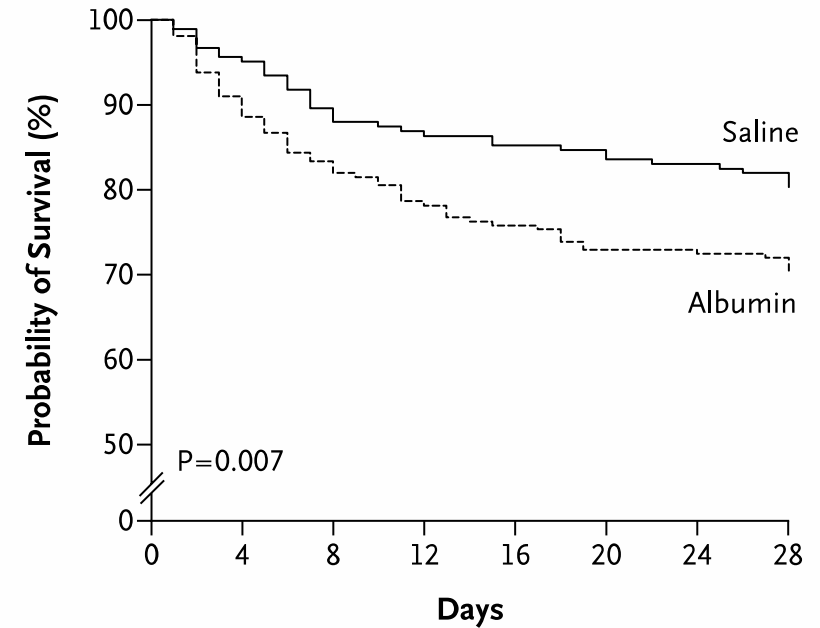
Albumin Better Saline Better

Saline or Albumin for Fluid Resuscitation in Patients with Traumatic Brain Injury

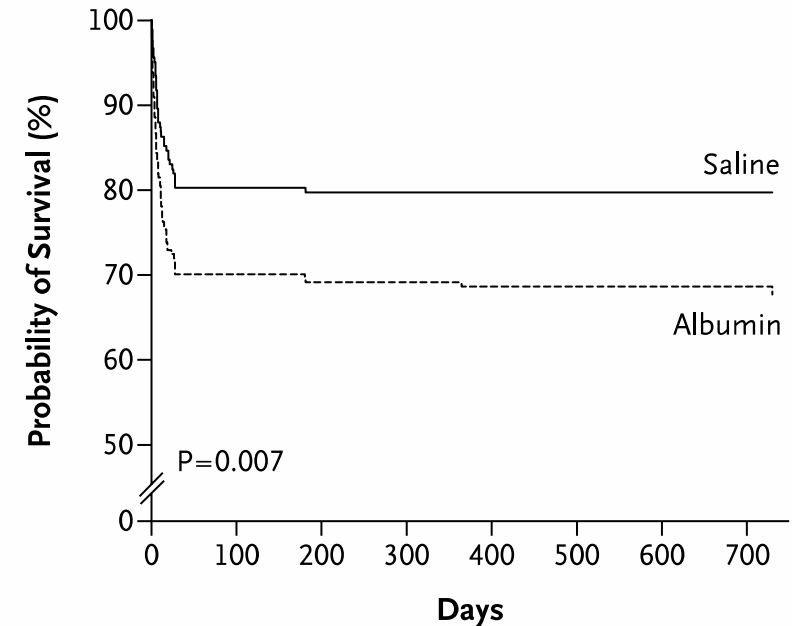
The SAFE Study Investigators*

- 461 TBI patients
- Alb 4% vs Isotonique
- HTIC
- Hypotonic/hypooncotic

A



B

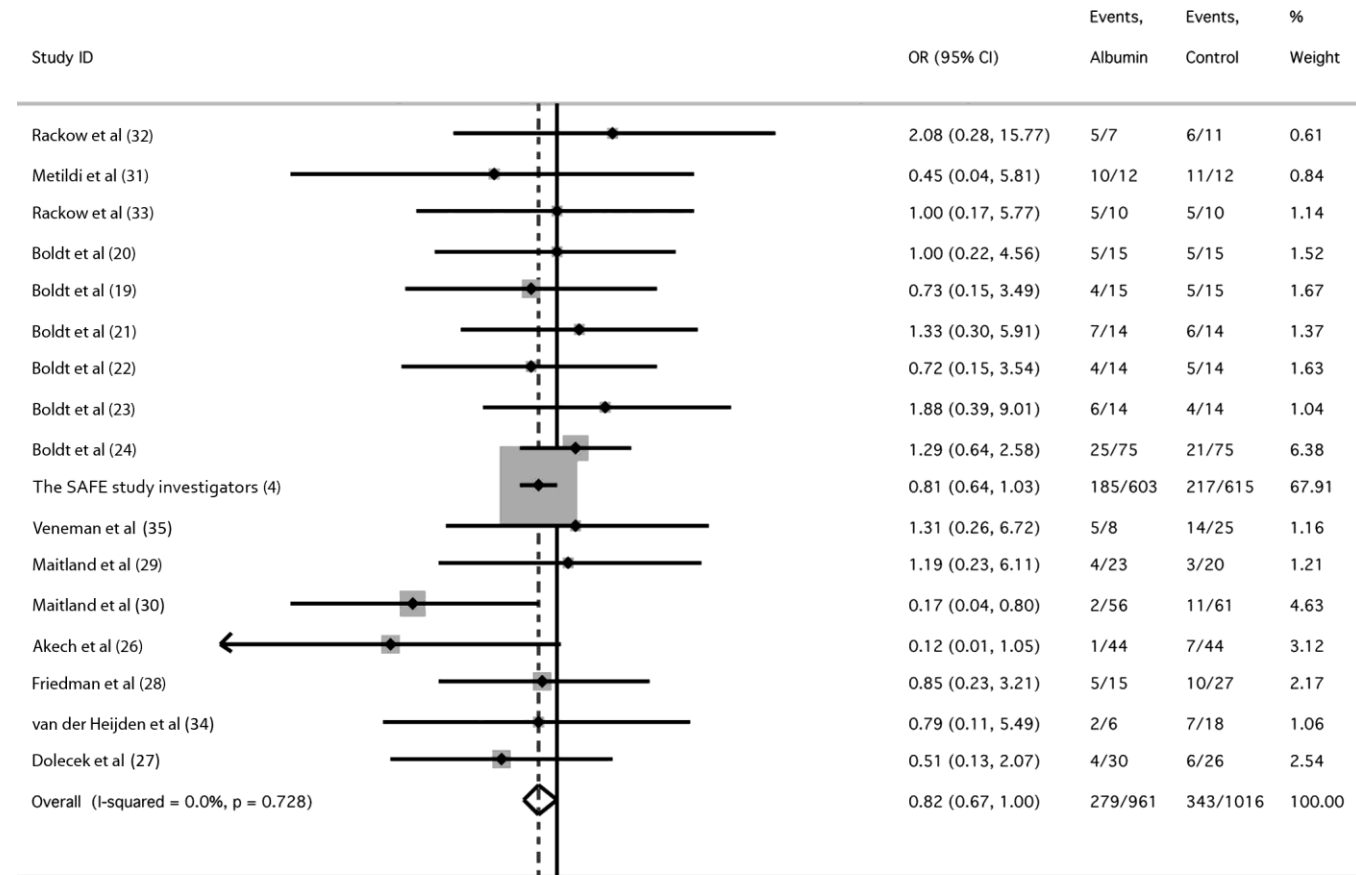


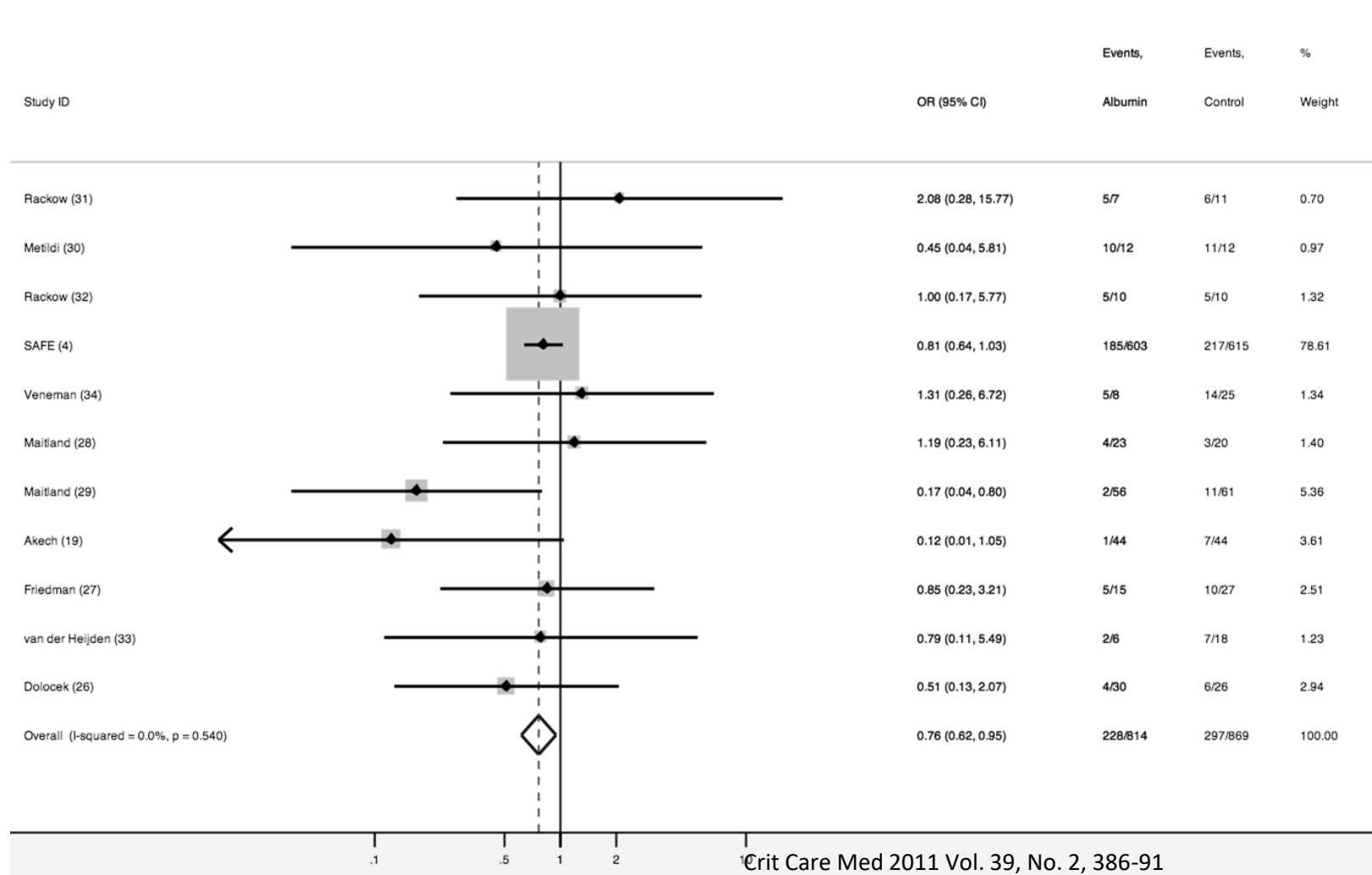
The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis*

Anthony P. Delaney, MD, FCICM; Arina Dan, MD, FCICM; John McCaffrey, MD, FCICM; Simon Finfer, MD, FCICM

Crit Care Med 2011 Vol. 39, No. 2

- Sepsis
- Alb vs tout le reste...
- 17 RCT









Morbidity in hospitalized patients receiving human albumin: A meta-analysis of randomized, controlled trials*

Jean-Louis Vincent, MD, PhD, FCCM; Roberta J. Navickis, PhD; Mahlon M. Wilkes, PhD

Crit Care Med 2004 Vol. 32, No. 10

Clinical Indication	Trials	Morbidity				RR (CI)	
		Albumin Group		Control Group			
		Events	Patients	Events	Patients		
Surgery or Trauma							
Albumin vs no albumin	12	44	245	72	249		0.58 (0.40-0.85)
Albumin vs low-dose albumin	10	27	143	28	153		0.95 (0.56-1.61)
Albumin vs moderate-dose albumin	18	561	530	520	518		1.06 (0.94-1.19)
<i>Pooled</i>	40	632	918	620	920		1.00 (0.89-1.11)
Other indications							

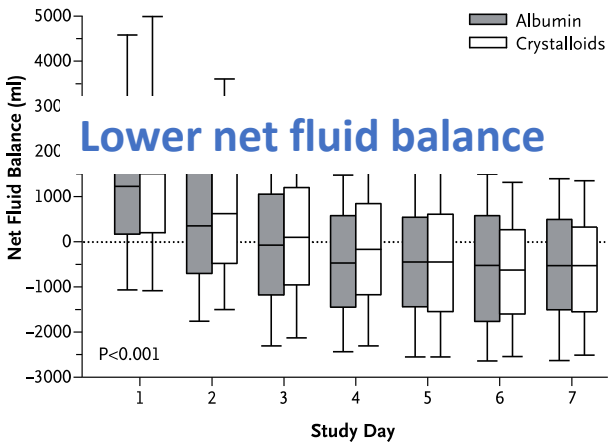
ORIGINAL ARTICLE

Albumin Replacement in Patients with Severe Sepsis or Septic Shock

Pietro Caironi, M.D., Gianni Tognoni, M.D., Serge Masson, Ph.D., Roberto Fumagalli, M.D., Antonio Pesenti, M.D., Marilena Romero, Ph.D., Caterina Fanizza, M.Stat., Luisa Caspani, M.D., Stefano Faenza, M.D., Giacomo Grasselli, M.D., Gaetano Iapichino, M.D., Massimo Antonelli, M.D., Vieri Parrini, M.D., Gilberto Fiore, M.D., Roberto Latini, M.D., and Luciano Gattinoni, M.D., for the ALBIOS Study Investigators*

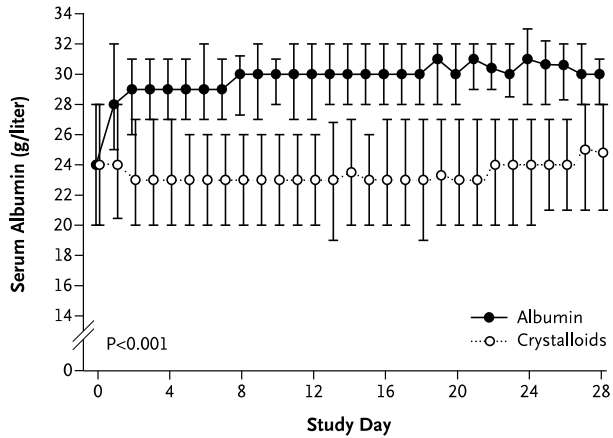
- 1818 patients sepsis sévère/shock
- 300 ml Alb 20%+cristalloides/j
- Réanimation agressive (Rivers)
- Maintien Alb>30 g/l

B

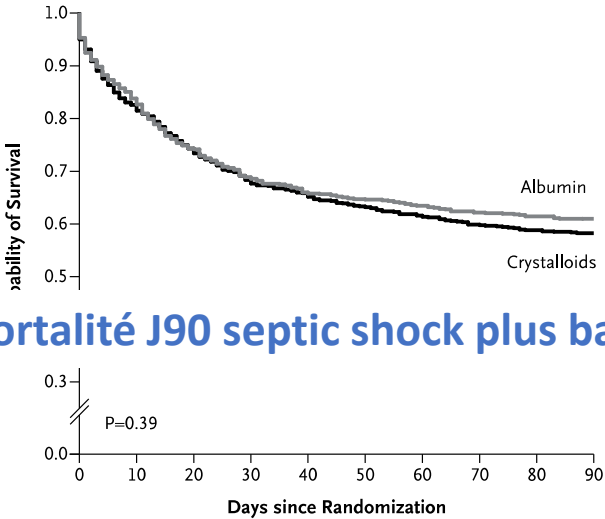


No. at Risk							
Albumin	840	789	742	701	639	586	542
Crystalloids	844	795	735	685	635	587	529

A



No. at Risk								
Albumin	821	677	483	335	239	198	148	107
Crystalloids	813	663	464	303	217	159	130	104



Mortalité J90 septic shock plus basse

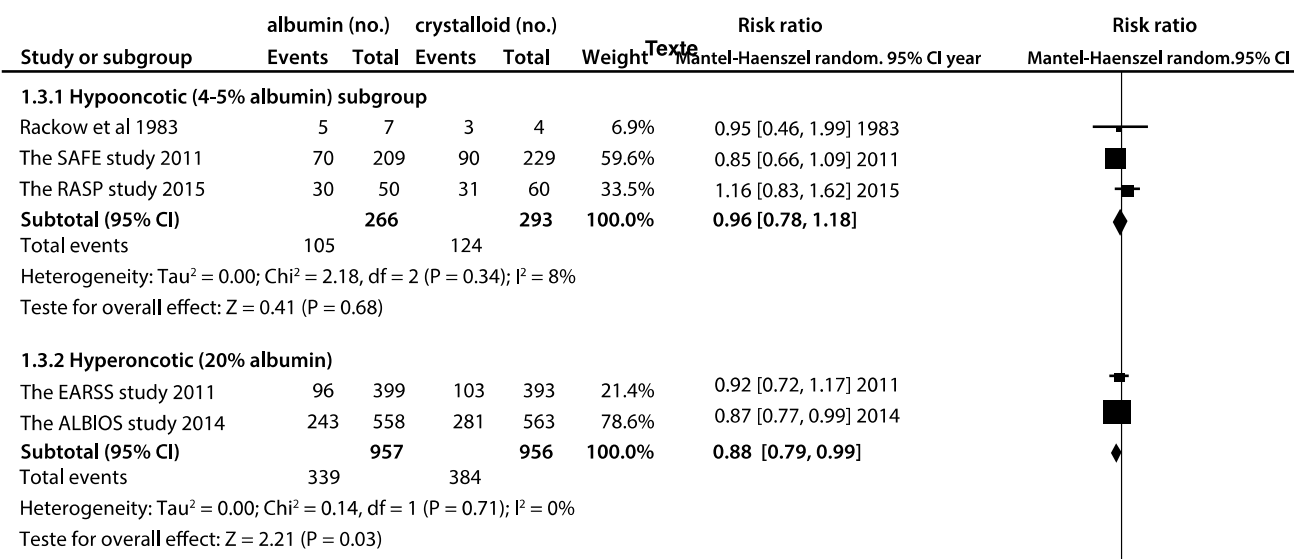
No. at Risk										
Albumin	903	733	647	597	567	556	545	535	529	523
Crystalloids	907	729	652	598	676	551	538	521	511	504

	Albumin			Saline			
	Dead	Survive	Total	Dead	Survive	Total	P
SAFE	185	418	603	217	398	615	0.09
EARSS	96	303	399	103	290	393	>0.05
ALBIOS	244	409	653	274	374	648	0.07
Total	525	1130	1655	594	1062	1656	

Comparison of the effects of albumin and crystalloid on mortality among patients with septic shock: systematic review with meta-analysis and trial sequential analysis

Yan Zou[†], Ke Ma[†], Ji-Bin Xiong[‡], Cai-Hua Xi[†], Xiao-Jun Deng[†]

Department of Emergency Medicine, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China



Choice of Fluids in Severe Septic Patients - A Cost-effectiveness Analysis
Informed by Recent Clinical Trials

Fluid	Life Expectancy (LY)	Total medical Costs	Incremental Costs	Total Costs per LY
Crystalloid	2.00	\$20,133	Reference	\$10,036
Albumin	2.21	\$20,403	\$270	\$9,253
Hydroxyethyl starch	1.15	\$28,091	\$76	\$24,363

*LY – Life Years

Heterogeneity and oxidation status of commercial human albumin preparations in clinical use*

David Bar-Or, MD; Raphael Bar-Or, BS; Leonard T. Rael, MS; David K. Gardner, PhD;
Denetta S. Slone, MD; Michael L. Craun, MD

Crit Care Med 2005 Vol. 33, No. 7

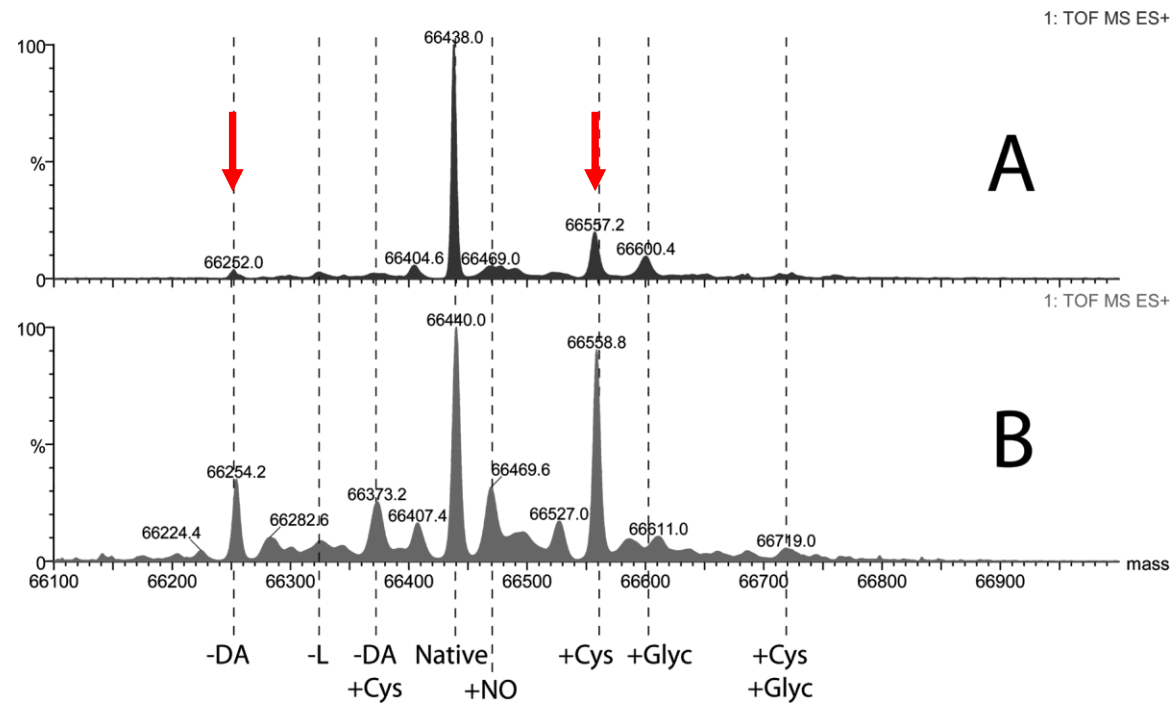


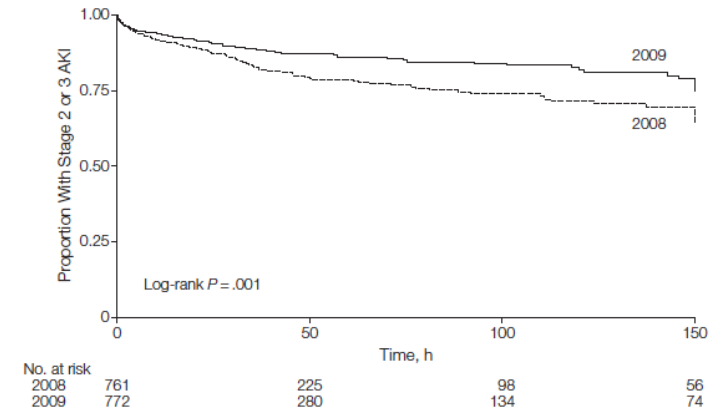
Figure 1. *A*, normal healthy volunteer human serum albumin (HSA) profile. *B*, typical commercial albumin preparation. HSA identification: *DA*, aspartate-alanine absent from N-terminus; *L*, leucine absent from C-terminus; *+Cys*, Cysteine 34 is bound by a free cysteine; *+NO*, cysteine 34 is bound by nitric oxide; *+Glyc*, glycated albumin.

En pratique

- Viser 1 cible Albuminémie > 30g/l (Albios)
- Alb 20%: 100 ml/8 h sur 3 j : Alb 26-29 g/l (EARSS)
- Privilégier Alb hyperoncotique (attention au Chlore)

Yunos et al. JAMA 2012

Figure 1. Development of Stage 2 or 3 Acute Kidney Injury (AKI) While in the Intensive Care Unit (ICU)



Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

Conclusion

- Pas de crainte concernant la safety, mais pas à tous les patient en choc...
- Pas de solutés iso/hypotoniques en particulier TBI (SAFE study)
- Recommandée si:
 - Cirrhose et péritonite bactérienne spontanée
 - Cirrhose et ascite réfractaire > 4-5 l
- Données de sous groupes/physiopathologie-données biologiques
 - Cirrhose et syndrome hépatorénal
 - Patients « hypo-oncotiques » en SDRA
 - Choc septique sévère et hypo albuminémie/oedemes