LES ÉTATS SEPTIQUES

INTRODUCTION: ÉPIDÉMIOLOGIE

VENDRREDIREA/29/10/2011

Pr .A :MOHAMED FEKIH HASSEN

Définitions

Réponse inflammatoire systémique

- T° > 38.5°C ou < 35°C
- Fréquence cardiaque > 90 batt/ min
- Fréquence respiratoire > 20 cycles/ min ou PaCO2 < 32 mmHg ou recours VM
- GB > 12 000/ mm3 ou < 4 000/ mm3 ou formes immatures > 10%

- Glycémie > 7.7mmol/L
- Altération des fonctions supérieures
- Temps de recoloration > 2sec
- Lactatémie > 2 mmol/L

sepsis

SRIS + infection présumée ou identifiée

Définitions

Sepsis grave

-Lactates > 4mmol/L **OU** Hypotension avant remplissage
-Dysfonction d'organe (**1 seule suffit**)

- respiratoire (PaO_2/FIO_2<300,FIO_2>0.5 pour SpO_2 > 92%)
- rénale (Créatinémie >176 µmol/L, > 2 x normale ou oligurie)
- coagulation (INR >1.5)
- hépatique (TP >60 s, bilirubine > 78mmol/L, transaminases > 2 x normale)
- thrombopénie (< 100 000/mm^3)
- fonctions supérieures (GCS < 13)

Choc septique

Sepsis grave + hypotension artérielle malgré le remplissage vasculaire : 20-40 ml/kg

Définitions

Sepsis grave

-Lactates > 4mmol/L **OU** Hypotension avant remplissage
-Dysfonction d'organe (**1 seule suffit**)

- respiratoire (PaO_2/FIO_2<300,FIO_2>0.5 pour SpO_2 > 92%)
- rénale (Créatinémie >176 mmol/L, > 2 x normale ou oligurie)
- coagulation (INR >1.5)
- hépatique (TP >60 s, bilirubine > 78mmol/L, transaminases > 2 x normale)
- thrombopénie (< 100 000/mm^3)
- fonctions supérieures (GCS < 13)

Choc septique

Sepsis grave + hypotension artérielle malgré le remplissage vasculaire : 20-40 ml/kg

Incidence

PP 2007

Incidences comparées

Incidence aux USA (pour 100.000 habitants)

- SIDA 17
- Cancer colorectal 48
- Cancer du sein 112
- Insuffisance cardiaque 196
- Sepsis sévère 300

Centers for Disease Control and Prevention. 2000. Incidence rate for 1999.
American Cancer Society. 2001. Incidence rate for 1993-1997.
American Heart Association. 2000.
Angus DC et al. 2001. Crit Care Med 29:1303-1310.
National Center for Health Statistics. 2001

Epidémiologie

AMERICAN JOURNAL OF
Respiratory and
Critical Care Medicine®

Estimation de l'incidence des SSG dans les hôpitaux français et selon secteur d'hospitalisation

	Sepsis grave
Hôpital	6(5.5-6.6)
services	2.9(2.5-3.2)
Réanimations	119(106-133)

Taux pour 1000 admissions (IC 95%)

sepsis grave complique 26% de l'ensemble des bactériémie dont 17 % de ceux survenant dans les services d'hospitalisation et 65% des épisodes survenant en réanimation

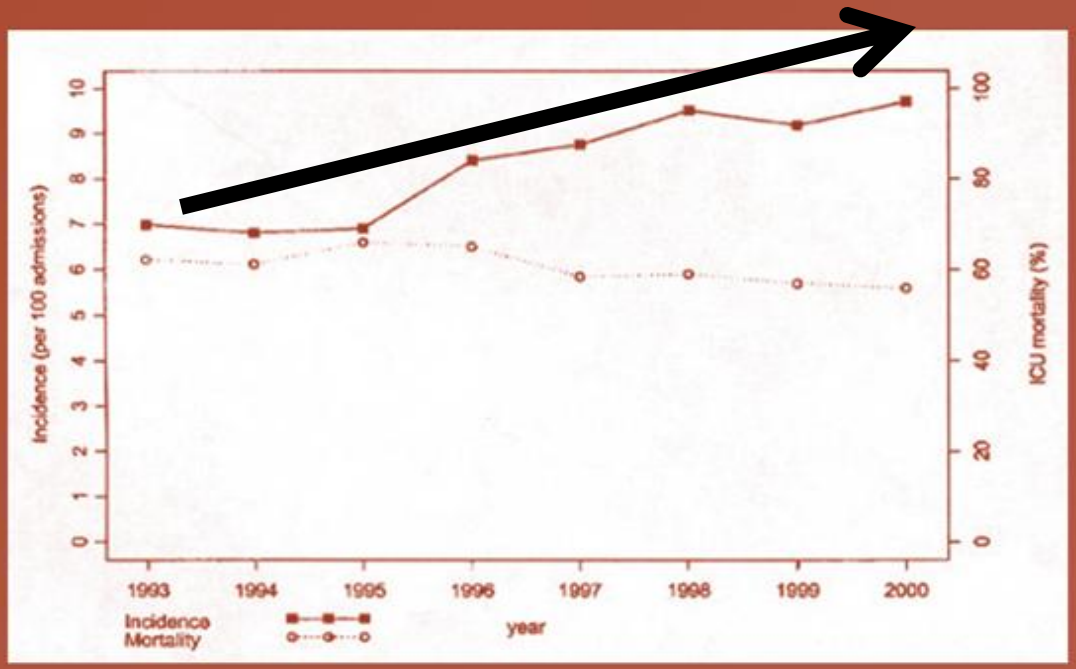
Brun Buisson C. et al AJRCCM 1996;154:617-

Epidémiologie. INCIDENCE

Auteur	Pays	Lieu	Année	Fréquence
Salvo, 1995	Italie	99 réa	12 mois, 93-94	12% des admissions en réanimation
Brun Buisson, 95	France	170 réa med	8 semaines, 93	9% des adm
Rangel-Frausto, 95	USA	1 hôpital	9 mois, 92-93	13% des adm
Sands, 1997	USA	8 hôpitaux	16 mois, 93-94	10% des adm
Angus, 2001	USA	936 hôpitaux, 7 états	12 mois, 95	11% des adm
Padkin, 2003	UK	91 réa	5 ans, 95-00	27% des adm
Martin, 2003	USA	Hôpital	22 ans, 79-00	
Alberti, 2002	Europe, Canada, Israël	28 réa	12 mois, 97-98	15% des adm
Brun Buisson, 2004	France	206 réa	2 semaines, 01	15% des adm
Finfer, 2004	Autralie, NZ	23 réa	5 mois, 99	12% des adm
Van Gestel, 2004	Pays-Bas	47 réa	1 jour, 01	11% des adm
Flatten, 2004	Norvège	Hôpitaux	12 mois, 99	
Silva, 2004	Brésil	5 réa	8 mois, 01-02	27% des adm>24H
Sundararajan, 05	Australie	Hôpitaux	4 ans, 99-03	
Vincent, 2006	Europe	198 réa	2 semaines, 02	30% des adm>24H

Epidémiologie

- **22** USI dans la région Parisienne. **100 554** entrées de 1993 à 2000
- Augmentation régulière du nombre des chocs septiques hospitalisés en USI : **7 à 9,7% (p<0,001)**
- **Diminution de la mortalité** au cours du sepsis en USI



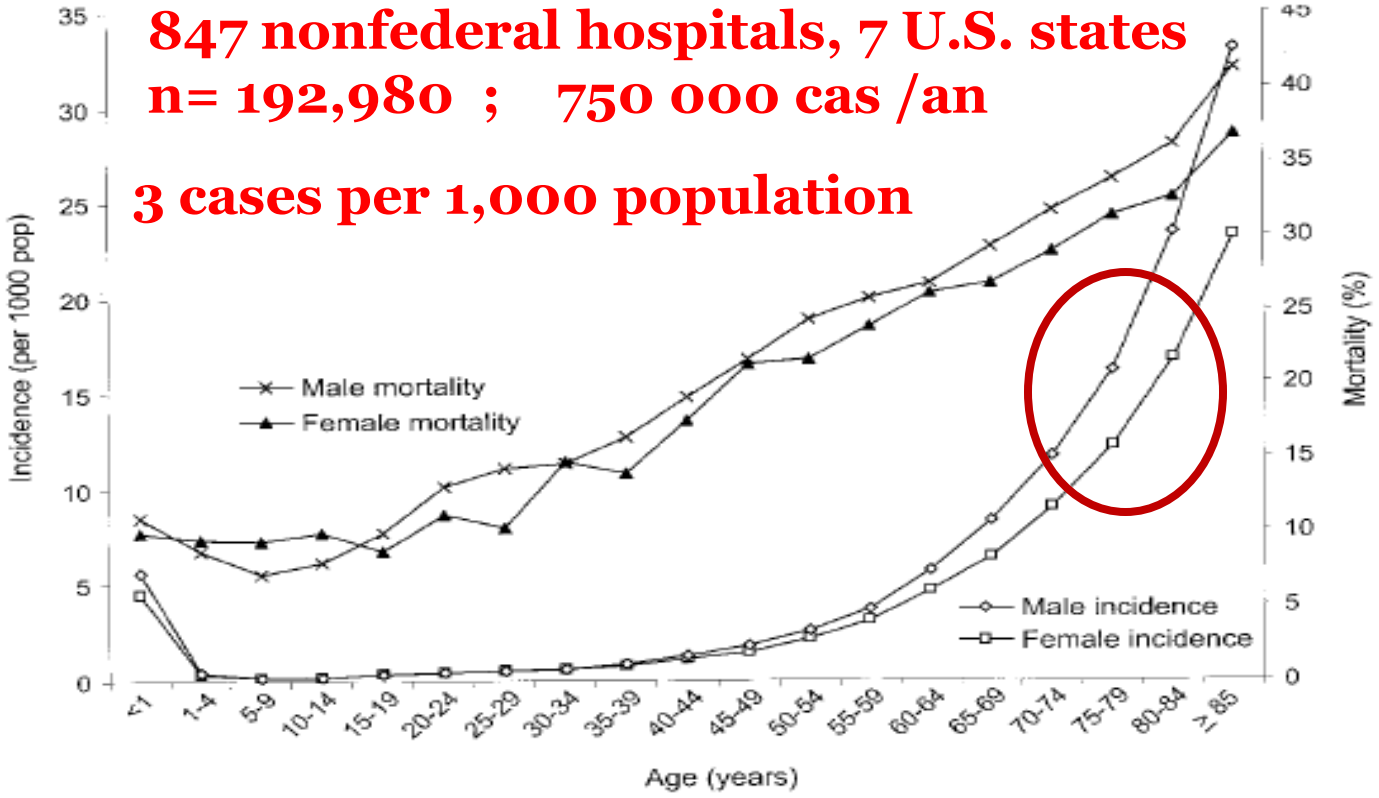
Annane for the CUB-Réa Network. AJRCCM. 2003; 168 : 165-72

Epidémiologie

Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care

847 nonfederal hospitals, 7 U.S. states
n= 192,980 ; 750 000 cas /an

3 cases per 1,000 population



Angus et al. Crit Care Med 2001; 29:1303–1310

Epidémiologie

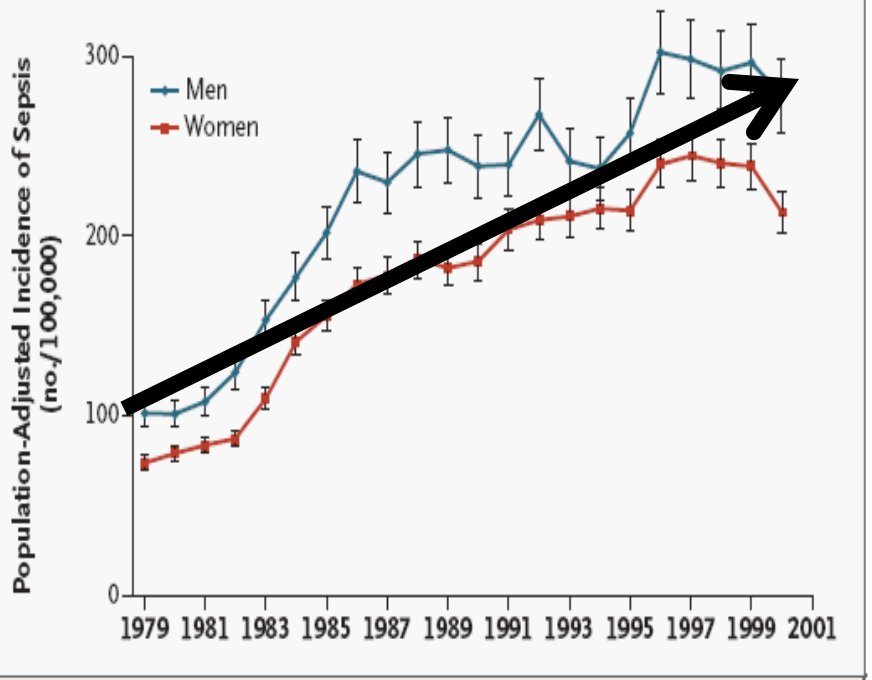


Figure 1. Population-Adjusted Incidence of Sepsis, According to Sex, 1979–2000.
Points represent the annual incidence rate, and I bars the standard error.

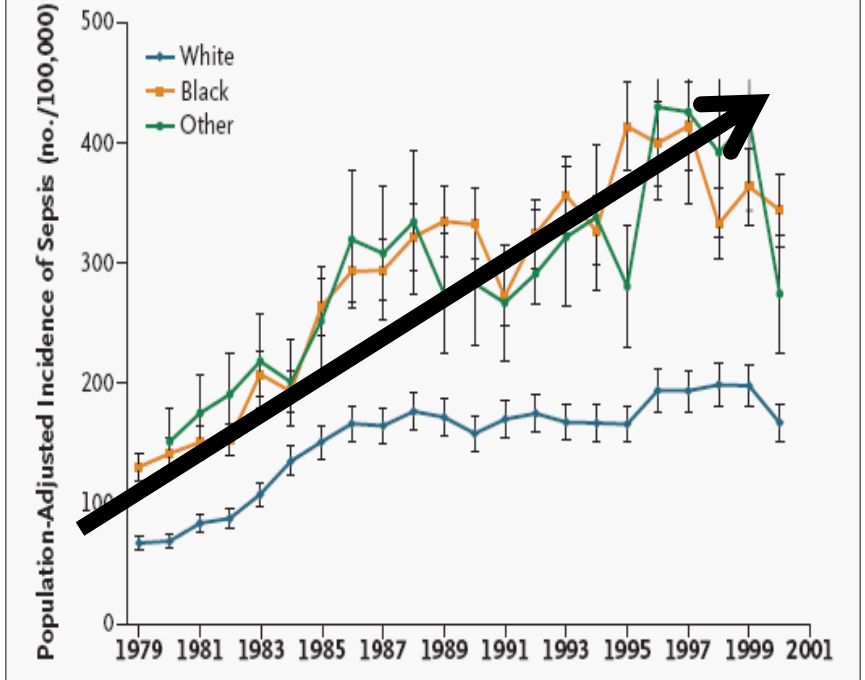
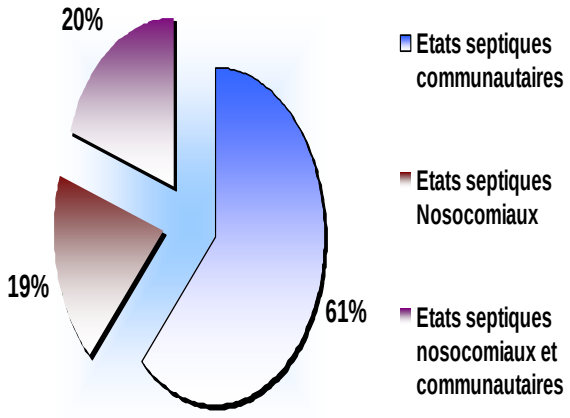
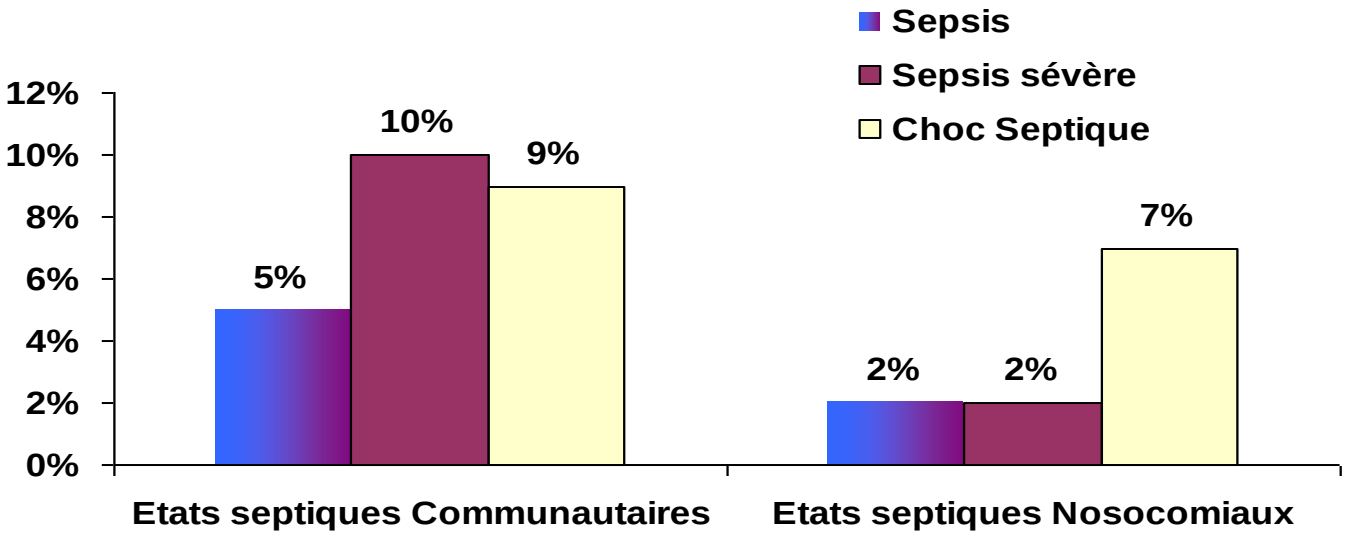


Figure 2. Population-Adjusted Incidence of Sepsis, According to Race, 1979–2000.
Points represent the annual incidence rate, and I bars the standard error.

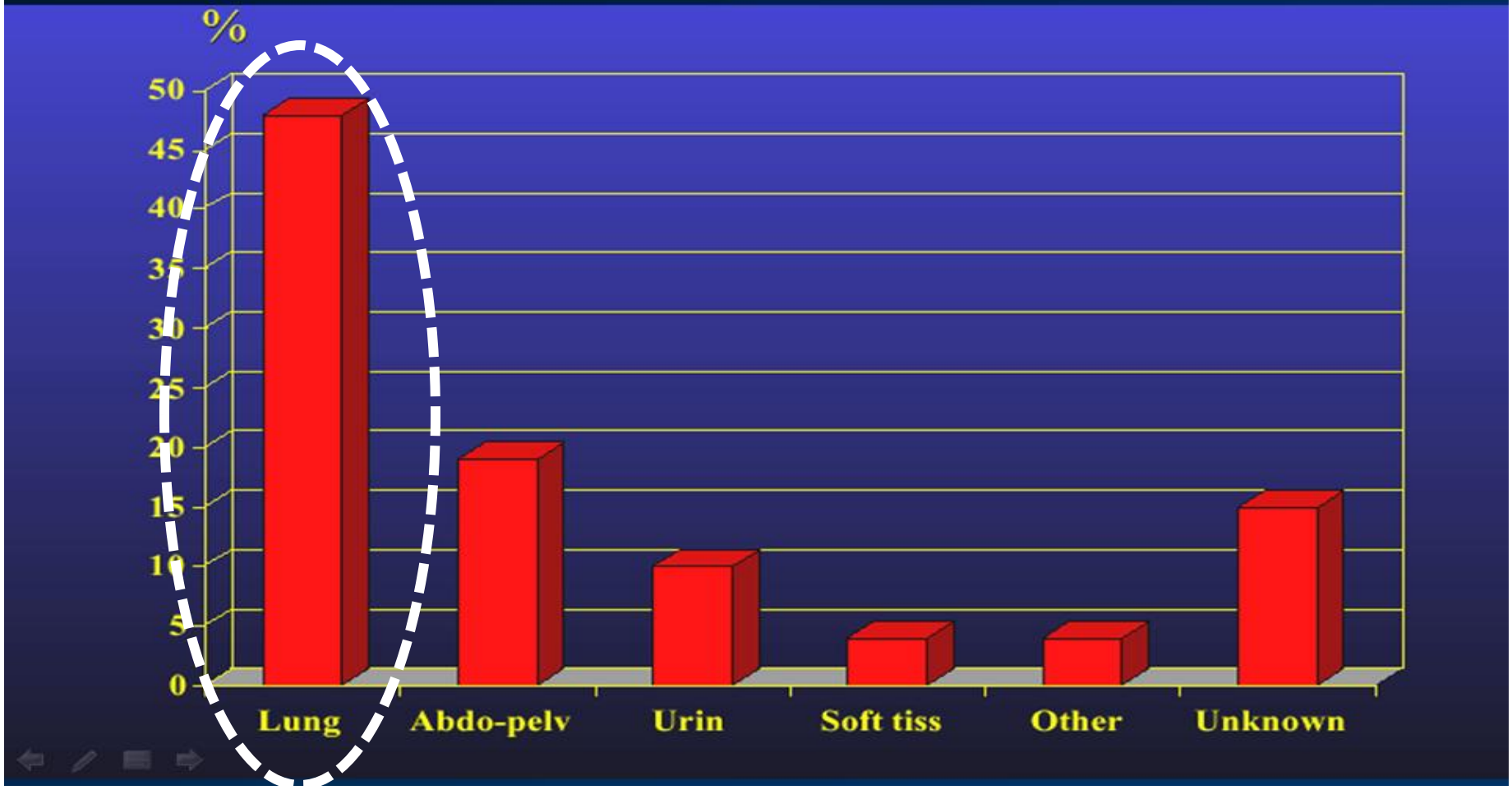
Incidence des états septiques. EN REANIMATION MAHDIA





Epidémiologie : PORTES D'ENTREES

Poumon >> abdomen > urines…..



Epidémiologie : PORTES D'ENTREES (Mahdia)

	Total N=122	États septiques Communautaires N=83	États septiques Nosocomiaux N=39
Pneumonies, n (%)	93 (76)	64 (64)	29 (74)
Pyélonéphrites, n (%)	23 (19)	14 (14)	9 (23)
Erysipèles, n (%)	3 (3)	3 (3)	0 (0)
Autres, n (%)	2 (2)	2 (2)	0 (0)

Microorganismes en cause

	Estimated frequency*
Gram-positive bacteria	30–50%
Meticillin-susceptible *S aureus*	14–24%
Meticillin-resistant *S aureus*	5–11%
Other *Staphylococcus* spp	1–3%
Streptococcus pneumoniae	9–12%
Other *Streptococcus* spp	6–11%
Enterococcus spp	3–13%
Anaerobes	1–2%
Other gram-positive bacteria	1–5%
Gram-negative bacteria	25–30%
E coli	9–27%
Pseudomonas aeruginosa	8–15%
Klebsiella pneumoniae	2–7%
Other *Enterobacter* spp	6–16%
Haemophilus influenzae	2–10%
Anaerobes	3–7%
Other gram-negative bacteria	3–12%
Fungus	
Candida albicans	1–3%
Other *Candida* spp	1–2%
Yeast	1%
Parasites	1–3%
Viruses	2–4%

en ↓

Cultures négatives dans 30% des cas

Annane, Lancet 2005;365

Microorganismes en cause

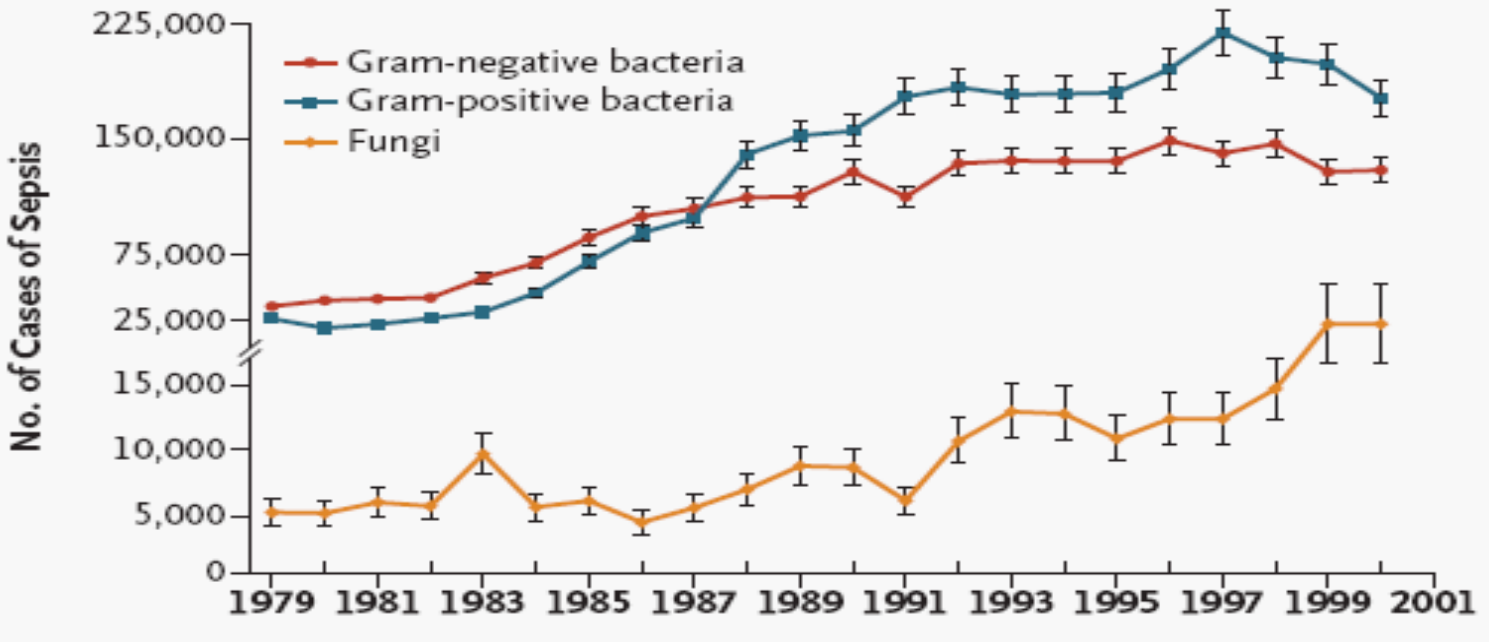


Figure 3. Numbers of Cases of Sepsis in the United States, According to the Causative Organism, 1979–2000.

Points represent the number of cases for the given year, and I bars the standard error.

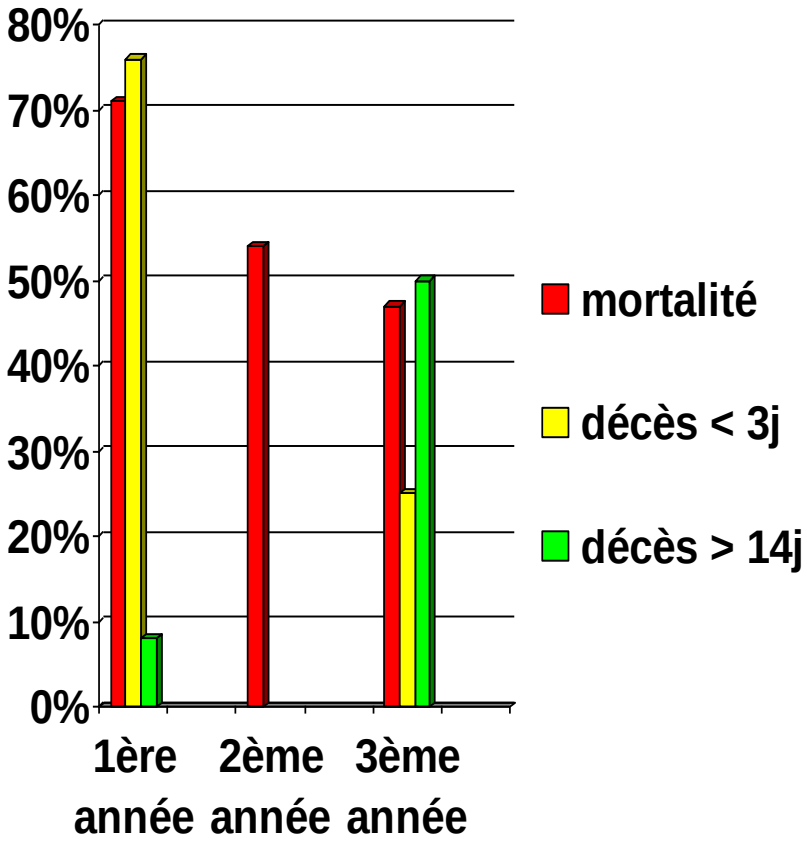
Microorganismes en cause

	Etats septiques Communautaires N=89	Etats septiques Nosocomiaux N=39
Streptococcus pneumoniae	1 (1)	0 (0)
Staphyloccocus Auréus	1 (1)	2 (5)
Entérobactéries*	5 (6)	7 (18)
Virus *A H1N1*	6 (7)	0 (0)
Pseudomonas Aeruginosa	0 (0)	9 (23)
Acinetobacter Baumannii	0 (0)	10 (26)
Pseudomonas Aeruginosa + *Acinetobacter Baumannii*	0 (0)	2 (5)
Entérobacteries+ *Acinetobacter Baumannii*	0 (0)	2 (5)
Autres	3 (3)	0 (0)
Autres BGN	0 (0)	3 (3)

Mortalité

Prospective study of the treatment of septic shock

- Étude prospective
- University department of surgery and intensive therapy unit
- Glasgow
- Étude sur 3 ans
- 113 patients en choc septique (n=35;35;43)
- Documentation bactériologique
- Modifications de la prise en charge: ventilation précoce avec PEP, chirurgie précoce, modification de l'antibiothérapie, remplissage vasculaire



I.Mca. Ledingham and C.S. Mcardle Lancet 1978;311:1194-1197

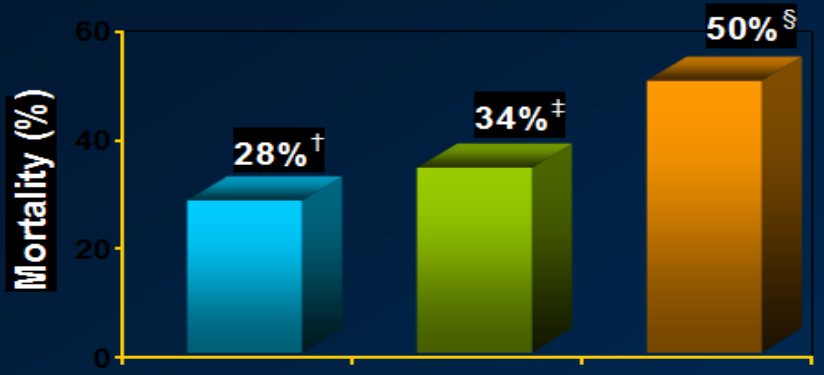
Mortalité

Référence	SIRS (%)	Sepsis (%)	Sepsis Sévère (%)	Choc septique
Rangel-Frausto	7	16	20	46
Pittet	6	0	[illegible]	58
Jones - Lowes	23	[illegible]	38	56
Muckart	[illegible]	10	18	53
Bossink	6	13	-	-

Mortalité à 28 jours **10-15%** **20-30%** **40-50%**

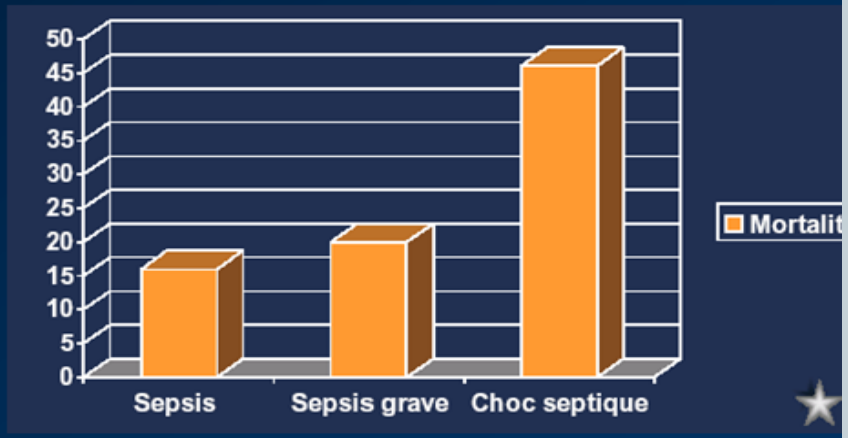
Matot, Sprung *ICM*. 2001

Mortalité



La mortalité est variable en fonction des séries :

- 28 à 50%
- DMV : 15%
- population hétérogène



La mortalité est variable en fonction de la gravité initiale

Elle est stable au cours du temps

1995 : 59%

2005 : 42%

† **Angus**. Crit Care Med. 2001
‡ **Sands**. JAMA. 1997
§ **Zeni** . Crit Care Med. 1997

Brun-Buisson. CCM. 1996

Mortalité

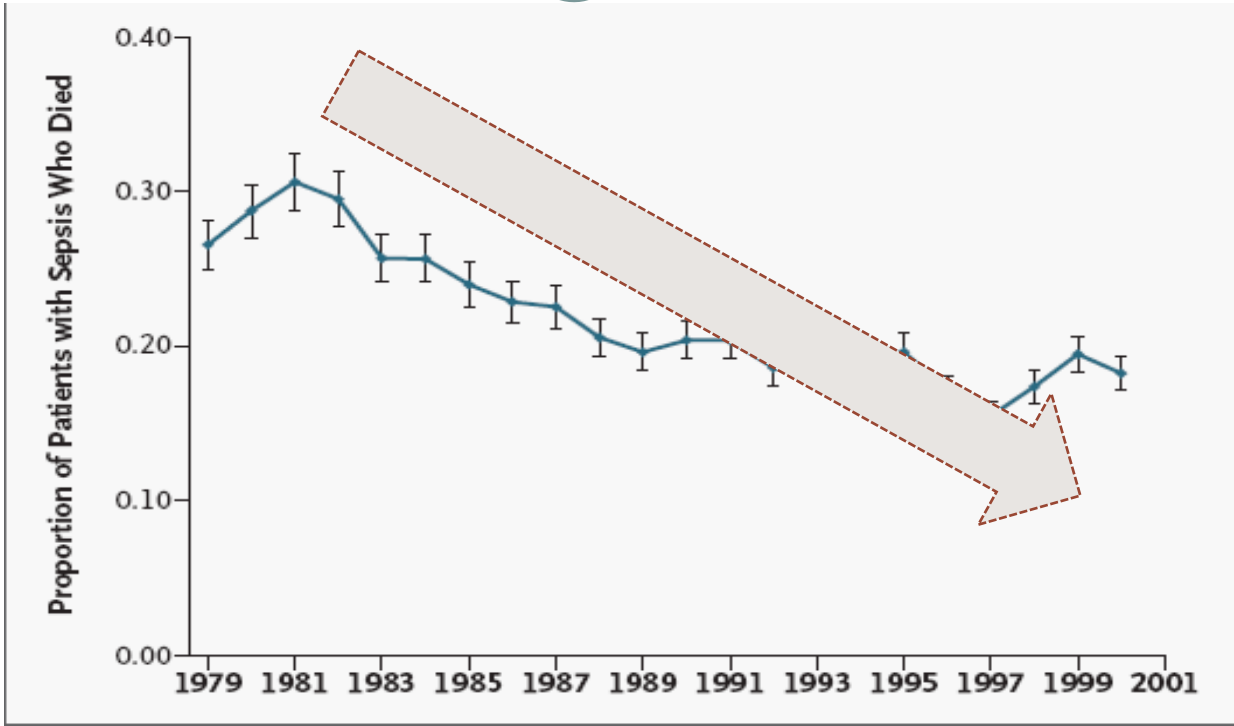


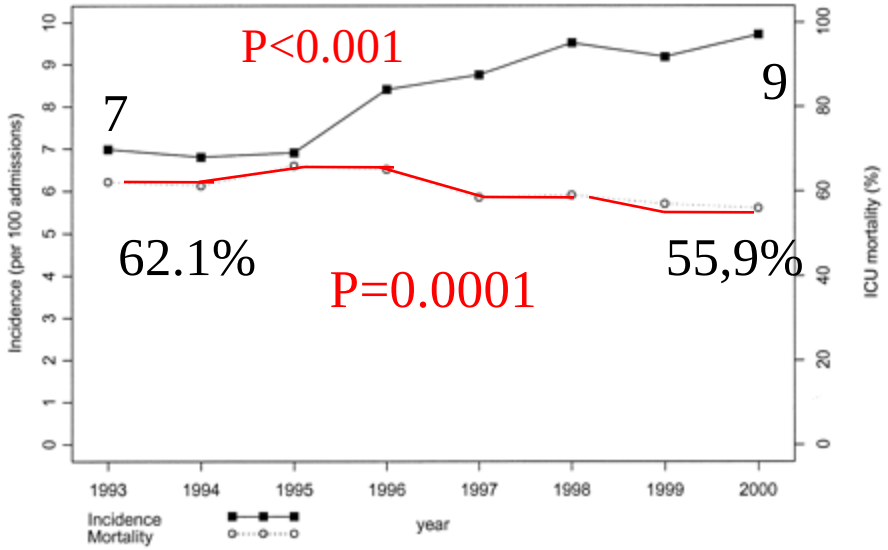
Figure 4. Overall In-Hospital Mortality Rate among Patients Hospitalized for Sepsis, 1979–2000.

Mortality averaged 27.8 percent during the first six years of the study and 17.9 percent during the last six years. The I bars represent the standard error.

N Engl J Med 2003;348:1546-54.

Mortalité

Épidémiologie et mortalité du choc septique: CUB -Réa



100554 admissions
1993-2000
22 hopitaux Ile de France

8.2 pour 100 admissions
mortalité: 60,1%
Risque X 3.9 (3.5-4.3)

Annane D. for the CUB -Réa network Am J Respir Crit Care Med 2003;168:165-172

Mortalité

Inter-relation entre mortalité en réanimation
et incidence du sepsis dans différents pays européens

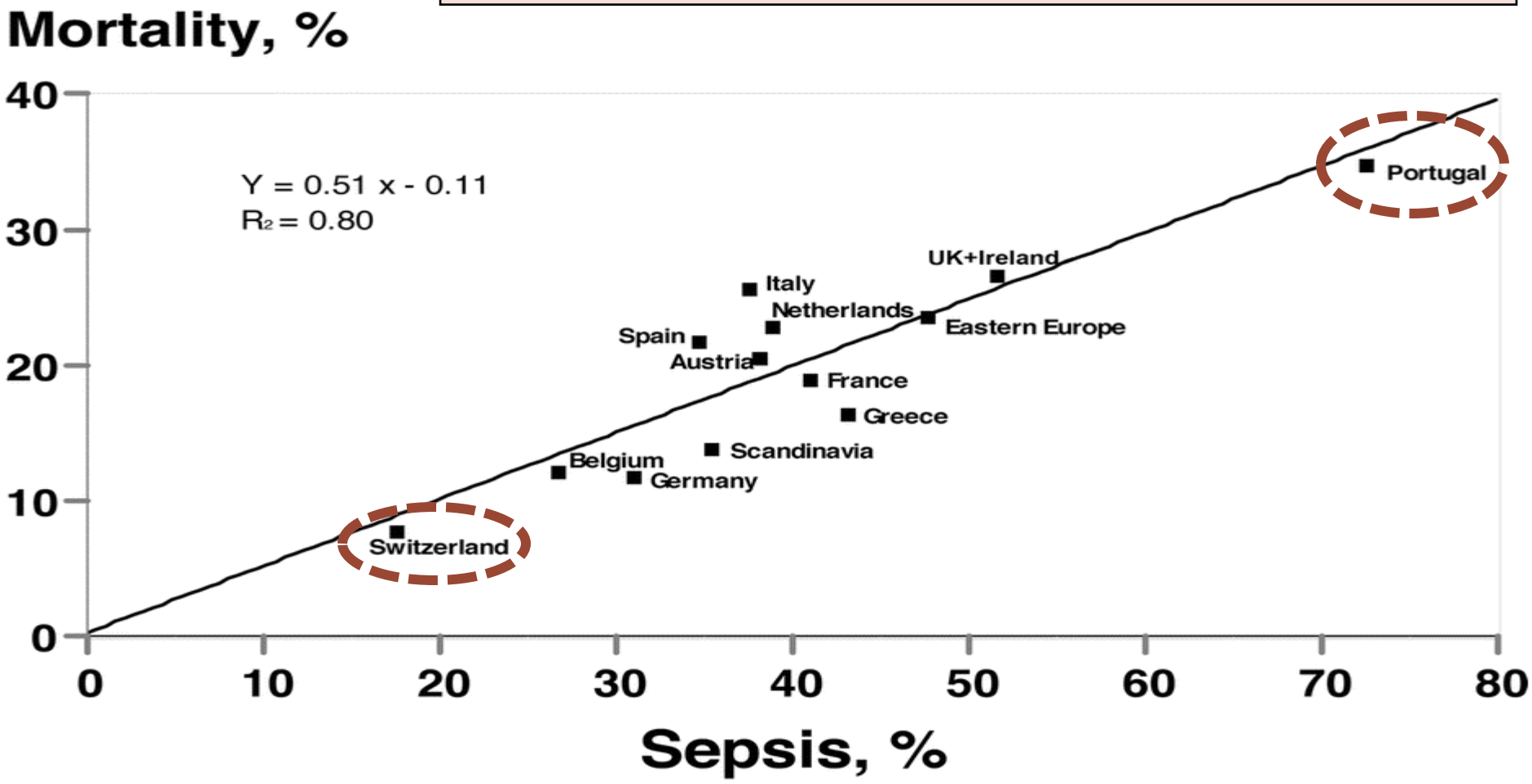


Figure 2. Relationship between intensive care unit mortality rates for all patients and frequency of sepsis in the various European countries.

Vincent JL et al: Crit Care Med 2006;34:344-353


Merci

Prise en charge thérapeutique du choc septique : optimisation hémodynamique

ANALYSE CRITIQUE

Pr .A :MOHAMED FEKIH HASSEN

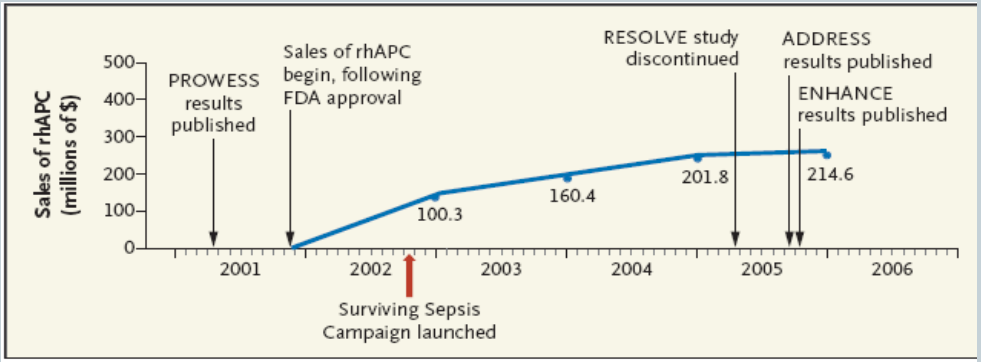
Optimisation hémodynamique

Recommandations pour la prise en charge du sepsis sévère et du choc septique

- Surviving Sepsis Campaign : guidelines for management of severe sepsis and septic shock. Intensive Care Med 2004, 30,536-55.

Surviving Sepsis — Practice Guidelines, Marketing Campaigns, and Eli Lilly

Peter Q. Eichacker, M.D., Charles Natanson, M.D., and Robert L. Danner, M.D.



Timeline of Controlled Trials of rhAPC, Regulatory Actions, Yearly Sales, and the Marketing Initiative by Eli Lilly.

N ENGL J MED 355;16 WWW.NEJM.ORG OCTOBER 19, 2006

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

Initial resuscitation (first 6 hrs)

- Begin resuscitation immediately in patients with hypotension or elevated serum lactate : mmol/L; do not delay pending ICU admission (1C)
- Resuscitation goals (1C)
  CVP 8–12 mm Hg[a]
  Mean arterial pressure ≥ 65 mm Hg
  Urine output ≥0.5 $mL \cdot kg^{-1} \cdot hr^{-1}$
  Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%
  - If venous oxygen saturation target is not achieved (2C)
    Consider further fluid
    Transfuse packed red blood cells if required to hematocrit of ≥30% and/or
    Start dobutamine infusion, maximum 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$

(Crit Care Med 2008; 36:296–327)

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

Fluid therapy

- Fluid-resuscitate using crystalloids or colloids (1B)
- Target a CVP of ≥8 mm Hg (≥12 mm Hg if mechanically ventilated) (1C)
- Use a fluid challenge technique while associated with a hemodynamic improvement (1D)
- Give fluid challenges of 1000 mL of crystalloids or 300–500 mL of colloids over 30 mins. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion (1D)
- Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement (1D)

Vasopressors

- Maintain MAP ≥65 mm Hg (1C)
- Norepinephrine and dopamine centrally administered are the initial vasopressors of choice (1C)
  - Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock (2C). Vasopressin 0.03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone
  - Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine (2B).
- Do not use low-dose dopamine for renal protection (1A)
- In patients requiring vasopressors, insert an arterial catheter as soon as practical (1D)

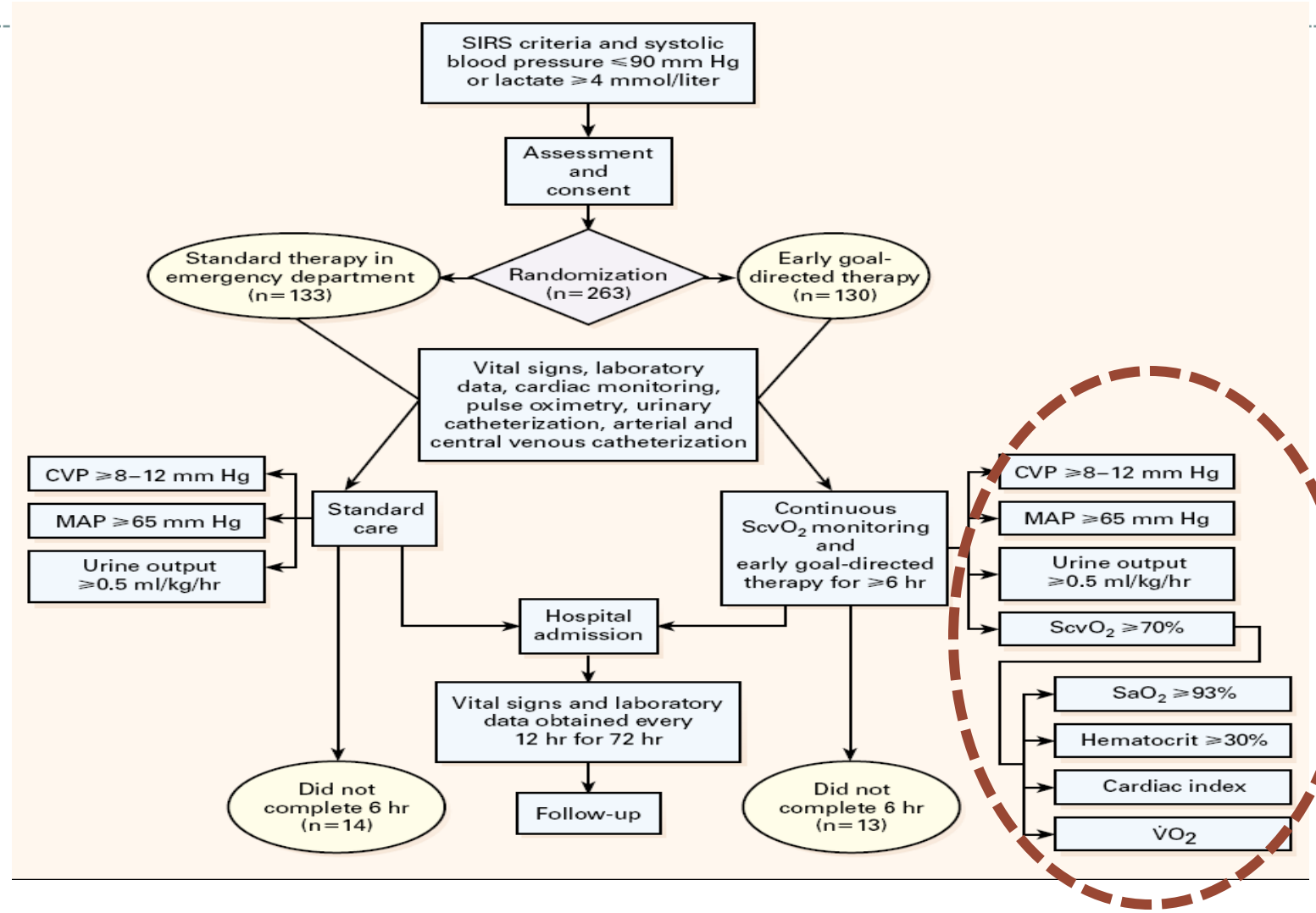
(Crit Care Med 2008; 36:296–327)

EBM et prise en charge du choc septique

- Pas d'étude contrôlée disponible
  - Antibiothérapie
  - Drogues vaso-actives
- Etudes contrôlées disponibles mais pas dans le domaine du sepsis
  - Remplissage vasculaire (SAFE)
  - Contrôle de la glycémie-
  - prise en charge du SDRA
  - Transfusion sanguine
- Etudes contrôlées disponibles mais controversées
  - Protéine C activée
  - Corticothérapie à faible dose

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*



The New England Journal of Medicine 2001;345:1368-77.)

TABLE 4. TREATMENTS ADMINISTERED.*

TREATMENT	HOURS AFTER THE START OF THERAPY		
	0–6	7–72	0–72
Total fluids (ml)			
Standard therapy	3499±2438	10,602±6,216	13,358±7,729
EGDT	4981±2984	8,625±5,162	13,443±6,390
P value	<0.001	0.01	0.73
Red-cell transfusion (%)			
Standard therapy	18.5	32.8	44.5
EGDT	64.1	11.1	68.4
P value	<0.001	<0.001	<0.001
Any vasopressor (%)†			
Standard therapy	30.3	42.9	51.3
EGDT	27.4	29.1	36.8
P value	0.62	0.03	0.02
Inotropic agent (dobutamine) (%)			
Standard therapy	0.8	8.4	9.2
EGDT	13.7	14.5	15.4
P value	<0.001	0.14	0.15
Mechanical ventilation (%)			
Standard therapy	53.8	16.8	70.6
EGDT	53.0	2.6	55.6
P value	0.90	<0.001	0.02
Pulmonary-artery catheterization (%)‡			
Standard therapy	3.4	28.6	31.9
EGDT	0	18.0	18.0
P value	0.12	0.04	0.01

*Plus–minus values are means ±SD. Because some patients received a specific treatment both during the period from 0 to 6 hours and during the period from 7 to 72 hours, the cumulative totals for those two periods do not necessarily equal the values for the period from 0 to 72 hours. EGDT denotes early goal-directed therapy.

†Administered vasopressors included norepinephrine, epinephrine, dopamine, and phenylephrine hydrochloride.

‡All pulmonary-artery catheters were inserted while patients were in the intensive care unit.

TABLE 3. KAPLAN–MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

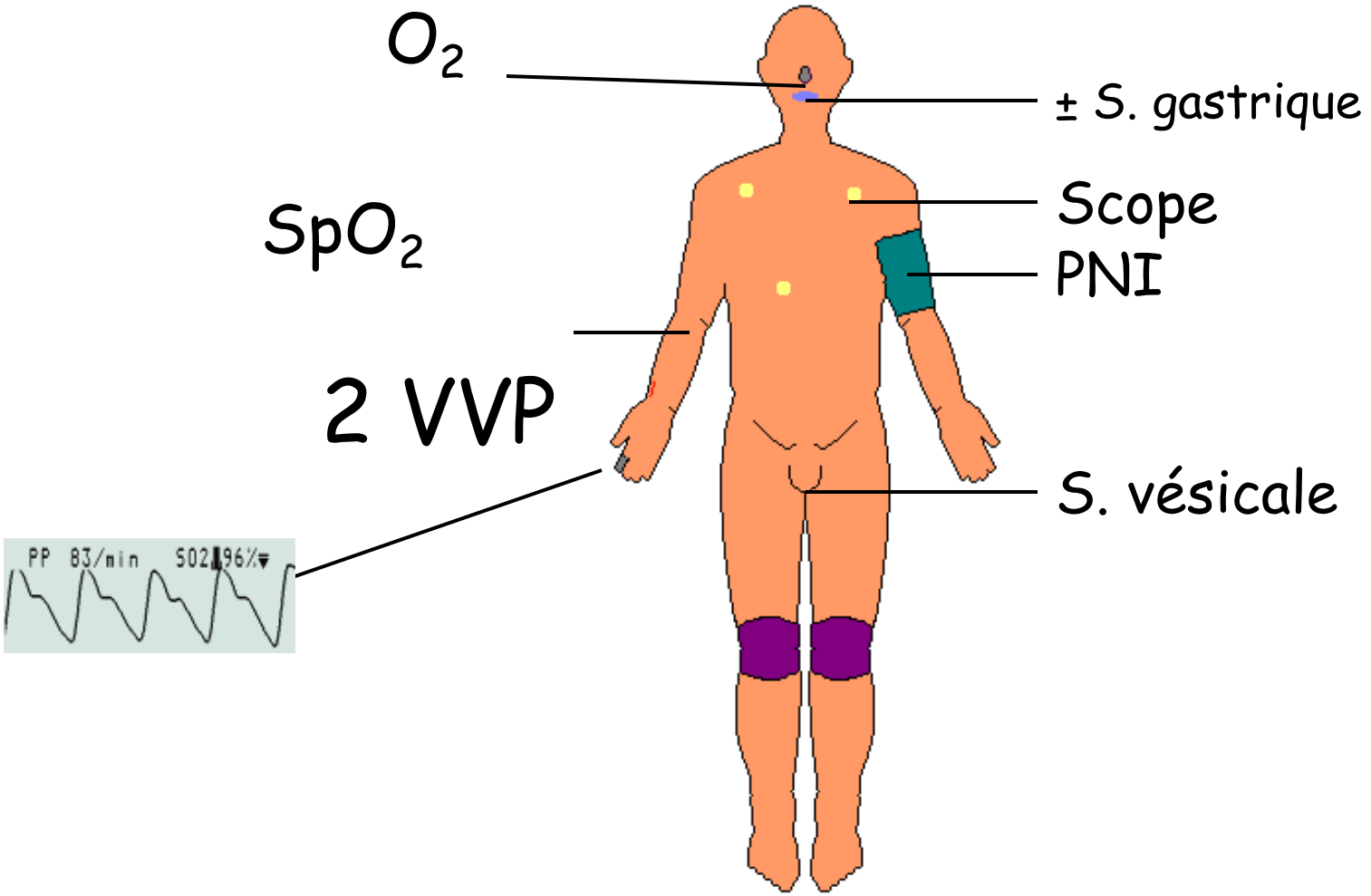
VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.6)	9 (14.9)	0.48 (0.21–1.05)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (21.0)	12/117 (10.3)	—	0.02
Multiorgan failure	26/119 (21.8)	19/117 (16.2)	—	0.27

*CI denotes confidence interval. Dashes indicate that the relative risk is not applicable.

†Percentages were calculated by the Kaplan–Meier product-limit method.

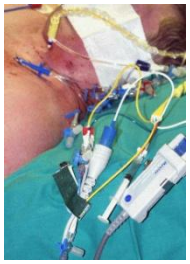
‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

Conditionnement



Déshabillage complet

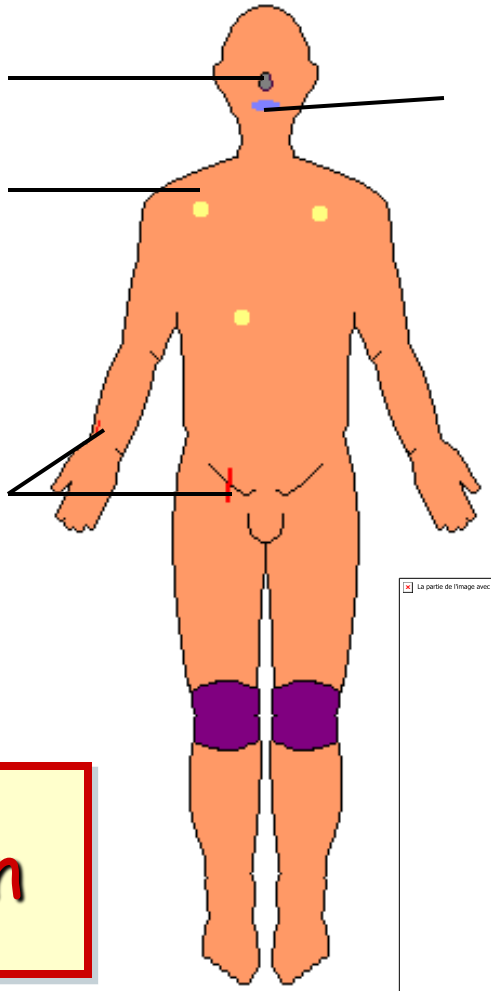
Conditionnement



SG

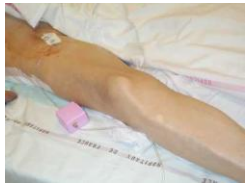
VVC ?

± PVC ?



IOT + VC + $EtCO_2$

Pression invasive



= Réanimation

La partie de l'image avec l'ID de relation rId4 n'a pas été trouvé dans le fichier.

REMPLISSAGE VASCULAIRE:

- **INITIALEMENT bolus : 30CC/Kg sur 30mn**
- **Pas d'étude chez l'adulte**
- **Chez l'enfant**

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

Table 1. (Continued.)

Variable	Albumin Bolus (N=1050)	Saline Bolus (N=1047)	No Bolus (N=1044)	Total (N=3141)
Laboratory assessments†††				
Positive for malaria parasitemia — no./total no. (%)‡‡	590/1044 (57)	612/1042 (59)	591/1037 (57)	1793/3123 (57)
Hemoglobin — no./total no. (%)				
<5 g/dl	323/1024 (32)	332/1015 (33)	332/1015 (33)	987/3054 (32)
>10 g/dl	231/1024 (23)	230/1015 (23)	244/1015 (24)	705/3054 (23)
Glucose — no./total no. (%)				
<2.5 mmol/liter (45 mg/dl)	43/990 (4)	46/991 (5)	42/989 (4)	131/2970 (4)
<3.0 mmol/liter (54 mg/dl)	67/990 (7)	61/991 (6)	59/989 (6)	187/2970 (6)
Lactate ≥5 mmol/liter — no./total no. (%)	357/1000 (36)	407/989 (41)	395/992 (40)	1159/2981(39)
Base deficit ≥8 mmol/liter — no./total no. (%)	380/710 (54)	360/689 (52)	330/680 (49)	1070/2079 (51)
Severe acidemia (pH <7.2) — no./total no. (%)	71/712 (10)	73/694 (11)	65/685 (9)	209/2091 (10)
Hyperkalemia (potassium >6.5 mmol/liter) — no./total no. (%)	67/686 (10)	68/687 (10)	65/670 (10)	200/2043 (10)
Positive for HIV antibody — no./total no. (%)	37/817 (5)	28/827 (3)	41/839 (5)	106/2483 (4)
Positive blood culture — no. of positive cultures/total no. of cultures (%)	38/347 (11)	52/360 (14)	36/363 (10)	126/1070 (12)
Positive cerebrospinal fluid culture — no. of positive cultures/total no. of cultures (%)	2/94 (2)	4/102 (4)	4/96 (4)	10/292 (3)

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

Table 2. Death and Other Adverse Event End Points at 48 Hours and 4 Weeks.

End Point	Albumin Bolus (N=1050)	Saline Bolus (N=1047)	No Bolus (N=1044)	Saline Bolus vs. No Bolus		Albumin Bolus vs. No Bolus		Albumin Bolus vs. Saline Bolus		Albumin and Saline Boluses vs. No Bolus	
				Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
		no. (%)									
48 Hours											
Death — no. (%)	111 (10.6)	110 (10.5)	76 (7.3)	1.44 (1.09–1.90)	0.01	1.45 (1.10–1.92)	0.008	1.00 (0.78–1.29)	0.96	1.45 (1.13–1.86)	0.003
Pulmonary edema — no. (%)	14 (1.3)	6 (0.6)	6 (0.6)								
Increased intracranial pressure — no. (%)	16 (1.5)	18 (1.7)	11 (1.1)								
Severe hypotension — no. (%)*	1 (0.1)	2 (0.2)	3 (0.3)								
Allergic reaction — no. (%)	3 (0.3)	4 (0.4)	2 (0.2)								
Pulmonary edema, increased intracranial pressure, or both — no. (%)†	27 (2.6)	23 (2.2)	17 (1.6)	1.34 (0.72–2.51)	0.34	1.57 (0.87–2.88)	0.10	1.17 (0.68–2.03)	0.49	1.46 (0.85–2.53)	0.17
4 Weeks											
Death — no. (%)	128 (12.2)	126 (12.0)	91 (8.7)	1.38 (1.07–1.78)	0.01	1.40 (1.08–1.80)	0.01	1.01 (0.80–1.28)	0.91	1.39 (1.11–1.74)	0.004
Neurologic sequelae — no./total no. (%)‡	22/990 (2.2)	19/996 (1.9)	20/997 (2.0)	0.95 (0.51–1.77)	0.87	1.10 (0.61–2.01)	0.74	1.16 (0.63–2.14)	0.62	1.03 (0.61–1.75)	0.92
Neurologic sequelae or death — no./total no. (%)‡	150/990 (15.2)	145/996 (14.6)	111/997 (11.1)	1.31 (1.04–1.65)	0.02	1.36 (1.08–1.71)	0.008	1.04 (0.84–1.28)	0.71	1.33 (1.09–1.64)	0.005

* Severe hypotension was defined as a systolic blood pressure of less than 50 mm Hg in children younger than 12 months of age, less than 60 mm Hg in children 1 to 5 years of age, and less than 70 mm Hg in children older than 5 years of age, plus one or more features of impaired perfusion.

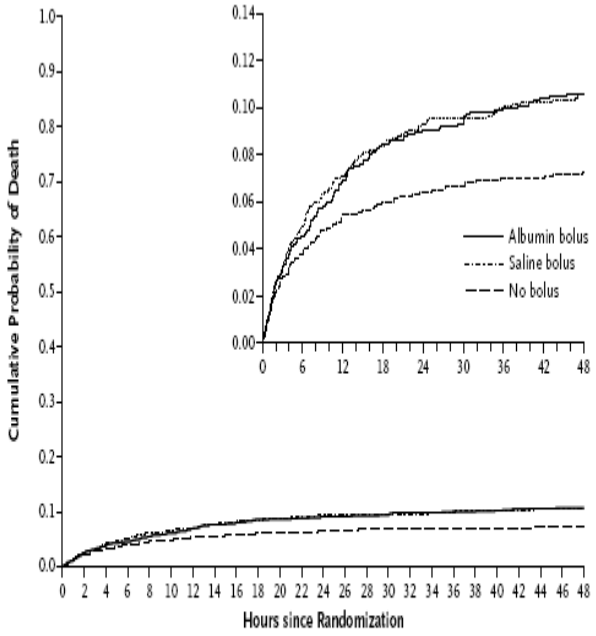
† Four children — three in the albumin-bolus group and one in the saline-bolus group — had both increased intracranial pressure and pulmonary edema.

‡ A total of 60 children in the albumin-bolus group, 51 in the saline-bolus group, and 47 in the control group did not have a neurologic assessment at 4 weeks.

Mortality after Fluid Bolus in African Children with Severe Infection

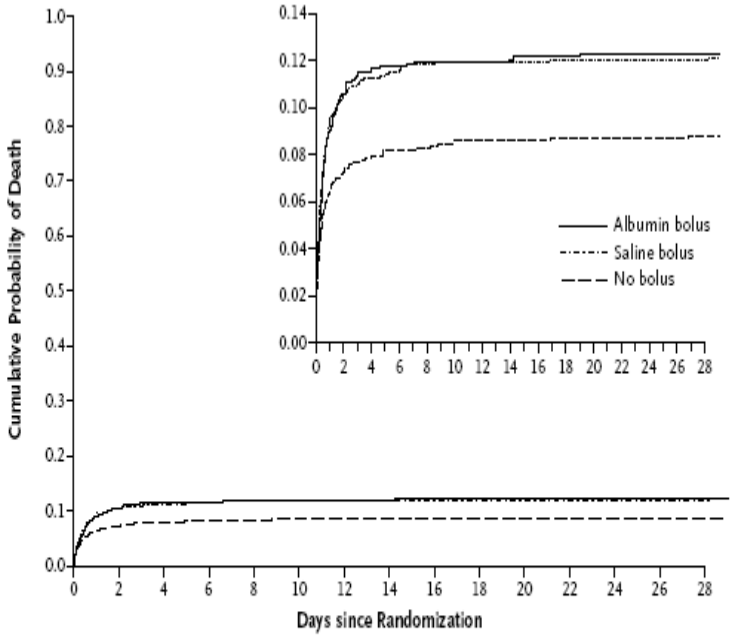
Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

A Mortality at 48 Hours



	Hr 1			Hr 2			Hr 3			Hr 4			Hr 5–8			Hr 9–24			Hr 24–48		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	1037	1033	1030	1024	1018	1021	1016	1010	1015	1010	1001	1011	992	980	996	954	945	975
Died	13	12	14	13	15	9	8	7	6	6	9	4	17	20	14	38	34	20	16	13	9
%	1.2	1.1	1.3	1.3	1.5	0.9	0.8	0.7	0.6	0.6	0.9	0.4	1.7	2.0	1.4	3.8	3.5	2.0	1.7	1.4	0.9

B Mortality at 4 Weeks



	Day 1			Day 2			Day 3–7			Day 8–14			Day 15–21			Day 21–28		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	954	945	975	914	917	947	901	909	940	899	902	933	897	901	934
Died	95	97	67	16	13	9	11	7	7	2	6	2	2	1	4	2	1	1
%	9.0	9.3	6.4	1.7	1.4	0.9	1.2	0.8	0.7	0.2	0.7	0.2	0.2	0.1	0.4	0.2	0.1	0.2

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

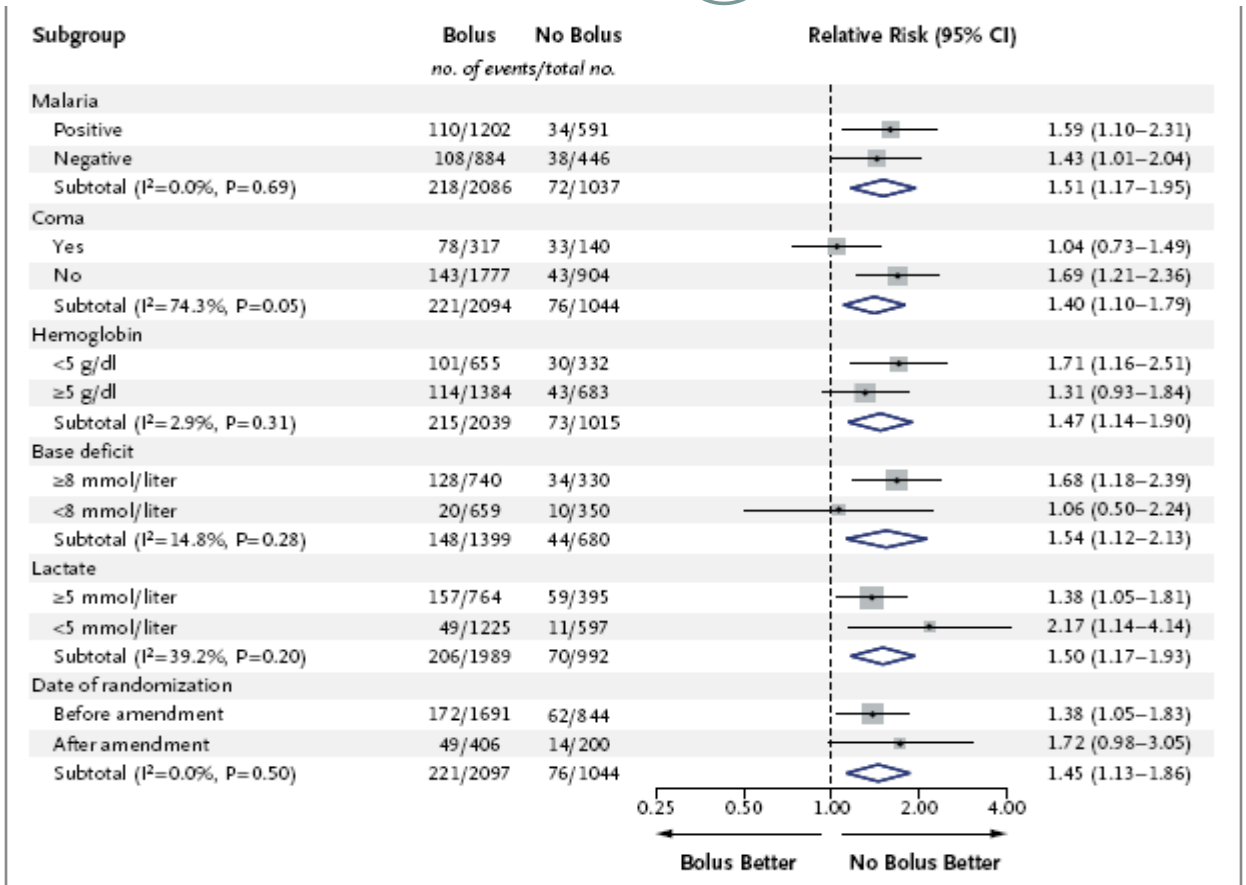


Figure 3. Mortality at 48 hours in Prespecified Subgroups.

The sizes of the boxes are proportional to the Mantel–Haenszel weights. The I^2 statistic indicates the percentage of total variation that was due to heterogeneity.

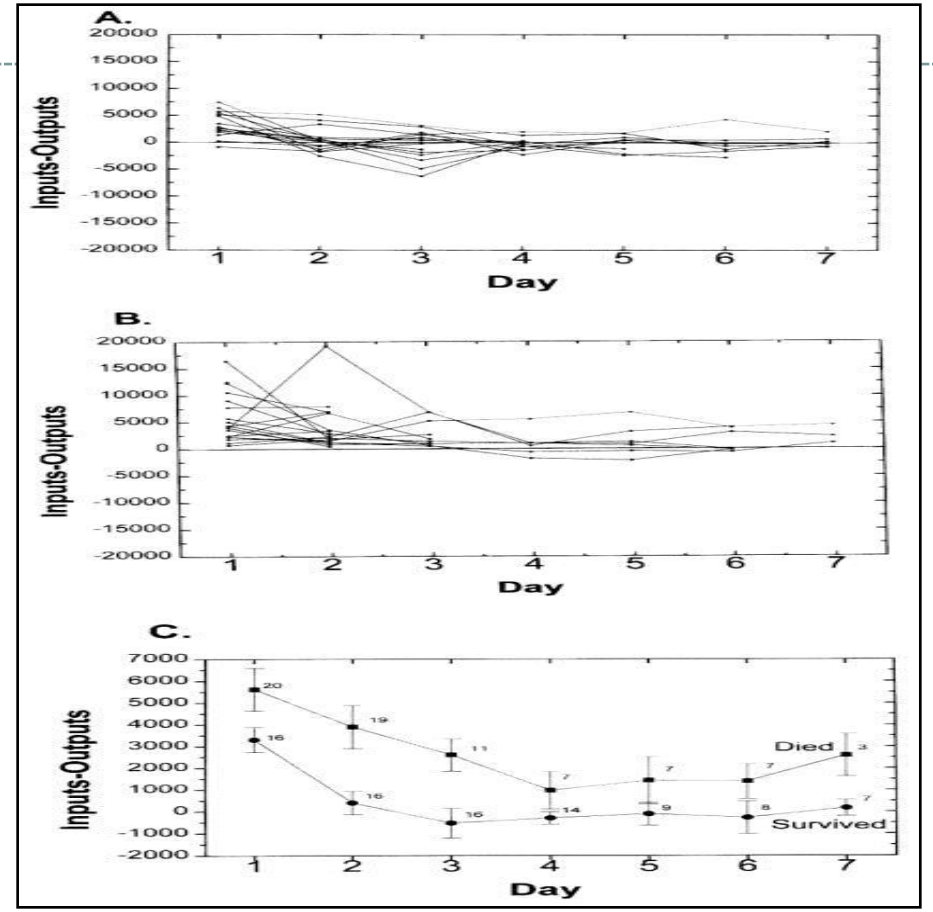
QUELLE QANTITÉ ?

- **Negative Fluid Balance Predicts Survival in Patients With Septic Shock*: A Retrospective Pilot Study.**
- Alsous, Fadi; Khamiees, Mohammad; DeGirolamo, Angela; Amoateng-Adjepong, Yaw; MD, PhD; Manthous, Constantine; MD, FCCP .

Characteristics	No. of Patients Who Survived (n = 16)	No. of Patients Who Died (n = 20)	p Value
Age, yr	61.1 ± 6.3 (72/16–85)	72.4 ± 2.9 (72/35–91)	0.12
Bacteriology			
GPC	4	5	1.0
GNR	9	6	0.13
Mixed GPC/GNR	0	3	0.12
Fungal	1	1	0.90
Unknown	2	5	0.35
Site of infection			
UTI	7	6	0.39
Pneumonia	5	8	0.58
Other/unknown	4	6	0.74
APACHE II score	20.4 ± 1.7 (19.5/11–34)	29.8 ± 1.7 (29.5/15–46)	0.0002
Day 1 SOFA score	6.9 ± 0.8 (7/3–13)	10.8 ± 1.2 (10/3–25)	0.01
Day 3 SOFA score†	5.4 ± 0.8‡ (4.5/1–11)	9.5 ± 1.91 (7/3–19)	0.06
Day 1 fluid balance (input-output), mL	3,305.6 ± 575.2 (2,668/−905–7449)	5,618.3 ± 981.2 (4,114/688–16,413)	0.05
Day 1 fluid inputs, mL	4,943.7 ± 506.0 (4,884/1,898–8,215)	6,227.3 ± 1037.4 (4,659/688–17,563)	0.26
≥ One day ≤ − 500-mL balance by day 3, No. of patients	11	0	0.0001
Any day with a ≤−500-mL fluid balance	14	2	0.0001
Admission creatinine level, mg/dL	1.9 ± 0.5 (1.7/0.5–5.1)	5.5 ± 0.6 (2.1/0.6–12.7)	0.05
Required hemodialysis	0	2	0.20
Required mechanical ventilation	7	17	0.01
ALI or ARDS (by day 3)	1	4	0.23
DIC (by day 3)	0	4	0.07
Encephalopathy (by day 3)	0	11	0.001
Any MAP < 60 mm Hg (days 2 and 3)	12	13	0.67
Any pressors by day 3	0	6	0.02
Diuretics	8	7	0.37

*Values are given as mean ±SE (median/range) or No. unless otherwise indicated. GPC = Gram-positive cocci; GNR = Gram-negative rod; UTI = urinary tract infection; ALI = acute lung infection; DIC = disseminated intravascular coagulation; MAP = mean arterial pressure.
†n = 14.
‡n = 11.

Chest. 117(6):1749-1754, June 2000.



- Figure 1 . Fluid balance in subgroups of 36 patients with septic shock. Top, A: net fluid balance (inputs-outputs) in patients who survived is shown. Middle, B: net fluid balance in patients who died is shown. Bottom, C: the aggregate daily mean (+/- SE) values comparing those who survived vs those who died are shown. Note that due to deaths and transfers from the ICU, the number of patients for whom accurate fluid balance data were available decreased with time. The small numbers over each point signify the number of patients included in the computation of the mean +/- SE.

Chest. 117(6):1749-1754, June 2000.

Characteristics	No. of Patients with ≥ 1 Day Net Negative by Day 3 (n = 11)	No. Days Net Negative Balance by Day 3 (n = 16)	p Value
Mortality rate, %	0	11 (69)	< 0.05
Age, yr	57.7 ± 7.5 (68/16–84)	72.6 ± 4.1 (75.5/20–88)	0.10
Bacteriology			
GPC	3	6	0.57
GNR	6	6	0.38
Mixed GPC/GNR	0	1	0.41
Fungal	1	0	0.23
Unknown	1	3	0.49
Site of infection			
UTI	5	5	0.46
Pneumonia	3	8	0.25
Other/unknown	3	3	0.61
APACHE II score	20.3 ± 2.1 (20/11–34)	26.2 ± 2.4 (24.5/14–46)	0.08
Day 1 SOFA score	7.5 ± 1.0 (7/3–13)	8.2 ± 1.1 (7.5/3–17)	0.63
Day 3 SOFA score	4.7 ± 0.9 (4/1–11)†	8.8 ± 1.4 (7/3–19)‡	0.03
Day 1 fluid balance (inputs-outputs), mL	3,172.8 ± 774.4 (2,538/−905–7,449)	3,818.1 ± 695.9 (3,490.5/688–12,296)	0.54
Day 1 fluid inputs, mL	4,660.2 ± 621.4 (4,747/1,898–8,215)	6,095.3 ± 843.5 (4,780/688–17,563)	0.18
Admission creatinine level, mg/dL	2.1 ± 0.4 (2.1/0.9–5.1)	2.1 ± 0.4 (1.7/0.5–4.9)	0.99
Required mechanical ventilation	4	11	0.11
Required hemodialysis	0	2	0.23
ALI or ARDS (by day 3)	2	3	0.97
DIC (by day 3)	0	2	0.23
Encephalopathy (by day 3)	1	4	0.31
Any MAP < 60 mm Hg (days 2 and 3)	4	7	0.70
Any pressors by day 3	0	2	0.23
Diuretics	5	7	0.93

*Values given as mean ± SE (median/range) or No., unless otherwise indicated. See Table 1 for abbreviations.
†n = 10.
‡n = 15.

Table 2 -Comparison of Selected Characteristics of Patients With Septic Shock Who Were Alive on Day 3 and Who Had at Least 1 Day of Net Negative Fluid Balance vs Those Who Did Not

The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock

Groupe 1: REMPLISSAGE > 20ml/K g pour avoir une PVC > 8
Groupe 2: bilan négatif pendant deux jours sur sept

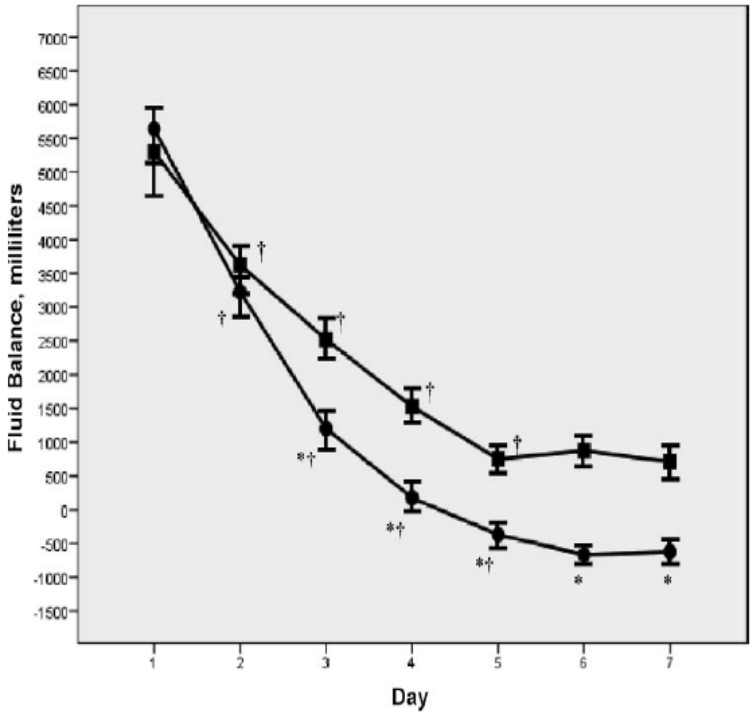


FIGURE 1. Mean (± SE) daily fluid balance (in milliliters) for days 1 through 7 following the onset of septic shock. Nonsurvivors are depicted by squares, and survivors by circles. * = $p < 0.05$ pairwise compared between survivors and nonsurvivors (ANOVA for repeated measures); † = $p < 0.05$ compared with the previous time point (ANOVA for repeated measures).

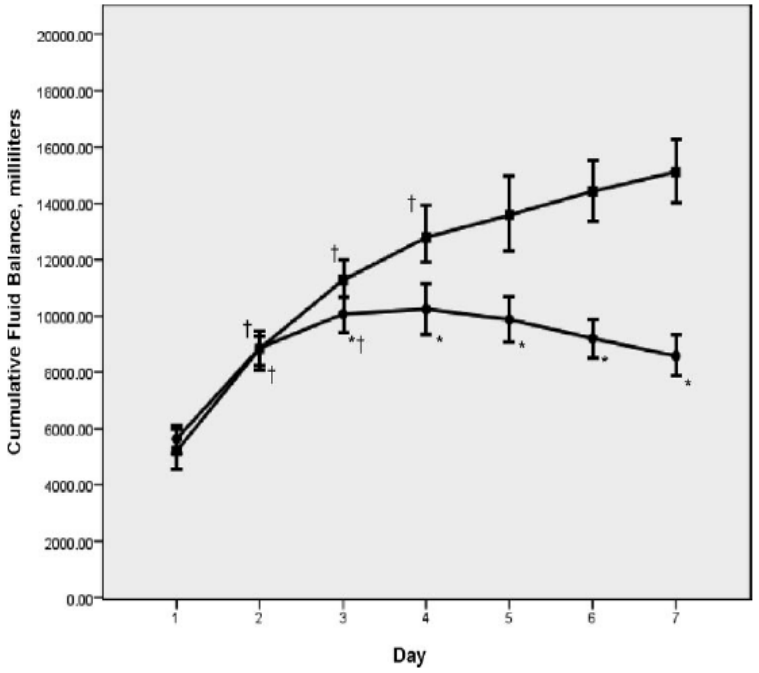


FIGURE 2. Mean (± SE) cumulative daily fluid balance (in milliliters) for days 1 through 7 following the onset of septic shock. Nonsurvivors are depicted by squares, and survivors by circles. * = $p < 0.05$ pairwise compared between survivors and nonsurvivors (ANOVA for repeated measures); † = $p < 0.05$ compared with the previous time point (ANOVA for repeated measures).

(CHEST 2009; 136:102–109)

The Importance of Fluid Management in Acute Lung Injury Secondary to Septic Shock

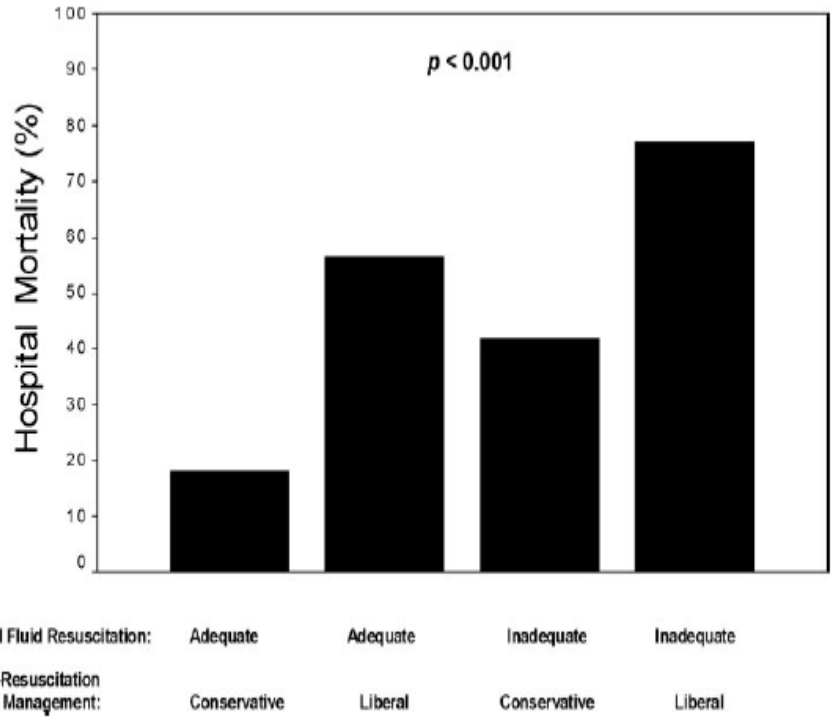


FIGURE 3. Hospital mortality according to whether or not patients achieved AIFR, CLFM, both, or neither.

Table 3—*Multivariate Analyses of Independent Risk Factors for Hospital Mortality*

Variables	Adjusted OR	95% CI	p Value
APACHE II score, 1-point increments	1.07	1.01–1.14	0.030
Charlson comorbidity score, 1-point increments	1.11	1.01–1.23	0.040
Renal replacement therapy	3.15	1.51–4.79	0.020
Colloid administration	2.94	1.41–4.47	0.011
AIFR not achieved	4.94	2.07–11.79	< 0.001
Duration of vasopressors, 1-day increments	1.24	1.04–1.47	0.017
CLFM not achieved	6.13	2.77–13.57	< 0.001

Other covariates not in the table had a p value < 0.5, including BMI ≥ 40 kg/m^2, patient location prior to ICU admission, medical ICU patients, and transfusion of packed RBCs (p = 0.588 [Hosmer-Lemeshow goodness-of-fit test]). CI = confidence interval; OR = odds ratio.

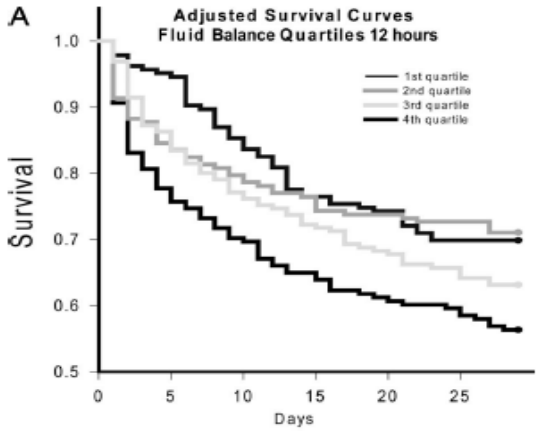
(CHEST 2009; 136:102–109)

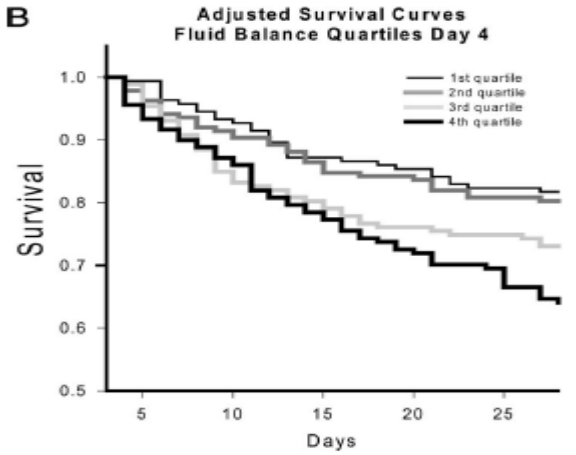
Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

Table 1. Fluid intake, urine output, and net fluid balance at 12 hrs and cumulative day 4 balance

	Quartile 1 (Dry)	Quartile 2	Quartile 3	Quartile 4 (Wet)
12 hrs				
Intake, mL	2900 (2050–3900)	4520 (3700–5450)	6110 (5330–7360)	10,100 (8430–12,100)
Output, mL	2200 (1100–3920)	1590 (960–2560)	1180 (600–2070)	1260 (600–2400)
Balance, mL	710 (−132–1480)	2880 (2510–3300)	4900 (4290–5530)	8150 (7110–10,100)
Day 4				
Intake, mL	16,100 (12,800–19700)	18,500 (15,700–22,500)	22,800 (19,700–26,700)	30,600 (26,200–36,000)
Output, mL	14,600 (11,500–20100)	11,000 (8210–14,500)	9960 (6940–12,900)	8350 (5100–12,300)
Balance, mL	1560 (−723–3210)	8120 (6210–9090)	13,000 (11,800–14,700)	20,500 (17,700–24,500)

Volumes are expressed as median (25–75%).





John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)

(Crit Care Med 2011; 39:259–265)

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

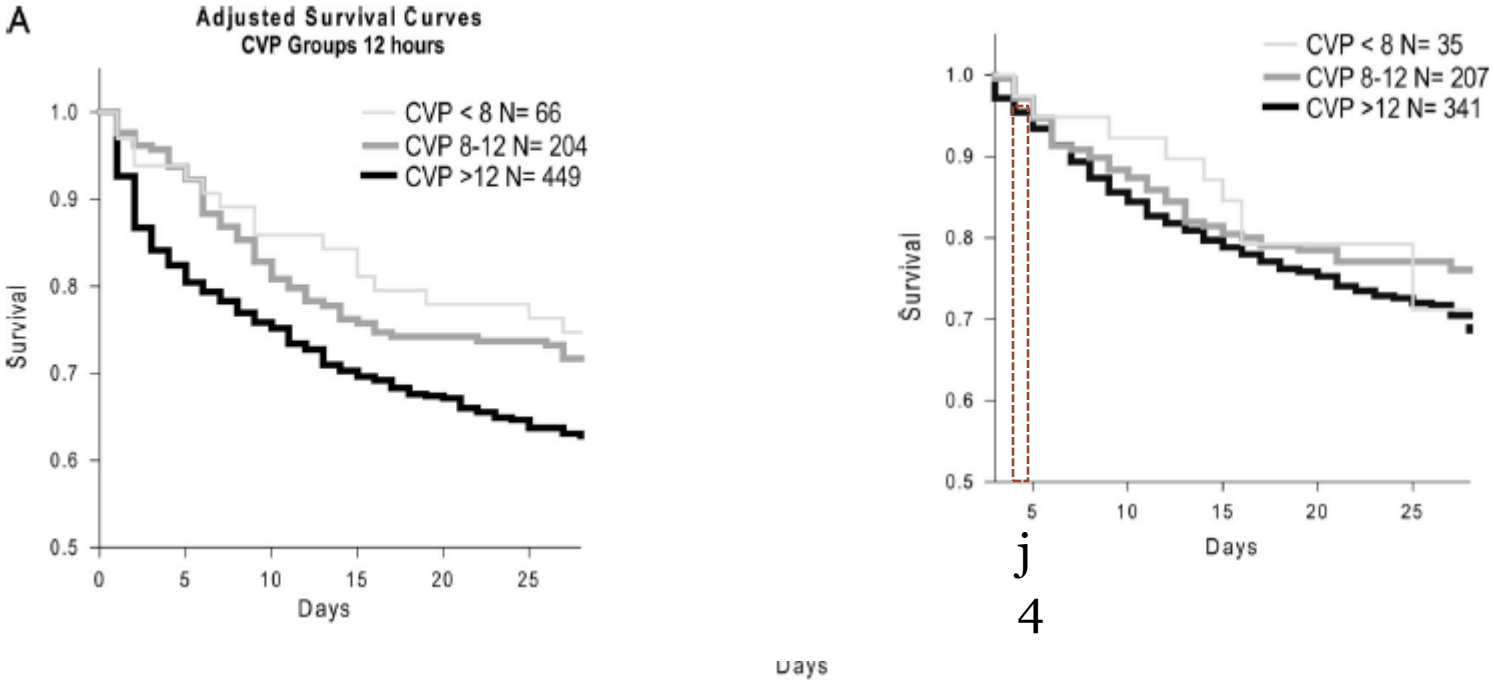


Figure 4. *A*, Cox survival curves, adjusted for age, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and severity of shock (dose of norepinephrine), are shown for central venous pressure (*CVP*) groups at 12 hrs. Patients with a CVP of <8 mm Hg at 12 hrs have the lowest mortality followed by those with CVP of 8–12 mm Hg and patients with a CVP >12 mm Hg had the highest mortality. B, Cox survival curves, adjusted for age, APACHE II score, and dose of norepinephrine, are shown for CVP groups on day 4. There were no significant differences in mortality among groups.

(Crit Care Med 2011; 39:259–265)

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

Table 2. Hazard ratio for death according to fluid balance quartiles

Fluid Balance Group	Adjusted Hazard Ratio versus Quartile 4
12 hrs	
Quartile 1	0.569 (0.405–0.799)
Quartile 2	0.581 (0.414–0.816)
Quartile 3	0.762 (0.562–1.033)
Day 4	
Quartile 1	0.466 (0.299–0.724)
Quartile 2	0.512 (0.339–0.775)
Quartile 3	0.739 (0.503–1.087)

Hazard ratios are shown with their 95% confidence intervals.

Table 3. Hazard ratio for death according to CVP group

CVP Group	Adjusted Hazard Ratio versus CVP >12 mm Hg
12 hrs	
CVP <8 mm Hg	0.606 (0.363–0.913)
CVP 8–12 mm Hg	0.762 (0.562–0.943)
Day 4	
CVP <8 mm Hg	0.903 (0.484–1.686)
CVP 8–12 mm Hg	0.764 (0.542–1.078)

CVP, central venous pressure.

Hazard ratios are shown with their 95% confidence intervals.

(Crit Care Med 2011; 39:259–265)

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Table 2. Furosemide Dose, Fluid Intake, Fluid Output, and Fluid Balance on Each Day during the Study.*

Day	Furosemide		Fluid Intake		Fluid Output		Fluid Balance	
	Liberal	Conservative	Liberal	Conservative	Liberal	Conservative	Liberal	Conservative
	mg/24 hr (no. of patients)		*ml/24 hr (no. of patients)*		*ml/24 hr (no. of patients)*		*ml/24 hr (no. of patients)*	
1	74.27±7.48 (133)	148.94±8.52 (312)	5029.8±132.98 (485)	4230.5±120.03 (491)	2501.9±73.23 (485)	3043.8±93.90 (491)	2529.5±148.99 (484)	1186.7±151.01 (491)
2	72.46±6.65 (146)	157.35±8.91 (304)	4467.4±136.11 (479)	3590.6±98.45 (480)	2824.5±101.44 (479)	3966.7±115.57 (480)	1642.9±151.71 (479)	−376.1±161.08 (480)
3	65.28±6.49 (140)	166.90±10.01 (269)	3997.1±103.40 (465)	3390.4±85.30 (464)	3060.9±103.23 (465)	3797.3±110.48 (465)	936.12±115.32 (465)	−408.5±135.90 (464)
4	80.74±10.23 (129)	154.25±10.61 (228)	3752.0±102.07 (444)	3430.8±96.49 (437)	3188.1±109.19 (444)	3606.1±113.38 (434)	563.88±100.98 (444)	−165.5±119.92 (434)
5	73.06±8.41 (119)	164.71±12.06 (197)	3825.3±110.62 (424)	3201.1±87.23 (411)	3358.7±115.49 (421)	3444.8±108.98 (408)	483.03±109.98 (421)	−226.3±115.22 (408)
6	58.20±6.68 (106)	158.87±13.45 (165)	3782.8±104.28 (411)	3159.4±88.12 (382)	3334.4±123.99 (411)	3316.9±103.81 (379)	508.04±111.75 (410)	−144.9±110.25 (378)
7	51.03±4.31 (87)	127.86±11.61 (137)	3639.7±93.96 (390)	3226.9±108.18 (355)	3216.8±98.36 (385)	3143.9±100.16 (346)	458.95±106.85 (385)	130.08±118.47 (346)

* Plus–minus values are means ±SE. Numbers in parentheses indicate the number of patients receiving at least one dose of furosemide on that day or the number of patients with a fluid measurement. $P<0.001$ for all comparisons except for fluid intake on day 4 ($P=0.02$) and day 7 ($P=0.004$); fluid output on day 4 ($P=0.008$), day 5 ($P=0.58$), day 6 ($P=0.94$), and day 7 ($P=0.61$); and fluid balance on day 7 ($P=0.04$). Negative fluid balance means that fluid output exceeded fluid intake.

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Table 3. Main Outcome Variables.*

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001
Organ-failure–free days†‡			
Days 1 to 7			
Cardiovascular failure	3.9±0.1	4.2±0.1	0.04
CNS failure	3.4±0.2	2.9±0.2	0.02
Renal failure	5.5±0.1	5.6±0.1	0.45
Hepatic failure	5.7±0.1	5.5±0.1	0.12
Coagulation abnormalities	5.6±0.1	5.4±0.1	0.23
Days 1 to 28			
Cardiovascular failure	19.0±0.5	19.1±0.4	0.85
CNS failure	18.8±0.5	17.2±0.5	0.03
Renal failure	21.5±0.5	21.2±0.5	0.59
Hepatic failure	22.0±0.4	21.2±0.5	0.18
Coagulation abnormalities	22.0±0.4	21.5±0.4	0.37
Dialysis to day 60			
Patients (%)	10	14	0.06
Days	11.0±1.7	10.9±1.4	0.96

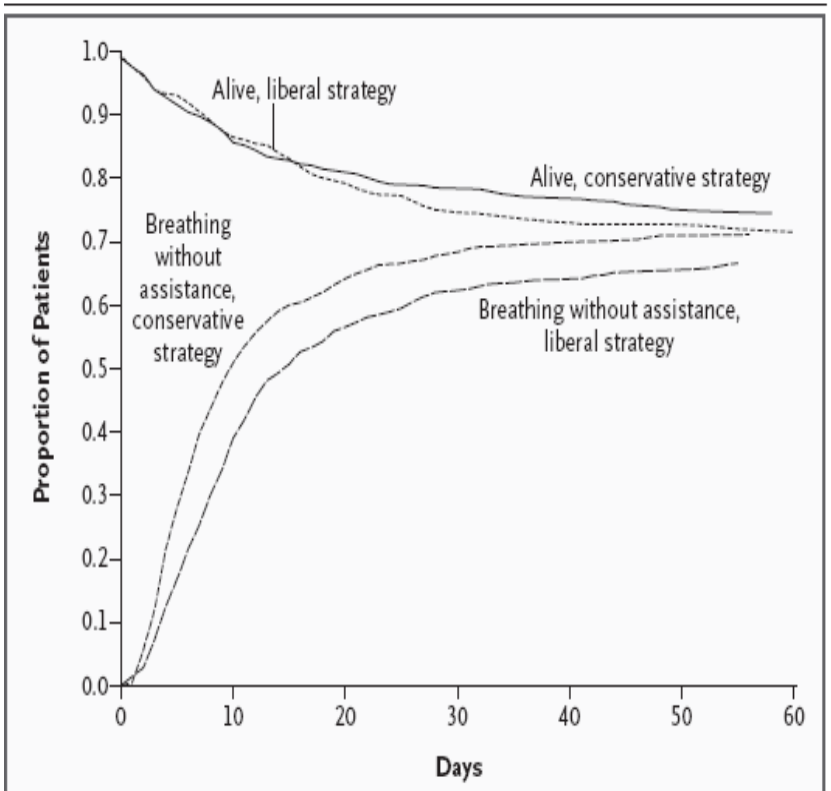


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

QUELLE VALEUR HEDYNAMIQUE DE LA SVO_2

$$\underline{SvO_2} = SaO_2 - (VO_2 / (Qc \times Hb \times PO))$$

ELEVATION OF SYSTEMIC OXYGEN DELIVERY IN THE TREATMENT OF CRITICALLY ILL PATIENTS

MICHELLE A. HAYES, F.R.C.A., ANDREW C. TIMMINS, F.R.C.A., ERNEST H.S. YAU, F.R.C.A., MARK PALAZZO, F.R.C.A., CHARLES J. HINDS, F.R.C.A., AND DAVID WATSON, F.R.C.A.

Table 2. Outcome Data.

OUTCOME	CONTROL GROUP (N = 50)	TREATMENT GROUP (N = 50)	NOT RANDOMIZED (N = 9)
Days in unit — median (range)	10 (1–64)	10 (1–48)	10 (1–29)
Ventilation			
No. of days — median (range)	8 (0–54)	8 (0–41)	2 (0–26)
No. of patients	44	46	7
Days in hospital — median (range)	23.5 (1–244)	19 (1–187)	20 (11–102)
Mortality — %			
In intensive care unit	30	50*	—
In hospital	34	54*	—
Predicted risk of death — median % (range)	34 (3–91)	34 (3–85)	6 (3–32)
Cause of death — no. of patients			
Intractable hypotension	4	4	—
Cardiac event	2	4	—
Multiple organ failure	9	17	—

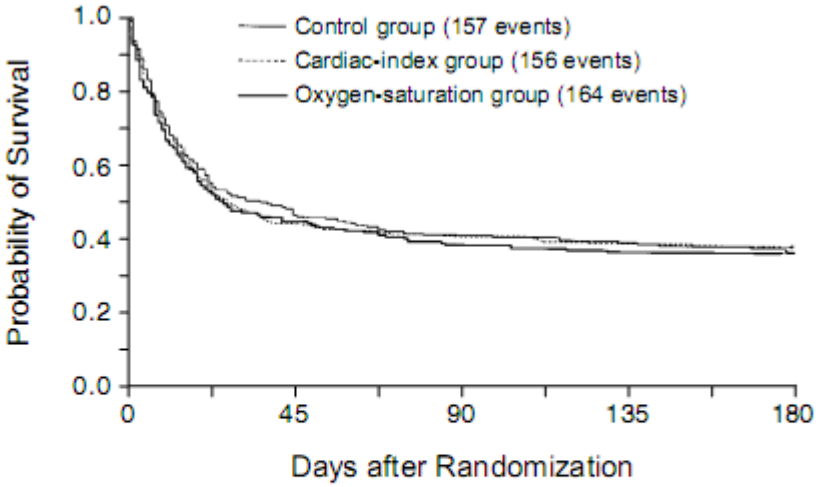
*P = 0.04 for the comparison between the control and treatment groups.

(N Engl J Med 1994;330:1717-22.)

A TRIAL OF GOAL-ORIENTED HEMODYNAMIC THERAPY IN CRITICALLY ILL PATIENTS

LUCIANO GATTINONI, M.D., LUCA BRAZZI, M.D., PAOLO PELOSI, M.D., ROBERTO LATINI, M.D., GIANNI TOGNONI, M.D., ANTONIO PESENTI, M.D., AND ROBERTO FUMAGALLI, M.D., FOR THE SVO2 COLLABORATIVE GROUP*

Groupe contrôle: IC:2.5-3.5
Groupe2: IC >4.5
Groupe3: SVO≥ 70%



PATIENTS AT RISK (NO. OF EVENTS)

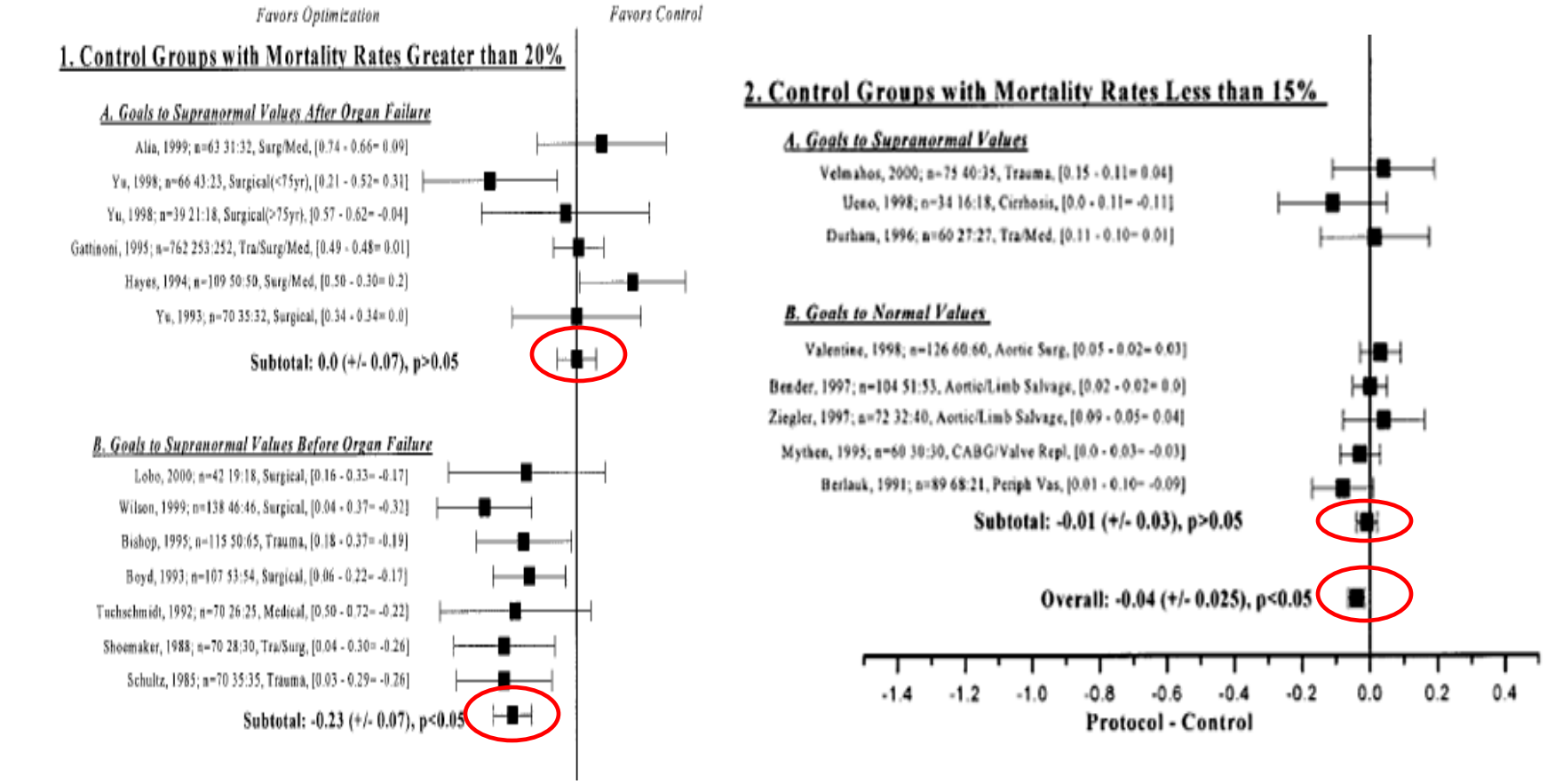
Control group	252 (129)	108 (13)	94 (4)	90 (3)	87
Cardiac-index group	253 (133)	102 (8)	90 (4)	86 (3)	83
Oxygen-saturation group	257 (133)	106 (16)	89 (4)	85 (1)	84

Figure 2. Survival Curves from Study Entry to the Six-Month Follow-up in the Three Study Groups.

(N Engl J Med 1995;333:1025-32.)

Meta-analysis of hemodynamic optimization in high-risk patients*

Jack W. Kern, PharmD; William C. Shoemaker, MD



Crit care Med 2002; 30:1686-1692

PVC ?

Les indices statiques de précharge

Les pressions de remplissage : PVC

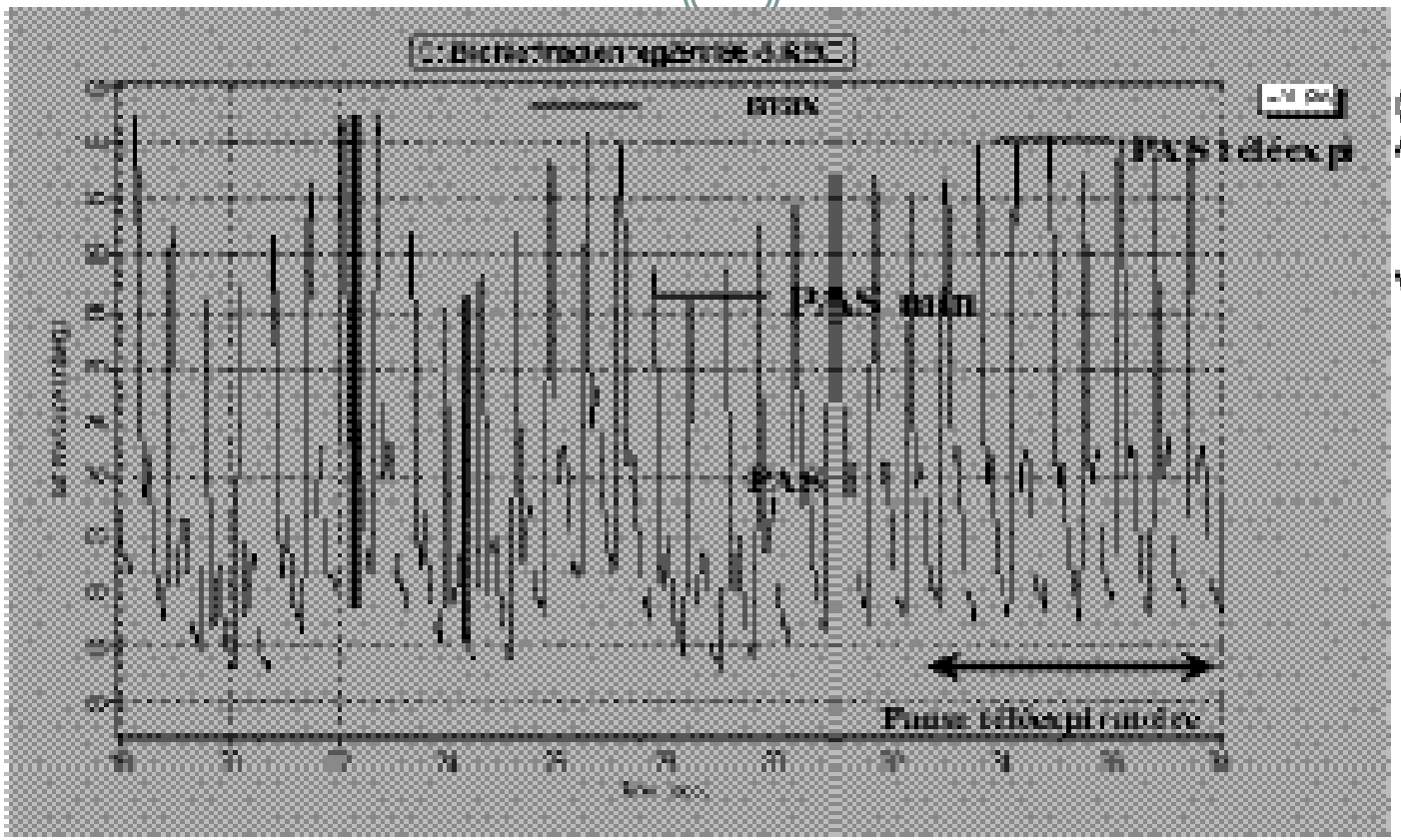
- même si correctement mesurées, PVC médiocres indices prédictifs de la réponse au RV.
- **Des valeurs en présence de valeurs (très) basses**
- **une efficacité du RV peut être raisonnablement attendue**

Annales Françaises d'Anesthésie et de Réanimation 24 (2005) 568–576

RECOMMANDATIONS

Recommandations d'experts de la SRLF
« Indicateurs du remplissage vasculaire au cours de l'insuffisance circulatoire »

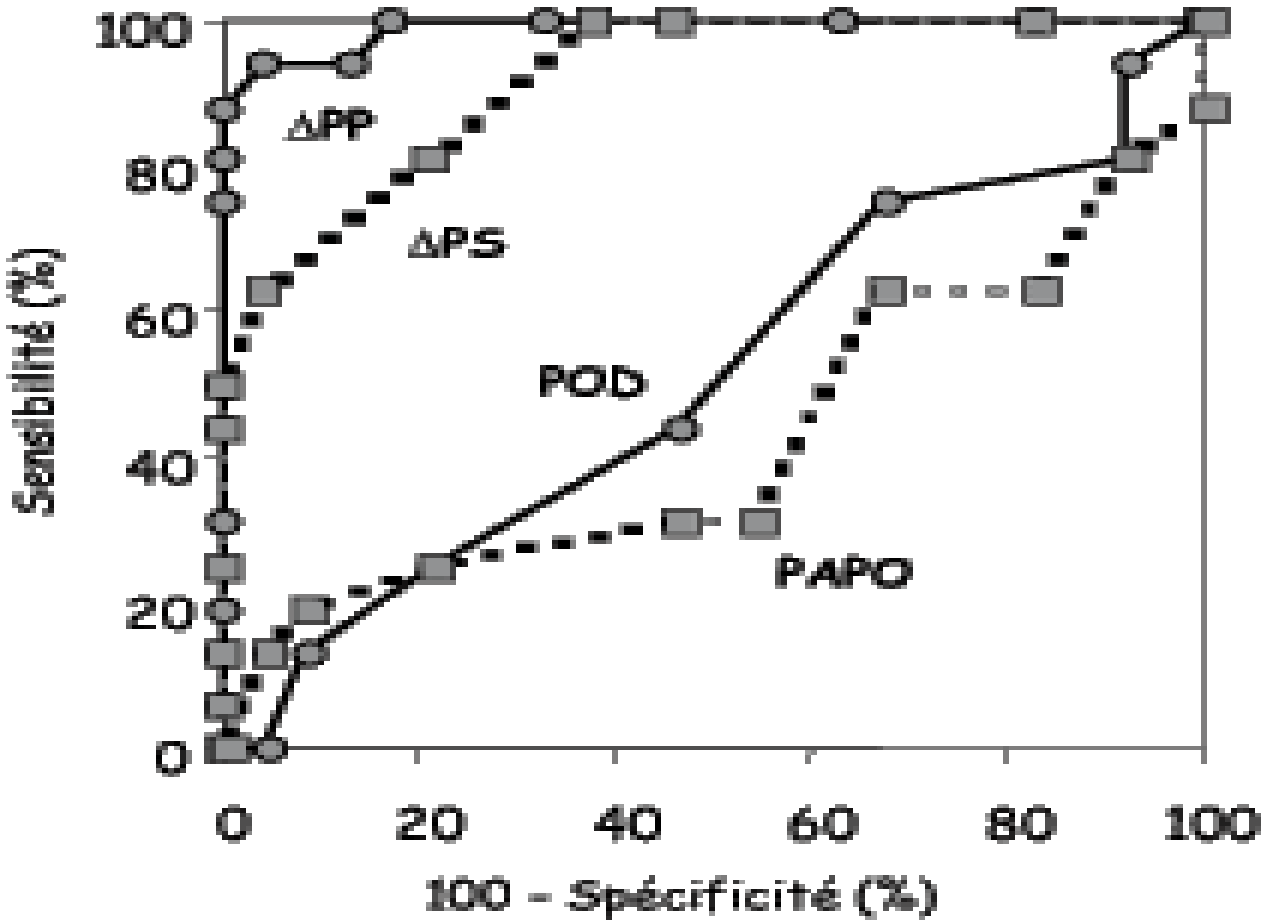
Méthodes dynamiques

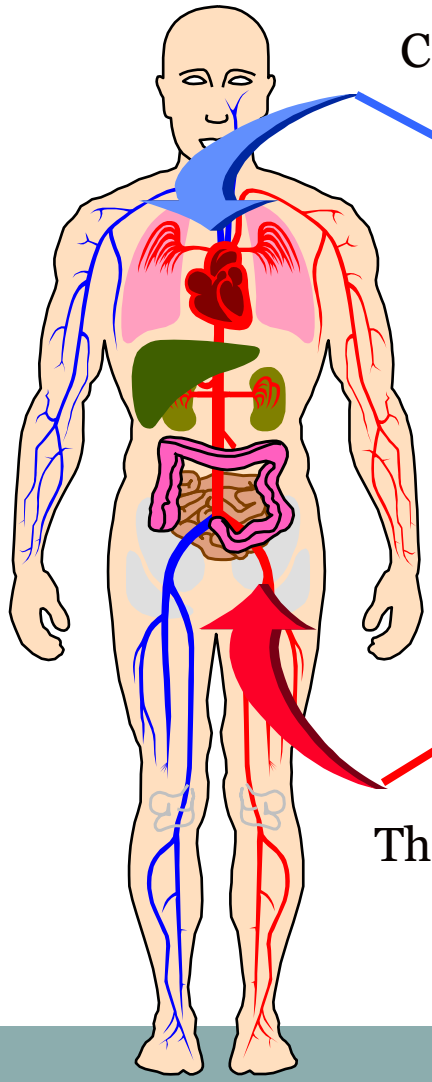


PP max PP min

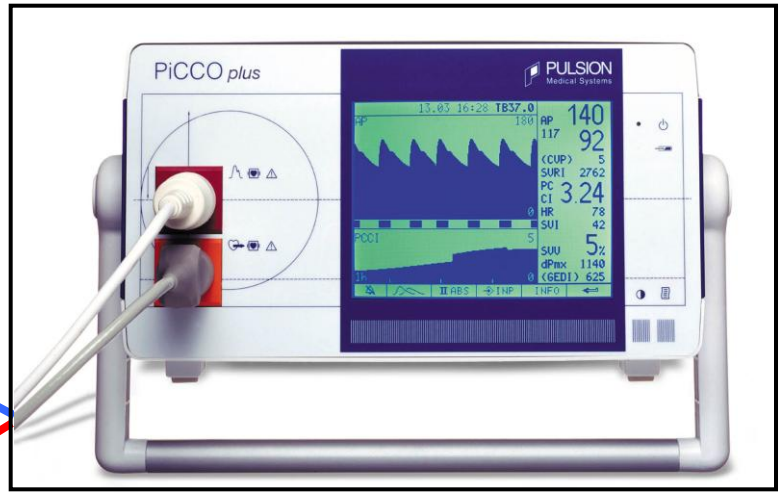
$$\Delta PP\ (\%) = (PPmax - PPmin) / [(PPmax + PPmin)/2]*100$$

Variations respiratoires de la POD,PAPO,deltaPS,et deltaPP





Central venous catheter



Thermodilution femoral arterial catheter


PHILIPS
Peha-soft

- Transfusion sanguine?

- Effect of Stored-Blood Transfusion on Oxygen Delivery in Patients With Sepsis
- Bone, Roger C.; Marik, Paul E.; Sibbald, William J.

Patient No.	Age, y	Diagnosis*	APACHE II	Baseline Lactate, mmol/L	ICU Outcome
1	65	Pulmonary embolus, *Pseudomonas* pneumonia	17	1.0	Alive
2	36	Pneumococcal pneumonia	22	2.4	Dead
3	23	HIV, septicemia	18	2.2	Alive
4	32	Burn, septicemia	24	3.2	Dead
5	54	Perforated peptic ulcer, septic abdomen	21	1.5	Dead
6	69	Perforated gallbladder, septic abdomen	15	1.7	Alive
7	49	Diabetes, necrotizing fasciitis	18	1.6	Alive
8	52	Gangrenous appendix	24	2.6	Alive
9	65	*Legionella* pneumonia	22	2.3	Alive
10	20	Home TPN, *Candida* septicemia	23	1.0	Alive
11	80	Pancreatitis, *Staphylococcus aureus* septicemia	26	8.7	Dead
12	77	*Legionella* pneumonia	18	1.1	Dead
13	68	Perforated colon, septic abdomen	24	4.9	Dead
14	70	CCF, *Candida* septicemia	18	1.9	Alive
15	40	Liver failure, pneumonia	28	2.7	Dead
16	68	Hepatitis, pneumococcal pneumonia	24	2.3	Dead
17	56	Metastatic carcinoid, *Pseudomonas* pneumonia	17	1.1	Dead
18	62	AAA, fibrosing alveolitis, septicemia	18	2.8	Alive
19	58	Polytrauma, ARDS, *Pseudomonas* pneumonia	20	1.1	Alive
20	62	Biliary pancreatitis, ARDS, *S aureus* septicemia	24	3.3	Dead
21	43	Pneumonia, *Escherichia coli* septicemia	19	5.5	Alive
22	73	Flail chest, pneumococcal pneumonia	14	1.3	Dead
23	79	AAA, *Pseudomonas* septicemia	21	5.7	Dead

*HIV indicates human immunodeficiency virus; TPN, total parenteral nutrition; CCF, congestive cardiac failure; AAA, abdominal aortic aneurysm; and ARDS, adult respiratory disease syndrome.

JAMA : Volume 269(23), 16 Jun 1993, pp 3024-3029 3024-3029

Effect of Stored-Blood Transfusion on Oxygen Delivery in Patients With Sepsis

Bone, Roger C.; Marik, Paul E.; Sibbald, William J.

	Mean (±SD)			
	Baseline	Immediate	3-Hour	6-Hour
All patients (n=23)				
Do_2I, mL/min·m²	565.1 (±224.4)	709.1 (±311.3)†	704.3 (±237.2)	690.3 (±237.6)
Calculated Vo_2I, mL/min·m²	162.9 (±47.6)	187.6 (±71.6)‡	183.7 (±50.6)	183.9 (±55.2)
Measured Vo_2I, mL/min·m²	138.9 (±35.5)	140.8 (±39.1)	138.4 (±34.5)	137.6 (±34.5)
Normal lactate (n=11)				
Calculated Vo_2I, mL/min·m²	141.8 (±14.7)	165.0 (±34.3)§	167.7 (±28.8)	162.0 (±34.1)
Measured Vo_2I, mL/min·m²	128.4 (±19.0)	131.4 (20.7)	130.1 (±19.0)	128.1 (±17.2)
Increased lactate (n=12)				
Calculated Vo_2I, mL/min·m²	182.3 (±58.9)	208.3 (±90.6)	198.4 (±62.2)	203.0 (±64.7)
Measured Vo_2I, mL/min·m²	148.5 (±44.6)	149.4 (±50.0)	146.1 (±43.8)	146.5 (±43.9)
Increase in gastric intramucosal pH (+Δ)(n=9)				
Measured Vo_2I, mL/min·m²	124.8 (±27.4)	124.6 (±28.4)	122.6 (±24.6)	122.2 (±24.7)

*Do_2I indicates systemic oxygen delivery indexed, and Vo_2I, systemic oxygen consumption indexed.
†$P<.001$.
‡$P<.01$.
§$P<.05$ for comparison of immediate with baseline values.

JAMA : Volume 269(23), 16 Jun 1993, pp 3024-3029 3024-3029

Age of Blood, d	Lactate, mmol/L	Baseline pHi	Immediate pHi	3-Hour pHi	6-Hour pHi
		Normal Lactate			
3	1.3	7.230	7.250	7.260	7.320
10	1.0	7.357	7.390	7.390	7.410
12	2.2	7.285	7.340	7.340	7.345
12	1.9	7.437	7.460	7.420	7.430
13	1.1	7.255	7.280	7.280	7.285
16	1.7	7.340	7.300	7.350	7.360
19	1.0	7.410	7.325	7.420	7.420
22	1.6	7.360	7.315	7.340	7.350
22	1.2	7.390	7.335	7.300	7.260
31	1.5	7.250	7.240	7.130	7.260
32	1.1	7.380	7.390	7.380	7.350
		Increased Lactate			
2	2.3	7.200	7.200	7.220	7.270
4	2.8	7.400	7.410	7.405	7.400
4	5.0	7.060	7.070	7.060	7.060
13	3.3	7.145	7.210	7.180	7.160
15	8.7	6.880	6.824	6.820	6.853
19	2.3	7.315	7.120	7.210	7.255
21	2.4	7.040	7.040	7.005	7.030
22	4.9	7.245	7.115	7.110	7.150
26	2.6	7.310	7.320	7.260	7.130
27	3.2	7.020	6.770	6.740	7.030
30	5.5	7.330	7.225	7.325	7.320
33	2.7	6.780	6.610	6.650	6.706

CONCLUSIONS: We failed to demonstrate a beneficial effect of red blood cell transfusion on measured systemic oxygen uptake in patients with sepsis. Patients receiving old transfused red blood cells developed evidence of splanchnic ischemia. We postulate that the poorly deformable transfused red blood cells cause microcirculatory occlusion in some organs, which may lead to tissue ischemia in some organs.

Association of mortality with age of blood transfused in septic ICU patients

F. Robert Purdy MSc DVM MD FRCPC,
Martin G. Tweeddale PhD MD FRCPC,
Pamela M. Merrick BSN

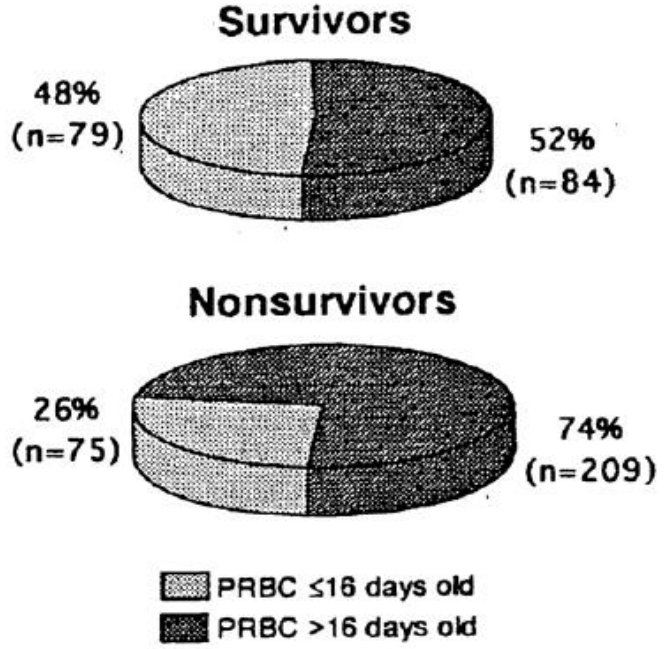


FIGURE 1 Proportion of PRBC units of different age transfused to survivors and nonsurvivors during sepsis ($P < .0001$). n = number of PRBC units in each subgroup.

CAN J ANAESTH 1997 / 44: 12 / pp 1256–1261

Acute lung injury following blood transfusion: Expanding the definition

Paul E. Marik, MD, FACP, FCCM, FCCP; Howard L. Corwin, MD, FACP, FCCM, FCCP

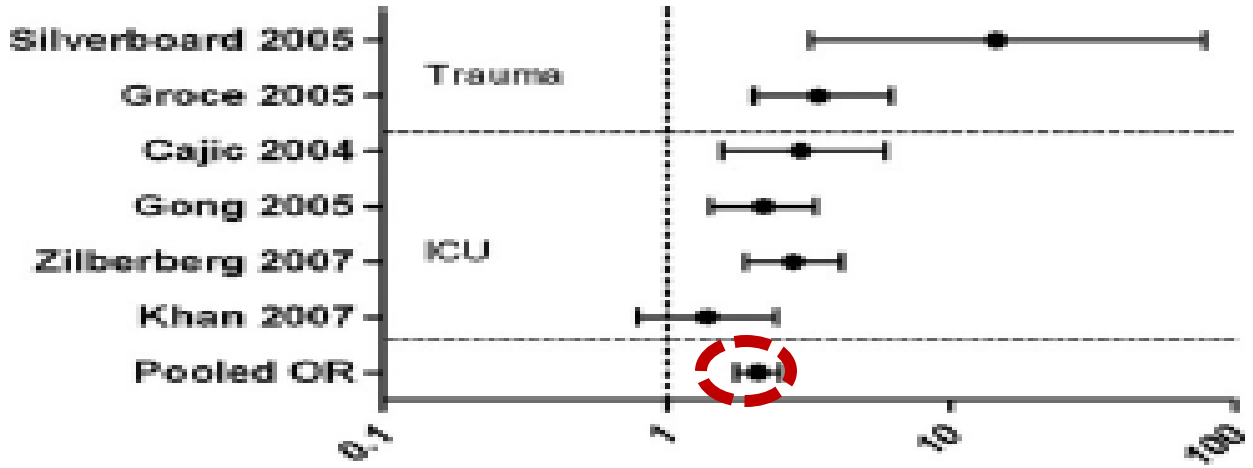


Figure 1. Effect of blood transfusions (any transfusion) on the risk of developing late transfusion-related acute lung injury (odds ratio and 95% confidence interval) (see reference 64). *ICU*, intensive care unit.

(Crit Care Med 2008; 36:3080–3084)

Efficacy of red blood cell transfusion in the critically ill: A systematic review of the literature*

Paul E. Marik, MD, FACP, FCCM, FCCP; Howard L. Corwin, MD, FACP, FCCM, FCCP

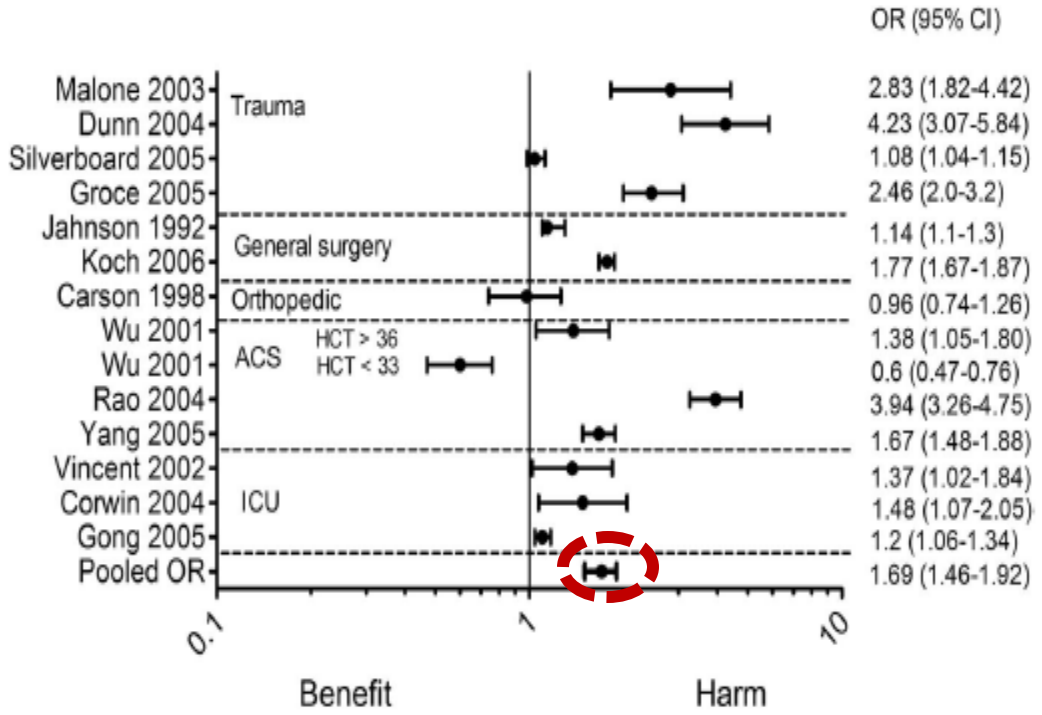


Figure 2. Association between blood transfusion and the risk of death (odds ratio [*OR*] and 95% confidence interval [*CI*]). *ACS*, abdominal compartment syndrome; *ICU*, intensive care unit.

(Crit Care Med 2008; 36:2667–2674)

- **Quelle drogue vasoactive ?**

Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial

*Djillali Annane, Philippe Vignon, Alain Renault, Pierre-Edouard Bollaert, Claire Charpentier, Claude Martin, Gilles Troché, Jean-Damien Ricard, Gérard Nitenberg, Laurent Papazian, Elie Azoulay, Eric Bellissant, for the CATS Study Group**

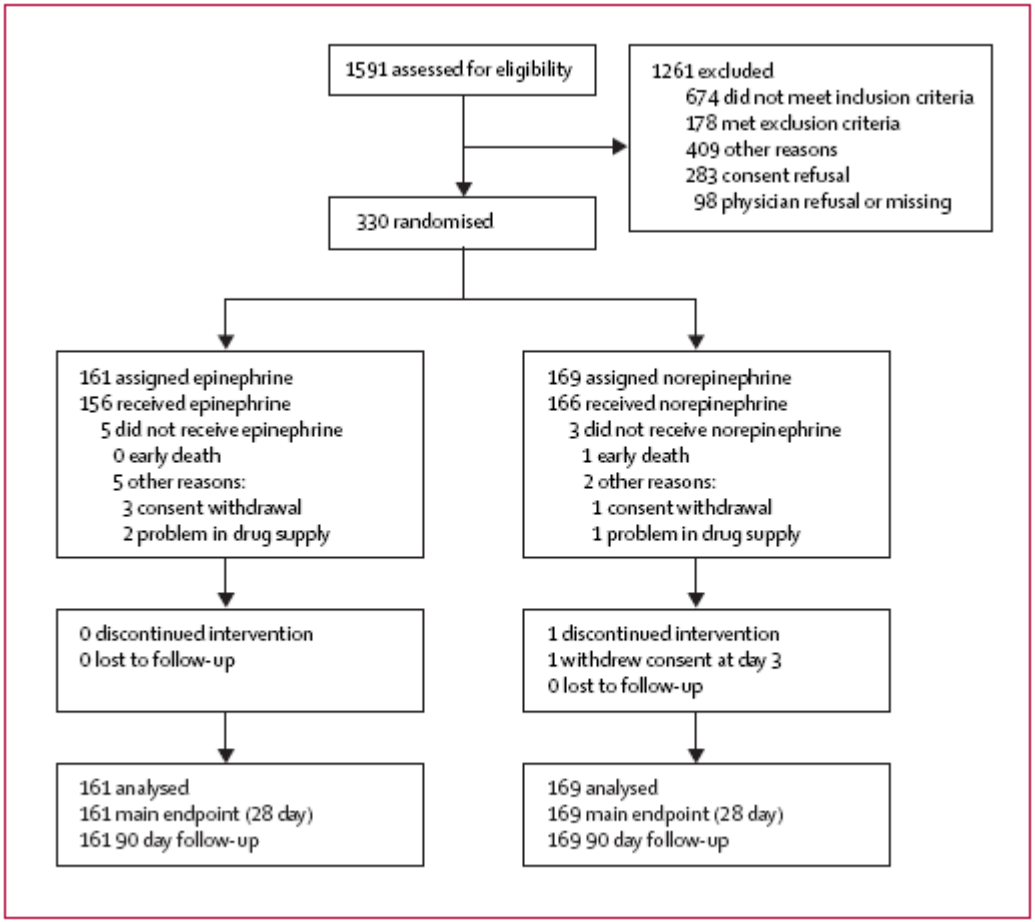


Figure 2: Trial profile

Lancet 2007; 370: 676–84

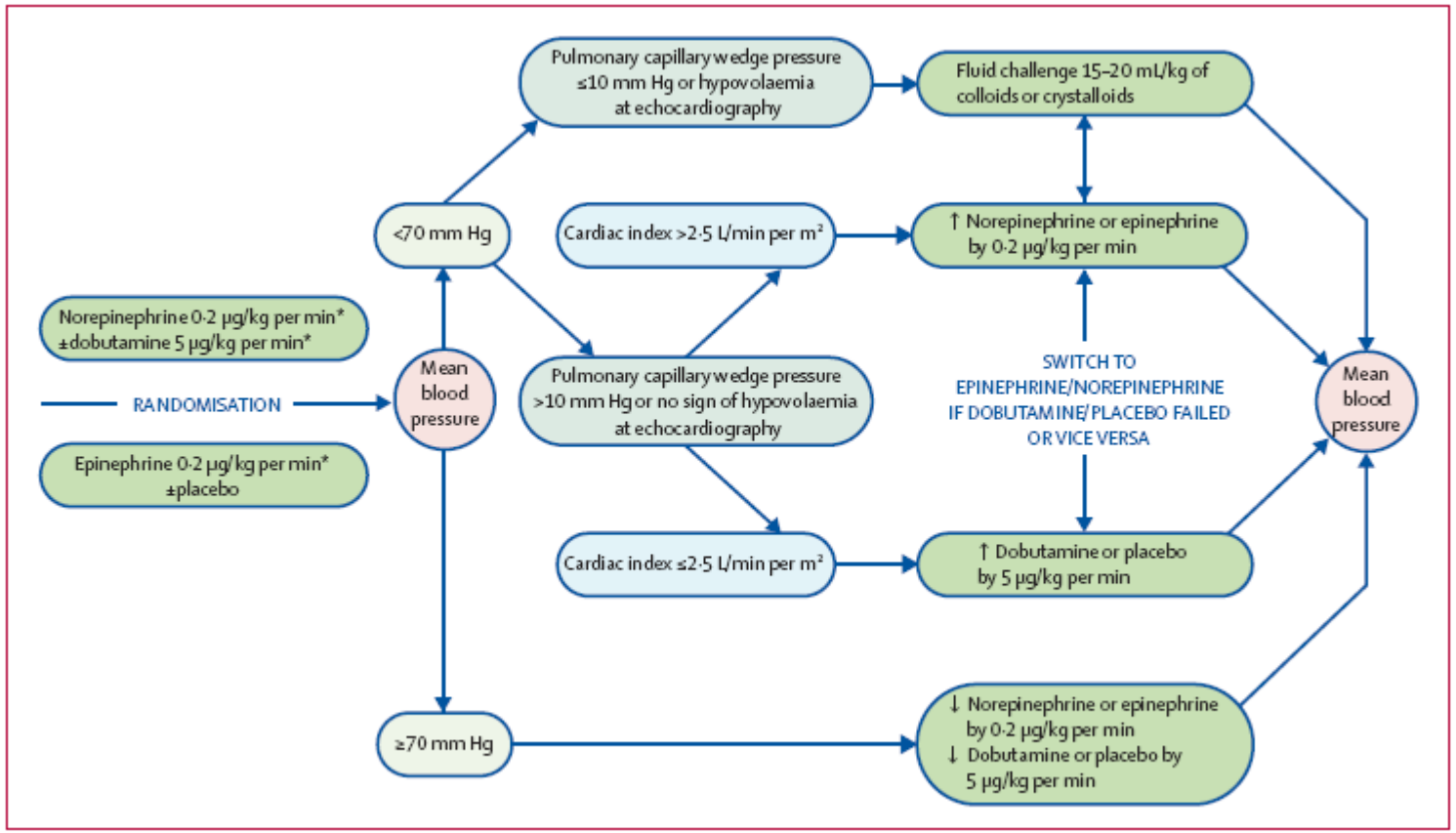


Figure 1: Treatment algorithm

	Overall (n=330)	Epinephrine (n=161)	Norepinephrine plus dobutamine (n=169)
Type of infection			
Community acquired	185 (56%)	88 (55%)	97 (57%)
Hospital acquired, postoperative	57 (17%)	31 (19%)	26 (15%)
Hospital acquired, others	88 (27%)	42 (26%)	46 (27%)
Primary source of infection			
Lung	155 (47%)	74 (46%)	81 (48%)
Abdomen	84 (25%)	45 (28%)	39 (23%)
Primary septicaemia	67 (20%)	28 (17%)	39 (23%)
Urinary tract	40 (12%)	19 (12%)	21 (12%)
Bones/joints/soft tissues	34 (10%)	12 (8%)	22 (13%)
Mediastinum/endocarditis	10 (3%)	6 (4%)	4 (2%)
Central nervous system	8 (2%)	4 (3%)	4 (2%)
Catheter related	6 (2%)	4 (3%)	2 (1%)
Head and neck	2 (0·6%)	1 (0·6%)	1 (0·6%)
Others	5 (2%)	3 (2%)	2 (1%)
Positive blood cultures	118 (36%)	64 (40%)	54 (32%)
Causal microorganism			
None	63 (19%)	30 (19%)	33 (20%)
One	174 (53%)	88 (55%)	86 (51%)
More than one	93 (28%)	43 (27%)	50 (30%)
Gram-positive bacteria	154 (47%)	69 (43%)	85 (50%)
Gram-negative bacteria	158 (48%)	83 (52%)	75 (44%)
Anaerobes	28 (9%)	11 (7%)	17 (10%)
Mycobacterium	3 (1%)	2 (1%)	1 (0·6%)
Fungi	28 (9%)	12 (8%)	16 (10%)
Parasite	1 (0·3%)	1 (0·6%)	0 (0%)
Virus	3 (1%)	3 (2%)	0 (0%)

Data are number of patients (%).

Table 2: Characteristics of infections

	Epinephrine (n=161)	Norepinephrine plus dobutamine (n=169)	p
At day 7	40 (25%)	34 (20%)	0·30
At day 14	56 (35%)	44 (26%)	0·08
At day 28	64 (40%)	58 (34%)	0·31
At discharge from intensive care	75 (47%)	75 (44%)	0·69
At discharge from hospital	84 (52%)	82 (49%)	0·51
At day 90	84 (52%)	85 (50%)	0·73

Data are number of deaths (%).

Table 3: All-cause mortality rates

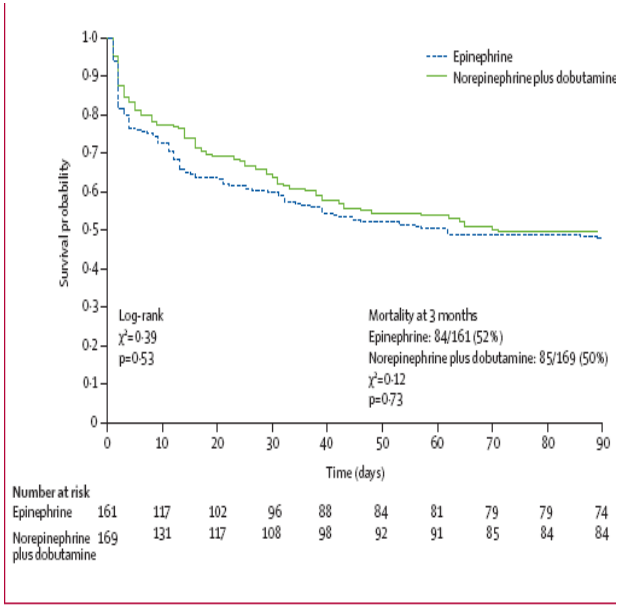


Figure 3: Survival from randomisation to day 90

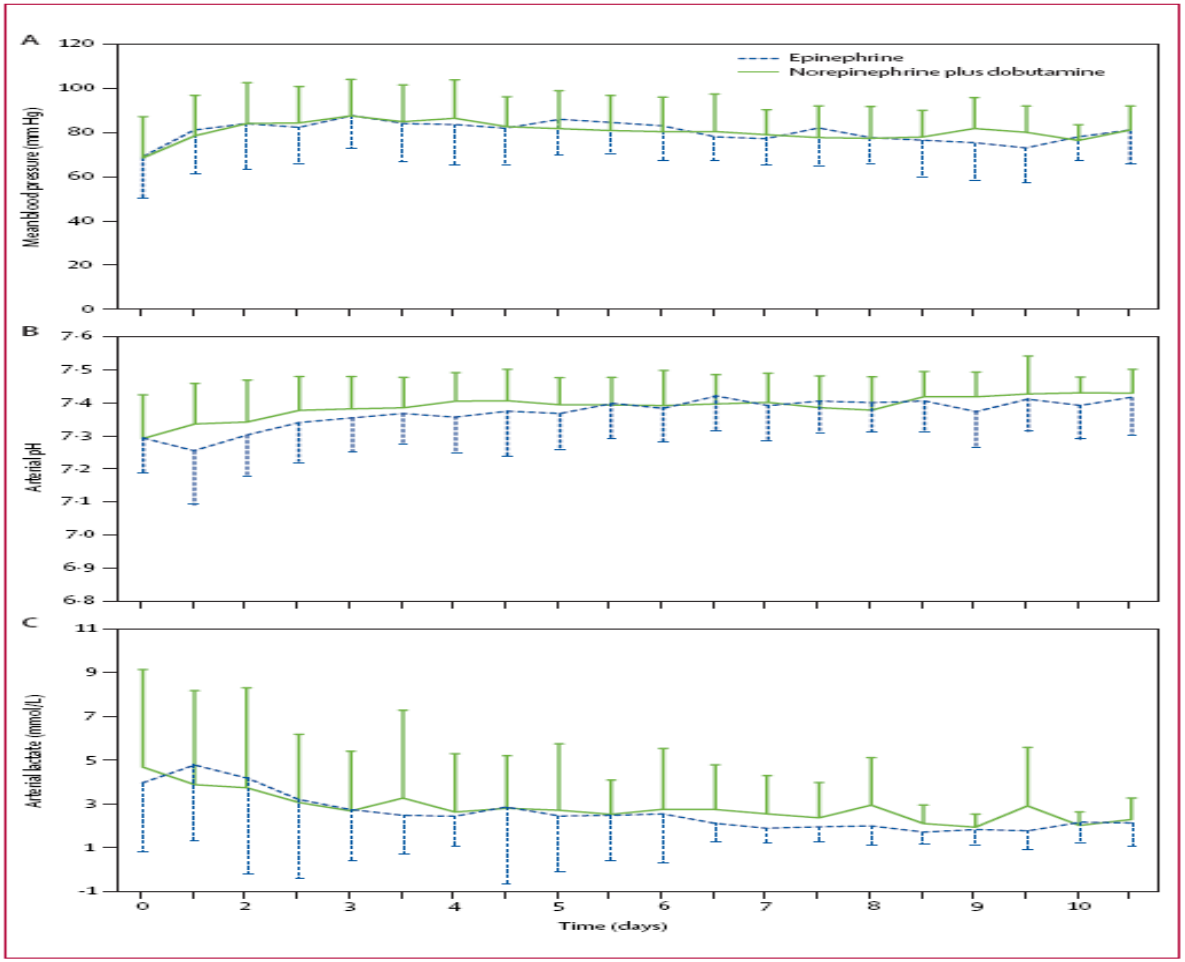


Figure 4: **Effects of treatment**
(A) Mean blood pressure. (B) Arterial pH. (C) Arterial lactate concentration. Error bars are SD.

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators*

Table 1. Baseline Characteristics of the Patients and Major Therapeutic Interventions at Baseline.*

Variable	Dopamine (N=858)	Norepinephrine (N=821)
Age — yr		
Median	68	67
Interquartile range	55–76	56–76
Male sex — no. (%)	507 (59.1)	449 (54.7)
APACHE II score†		
Median	20	20
Interquartile range	15–28	14–27
SOFA score‡		
Median	9	9
Interquartile range	7–12	6–12
Reason for admission — no. (%)		
Medical	565 (65.9)	532 (64.8)
Scheduled surgery	168 (19.6)	161 (19.6)
Emergency surgery	125 (14.6)	128 (15.6)
Cause of shock — no. (%)		
Sepsis	542 (63.2)	502 (61.1)
Lungs	278 (32.4)	246 (30.0)
Abdomen	138 (16.1)	135 (16.4)
Urine	51 (5.9)	42 (5.1)
Catheter	14 (1.6)	10 (1.2)
Endocardium	9 (1.0)	11 (1.3)
Mediastinum	10 (1.2)	15 (1.8)
Soft tissues	11 (1.3)	13 (1.6)
Other	15 (1.7)	20 (2.4)
Cardiogenic source	135 (15.7)	145 (17.6)
Myocardial infarction	75 (8.7)	86 (10.5)
Dilated cardiomyopathy	25 (2.9)	19 (2.3)
Tamponade	2 (0.2)	7 (0.9)
Pulmonary embolism	10 (1.2)	8 (1.0)
Valvular disease	4 (0.5)	5 (0.6)
After cardiopulmonary bypass	19 (2.2)	20 (2.4)
Other		
Hypovolemia	138 (16.1)	125 (15.2)
Hemorrhage	130 (15.2)	116 (14.1)
Trauma	17 (2.0)	23 (2.8)
Gastrointestinal bleeding	31 (3.6)	22 (2.7)
Bleeding at surgical site	64 (7.5)	57 (6.9)
Other	18 (2.1)	14 (1.7)
Dehydration	8 (0.9)	9 (1.1)
Other	48 (5.9)	44 (5.0)
Spinal	6 (0.7)	8 (1.0)
Peridural§	13 (1.5)	4 (0.5)
Intoxication-related¶	7 (0.8)	4 (0.5)
Anaphylactic	3 (0.3)	4 (0.5)
Miscellaneous	13 (1.5)	29 (3.5)
Hemodynamic, respiratory, and biologic variables		
Temperature — °C	36.6±1.5	36.6±1.5
Heart rate — beats/min	97±27	95±25
Mean arterial pressure — mm Hg	58±13	58±13
Mean pulmonary-artery pressure — mm Hg**	27±9	29±8

N Engl J Med 2010;362:779-89.

Table 2. Mortality Rates.*

Time Period	Dopamine	Norepinephrine	Odds Ratio (95% CI)†	P Value
	percent mortality			
During stay in intensive care unit	50.2	45.9	1.19 (0.98–1.44)	0.07
During hospital stay	59.4	56.6	1.12 (0.92–1.37)	0.24
At 28 days	52.5	48.5	1.17 (0.97–1.42)	0.10
At 6 mo	63.8	62.9	1.06 (0.86–1.31)	0.71
At 12 mo	65.9	63.0	1.15 (0.91–1.46)	0.34

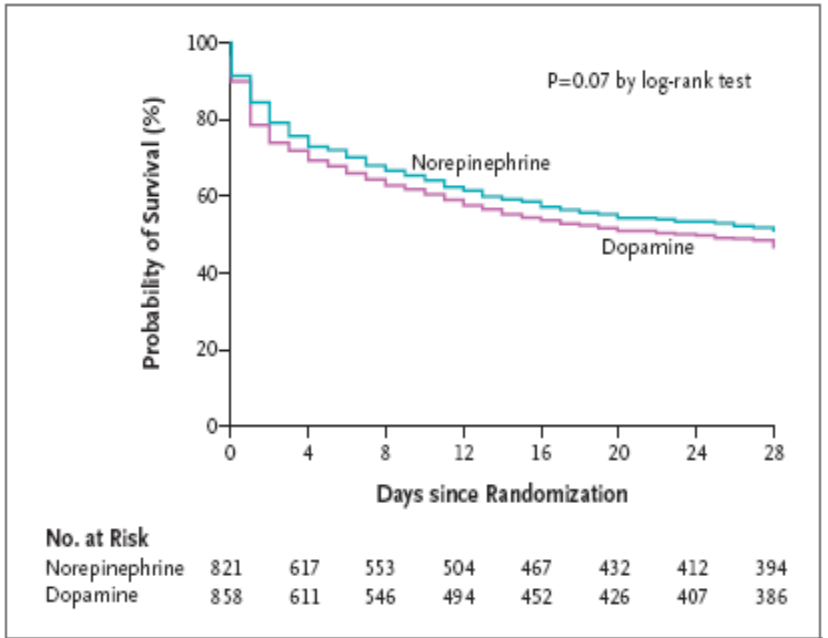


Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

Table 3. Secondary Outcomes and Adverse Events.*

Variable	Dopamine (N=858)	Norepinephrine (N=821)	P Value
Support-free days through day 28			
Vasopressors not needed			
Trial drug	11.0±12.1	12.5±12.1	0.01
Open-label vasopressors	12.6±12.5	14.2±12.3	0.007
Mechanical ventilation not needed	8.5±11.2	9.5±11.4	0.13
Renal support not needed	12.8±12.4	14.0±12.3	0.07
Intensive care not needed	8.1±10.3	8.5±10.3	0.43
Length of stay — no. of days			
Intensive care unit			0.12
Median	5	5	
Interquartile range	1–11	2–12	
Hospital			0.22
Median	11	12	
Interquartile range	2–28	3–28	
Cause of death in hospital — no./total no. (%)			0.31
Refractory shock	196/426 (46)	155/381 (41)	
Withdrawal or withholding of therapy	193/426 (45)	190/381 (50)	
Brain death or severe postanoxic lesions	37/426 (9)	36/381 (9)	
Adverse events			
Arrhythmias — no. (%)	207 (24.1)	102 (12.4)	<0.001
Atrial fibrillation	176 (20.5)	90 (11.0)	
Ventricular tachycardia	21 (2.4)	8 (1.0)	
Ventricular fibrillation	10 (1.2)	4 (0.5)	
Myocardial infarction — no. (%)	19 (2.2)	25 (3.0)	0.29
New infectious episode			
No. of episodes			0.69
Median	1	1	
Interquartile range	0–1	0–1	
Patients with at least one episode — no. (%)	674 (78.6)	619 (75.4)	0.35
Skin ischemia — no. (%)	56 (6.5)	34 (4.1)	0.09
Mild†	46 (5.4)	28 (3.4)	
Severe‡	10 (1.2)	6 (0.7)	
Arterial occlusion — no. (%)§	23 (2.7)	20 (2.4)	0.12
Arms or fingers	5 (0.6)	1 (0.1)	
Legs	7 (0.8)	13 (1.6)	
Bowel	11 (1.3)	6 (0.7)	

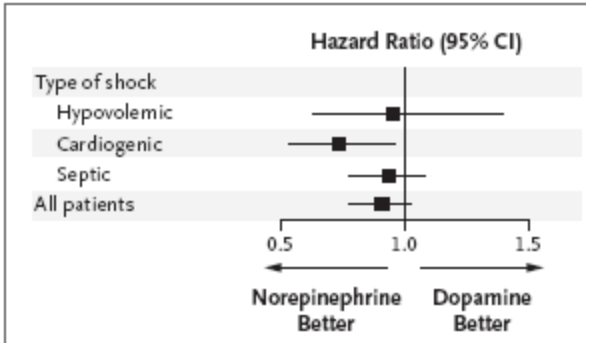


Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.

Norephinephrine or Dopamine for Septic Shock: A Systematic Review of Randomized Clinical Trials

Tajender S. Vasu, Rodrigo Cavallazzi, Amyn Hirani, Gary Kaplan, Benjamin Leiby and Paul E. Marik

J Intensive Care Med published online 24 March 2011
DOI: 10.1177/0885066610396312

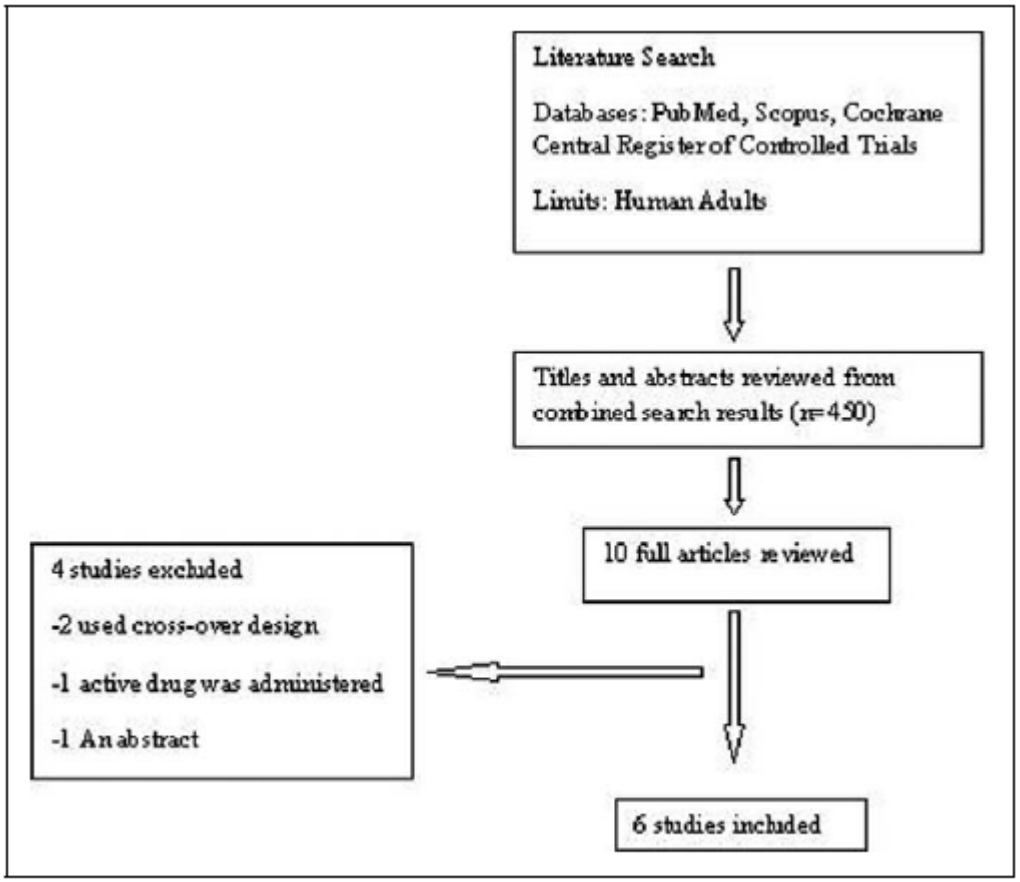


Figure 1. Flowchart of study selection for the systematic review.

Table 1. Randomized Control Trials Comparing Norepinephrine With Dopamine in Patients With Septic Shock: Baseline Characteristics of Studies Included in the Meta-Analysis

Author	Year	Population	Country	Number (NE)	Deaths (NE)	Arrhythmia (NE)	Number (DA)	Deaths (DA)	Arrhythmia (DA)	Mean Age (NE)	Mean age (DA)	Male (NE)	Male (DA)	APACHE II (NE)	APACHE II (DA)
Martin[12]	1993	Septic Shock	France	16	7	NR	16	10	NR	52 ± 12	53 ± 19	12	12	31 ± 1.3	30 ± 1.2
Ruokoacn[13]	1993	Septic Shock	USA Finland	5	4	NR	5	3	NR	42.2 ± 28	44.6 ± 6	NR	NR	NR	NR
Marik[14]	1994	Septic Shock	USA	10	5	NR	10	6	NR	46 ± 22	46 ± 13	6	5	18 ± 3	17 ± 6
Mathur[15]	2007	Septic Shock	India	25	14	NR	25	19	NR	52.8 ± 10.4	54.6 ± 10.9	15	17	25.6 ± 2.3	24.5 ± 2.9
Paid[16]	2010	Septic Shock	USA	118	51	14	134	67	51	NR	NR	52	64	27 ± 6.1	28 ± 6.7
Dc Backer[17]	2010	Shock	Europe	821	393	102	838	450	207	67[a]	68[a]	449	507	20[a]	20[a]

Abbreviations: NE, Norepinephrine; DA, Dopamine; NR, not reported.

Table 2. Cochrane Risk of Bias in Included Studies

Author	Adequate Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data Assessed	Free of Selective Outcome Reporting	Free of Other Biases
Martin	Yes	Unclear	Yes	Yes	Yes	Yes
Ruokonen	Yes	No	Unclear	Yes	Yes	Yes
Marik	Yes	Unclear	Unclear	Yes	Yes	No
Mathur	Unclear	Unclear	Yes	Yes	Yes	No
Patel	No	No	No	Yes	Yes	No
Debacker	Yes	Yes	Yes	Yes	No	No

Norephinephrine or Dopamine for Septic Shock: A Systematic Review of Randomized Clinical Trials

Tajender S. Vasu, Rodrigo Cavallazzi, Amyn Hirani, Gary Kaplan, Benjamin Leiby and Paul E. Marik

J Intensive Care Med published online 24 March 2011
DOI: 10.1177/0885066610396312

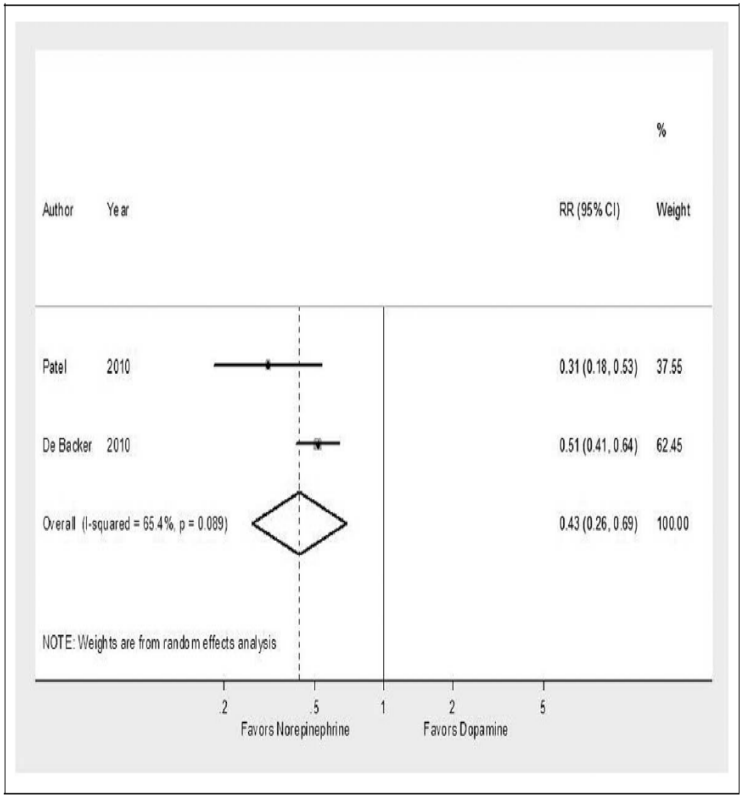


Figure 2. Comparison of mortality between norepinephrine and dopamine in patients with septic shock.

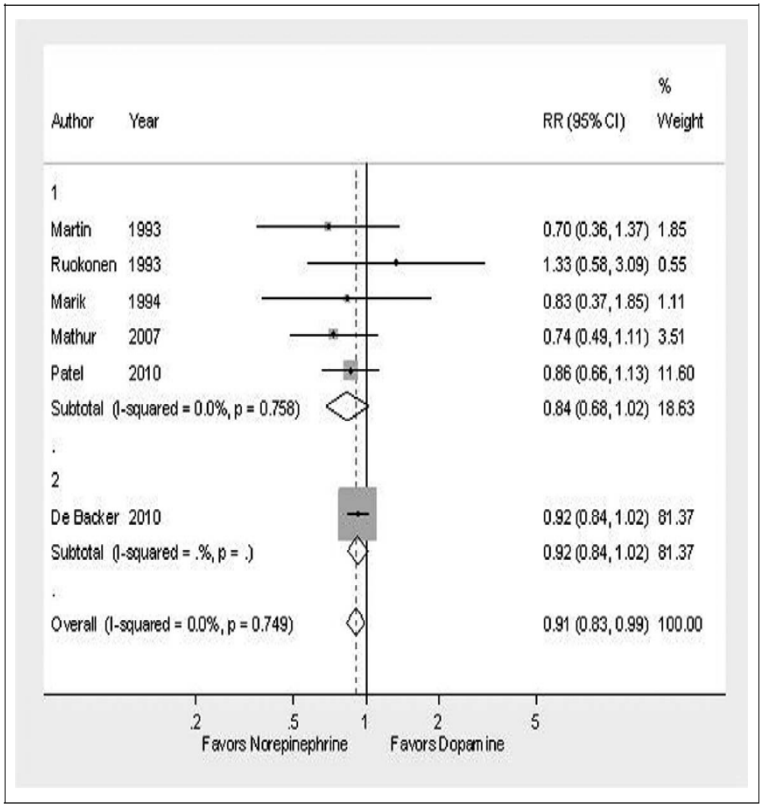


Figure 3. Rate of cardiac arrhythmia (comparison between norepinephrine and dopamine).

Critères de sepsis sévère ou choc septique

Biologie
Bactériologie
Radiologie

Conditionnement

Avant

Remplissage vasculaire
Cristoilide <30cc/kg sur 30min

Antibiothérapie

PAM <70mmHg → Voie centrale

Noradrénaline
0.02µg/kg/min → Hydrocortisone 50mgx6/j

En service de Réanimation

Pas d'amélioration
Monitorage → PICCO ou écho cœur

- Hypovolémie → Remplissage
- Fonction VG altérée → Dobutamine Ou adrénaline
- Vasoplégie → Noradrénaline

SURVEILLANCE: CLINIQUE, biologique

Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy

A Randomized Clinical Trial

Table 5. Hospital Mortality and Length of Stay

Variable	Lactate Clearance Group (n = 150)	$Scvo_2$ Group (n = 150)	Proportion Difference (95% Confidence Interval)	*P* Value[b]
In-hospital mortality, No. (%)[a]				
Intent to treat	25 (17)	34 (23)	6 (–3 to 15)	
Per protocol	25 (17)	33 (22)	5 (–3 to 14)	
Length of stay, mean (SD), d				
ICU	5.9 (8.46)	5.6 (7.39)		.75
Hospital	11.4 (10.89)	12.1 (11.68)		.60
Hospital complications				
Ventilator-free days, mean (SD)	9.3 (10.31)	9.9 (11.09)		.67
Multiple organ failure, No. (%)	37 (25)	33 (22)		.68
Care withdrawn, No. (%)	14 (9)	23 (15)		.15

Abbreviations: ICU, intensive care unit; $Scvo_2$, central venous oxygen saturation.
[a] Primary study end point.
[b] Continuous data are compared using an unpaired *t* test; categorical variables, using the χ^2 test.

JAMA. 2010;303(8):739-746


Merci

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D., Paul C. Hébert, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holmes, M.D., Sangeeta Mehta, M.D., John T. Granton, M.D., Michelle M. Storms, B.Sc.N., Deborah J. Cook, M.D., Jeffrey J. Presneill, M.B., B.S., Ph.D., and Dieter Ayers, M.Sc., for the VASST Investigators*

Table 2. Analysis of the Rates and Risks of Death from Any Cause and Secondary Outcomes.*

Variable	Norepinephrine Group (N=382)	Vasopressin Group (N=396)	P Value†	Absolute Risk Reduction (95% CI)‡	Relative Risk (95% CI)§	Adjusted Odds Ratio¶
	no./total no. (%)			%		
Patients who underwent randomization and infusion						
28-day mortality	150/382 (39.3)	140/396 (35.4)	0.26	3.9 (−2.9 to 10.7)	0.90 (0.75 to 1.08)	0.88 (0.62 to 1.26)
90-day mortality	188/379 (49.6)	172/392 (43.9)	0.11	5.7 (−1.3 to 12.8)	0.88 (0.76 to 1.03)	0.81 (0.57 to 1.16)
Patients who underwent randomization						
28-day mortality	154/395 (39.0)	144/404 (35.6)	0.33	3.3 (−3.4 to 10.1)	0.91 (0.76 to 1.09)	
90-day mortality	194/392 (49.5)	177/400 (44.2)	0.14	5.2 (−1.7 to 12.2)	0.89 (0.77 to 1.04)	
	median (interquartile range)					

N Engl J Med 2008;358:877-87.

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D., Paul C. Hébert, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holmes, M.D., Sangeeta Mehta, M.D., John T. Granton, M.D., Michelle M. Storms, B.Sc.N., Deborah J. Cook, M.D., Jeffrey J. Presneill, M.B., B.S., Ph.D., and Dieter Ayers, M.Sc., for the VASST Investigators*

Days alive‖			
Free of organ dysfunction			
Cardiovascular	17 (0–24)	19 (0–24)	0.58
Vasopressor use**	17 (0–24)	19 (0–24)	0.61
Respiratory	2 (0–14)	3.5 (0–16)	0.15
Ventilation††	6 (0–20)	8.5 (0–20)	0.24
Renal	18.5 (3–28)	21.5 (4–28)	0.54
Renal-replacement therapy	23 (5–28)	25 (6–28)	0.64
Hepatic	24.5 (3–28)	25 (5–28)	0.80
Hematologic	23 (3–28)	24 (5–28)	0.48
Neurologic	15 (0–24)	15 (0–24)	0.57
Free of any organ failure	0 (0–6)	0 (0–9)	0.14
Free of the systemic inflammatory response syndrome‡‡	6 (0–15)	6 (0–18)	0.21
Free of corticosteroid use	13.5 (1–24)	16 (1–25)	0.33
Length of stay (days)			
In ICU	16 (8–32)	15 (7–29)	0.14
In hospital	26 (15–53)	27 (13–52)	0.23

N Engl J Med 2008;358:877-87.

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D., Paul C. Hébert, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holmes, M.D., Sangeeta Mehta, M.D., John T. Granton, M.D., Michelle M. Storms, B.Sc.N., Deborah J. Cook, M.D., Jeffrey J. Presneill, M.B., B.S., Ph.D., and Dieter Ayers, M.Sc., for the VASST Investigators*

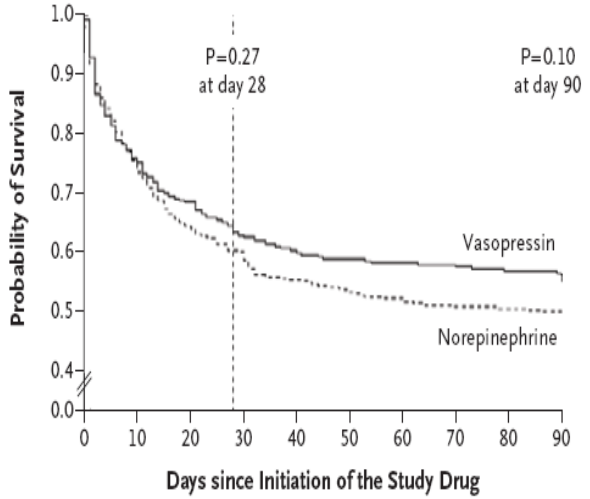


Figure 2. Kaplan–Meier Survival Curves for Patients Who Underwent Randomization and Infusion.

The dashed vertical line marks day 28. P values were calculated with the use of the log-rank test.

Table 3. Serious Adverse Events in Patients Who Had Septic Shock.

Variable	Norepinephrine Group (N=382)	Vasopressin Group (N=396)	P Value*
	no. (%)		
At least one serious adverse event	40 (10.5)	41 (10.3)	1.00
Acute myocardial infarction or ischemia	7 (1.8)	8 (2.0)	1.00
Cardiac arrest	8 (2.1)	3 (0.8)	0.14
Life-threatening arrhythmia	6 (1.6)	8 (2.0)	0.79
Acute mesenteric ischemia	13 (3.4)	9 (2.3)	0.39
Hyponatremia†	1 (0.3)	1 (0.3)	1.00
Digital ischemia	2 (0.5)	8 (2.0)	0.11
Cerebrovascular accident	1 (0.3)	1 (0.3)	1.00
Other‡	2 (0.5)	5 (1.3)	0.45

N Engl J Med 2008;358:877-87.

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D., Paul C. Hébert, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holmes, M.D., Sangeeta Mehta, M.D., John T. Granton, M.D., Michelle M. Storms, B.Sc.N., Deborah J. Cook, M.D., Jeffrey J. Presneill, M.B., B.S., Ph.D., and Dieter Ayers, M.Sc., for the VASST Investigators*

Table 4. Rates and Risks of Death from Any Cause According to the Severity of Shock.*

Stratum	Norepinephrine Group	Vasopressin Group	P Value†	Absolute Risk Reduction (95% CI)	Relative Risk (95% CI)
	no./total no. (%)			%	
More severe septic shock					
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76	−1.5 (−11.2 to 8.2)	1.04 (0.83 to 1.3)
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84	1.0 (−8.8 to 10.8)	0.98 (0.81 to 1.18)
Less severe septic shock					
28-day mortality	65/182 (35.7)	52/196 (26.5)	0.05	9.2 (−0.1 to 18.5)	0.74 (0.55 to 1.01)
90-day mortality	83/180 (46.1)	69/193 (35.8)	0.04	10.4 (0.4 to 20.3)	0.78 (0.61 to 0.99)

ANTIBIOTHÉRAPIE:

QUAND DEBUTER?

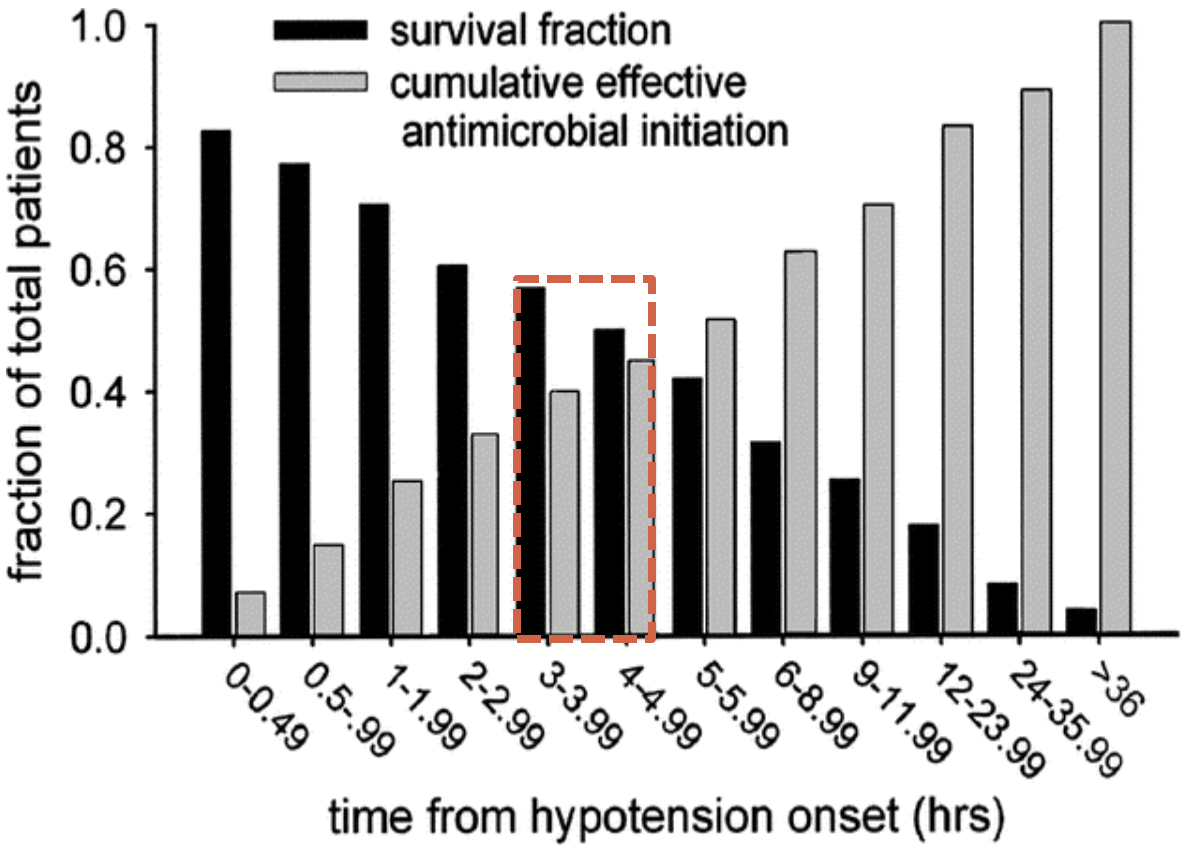
Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

- Choc septique
- étude rétrospective sur 5 ans (1989-2004)
- 24 ICU
- 2154 patients avec une antibiothérapie adéquate

Crit Care Med 2006; 34:1589–1596

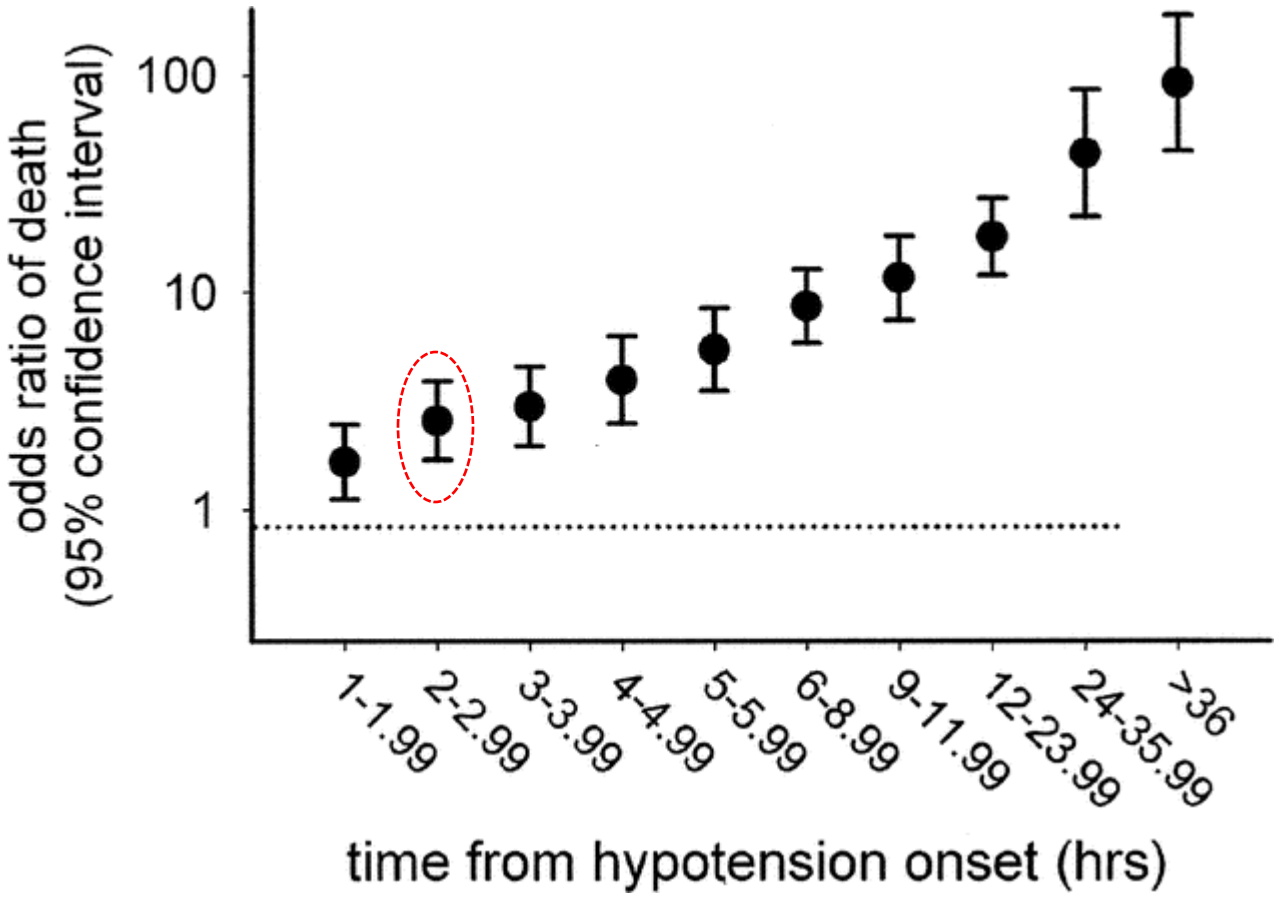
Précocité antibiothérapie probabiliste et mortalité



mort. 7.6%/ H

Crit Care Med 2006; 34:1589–1596

Précocité antibiothérapie probabiliste et mortalité



Crit Care Med 2006; 34:1589–1596

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

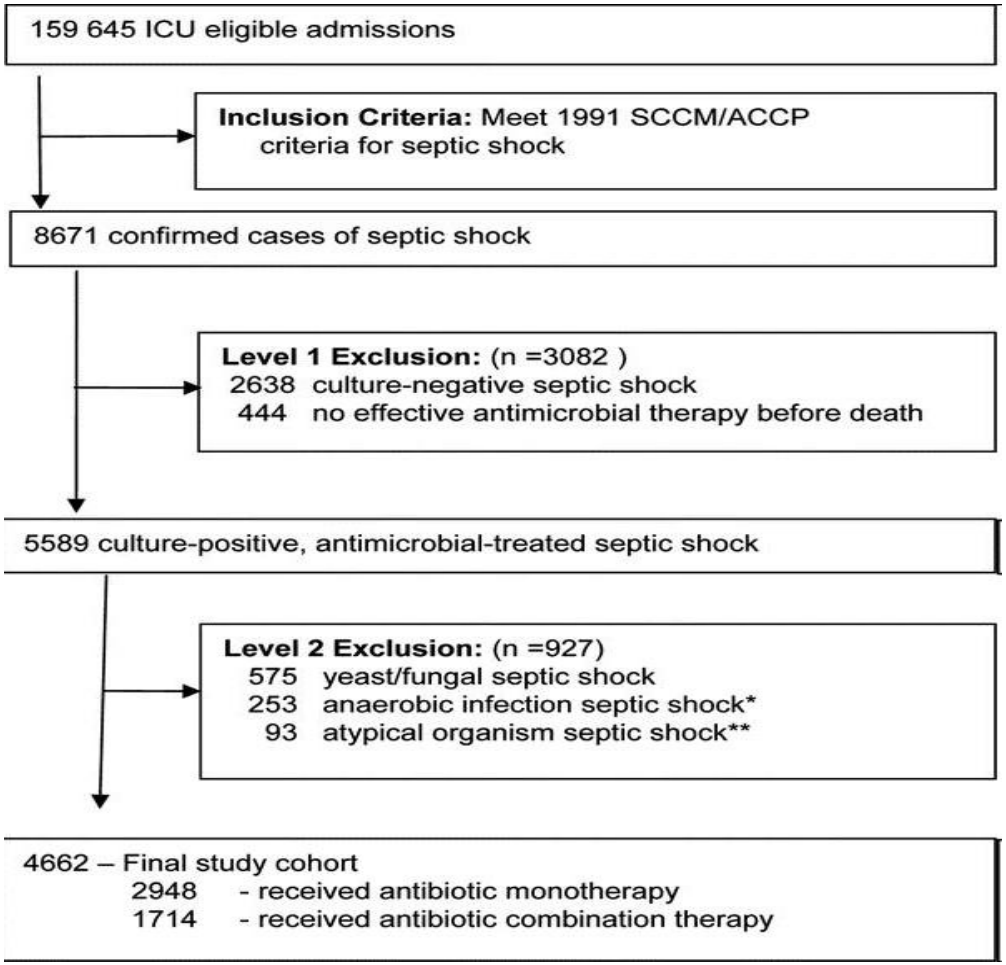
Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

Conclusions: Effective antimicrobial administration within the first hour of documented hypotension was associated with increased survival to hospital discharge in adult patients with septic shock. Despite a progressive increase in mortality rate with increasing delays, only 50% of septic shock patients received effective antimicrobial therapy within 6 hrs of documented hypotension. (Crit Care Med 2006; 34:1589–1596)

ANTIBIOTHÉRAPIE:

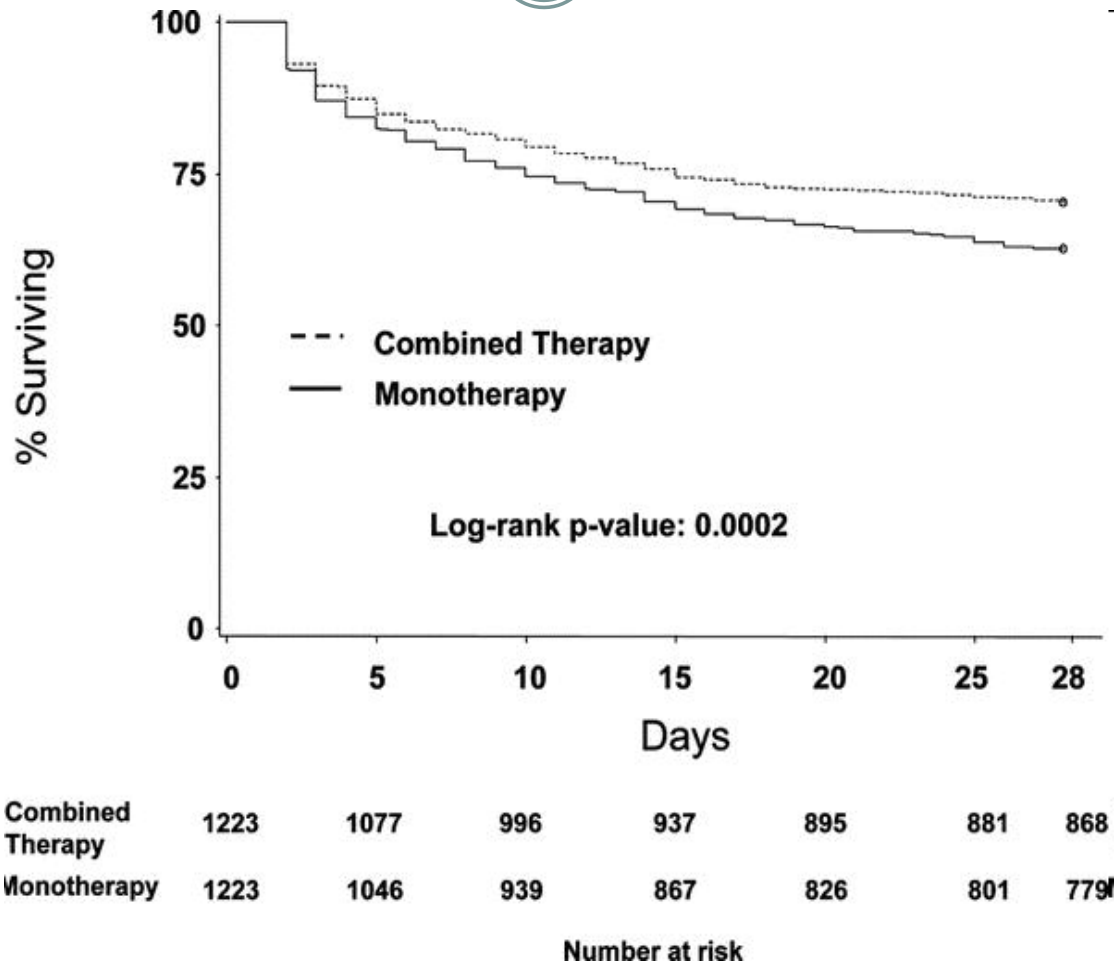
MONOTHERAPIE VERSUS BITHERAPIE

Early combination antibiotic therapy yields improved survival compared with monotherapy in septic shock : a propensity-matched analysis (I)

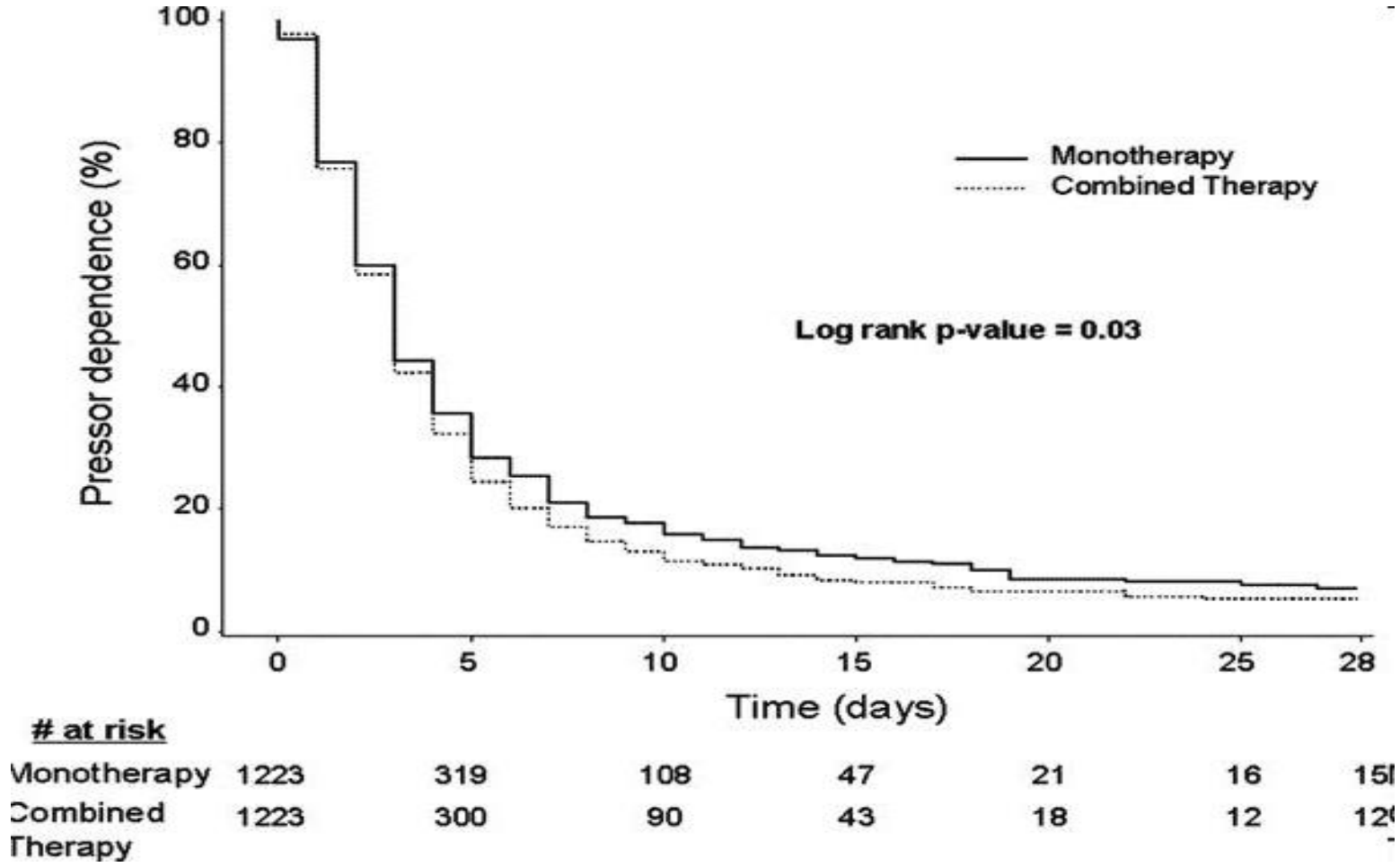


Kumar A et coll Crit Care Med 2010 ;38:1773-1785

- Adjusted cox proportional hazards of mortality associated with combination antibiotic therapy of septic shock



- **Log-rank assessment of persistence of pressor/inotrope dependence associated with combination therapy of septic shock. Combination therapy was associated**



ANTIBIOTHÉRAPIE:

ADAPTEE:

Bactériémies :
analyse multivariée des facteurs pronostiques

843 épisodes de bactériémies et de fongémies, 17,5% de mortalité globale

Facteurs significatifs	Risque Relatif
Age > 70 ans	1.80
Agents fongiques ou Entérobactéries autres qu'*E.coli*	2.27
Origine inconnue, respiratoire, péritonéale ou colique	2.86
Néoplasie, SIDA ou insuffisance rénale sous-jacents	1.98
Etat de choc	2.29
Absence de réaction fébrile (< 37.9°C)	2.04
Antibiothérapie inadéquate à au moins 2 évaluations (probabiliste initiale, résultat des HC, données antibiogramme)	2.72

Weinstein, CID 1997.24:584 - 602

Infections sévères en réanimation:
conséquences d'une antibiothérapie inadéquate

Étude prospective, 2000 patients dont 655 avec une antibiothérapie

- Mortalité liée à l'infection
  - patients avec ATB adéquate = 17.7%
  - patients avec ATB inadéquate = 42.0% (RR = 2.37 ; p<0.001)
- Défaillances viscérales plus nombreuses
  - 2.5+/-1.5 vs 0.9+/-1.4 (p<0.0001)
- Durée de séjour en réanimation accrue
  - 10.2+/-10.2 vs 7.1+/-8.2 j (p<0.0001)
- Durée de ventilation accrue
  - 11.1+/-10.6 vs 7.6 +/- 9.2 j (p<0.0001)

Kollef chest: 1999; 115: 462 – 74

Impact of adequate empirical antibiotic therapy on the outcome of patients admitted to the intensive care unit with sepsis*

Jose Garnacho-Montero, MD, PhD; Jose Luis Garcia-Garmendia, MD, PhD; Ana Barrero-Almodovar, MD; Francisco J. Jimenez-Jimenez, MD, PhD; Carmen Perez-Paredes, MD; Carlos Ortiz-Leyba, MD, PhD

Table 2. In-hospital mortality rates for the different sites of infections and mortality rates depending on the adequacy of empirical antibiotic therapy

Septic Source Empirical Antibiotic Therapy	Nonsurvivors (n = 196) No. (%)	Survivors (n = 210) No. (%)
Pulmonary	49 (63.6)	28 (36.4)
Adequate	23 (46.9)	17 (60.7)
Inadequate	8 (16.3)	1 (3.6)
Not evaluable	18 (36.7)	10 (35.7)
Unknown origin	22 (59.5)	15 (40.5)
Adequate	6 (27.3)	8 (53.3)
Inadequate	5 (22.7)	1 (6.7)
Not evaluable	11 (50)	6 (40)
Catheter	8 (50)	8 (50)
Adequate	7 (87.5)	7 (87.5)
Inadequate	1 (12.5)	1 (12.5)
Not evaluable	—	—
Abdomen	90 (47.4)	100 (52.6)
Adequate	42 (46.7)	54 (54)
Inadequate	10 (11.1)	10 (10)
Not evaluable	38 (42.2)	36 (36)
Soft tissue	11 (47.8)	12 (52.2)
Adequate	8 (72.7)	11 (91.7)
Inadequate	1 (9.1)	1 (8.3)
Not evaluable	2 (18.2)	—
CNS	4 (26.7)	11 (73.3)
Adequate	3 (75)	5 (45.5)
Inadequate	1 (25)	—
Not evaluable	—	6 (54.6)
Urologic	10 (24.4)	31 (75.6)
Adequate	6 (60)	24 (77.4)
Inadequate	3 (30)	2 (6.5)
Not evaluable	1 (10)	5 (16.1)
Others	2 (28.5)	5 (71.5)
Adequate		4 (80)
Inadequate		—
Not evaluable	2 (100)	1 (20)

CNS, central nervous system.

Table 7. Risk factors independently associated with 28-day and in-hospital death by multivariate analysis

	28-Day Mortality	In-Hospital Mortality
Risk Factor	OR (95% CI)	OR (95% CI)
SOFA (1st day)	1.43 (1.32–1.55)	1.29 (1.19–1.40)
ΔSOFA (3)	1.52 (1.34–1.72)	1.40 (1.19–1.65)
Urological sepsis	0.11 (0.04–0.35)	0.14 (0.05–0.41)
IEAT in nonsurgical sepsis	4.42 (1.17–16.7)	8.14 (1.98–33.5)
AEAT in surgical sepsis	0.35 (0.16–0.76)	0.37 (0.18–0.77)
Respiratory failure		3.12 (1.54–6.33)

OR, odds ratio; CI, confidence interval; SOFA, Sepsis-related Organ Failure Score; ΔSOFA (3), increase in SOFA over the first 3 days in the intensive care unit; IEAT, inadequate empirical antibiotic therapy; AEAT denotes adequate empirical antibiotic therapy.

(Crit Care Med 2003; 31:2742–2751)

Impact of adequate empirical antibiotic therapy on the outcome of patients admitted to the intensive care unit with sepsis*

Jose Garnacho-Montero, MD, PhD; Jose Luis Garcia-Garmendia, MD, PhD; Ana Barrero-Almodovar, MD; Francisco J. Jimenez-Jimenez, MD, PhD; Carmen Perez-Paredes, MD; Carlos Ortiz-Leyba, MD, PhD

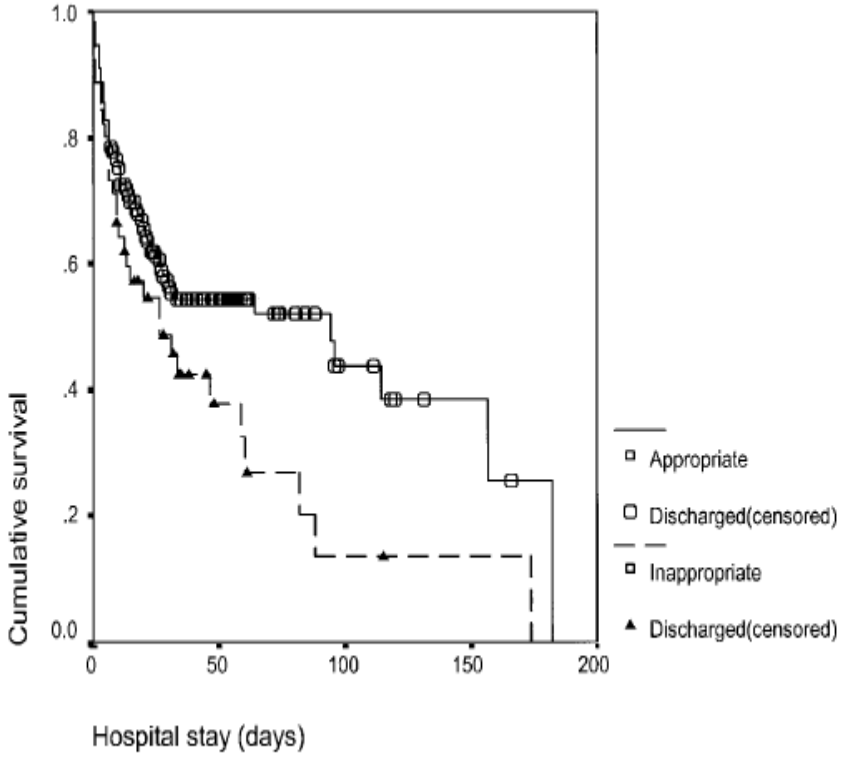


Figure 1. Kaplan-Meier survival curve for hospital stay in patients with adequate empirical antibiotic therapy vs. inadequate/not evaluable. Log-rank $p = .0007$.

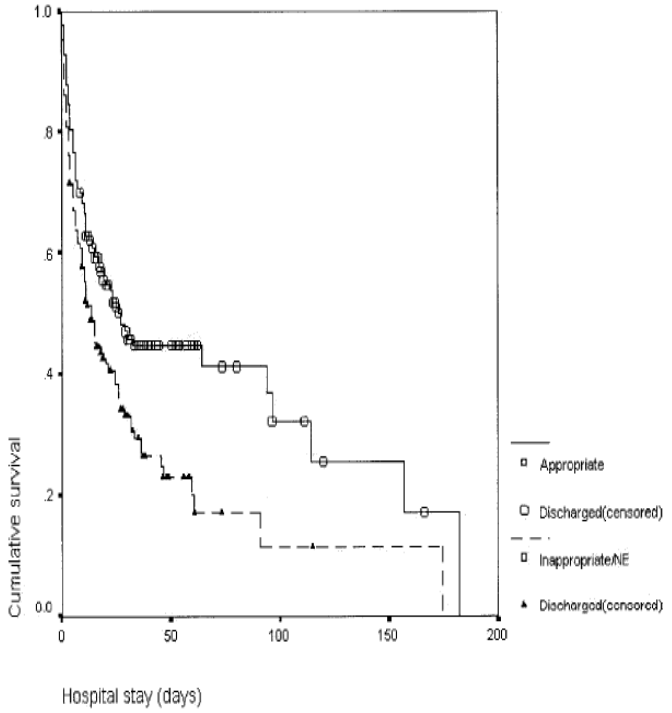
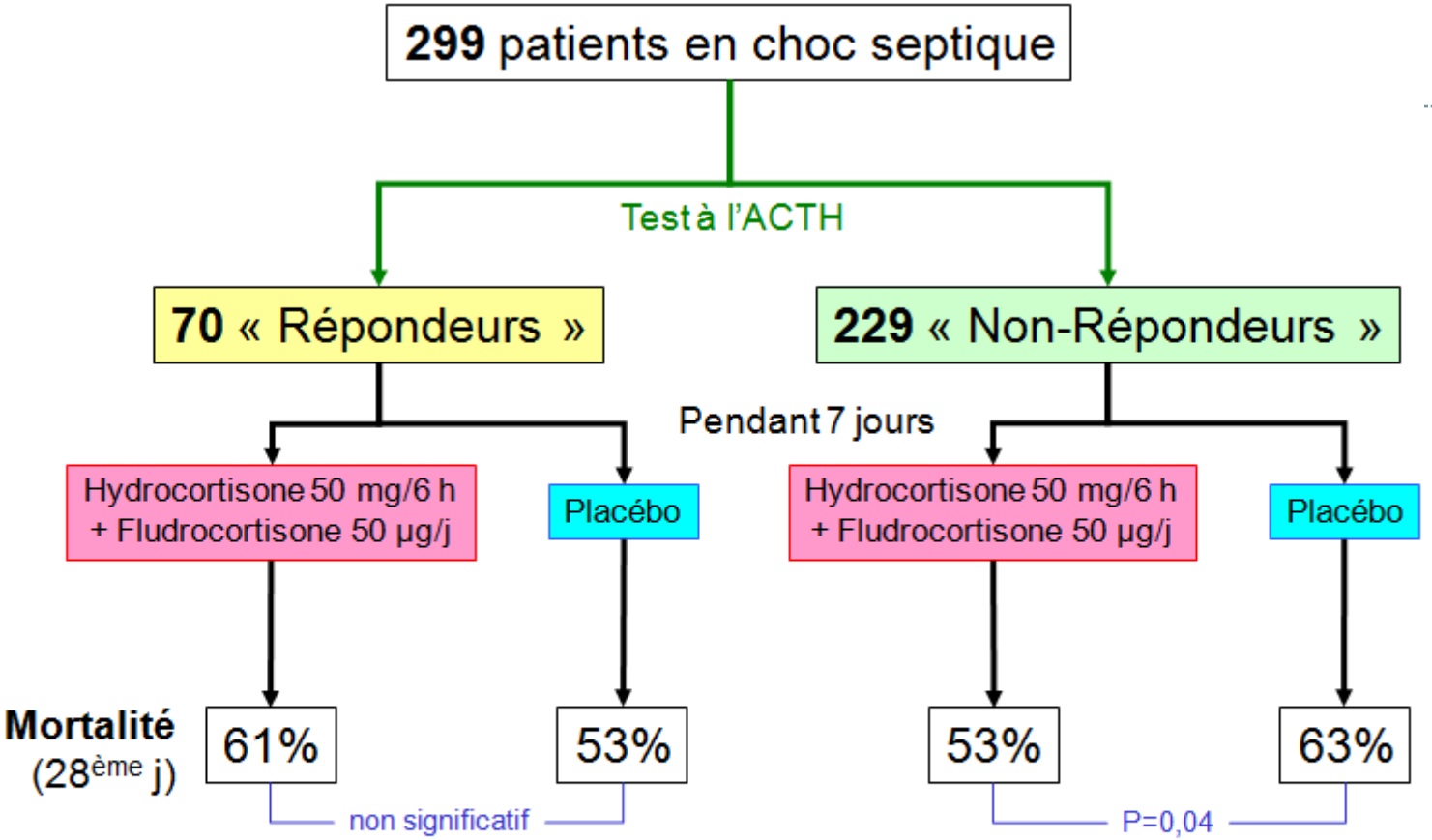


Figure 2. Kaplan-Meier survival curve for hospital stay in patients who were admitted to the intensive care unit with severe sepsis or septic shock comparing appropriate empirical antibiotic therapy vs. inappropriate/not evaluable. Log-rank $p = .0007$.

(Crit Care Med 2003; 31:2742–2751)

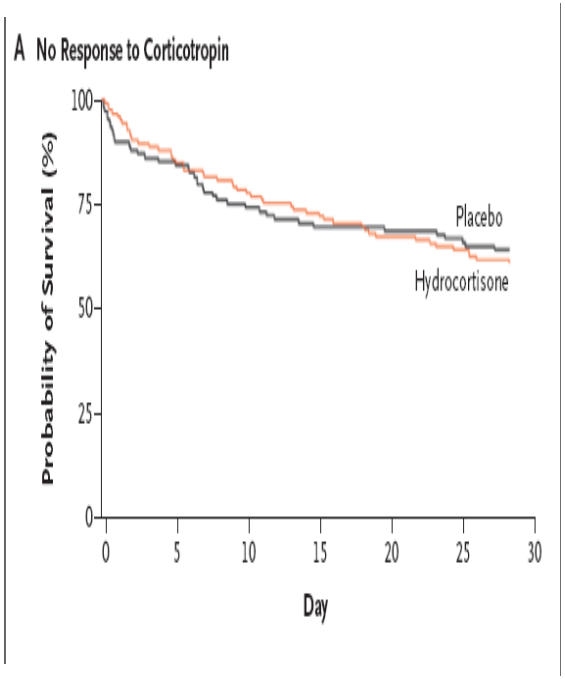


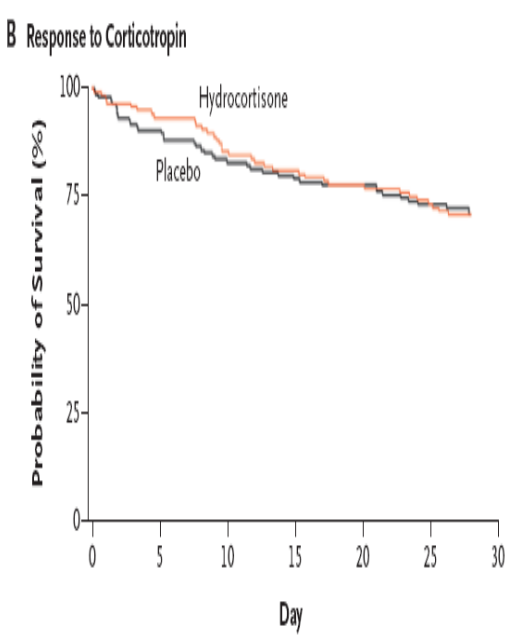
Indication de traitement substitutif par Hydrocortisone chez les non-répondeurs

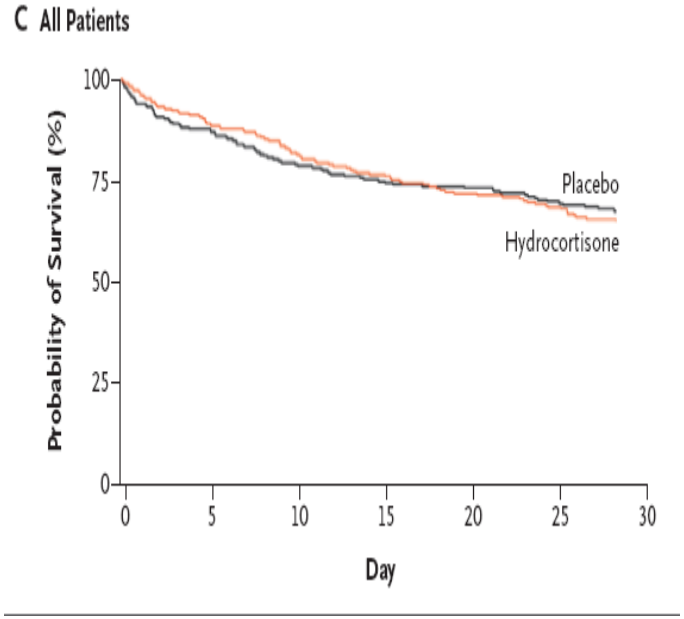
Annane D, JAMA, 2002; 288: 862

Hydrocortisone Therapy for Patients with Septic Shock

Charles L. Sprung, M.D., Djillali Annane, M.D., Ph.D., Didier Keh, M.D., Rui Moreno, M.D., Ph.D., Mervyn Singer, M.D., F.R.C.P., Klaus Freivogel, Ph.D., Yoram G. Weiss, M.D., Julie Benbenishty, R.N., Armin Kalenka, M.D., Helmuth Forst, M.D., Ph.D., Pierre-Francois Laterre, M.D., Konrad Reinhart, M.D., Brian H. Cuthbertson, M.D., Didier Payen, M.D., Ph.D., and Josef Briegel, M.D., Ph.D., for the CORTICUS Study Group*







N Engl J Med 2008;358:111-24.

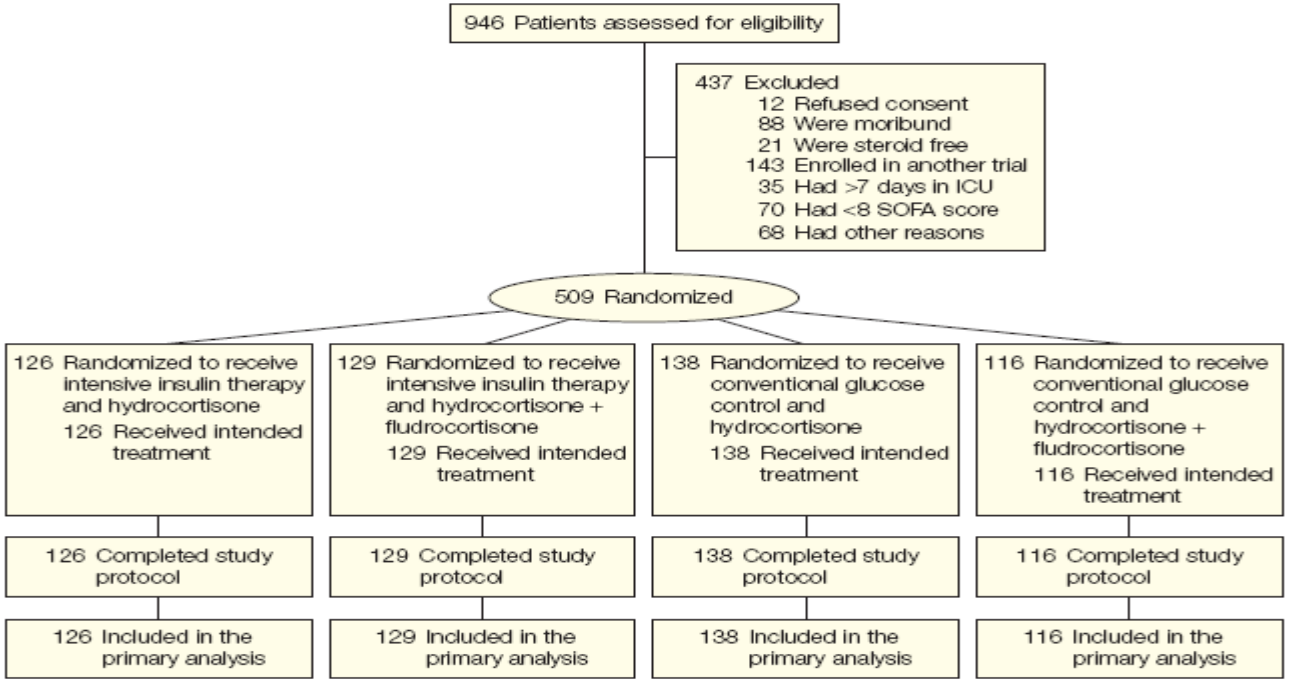
La partie de l'image avec l'ID de relation rId2 n'a pas été trouvé dans le fichier.

N Engl J Med 2008;358:111-24.

Corticosteroid Treatment and Intensive Insulin Therapy for Septic Shock in Adults

A Randomized Controlled Trial

Figure 1. Flowchart of the Trial



ICU indicates intensive care unit; SOFA, Sequential Organ Failure Assessment.

JAMA. 2010;303(4):341-348

Table 1. Baseline Characteristics of Randomized Groups[a]

	Intensive Insulin Therapy (n = 255)	Conventional Glucose Control (n = 254)	Hydrocortisone + Fludrocortisone (n = 245)	Hydrocortisone Alone (n = 264)
Age, mean (95% CI), y	63.7 (61.9-65.4)	64.3 (62.4-66.1)	64.0 (62.2-65.8)	63.9 (62.1-65.7)
Male sex, No. (%)	170 (66.7)	160 (63.0)	167 (68.2)	163 (61.7)
Admission days, median (IQR)				
In hospital before ICU admission	0 (0-1)	0 (0-2)	0 (0-1)	0 (0-2)
In ICU before randomization	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)
Physiology scores, mean (95% CI)				
SAPS II	58.9 (56.9-60.9)	60.4 (58.2-62.6)	58.9 (56.7-61.0)	60.4 (58.3-62.5)
SOFA	10.4 (10.0-10.8)	10.8 (10.3-11.2)	10.6 (10.2-11.1)	10.1 (10.1-11.0)
Type of patients, No. %	218	220	207	231
Medical	193 (88.5)	189 (85.9)	186 (89.9)	196 (84.9)
Unscheduled surgery	22 (10.1)	26 (11.8)	17 (8.2)	31 (13.4)
Scheduled surgery	3 (1.4)	5 (2.3)	4 (1.9)	4 (1.7)
Type of infection, No./total (%)				
Community acquired	134/246 (54.5)	115/247 (46.6)	120/234 (51.3)	129/259 (49.8)
Hospital acquired	112/246 (45.5)	132/247 (53.4)	114/234 (48.7)	130/259 (50.2)
Infected patient, No.	245	246	233	258
Infection per patient, mean (95% CI)	1.5 (1.4-1.6)	1.6 (1.5-1.8)	1.6 (1.4-1.7)	1.5 (1.4-1.7)
Sites of infection, No.				
Chest	173	180	168	185
Urogenital	41	35	36	40
Septicemia	32	36	37	31
Pathogens				
Gram negative	107	97	98	106
Blood glucose levels, mean (95% CI), mg/dL [No. of patients]	12.0 (11.0-13.0)	11.3 (10.7-11.9) [253]	11.8 (11.0-12.6)	11.5 (10.7-12.4)
Lactate levels, mean (95% CI), mg/dL	44.2 (33.3-55.0) [248]	35.1 (30.6-38.7) [244]	36.7 (27.0-45.1) [236]	42.1 (36.0-54.1) [256]
Cortisol levels, mean (SD), µg/dL [No. of patients]				
Basal	39.8 (34.0-45.7) [227]	36.7 (35.6-43.8) [230]	41.1 (34.9-47.4) [215]	38.5 (34.7-42.4) [242]
Peak	50.7 (45.0-56.3) [223]	50.1 (45.1-55.1) [225]	50.1 (44.8-55.4) [211]	50.7 (45.3-56.0) [237]
Change	10.7 (5.5-16.0) [223]	10.5 (7.5-13.5) [225]	9.2 (3.9-14.3) [211]	11.9 (8.6-15.3) [237]
Nonresponders, No. (%)	173 (67.8)	169 (66.5)	167 (68.2)	175 (66.3)
Mechanical ventilation, No. (%)	218 (85.5)	220 (86.6)	213 (86.9)	225 (85.2)
Renal replacement therapy, No. (%)	46 (18.7) [246]	53 (21.5) [246]	41 (17.2)	58 (22.9)

Abbreviations: CI, confidence interval; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; SAPS, Simplified Acute Physiology Score.
SI conversion factors: To convert blood glucose levels from mg/dL to mmol/L, multiply by 0.0555; cortisol levels from µg/dL to nmol/L, multiply by 27.588; lactate levels from mg/dL to mmol/L, multiply by 0.111.
[a] Each statistic was computed on the nonmissing value, ie, the whole sample unless specifically indicated.

Table 2. Primary and Secondary Outcomes

Variables	Intensive Insulin Therapy (n = 255)	Conventional Glucose Control (n = 254)	*P* Value Unadjusted	*P* Value Adjusted[a]	Hydrocortisone + Fludrocortisone (n = 245)	Hydrocortisone Alone (n = 264)	*P* Value Unadjusted	*P* Value Adjusted[a]
In-hospital death, No./total (%)	117/255 (45.9)	109/254 (42.9)	.50	.37	105 (42.9)	121 (45.8)	.50	.91
Overall survival								
Deaths, No. (%)	122 (47.9)	118 (46.5)			112 (45.7)	128 (48.5)		
Kaplan-Meier estimate of survival rates, HR (95% CI), d	1.04 (0.80-1.34)	1 [Reference]	.78	.39	0.94 (0.73-1.21)	1 [Reference]	.61	.67
28	62.2 (56.4-68.5)	61.1 (55.3-67.5)			62.5 (56.6-68.9)	60.9 (55.2-67.1)		
90	51.8 (45.9-58.4)	54.8 (48.9-61.4)			54.2 (48.2-61.0)	52.4 (46.6-58.9)		
180	50.9 (45.0-57.6)	52.1 (46.2-58.8)			52.9 (46.9-59.7)	50.2 (44.4-56.8)		
No. of patients who died	103	82			105	121		
Causes of death, No. (%)								
Multiple organ failure	92 (78.6)	66 (60.6)	.004[b]	.005[b]	75 (71.4)	83 (68.6)	.67[b]	.74[b]
Cardiovascular	9 (8.7)	7 (8.5)			7 (6.7)	9 (7.4)		
Stroke	1 (1.0)	2 (2.4)			3 (2.9)	0		
Brain hemorrhage	0	2 (2.4)			0	2 (1.7)		
Refractory hypoxia	1 (1.0)	2 (2.4)			2 (1.9)	1 (0.8)		
Unknown	0	3 (3.7)			3 (2.9)	0		
No. of days, median (IQR)								
Vasopressor-free within the first 7 days	4 (1-6)	4 (2-5)	.58	.60	4 (2-5)	4 (1-5)	.62	.61
Mechanical ventilation-free within 28 days	10 (2-22)	13 (2-23)	.51	.29	12 (2-23)	12 (2-22.5)	.50	.81
Cumulative incidence of SOFA <8 at day 7 (95% CI)	64.3 (58.6-70.1)	60.6 (54.7-66.6)	.38	.75	63.3 (57.3-69.2)	61.7 (56.0-67.5)	.75	.78
Length of stay, median (IQR), d								
ICU								
All patients	9 (4-19)	9 (4-15)	.70	.39	9 (4-16)	9 (4-17.5)	.86	.35
Survivors	10 (6-19)	9 (5-15)	.68	.46	10 (6-16)	9 (5-17)	.52	.10
Hospital								
All patients	16 (6-34)	15 (7-30)	.87	.94	14 (6-25)	18 (7-34)	.15	.07
Survivors	24 (12-43)	22 (11-39)	.87	.57	19 (5-40)	25.5 (14-42)	.09	.13

Abbreviations: CI, confidence interval; HR, hazard ratio, IQR, interquartile range; SOFA, Sequential Organ Failure Assessment

[a] Adjusted on baseline prognostic variables, namely age, time in hospital prior to ICU admission, time in ICU prior to randomization, Simplified Acute Physiology Score II, SOFA score, lactate level and mechanical ventilation, and a random center effect.

[b] Comparison of multiple organ failure vs other causes.

Table 3. Serious Adverse Events

Variables	Intensive Insulin Therapy (n = 255)	Conventional Glucose Control (n = 254)	*P* Value	Hydrocortisone + Fludrocortisone (n = 245)	Hydrocortisone Alone (n = 264)	*P* Value
Superinfection, No. of patients/episodes						
Total	47/106	43/132	.66	53/144	37/94	.02
Lung	35/59	29/94	.43	36/82	28/71	.18
Peritoneal	4/10	1/1	.37	4/10	1/1	.20
Urinary tract	7/8	13/16	.18	15/17	5/7	.02
Central nervous system	0/0	1/1	.50	1/1	0/0	.48
Blood	9/10	4/5	.26	8/9	5/6	.40
Others	14/19	8/15	.28	15/25	7/9	.08
In-hospital death among patients with superinfection, No./total (%)	26/47 (55.3)	21/43 (48.8)	.67	27/53 (50.9)	20/37 (54.1)	.83
Hypoglycemia, glucose <40 mg/dL						
No. of measures per patient, median (IQR)	72 (43-110)	44 (32-56)	<.001	51 (31-79)	53 (38-81)	.36
No. of patients/episodes	42/72	20/44	.003	32/51	30/53	.59
No. of episodes						
0	211	234	.002	212	233	.54
1	26	13		19	20	
2	9	3		8	4	
3	5	1		3	3	
4	1	2		2	2	
>4	1	1		1	1	
Episodes, mean (SD)	0.289 (0.90)	0.139 (0.58)	.003	0.238 (0.86)	0.198 (0.68)	.63
In-hospital death among patients with hypoglycemia, No./total (%)	19/42 (45.2)	10/20 (50.0)	.79	14/32 (43.8)	15/30 (50.0)	.80
MDRS day 28						
1	3	11	.06	5	9	.10
2	3	3		4	2	
3	3	1		2	2	
4	9	3		1	1	
5	5	3		6	6	

Abbreviations: IQR, interquartile range; MDRS, muscular disability rating score.
SI conversion factor: To convert blood glucose levels from mg/dL to mmol/L, multiply by 0.0555.