Choc septique

Cas particulier du choc septique

Etat hémodynamique
hyperdynamique

Sepsis et sepsis sévère définition de 1992

- **SIRS** (syndrome de réponse inflammatoire systémique) : si deux ou plus des conditions suivantes sont remplies (1992)
  - température < 36°C ou > 38°C
  - fréquence cardiaque > 90/min
  - fréquence respiratoire > 20/min ou PaCO2 < 32 mm Hg
  - leucocytose > 12.000/mm3, < 4.000/mm3 ou présence de formes immatures circulantes (> 10 % des cellules)
- **Sepsis** : si le SIRS est dû à une infection: voir tableau 2003
- **Sepsis sévère** : si le sepsis est associé à une dysfonction organique, de l'hypoperfusion (acidose lactique, oligurie, troubles de conscience,...) ou de l'hypotension artérielle (TAs < 90 mmHg ou chute de > 40 mmHg de la valeur de base sans autre raison connue)
- **Choc septique** : sepsis avec hypotension, malgré un remplissage adéquat, avec des signes d'hypoperfusion
  - l'hypotension peut manquer si des agents vasopresseurs sont administrés

Evolution des concepts

- Le sepsis n'est plus considéré comme seulement une réaction inflammatoire systémique. Il y a également une réponse anti-inflammatoire et une réponse immunitaire à l'agression.
- Il est plutôt la conséquence d'une réaction « inadaptée » avec dysfonction d'un ou de plusieurs organes

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Developing a New Definition and Assessing New Clinical Criteria for Septic Shock

For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Manu Shankar-Hari, MD, MSc; Gary S. Phillips, MAS; Mitchell L. Levy, MD; Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Clifford S. Deutschman, MD; Derek C. Angus, MD, MPh; Gordon D. Rubenfeld, MD, MSc; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force

JAMA. 2016;315(8):775-787. doi:10.1001/jama.2016.0289

Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

PROCESS A task force (n = 19) with expertise in sepsis pathobiology, clinical trials, and epidemiology was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. Definitions and clinical criteria were generated through meetings, Delphi processes, analysis of electronic health record databases, and voting, followed by circulation to international professional societies, requesting peer review and endorsement (by 31 societies listed in the Acknowledgment).

Définitions

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
  - A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
- In lay terms, sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.
- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, ie, alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.
- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
- Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

Abbreviations: MAP, mean arterial pressure; qSOFA, quick SOFA; SOFA: Sequential [Sepsis-related] Organ Failure Assessment.

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

System	Score 0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

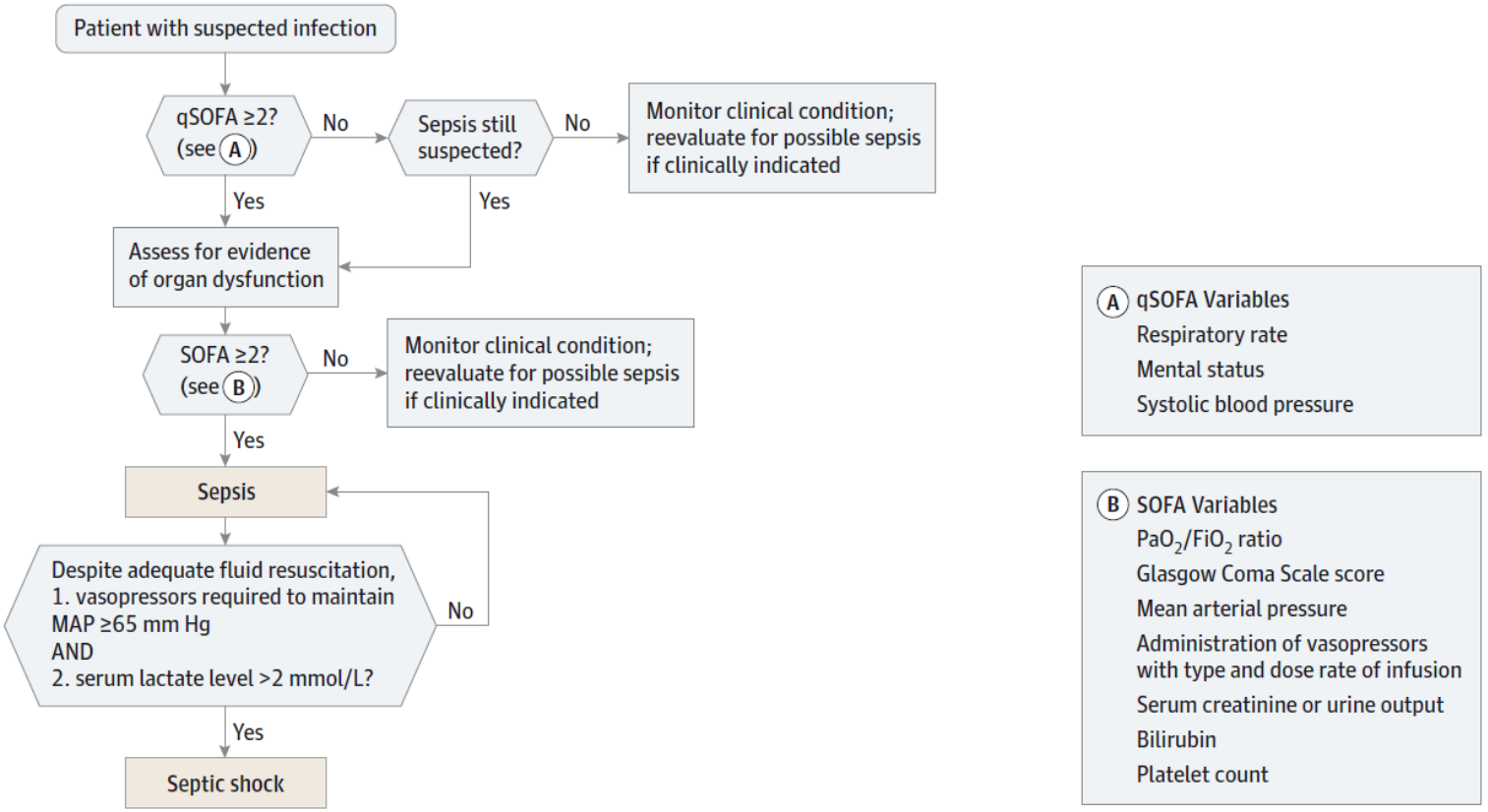
Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

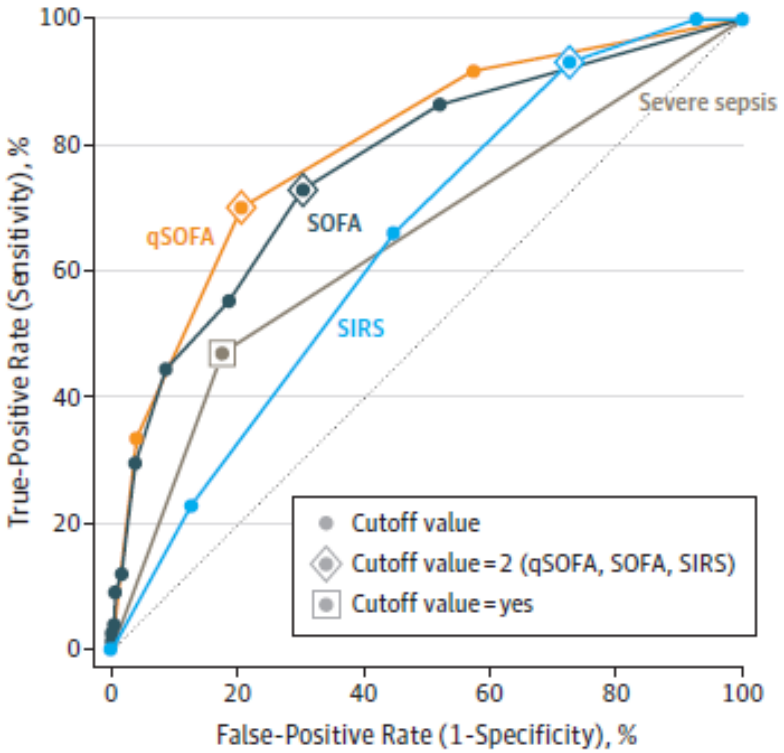
Systolic blood pressure ≤100 mm Hg

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

Figure 2. Receiver Operating Characteristic Curves for In-Hospital Mortality



qSOFA indicates quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; and SOFA, Sequential [Sepsis-related] Organ Failure Assessment. The area under the receiver operating characteristic curves for qSOFA is 0.80 (95% CI, 0.74-0.85); SOFA, 0.77 (95% CI, 0.71-0.82); SIRS, 0.65 (95% CI, 0.59-0.70); and severe sepsis, 0.65 (95% CI, 0.59-0.70).

Les principaux foyers sources

- Cutanés
- Digestifs : angiocholite, diverticulite, entérite
- Respiratoires : pneumonie, pleurésie, abcès
- Urinaires : pyélonéphrite, prostatite, sonde
- Gynécologiques : salpingite, post-partum
- Veineux : cathéter
- Cardiaque : endocardite
- Cervico-facial : pharyngite, angine, otite, sinusite
- Neuro-méningé
- Ostéo-articulaire

Chez l'opéré récent

- Infection site opératoire
- Pneumopathie
- Infection urinaire
- Phlébite
- Infection sur cathéter

Signes cliniques du choc

- hypotension artérielle
- tachycardie (pouls filant)
- « choc chaud »: extrémités vasodilatées, rouges, chaudes, sèches
- hyperventilation (acidose métabolique)
- lipothymie, apathie, agitation
- oligurie, anurie

Prélèvements à réaliser

A. Microbiologiques:

- hémocultures : périphériques et par toutes les voies des cathéters en place (à mettre également en culture en cas de retrait)
- urines (avec EMU)
- si indiqué : expectorations, LCR, frottis de gorge ...

B. Biologiques:

- fonction rénale : ionogramme, urée, créatinine
- examen hématologique complet avec formule
- tests inflammatoires : CRP, fibrinogène
- tests hépatiques
- coagulation
- gazométrie artérielle et acide lactique

Traitement spécifique

- identifier le foyer infectieux :
  - pulmonaire (radiographie, expectorations)
  - urinaire (EMU, culture)
  - cutané (purpura, macropapules, pustules)
  - neuroméningé (PL)
  - abdominal (RX abdomen à blanc, échographie)
  - endocardite (échographie cardiaque)
  - ....
- toujours faire des hémocultures
- débuter l'antibiothérapie sur un pari bactériologique

Choix des antibiotiques

- sepsis sans foyer : une β-lactamine à large spectre (céphalosporine ou Méronem^{R} ou Tazocin^{R}) + aminoside (Amikacine-Amukin^{R}) : 15 mg/kg 1 x/j (DT 1,5 g/j)
- infections abdominales pelviennes (anaérobies) : Tienam^{R}/Méronem^{R} ou Tazocin^{R} + aminoside
- suspicion d'infection à staphylocoque : β-lactamine à large spectre + vancomycine (Vancocin^{R} 20 mg/kg puis 2x 15 mg/kg i.v.)
- neutropénie fébrile : céphalosporine ou Méronem^{R} ou Tazocin^{R} + amikacine

Le pronostic est lié à la durée de l'hypotension avant l'antibiothérapie

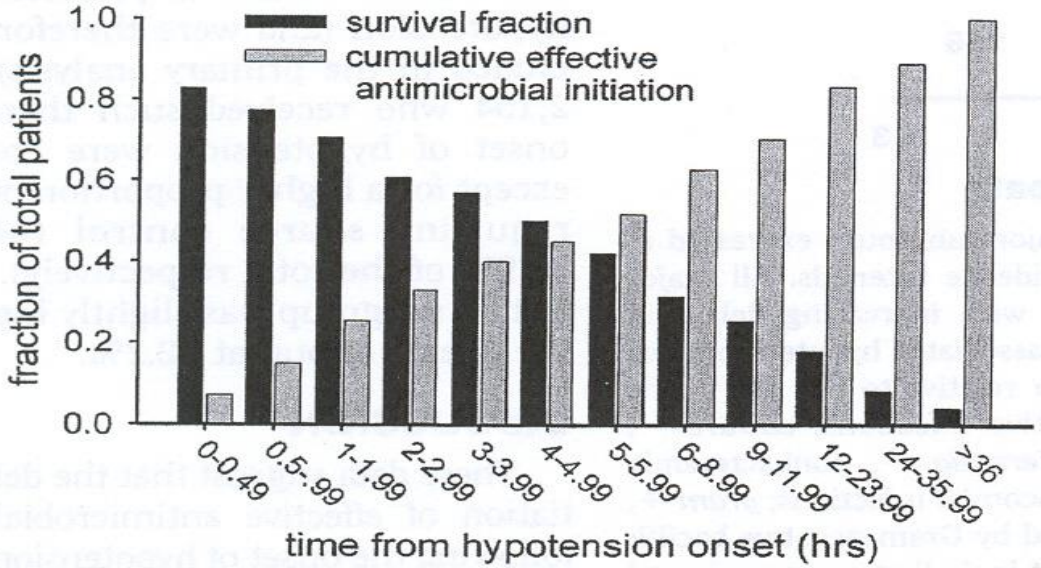


Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

Kumar; 2006; 34 : 1589-96

Traitement du choc

- monitorer la lactatémie : dosages réguliers (toutes les 2 h, selon la clinique), la TAM, la diurèse
- oxygénothérapie, éventuellement ventilation artificielle
- 4 phases successives :

1ère phase

remplissage adéquat

- par exemple 30 ml/kg les 3 premières heures (par pallier 250-500 ml d'un expanseur cristalloïdes en 15-30 min)
- Transfusion de GR si l'Hb<7g/dl

2ème phase

en cas de réponse non satisfaisante au remplissage adéquat : noradrénaline i.v. : 0,02 à 0,1 µg/kg/min

objectifs :

PAS > 90 mm Hg et/ou PAM > 65 mm Hg

lactatémie < 2 mEq/L

diurèse > 20 ml/h

3ème phase

en cas d'échec: évaluation hémodynamique (échographie cardiaque et/ou méthode invasive):

- une hypovolémie (↓ PVC, ↓ PAPO, ↓ IC) : poursuivre le remplissage sous cathécolamines, en recherchant une cause à l'hypovolémie (ex. hémorragie)
- une dysfonction ventriculaire gauche (dilatation ventriculaire, hypokinésie globale ou segmentaire, ↓ IC avec ↑ PAPO) : dobutamine (5 à 20 γ/kg/min) et noradrénaline
- **un profil hémodynamique classique de choc septique après remplissage vasculaire** (hyperdynamique : IC > 4,5 L/min et RVS < 800 dynes. sec/$cm^5.m^2$) : augmenter la noradrénaline … ou **corticoïdes** (pour renverser l'insensibilité aux catécholamines) : Solucortef^R 200 mg /j (durée minimale : 5 jours)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and E. Bellissant, for the CRICS-TRIGGERSEP Network*

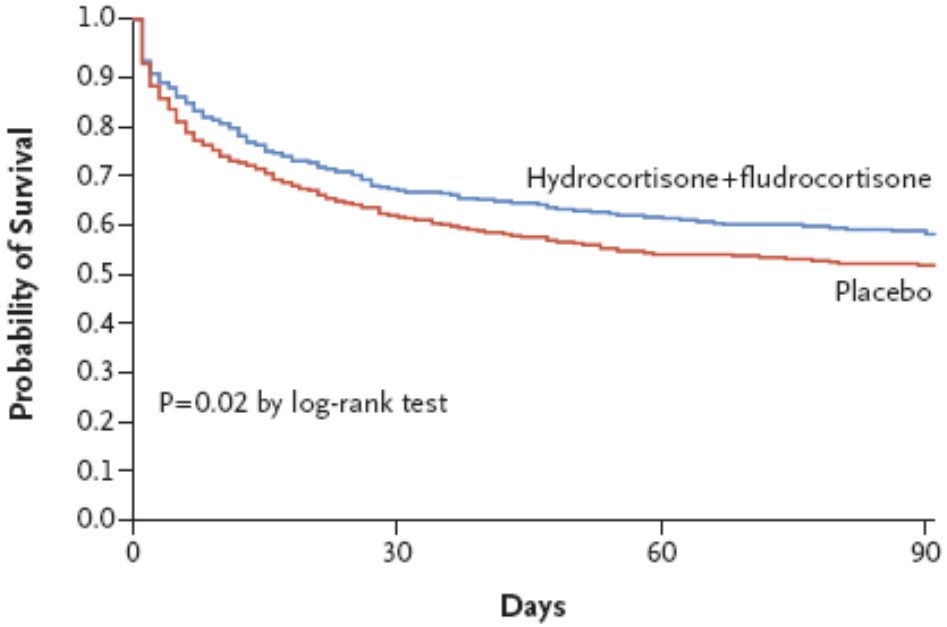
N Engl J Med 2018;378:809-18.
DOI: 10.1056/NEJMoa1705716

METHODS

In this multicenter, double-blind, randomized trial with a 2-by-2 factorial design, we evaluated the effect of hydrocortisone-plus-fludrocortisone therapy, drotrecogin alfa (activated), the combination of the three drugs, or their respective placebos. The primary outcome was 90-day all-cause mortality. Secondary outcomes included mortality at intensive care unit (ICU) discharge and hospital discharge and at day 28 and day 180 and the number of days alive and free of vasopressors, mechanical ventilation, or organ failure. After drotrecogin alfa (activated) was withdrawn from the market, the trial continued with a two-group parallel design. The analysis compared patients who received hydrocortisone plus fludrocortisone with those who did not (placebo group).

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Placebo (N = 627)	Hydrocortisone plus Fludrocortisone (N = 614)	All Patients (N = 1241)
Male sex — no./total no. (%)	424/626 (67.7)	402/614 (65.5)	826/1240 (66.6)
Age — yr†	66±15	66±14	66±14
Admission from a medical ward — no./total no. (%)	499/616 (81.0)	495/601 (82.4)	994/1217 (81.7)
SAPS II‡	56±19	56±19	56±19
SOFA score§	11±3	12±3	12±3
Community-acquired infection — no./total no. (%)	459/608 (75.5)	468/602 (77.7)	927/1210 (76.6)
Site of infection — no./total no. (%)¶			
Unknown	18/626 (2.9)	11/614 (1.8)	29/1240 (2.3)
Lung	363/626 (58.0)	373/614 (60.7)	736/1240 (59.4)
Abdomen	68/626 (10.9)	74/614 (12.1)	142/1240 (11.5)
Urinary tract	118/626 (18.8)	102/614 (16.6)	220/1240 (17.7)
Positive blood culture — no./total no. (%)	229/626 (36.6)	225/614 (36.6)	454/1240 (36.6)
Documented pathogen — no./total no. (%)	441/626 (70.4)	450/614 (73.3)	891/1240 (71.9)
Gram-positive bacteria — no./total no. (%)	228/626 (36.4)	235/614 (38.3)	463/1240 (37.3)
Gram-negative bacteria — no./total no. (%)	264/626 (42.2)	261/614 (42.5)	525/1240 (42.3)
Adequate antimicrobial therapy — no./total no. (%)	602/626 (96.2)	595/614 (96.9)	1197/1240 (96.5)
Vasopressor administration			
Epinephrine			
No. of patients	58	53	111
Dose — μg/kg/min	1.74±2.41	2.31±6.62	2.01±4.88
Norepinephrine			
No. of patients	552	534	1086
Dose — μg/kg/min	1.14±1.66	1.02±1.61	1.08±1.63
Mechanical ventilation — no./total no. (%)	569/623 (91.3)	567/614 (92.3)	1136/1237 (91.8)
Renal-replacement therapy — no./total no. (%)	168/598 (28.1)	161/596 (27.0)	329/1194 (27.6)



No. at Risk				
Hydrocortisone+ fludrocortisone	614	405	372	353
Placebo	627	381	333	319

Figure 1. 90-Day Survival Distributions.

Shown are survival curves from randomization up to 90 days. The survival rate was significantly higher in the hydrocortisone-plus-fludrocortisone group than in the placebo group.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

ABSTRACT

BACKGROUND

Whether hydrocortisone reduces mortality among patients with septic shock is unclear.

METHODS

We randomly assigned patients with septic shock who were undergoing mechanical ventilation to receive hydrocortisone (at a dose of 200 mg per day) or placebo for 7 days or until death or discharge from the intensive care unit (ICU), whichever came first. The primary outcome was death from any cause at 90 days.

RESULTS

From March 2013 through April 2017, a total of 3800 patients underwent randomization. Status with respect to the primary outcome was ascertained in 3658 patients (1832 of whom had been assigned to the hydrocortisone group and 1826 to the placebo group). At 90 days, 511 patients (27.9%) in the hydrocortisone group and 526 (28.8%) in the placebo group had died (odds ratio, 0.95; 95% confidence interval [CI],

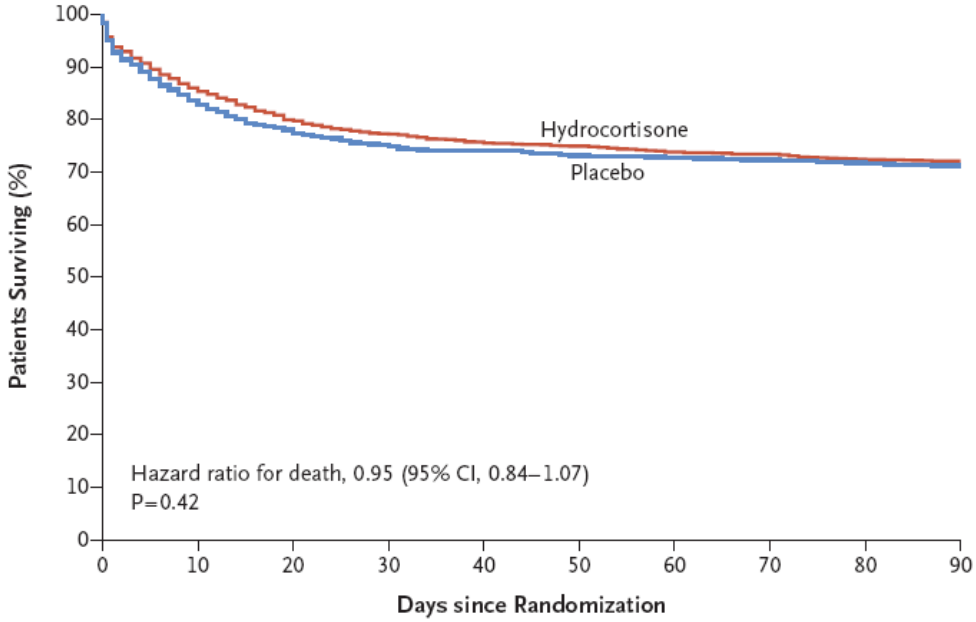
The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Venkatesh at the Department of Intensive Care, Wesley Hospital, 451 Coronation Dr., Auchenflower, Brisbane, QLD 4066, Australia, or at bvenkatesh@georgeinstitute.org.au.

*A full list of investigators in the ADRENAL Trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on January 19, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1705835

A Survival

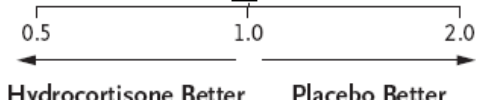


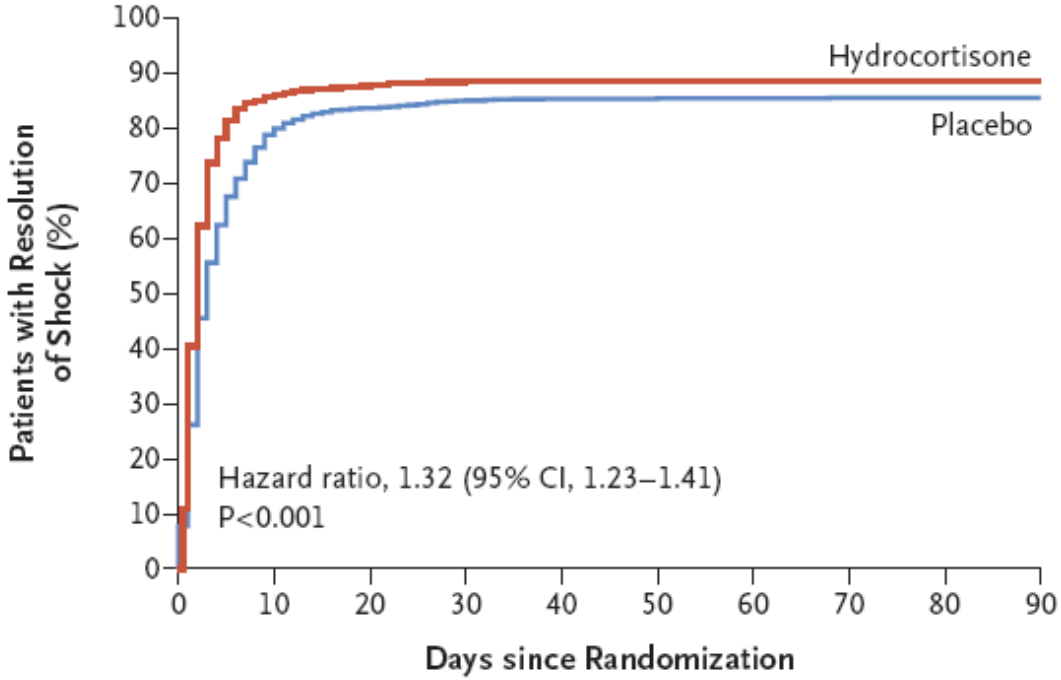
No. at Risk

Hydrocortisone	1832	1591	1481	1418	1388	1374	1356	1348	1328	1321
Placebo	1826	1546	1433	1376	1354	1337	1330	1322	1312	1300

B Subgroup Analysis of Death at 90 Days

Subgroup	Hydrocortisone	Placebo	Odds Ratio (95% CI)	P Value for Interaction
	no. of patients with event/total no. of patients (%)			
Sex				0.53
Male	312/1106 (28.2)	336/1122 (29.9)	0.92 (0.76–1.10)	
Female	199/726 (27.4)	190/704 (27.0)	1.01 (0.80–1.28)	
Admission type				0.73
Surgical	125/568 (22.0)	138/580 (23.8)	0.91 (0.69–1.21)	
Medical	386/1264 (30.5)	388/1245 (31.2)	0.97 (0.81–1.15)	
Catecholamine dose				0.25
≤15 μg/min	224/968 (23.1)	228/995 (22.9)	1.02 (0.82–1.26)	
>15 μg/min	281/849 (33.1)	291/805 (36.1)	0.86 (0.70–1.05)	
Site of sepsis				0.63
Pulmonary	243/799 (30.4)	250/828 (30.2)	0.99 (0.80–1.23)	
Other	268/1033 (25.9)	276/998 (27.7)	0.92 (0.76–1.12)	
APACHE II score				0.17
≥25	326/840 (38.8)	297/785 (37.8)	1.01 (0.83–1.24)	
<25	184/990 (18.6)	229/1039 (22.0)	0.82 (0.66–1.02)	
Time from shock onset to randomization				0.08
<6 hr	110/352 (31.2)	96/344 (27.9)	1.16 (0.83–1.61)	
6 to <12 hr	127/511 (24.9)	153/486 (31.5)	0.71 (0.54–0.94)	
12 to <18 hr	119/437 (27.2)	106/423 (25.1)	1.13 (0.83–1.54)	
≥18 hr	154/525 (29.3)	167/566 (29.5)	0.99 (0.76–1.29)	





No. at Risk

Hydrocortisone	1843	104	34	9	6	3	3	2	1	0
Placebo	1854	213	53	19	8	6	4	0	0	0

Figure 2. Cumulative Incidence Function of Time from Randomization to Resolution of Shock.

The cumulative incidence function plot was created by treating death as a competing risk.

dysfonction ventriculaire gauche

- la dysfonction cardiaque apparaît secondairement, nécessitant un support inotrope d'environ 48 h
- mécanisme : hypersécrétion NOS-2 dans les cavités cardiaques et autres muscles (diaphragme, grand droit) : NO se transforme en un dérivé peroxynitrite $ONOO^-$ réagissant avec les tyrosines des protéines musculaires avec formation de nitrotyrosine … et le muscle est bloqué
- BNP : taux très élevé non lié à la dépression myocardique mais à une diminution de son catabolisme par baisse de l'activité d'une endopeptidase vasculaire responsable de la destruction du BNP : donc rôle pronostic mais pas prédicteur de la dysfonction cardiaque
- détection : troponine circulante
- confirmation : échocardiographie (dilatation ventriculaire, hypokinésie globale ou segmentaire) ou hémodynamique invasive (baisse IC avec augmentation PAPO)

Penser à une étiologie infectieuse non couverte

- Abcès profond ou collection non drainée
- Fungémie ou autre infection non bactérienne
- Infection à staphylocoque
- Bactérie résistante aux antibiotiques prescrits

4ème phase

en cas d'insuffisance circulatoire persistante malgré la correction de l'hypovolémie et de la fonction ventriculaire gauche :

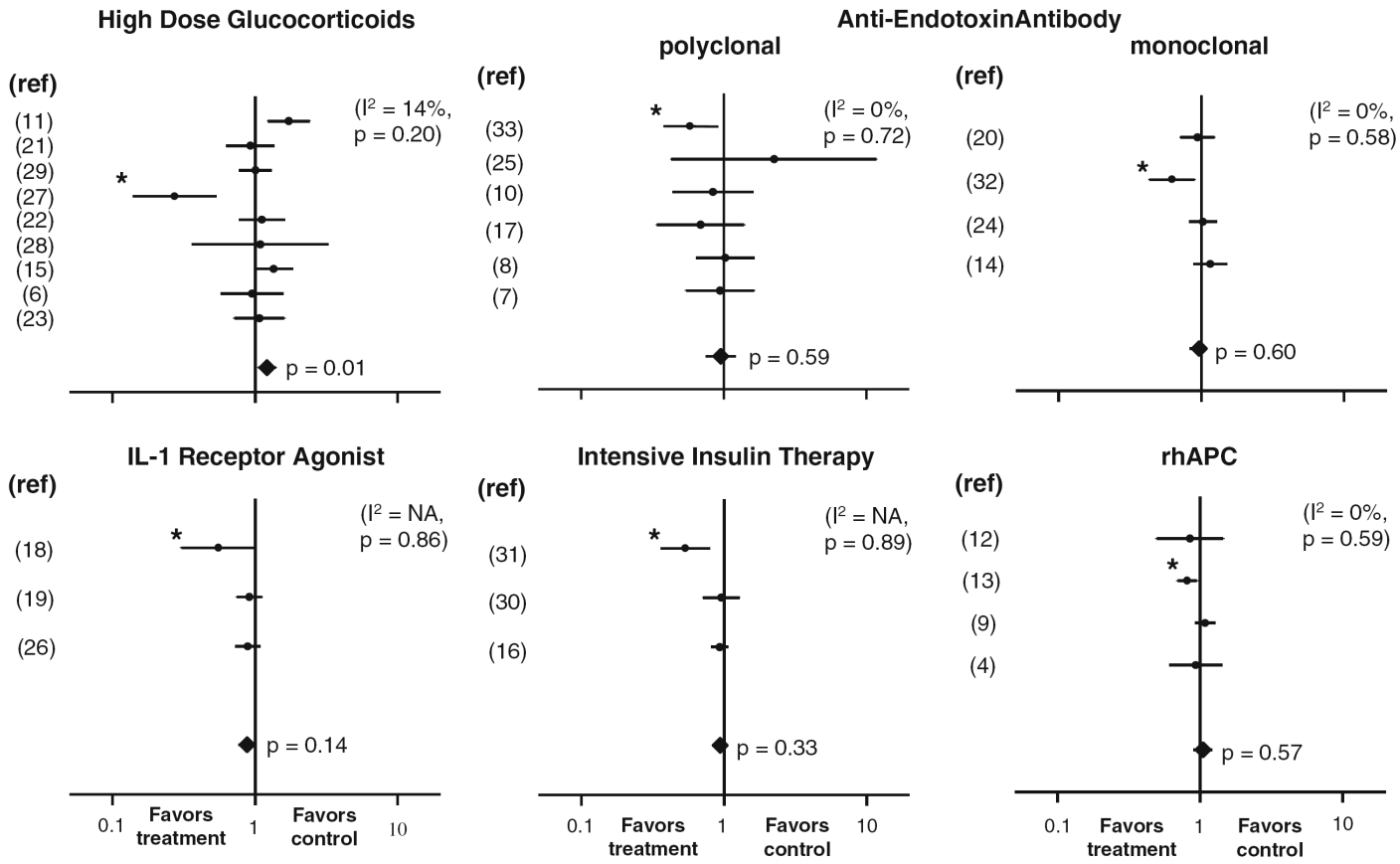
- passer à l'adrénaline
- sinon envisager :
  - augmentation les doses de catécholamines à niveaux très importants
  - associations de plusieurs catécholamines (ex. vasopressin (jusqu'à 0.03 U/min), adrénaline, ...)

Intensive Care Med (2008) 34:1955–1960
DOI 10.1007/s00134-008-1274-6

EDITORIAL

Daniel A. Sweeney
Robert L. Danner
Peter Q. Eichacker
Charles Natanson

Once is not enough: clinical trials in sepsis


High Dose Glucocorticoids
(ref)
(11)
(21)
(29)
(27)
(22)
(28)
(15)
(6)
(23)
*
(I² = 14%, p = 0.20)
p = 0.01
Anti-EndotoxinAntibody
polyclonal
(ref)
(33)
(25)
(10)
(17)
(8)
(7)
*
(I² = 0%, p = 0.72)
p = 0.59
monoclonal
(ref)
(20)
(32)
(24)
(14)
*
(I² = 0%, p = 0.58)
p = 0.60
IL-1 Receptor Agonist
(ref)
(18)
(19)
(26)
*
(I² = NA, p = 0.86)
p = 0.14
0.1
Favors treatment
1
Favors control
10
Intensive Insulin Therapy
(ref)
(31)
(30)
(16)
*
(I² = NA, p = 0.89)
p = 0.33
0.1
Favors treatment
1
Favors control
10
rhAPC
(ref)
(12)
(13)
(9)
(4)
*
(I² = 0%, p = 0.59)
p = 0.57
0.1
Favors treatment
1
Favors control
10
Relative Risk of Death (95% Confidence Interval)

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CONFERENCE REPORTS AND EXPERT PANEL

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

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]