

Evaluation des nouvelles définitions du sepsis



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Service de Réanimation Médicale
CHU La Rabta de Tunis

16-17 Février 2018 - Hôtel Le Royal Hammamet

09h00-09h30

Plan

1

Introduction

2

History of sepsis

3

Définitions du sepsis

4

Validation du sepsis-3

5

Les points forts

6

Les points faibles

7

Conclusions



ICU costs in the United States

2015

the **most expensive** condition treated in US hospitals

40 percent of all ICU costs

\$25.7 billion

Six times greater than that for ICU patients that do not have sepsis

62 percent readmission rate

(Sutton & Friedman, 2013; Sepsis Alliance, 2014)



31.5 million people are treated each year
5.3 million end up dying

Most expensive condition treated in US hospitals

Pour bien le traiter, il faut l'étudier

SEPTIS

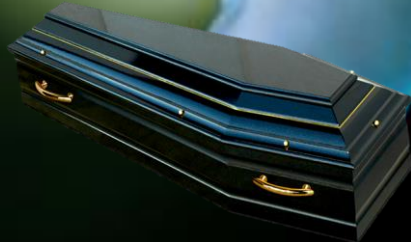


62 % readmission rate

Pour bien l'étudier il faut le définir

40 % of all ICU costs

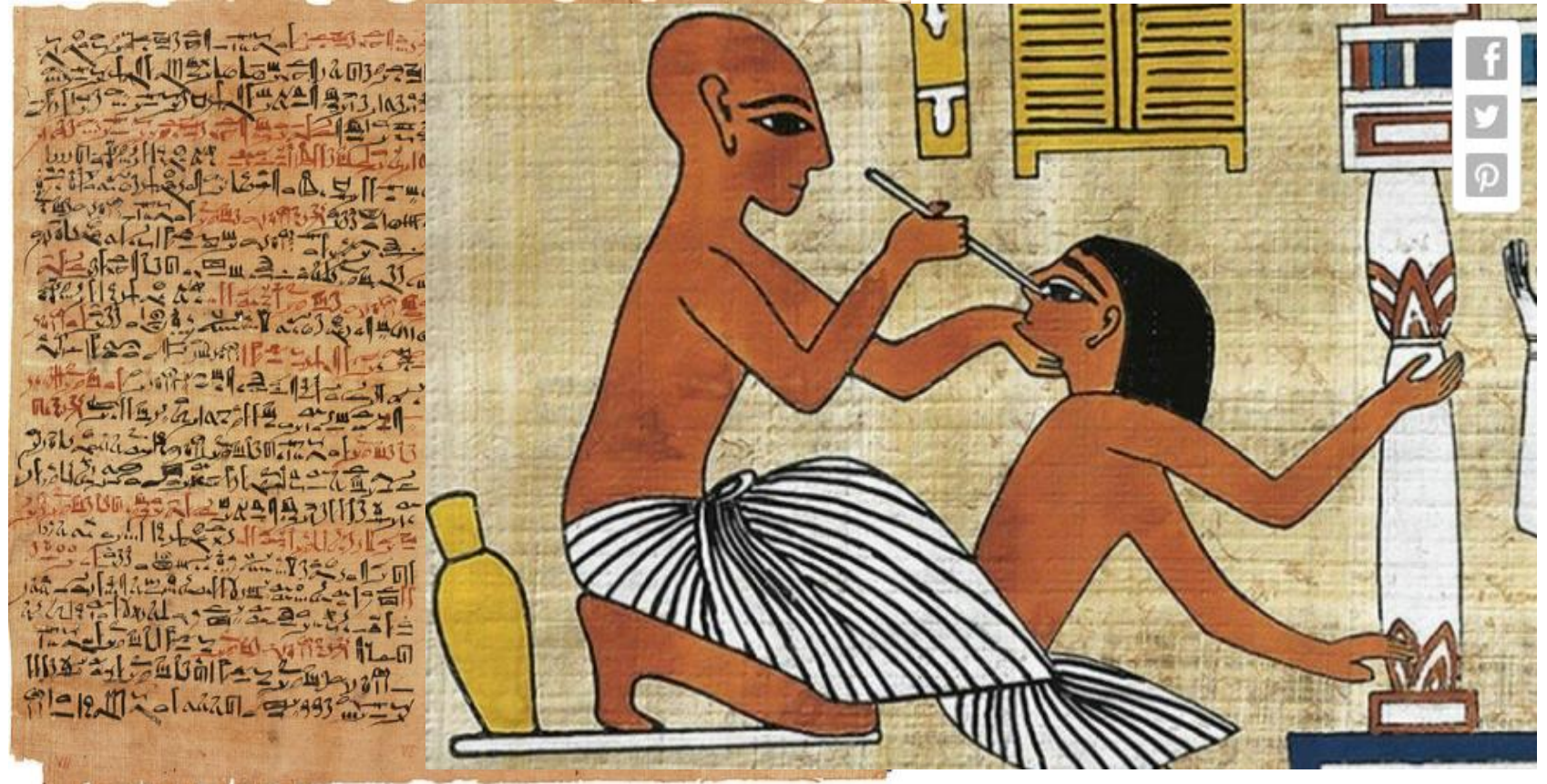
One person dying every **2 minutes**



History of sepsis



First descriptions of sepsis are found in Egyptian papyrus as early as **1600 BC**



Le papyrus Edwin Smith They used **honey** and **human brains** to cure eye infections



Hippocrate



460-470 av. JC

Galien



130-200

Avicenne



979-1037 BC

Sepsis (σηψις) =
« putréfaction »

Greek word

Sipsis

Make rotten

« *Pus bonum et laudabile* »

Faire pourrir

Coincidence of blood putrefaction and fever

Pepsis

Good digestion

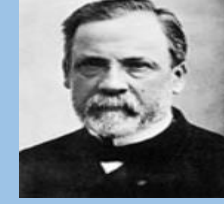
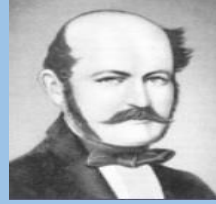
Bonne digestion



Semmelweiss

Pasteur

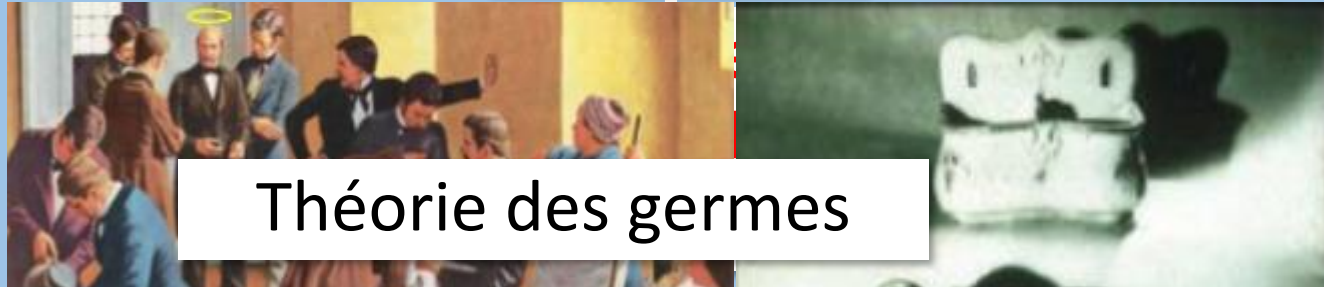
Robert Koch



1818-1865

1870

Hungary



Théorie des germes

Les processus d'infection et de suppuration étaient causés par des micro-organismes

Le terme de sepsis devenant synonyme d'infection invasive.



HUGO Schottmuller

1867-1936 Germany

Modern definition of
sepsis (1914)

Le sepsis survenait si des **germes pathogènes** envahissaient d'une façon constante ou périodiquement la **circulation sanguine** à partir d'un **foyer infectieux** et provoquaient des **symptômes** subjectifs et objectifs

Le traitement ne doit pas être dirigé contre les **bactéries** dans le sang, mais contre les **toxines bactériennes libérées**



Des

Rising incidence,
new etiologies

termes

Changing
demographics

ment

pour décrire le patient avec septicémie

= the **most common cause of death** in the noncoronary intensive care unit

été

↗ use of **ATB**, **immunosuppressive** agents, and invasive technology in the treatment



Septicémique

Bactériémique

Définition opérationnelle et universelle

American College Of Chest Physicians

Society of Critical Care Medicine



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Table 1 – Definitions

1992

SEPSIS-1

Infection = microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

Bacteremia = the presence of viable bacteria in the blood.

Systemic inflammatory response syndrome (SIRS) = the systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: (1) temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO_2

<32 mmHg

$<4,000$ cells/mm³ or $>10\%$ immature (band) forms.

Sepsis = the presence of a systemic inflammatory response to infection.

more of the following conditions: (1) temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO_2

<32 mmHg

$<4,000$ cells/mm³ or $>10\%$ immature (band) forms.

<32 mmHg

$<4,000$ cells/mm³ or $>10\%$ immature (band) forms.

Température $< 36^{\circ}\text{C}$ ou $\geq 38,5^{\circ}\text{C}$

FC > 90 battements/minute

FR $> 20/\text{mn}$ ou $\text{PaCO}_2 < 32$ mmHg

GB $> 12000/\text{mm}^3$ ou $< 4000/\text{mm}^3$
ou cellules immatures $> 10\%$

Severe sepsis = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.

Septic shock = sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

Sepsis-induced hypotension = a systolic blood pressure <90 mm Hg or a reduction of ≥ 40 mm Hg from baseline in the absence of other causes for hypotension.

Multiple organ dysfunction syndrome (MODS) = presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

In 2001, a second consensus conference validated most of the previous concepts

but drew attention to the fact that systemic inflammatory response is not specific of sepsis and could be seen in many diseases.



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

CHEST / 101 / 6 / JUNE, 1992

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:

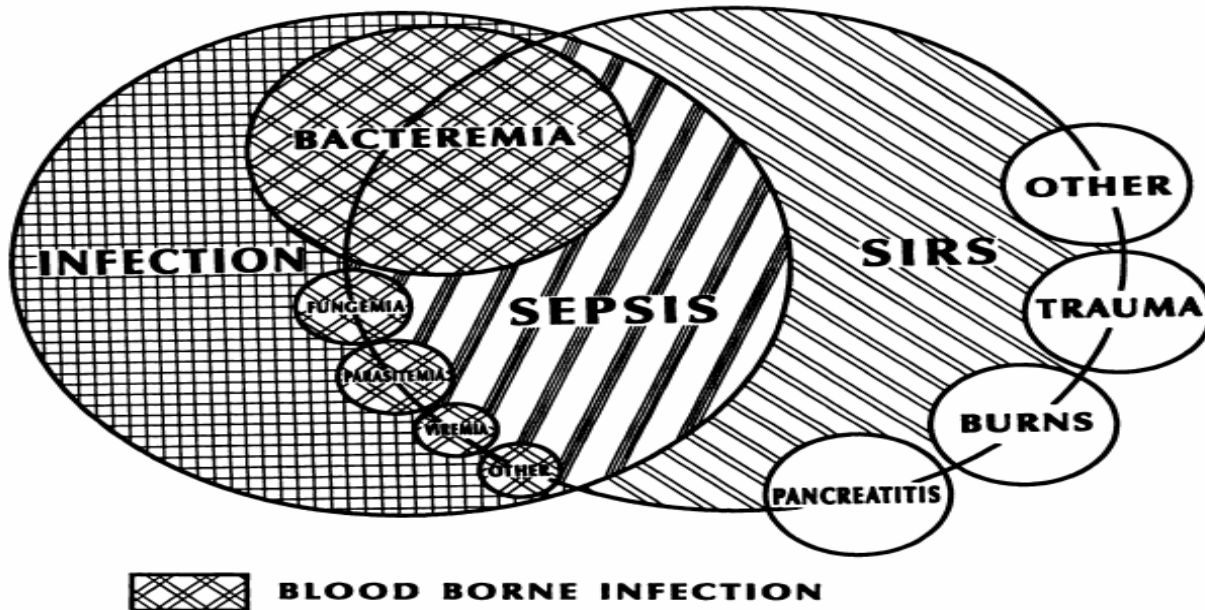
- | | |
|---|------------------------------------|
| Roger C. Bone, M.D., F.C.C.P., Chairman | Alan M. Fein, M.D., F.C.C.P. |
| Robert A. Balk, M.D., F.C.C.P. | William A. Knaus, M.D. |
| Frank B. Cerra, M.D. | Roland M. H. Schein, M.D. |
| R. Phillip Dellinger, M.D., F.C.C.P. | William J. Sibbald, M.D., F.C.C.P. |

1992

SEPSIS-1

2001

International Sepsis Definitions Conference



Peu sensible

SIRS criteria are **missing**
in **1 in 8** patients

34 % des patients en sepsis sévère et **24 %** en choc septique
DEC AUX URGENCES ne présentent pas les critères de SIRS

SIRS

Table 1. Baseline Characteristics and Hospital Outcomes of Patients with Severe Sepsis, According to Status with Respect to Criteria for the Systemic Inflammatory Response Syndrome (SIRS).*

Characteristic	All Patients <i>no. of patients with data</i>	Patients with SIRS-Positive Sepsis <i>no. of patients with data</i>	Patients with SIRS-Negative Sepsis <i>no. of patients with data</i>	P Value
Hospital outcome — no. (%)	109,663	96,385	13,278	
Death	25,713 (23.4)	23,577 (24.5)	2136 (16.1)	<0.001

study

ML
MI

D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.

Long Ngo, PhD
Daniel Talmor, MD, MPH

Pittsburgh, PA (Angus); The Division of General Internal Medicine; Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, MA (Ngo); and Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess

Volume 48, NO. 5 : November 2006

This lack of positivity was **associated** with **highest** hospital **morbidity** and **mortality**

Peu sensible

Peu spécifique

Dépend Recueil

SIRS

Sepsis

43 %

Intensive Care Med (2012) 38:811-819
DOI 10.1007/s00134-012-2549-5

ORIGINAL

Sepsis et sepsis sévère étaient utilisés de façon interchangeable par les cliniciens

Sepsis severe

variations in data capture and definition
S criteria

Vol 381 March 2, 2013

Sepsis definitions: time for change

Jean-Louis Vincent, Steven M Opal, John C Marshall, Kevin J Tracey

N ENGL J MED 369:9 NEJM.ORG AUGUST 29, 2013

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., Editors

Severe Sepsis and Septic Shock

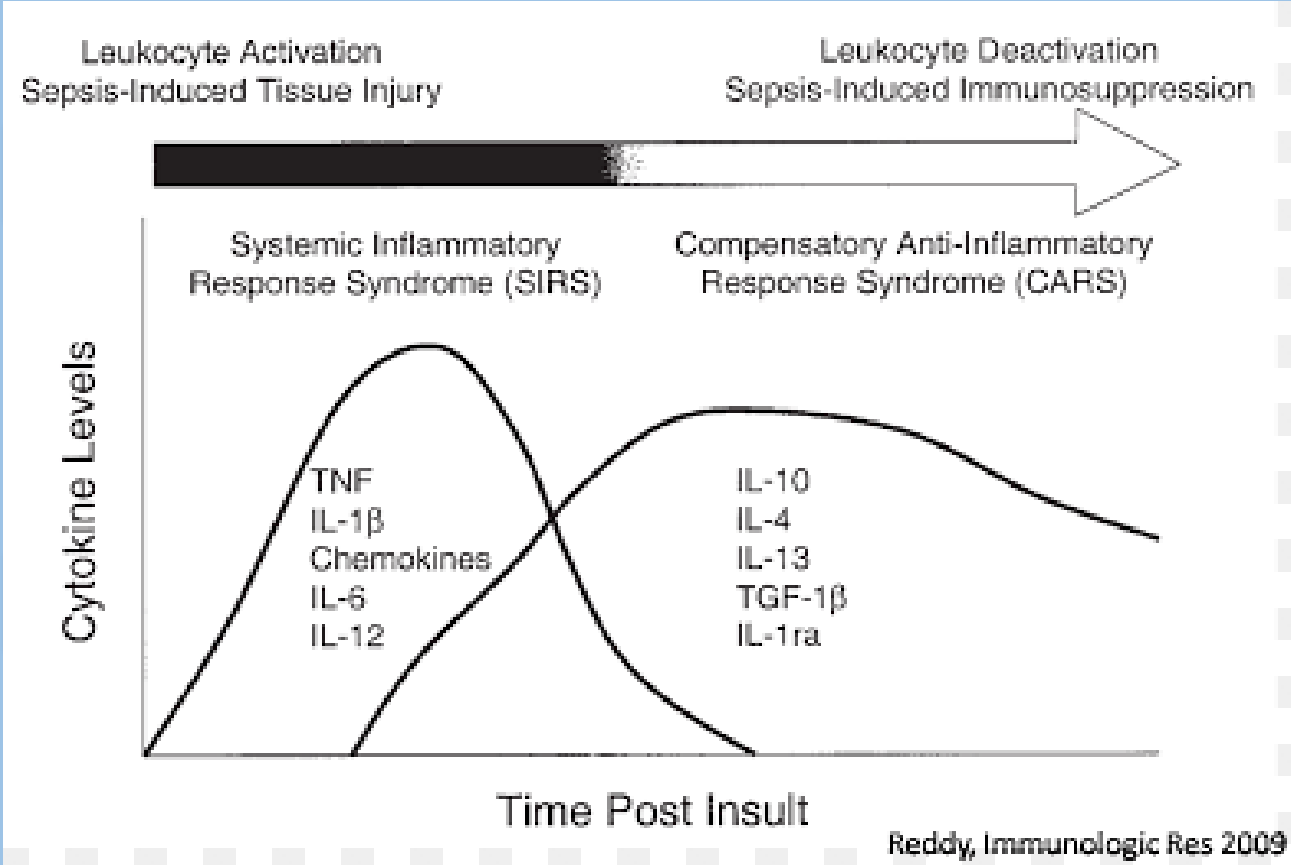
Derek C. Angus, M.D., M.P.H., and Tom van der Poll, M.D., Ph.D.

1992

SEPSIS-1

2001

SEPSIS-2



NEW

Méthodologie

Un groupe international de 19 experts

Critic

Données issues de l'analyse rétrospective

alists

Plusieurs cohortes de patients américains et allemands

Special Communication

Journal of Intensive Care Medicine, Number 8

Table 2. Summary of Data Sets

Characteristics	UPMC ^a	KPNC	VA	ALERTS	KCEMS
Years of cohort	2010-2012	2009-2013	2008-2010	2011-2012	2009-2010
No. of hospitals	12	20	130	1	14
Total No. of encounters	1 309 025	1 847 165	1 640 543	38 098	50 727
Data source and study design	Retrospective study of EHR	Retrospective study of EHR	Retrospective study of EHR	Prospective cohort study	Retrospective study of administrative records

Mervyn Singer, MD, FRCP; Clifford B. Newnam, MD, FICM; Djillali Annane, MD, PhD; Michael B. Singer, MD, FICM; 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



definitions du sepsis et choc septique dites SEPSIS-3

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

Sepsis

=

Dysfonction d'organe secondaire à une **réponse inappropriée** de l'hôte envers une infection

SEPSIS - 3

SEPSIS 1 et 2

Sepsis

=

~~SIRS~~

+

Infection

On oublie le SIRS

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, ×10 ³ /μL	≥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: FIO₂, fraction of inspired oxygen; MAP, mean arterial pressure; PaO₂, 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.

La complexité du score SOFA

Prélèvements biologiques

Limitent son a Une version simplifiée du SOFA e réanimation

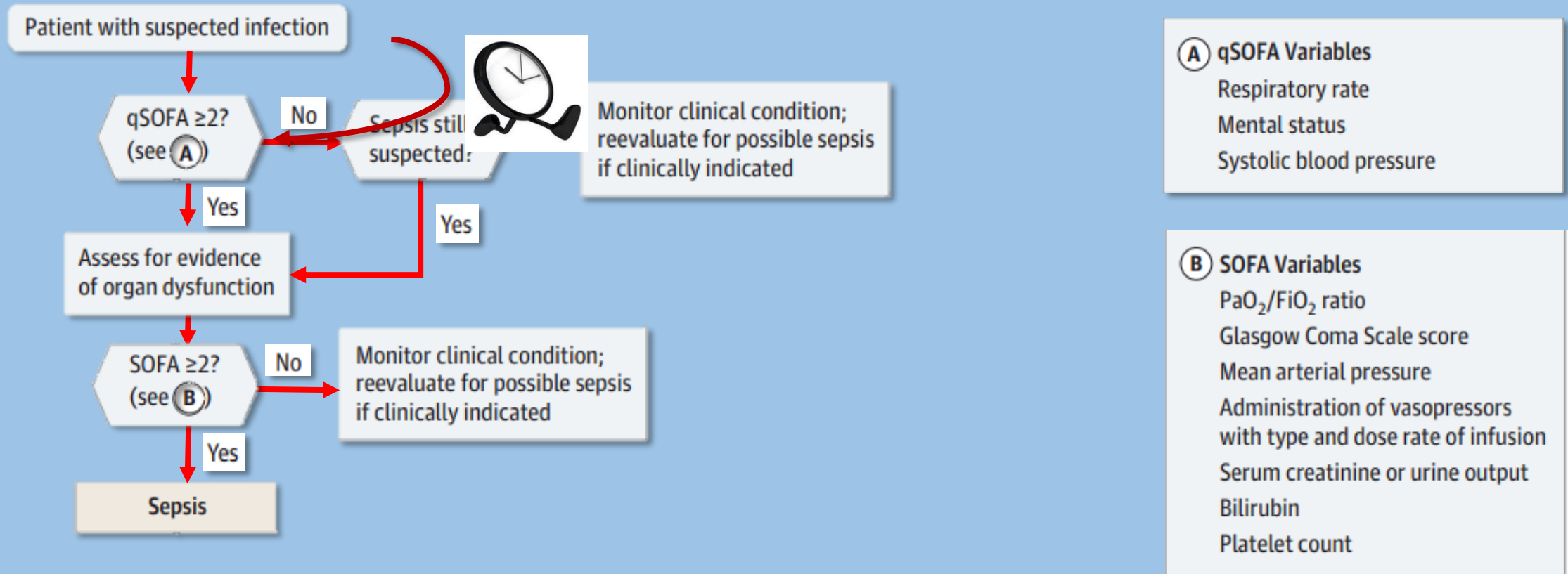
Altér Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study

Vol 12 December 2012

Mitchell M Levy, Antonio Artigas, Gary S Phillips, Andrew Rhodes, Richard Beale, Tiffany Osborn, Jean-Louis Vincent, Sean Townsend, Stanley Lemeshow, R Phillip Dellinger

	USA	Europe	p value*
Count	18 766 (74.0%)	6 609 (26.0%)	
Hospital mortality	5 313 (28.3%)	2 719 (41.1%)	<0.0001
Origin			<0.0001
Emergency department	12 218 (65.1%)	2 159 (32.7%)	
Ward	4 763 (25.4%)	3 405 (51.5%)	
ICU	1 785 (9.5%)	1 045 (15.8%)	

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

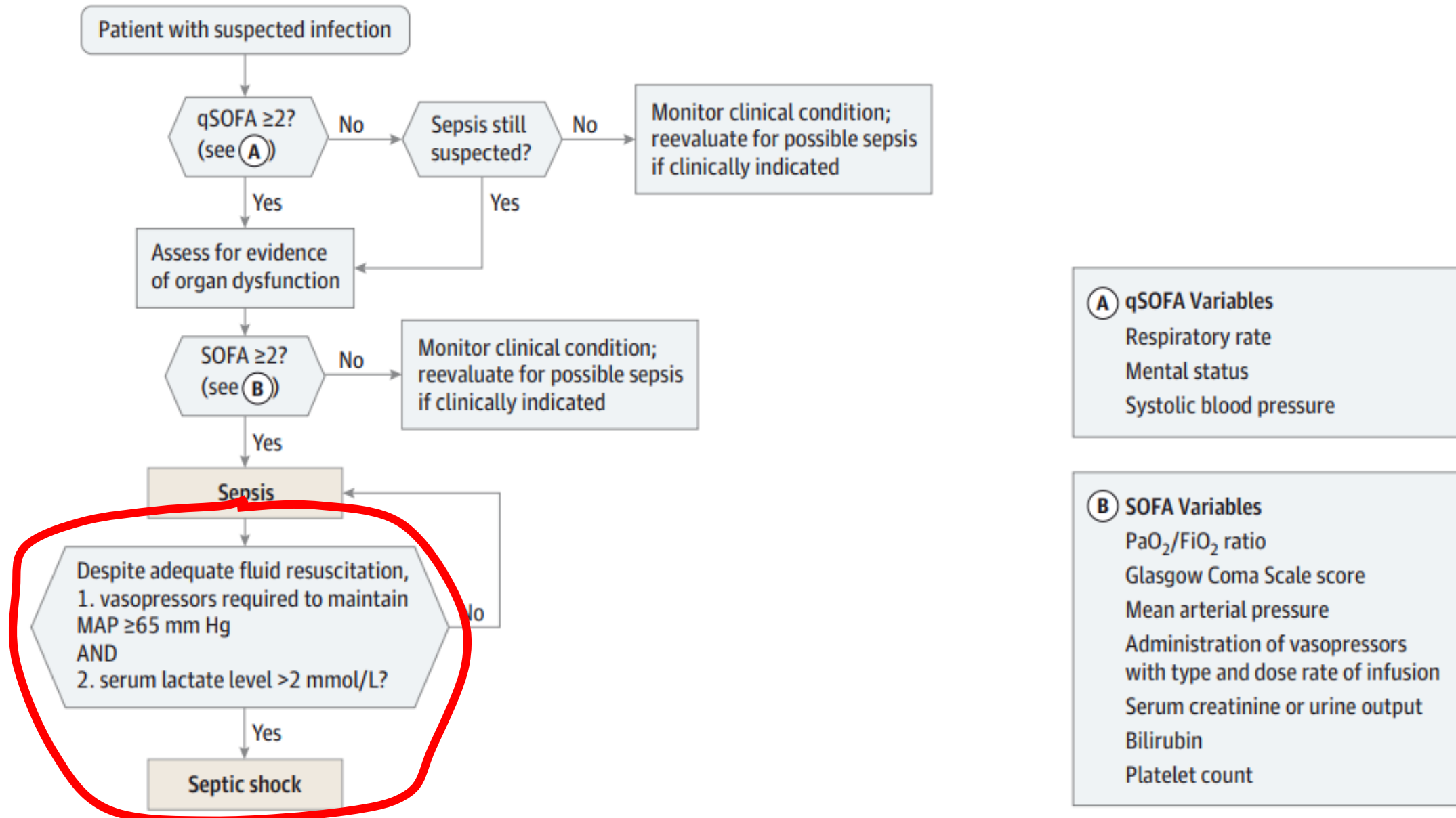


qSOFA

Cette stratification du risque a pour but de mettre l'accent sur la précocité de la prise en charge

Identification rapide patients les + graves/susceptibles de s'aggraver

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



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

Validation des critères SEPSIS-3

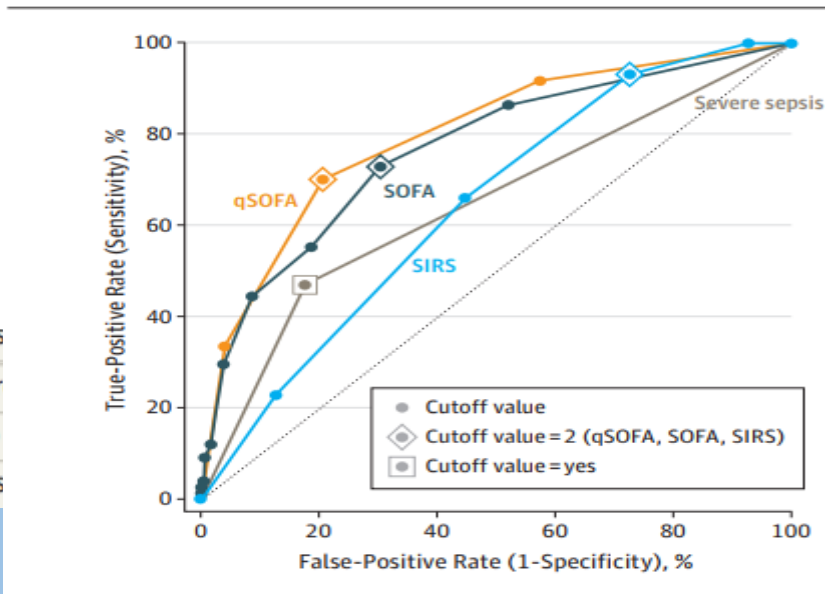


Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department

Table 3. Diagnostic Performances for the Prediction of In-Hospital Death

For Prediction of Death	qSOFA	SOFA	SIRS	Severe Sepsis	P Value
Sensitivity, % (95% CI)	70 (59-80)	73 (61-83)	93 (85-98)	47 (36-59)	
Specificity, % (95% CI)	79 (76-82)	70 (67-73)	27 (24-31)	82 (80-85)	
Area Under the Curve	0.80 (0.74-0.85)	0.77 (0.71-0.82)	0.65 (0.59-0.70)	0.65 (0.59-0.70)	<.001
Number of Patients	39 (53)	664 (82)	35 (47)	141 (18)	<.001

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



Étude de c

30 ser

2
2
%

Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit

Eamon P. Raith, MBBS, MACCP; Andrew A. Udy, MBChB, PhD, FCICM; Michael Bailey, PhD; Steven McGloughlin, BMed FRACP, FCICM, MPHTM; Christopher MacIsaac, MBBS, PhD, FRACP, FCICM; Rinaldo Bellomo, MD, FRACP, FCICM, FAHMS; David V. Pilcher, MBBS, FRACP, FCICM; for the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes and Resource Evaluation (CORE)

Étude rétrospective

190 000 patients

182 services de réanimation

2000 - 2015

Les performances **pronostiques** de l'item diagnostique **score SOFA ≥ 2**

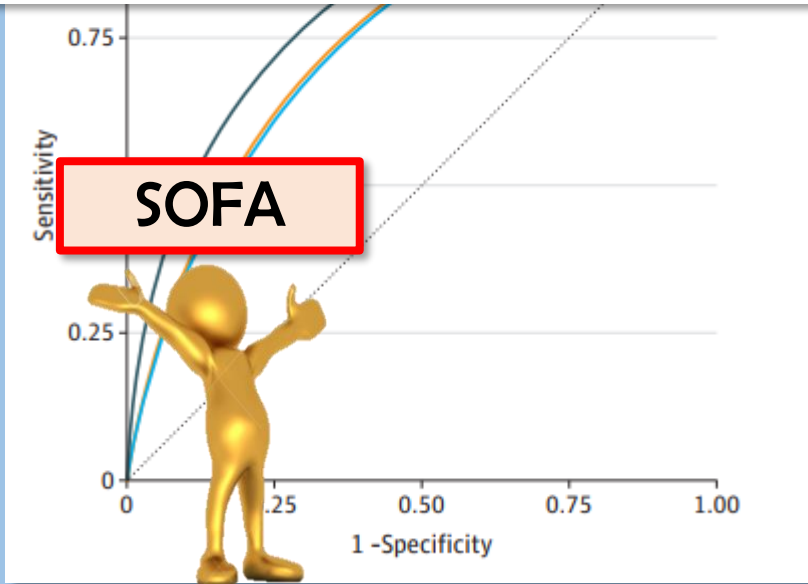
2critères ou plus de SIRS

qSOFA ≥ 2

Etude australienne et néozélandaise

Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit

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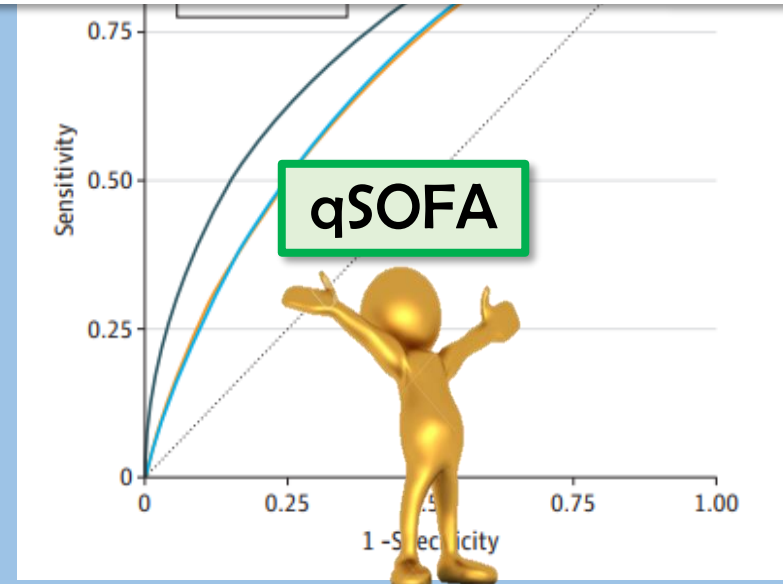


SOFA 0,811 (95%CI 0,811-0,818)

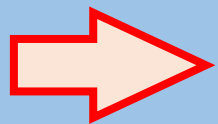


Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department

Jonathan Freund, MD, PhD; Najla Lemachatti, MD; Evguenia Krastinova, MD, PhD; Marie Van Laer, MD; Yann-Erick Claessens, MD, PhD; Aurélie Avondo, MD; Céline Ocelli, MD; Anne-Laure Feral-Pierssens, MD; Jennifer Truchot, MD; Mar Ortega, MD; Bruno Carneiro, MD; Julie Pernet, MD; Pierre-Géraud Claret, MD, PhD; Fabrice Dami, MD; Ben Bloom, MD; Bruno Riou, MD, PhD; Sébastien Beaune, MD, PhD; for the French Society of Emergency Medicine Collaborators Group



SOFA 0,761 (95%CI 0,761-0,764)

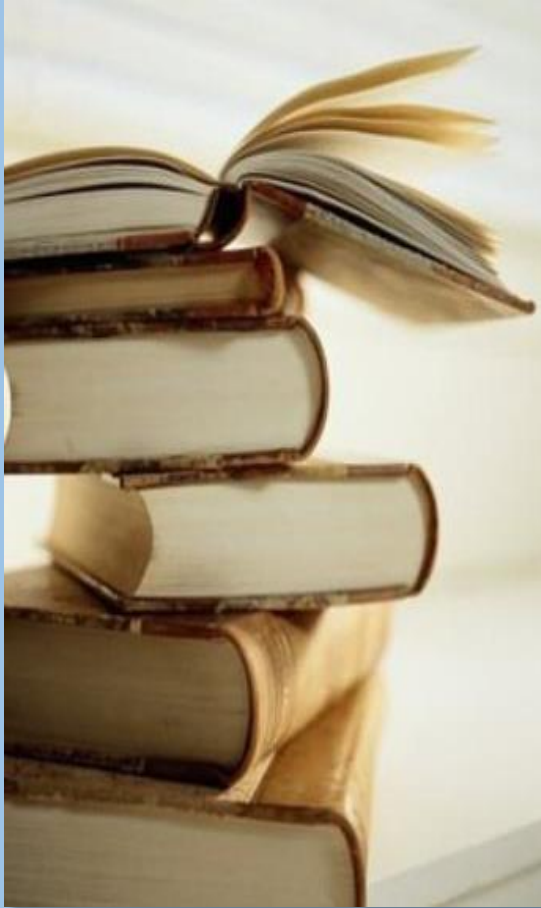


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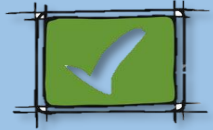
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The good





La définition du sepsis

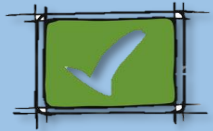


Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

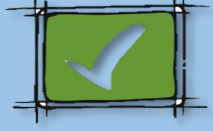
qSOFA

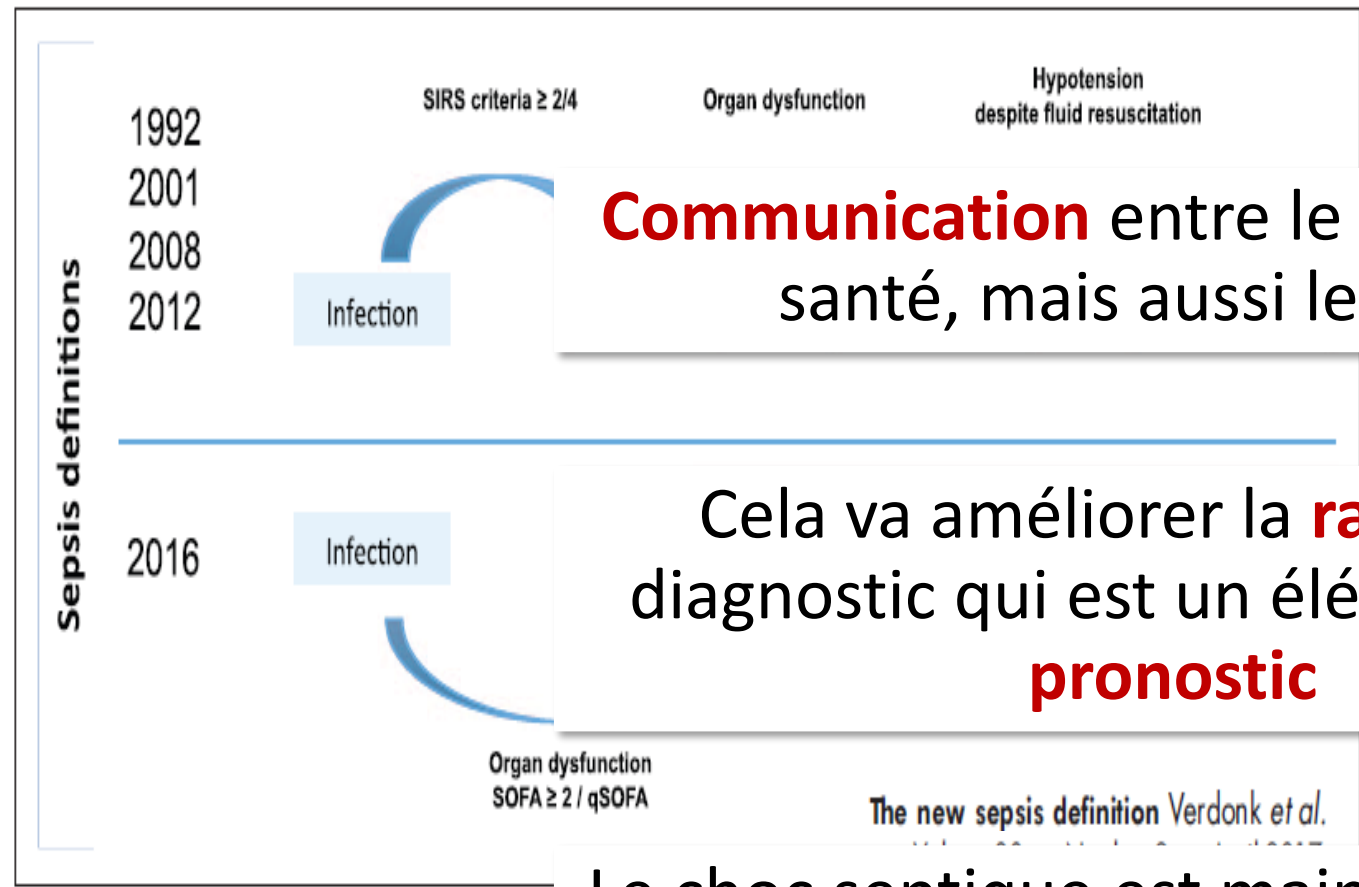


qSOFA et SOFA



Meilleure comparabilité des études





Communication entre le personnel de santé, mais aussi le public.

Cela va améliorer la **rapidité** du diagnostic qui est un élément clé de **pronostic**

Le choc septique est maintenant défini comme un sous-ensemble de sepsis (hyperleucocytose, fièvre)

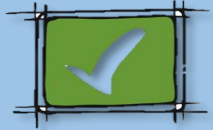
FIGURE 1. Diagram comparing the different definitions (1992, 2001 and 2016) [5,7,8], and during the S...

La définition des **différentes étapes de la sévérité** est simplifiée

Les critères SIRS



La définition du sepsis

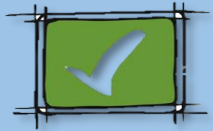


Physiopathologie (SOFA)

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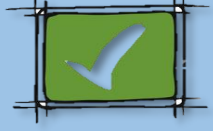
qSOFA



qSOFA et SOFA



Meilleure comparabilité des études



Déterminé à partir d'analyses de **grandes bases de données**

Trois éléments cliniques

Simple et facile à utiliser

qSOFA

SOFA

Mécanisme
Any 2 of 3 clinical variables

non-mécanisme
= la **détection**

The full SOFA score
outside the ICU

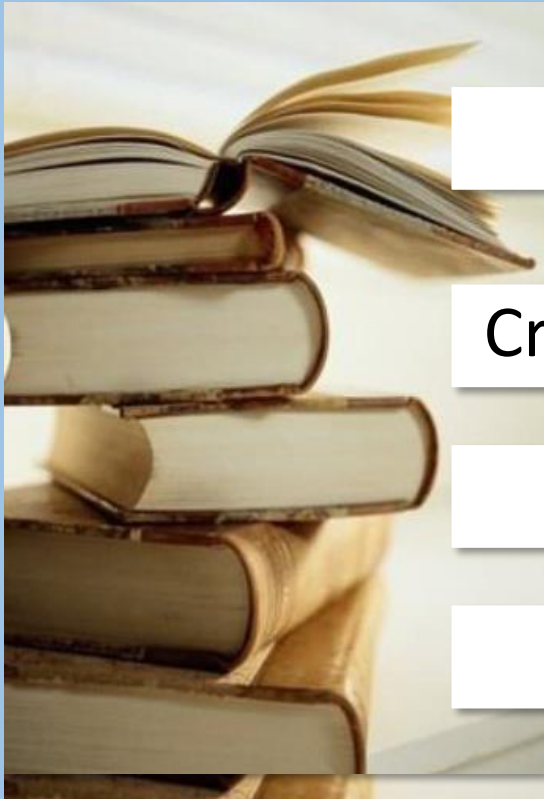
sepsis

Predictive validity

(du patient)

(AUROC = 0.81; 95% CI, 0.80-0.82)

Seymour CW, Liu VX, Iwashyna TJ, et al (2016) Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315:762–74



La définition du sepsis

Etudes SEPSIS

Physiopathologie (SOFA)

Critères de recrutement plus simples

Des de SIRS et de sepsis sévère

Etudes reproductibles

qSOFA

Meilleure comparabilité

qSOFA et SOFA



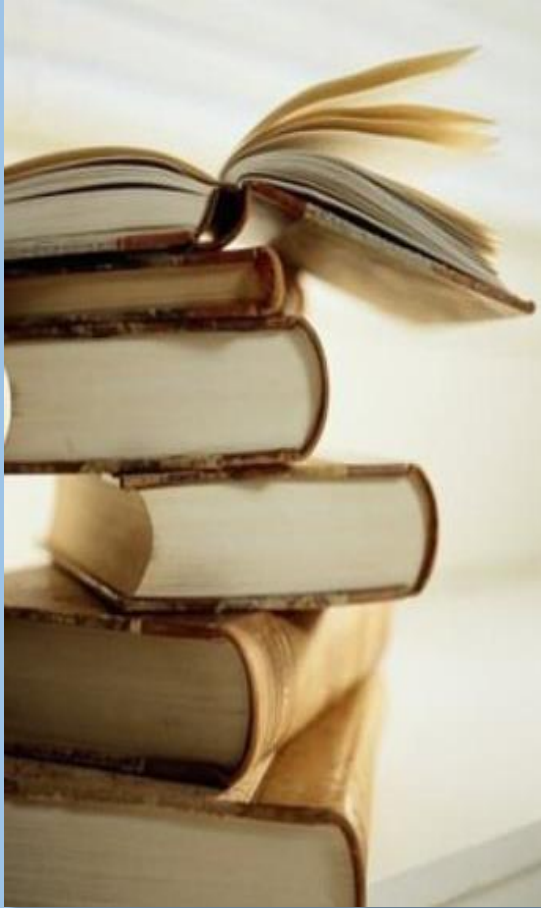
Ils présentent deux avantages: leurs **mesures** peut être **automatisés** et il peut être réalisé **rétrospectivement**

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The bad





La définition du sepsis

Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA

qSOFA et SOFA

Meilleure comparabilité des études

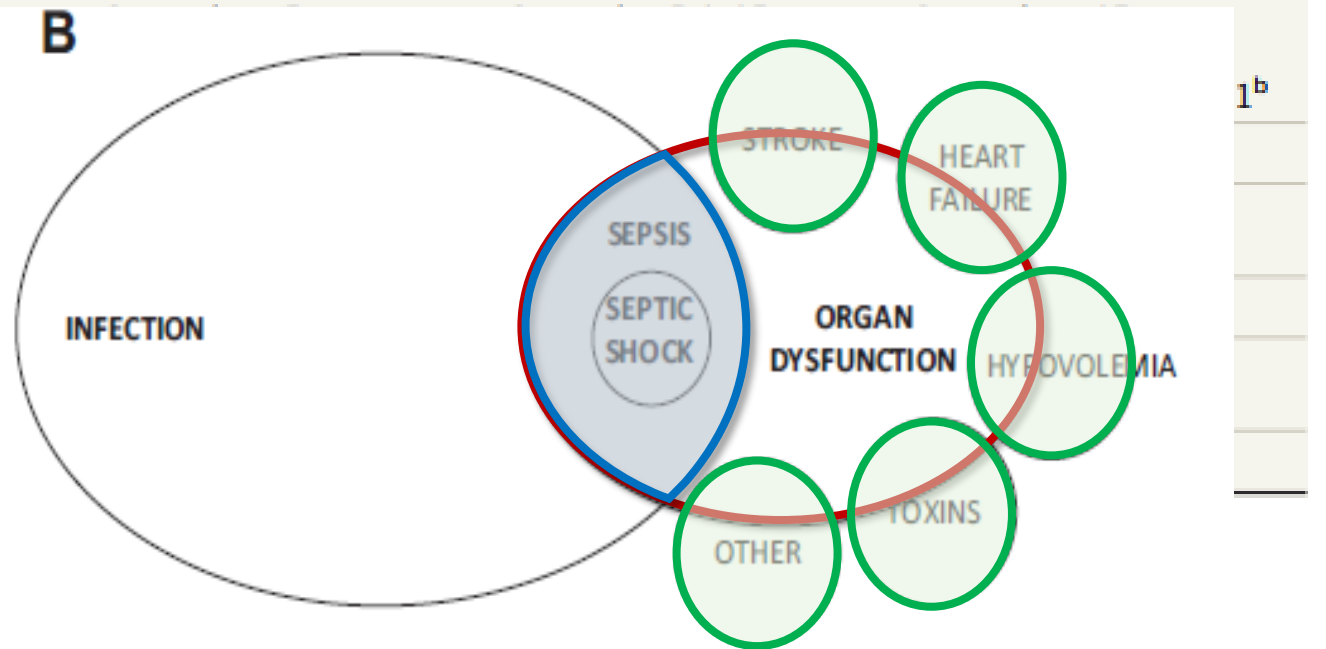


Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score^a

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, ×10 ³ /μL	≥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			
Central nervous system					
Glasgow Coma Scale score ^F	15	13-14			
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9			
Urine output, mL/d					

Abbreviations: FIO₂, fraction of inspired oxygen; MAP, mean arterial pressure; PaO₂, partial pressure of oxygen.

^a Adapted from Vincent et al.²⁷



Détecter un dysfonctionnement organique

Sepsis

=

Dysfonction d'organe secondaire à une réponse inappropriée de l'hôte envers une infection

Avec l'espoir qu'elle a été causée par une infection

Ce patient est-il infecté ou non?

Les nouvelles définitions n'offrent aucune indication sur l'identification de l'infection

When the infection is not certain and organ dysfunction is present

Des progrès importants ont été réalisés ces dix dernières années dans l'utilisation de biomarqueurs (Dg et AT/Bpie)

It is difficult to exclude a sepsis diagnosis

REVIEW

De
ma
Jae
And
**Procalcitonin: a p
marker for sepsis**

Ashitha L. Vijayan, Vanimaya, Shilpa Ra

Abstract

Background: Sepsis is a global health microbial infection, which leads to orga Early and differential diagnosis of sepsis proper antibiotic treatments through th

Main body of abstract: Current target factor- α , interleukins, etc.) are non-speci family could be a critical tool for the di procalcitonin alone may not be effective biomarkers during an infection and it infection. Beside this, the procalcitonin l of secondary inflammations, diagnosis (The present article summarizes the rele determining the therapeutic approach

Conclusion: Further studies are neede differentiating between microbial and for sepsis.

Keywords: Procalcitonin, Sepsis, Antil



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Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb



Mini review <http://dx.doi.org/10.1016/j.apjtb.2016.04.005>

New sepsis biomarkers

Dolores Limongi¹, Cartesio D'Agostini², Marco Ciotti^{3*}

¹Telematic University San Raffaele Rome, Via di Val Cannuta, 00167, Rome, Italy

²Clinical Microbiology and Virology, Polyclinic Tor Vergata Foundation, Viale Oxford 81, 00133, Rome, Italy

³Laboratory of Molecular Virology, Polyclinic Tor Vergata Foundation, Viale Oxford 81, 00133, Rome, Italy



The importance of pr

Funda

¹Inonu University Faculty of M
²Malatya State Hos

Received 03 N
Available online 29.1.

Abstract

Despite the advances and a wide range of studies conducted, sep diagnosis, rapid and effective treatment are extremely importan Procalcitonin is an important test as "point-of-care testing (PO released from the parenchymal cells of the liver, kidneys and m bacterial infection, the serum procalcitonin level may increase interleukin-6 (IL-6) trigger due to tissue injury, inflammation an in patients suspicious of sepsis in the early period. A total of 64 Medical Faculty Turgut Özal Medical Center Investigation H diagnostic criteria of systemic inflammatory response syndrome were investigated on the first day after having been included in 108.39 and 83.47 mg/l on the 1st, 3rd and 7th days, respectively. 1 was 316.054 ng/ml. The minimum/maximum levels were 0.091 No statistically significant difference was observed between t difference was observed between its levels between the 1st and th significant (p<0.005). C-reactive protein levels revealed a signifi (p<0.010). The Wilcoxon Signed test was used to investigate s patients. Although conflicting results have been obtained in diffe of sepsis, we believe that PCT is an appropriate and important in

Keywords: Procalcitonin, early diagnosis, sepsis

ARTICLE INFO

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Biomarker

Sepsis

Plasma chitotriosidase

ABSTRACT

Sepsis remains a leading cause of death in the intensive care units and in all age groups worldwide. Early recognition and diagnosis are key to achieving improved outcomes. Therefore, novel biomarkers that might better inform clinicians treating such patients are surely needed. The main attributes of successful biomarkers would be high sensitivity, specificity, possibility of bedside monitoring and financial accessibility. A panel of sepsis biomarkers along with currently used laboratory tests will facilitate earlier diagnosis, timely treatment and improved outcome may be more effective than single biomarkers. In this review, we summarize the most recent advances on sepsis biomarkers evaluated in clinical and experimental studies.



La définition du sepsis

Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA

qSOFA et SOFA

Meilleure comparabilité des études



Choc septique = forme grave et continuum du sepsis

Infection

~~SIRS~~

Sepsis

~~Sepsis sévère~~

Choc septique

Lactate Level Versus Lactate Clearance for Predicting Mortality in Patients With Septic Shock

TABLE 2. Prognostic Value of Measuring the Serum Lactate Level and Clearance After 6 Hours of Sep

6 hr From Shock	Receiver Operating	Sensitivity	Specificity	Predictive	Predictive	Positive Likelihood Ratio	Negative Likelihood Ratio
Lactate (mmol/L)							
Lactate over 2						1.26	0.40
Lactate over 3						1.60	0.60
Lactate over 4	0.64 (0.60–0.68)	55.9	72.3	40.2	83.1	1.39	0.42
Clearance (%)							
Clearance under						1.78	0.72
Clearance under						1.63	0.68
Clearance under						1.50	0.60

Volémie adéquate?

Évaluation HD invasive?
Non invasive?

Perte de temps % transfert
en USI (pronostic)

Vasopresseurs

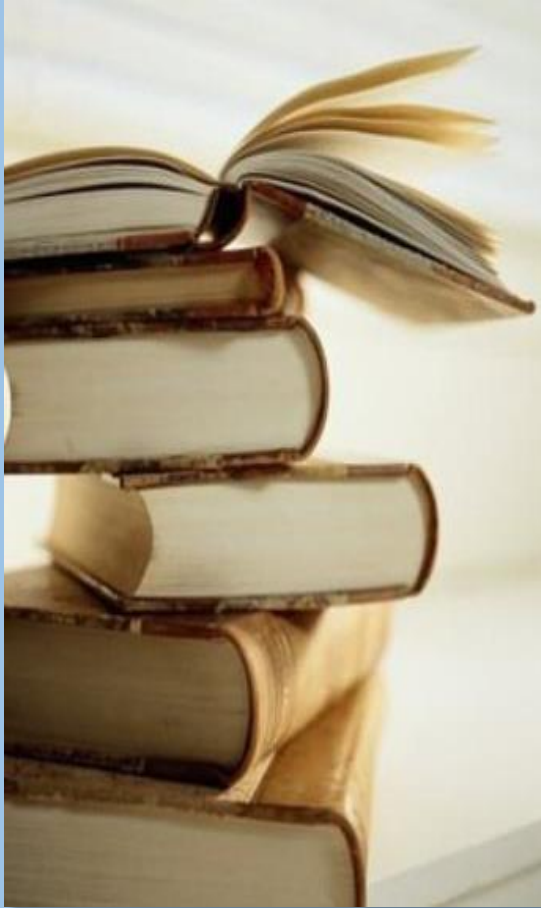
PAM \geq 65 mmHg

Lactate $>$ 2 mmol/L
(18 mg/dL)

Malgré la correction
d'une hypovolémie

Figure 1 for prognosis of septic shock patients who were treated with protocol-driven resuscitation bundle therapy.

3
.0



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Systemic Inflammatory Response Syndrome, Quick Sequential Organ Function Assessment, and Organ Dysfunction

Insights From a Prospective Da

Editorial

Julian M. Williams, MBBS; Jaimi H. Greenslade, PhD
Anthony F. T. Brown, MBChB; and Jeffrey Lipman, MD

Table 1 Sensitivity and specificity for mortality of diagnostic criteria for sepsis/severe sepsis in non-ICU settings

Criteria	Source	Sensitivity (%)	Specificity (%)
SIRS ≥ 2	Sepsis-3	64.0	65.0
	U of C	93.8	12.3
qSOFA ≥ 2	Sepsis-3	55.0	84.0
	U of C	68.7	63.5
		86.6	47.5
		71.4	65.0
		92.0	84.0

Systemic Inflamm Quick Sequential Assessment, and Insights From a Prospe

Julian M. Williams, MBBS; Jaimi H. Gr
Anthony F. T. Brown, MBChB; and Jeff

RESULTS: We enrolled 8,871 patients, wit

CONCLUSIONS: SIRS was associated with organ dysfunction and mortality, and abandoning the concept appears premature. A qSOFA score ≥ 2 showed high specificity, but poor sensitivity may limit utility as a bedside screening method. Although mortality for organ dysfunction was comparable between Sepsis-2 and Sepsis-3, more prognostic and clinical information is conveyed using Sepsis-2 regarding number and type of organ dysfunctions. The SOFA score may require recalibration.

CHEST 2017; 151(3):586-596

The SOFA score may require recalibration.

CHEST 2017; 151(3):586-596

KEY WORDS: emergency medicine; infection; organ dysfunction; qSOFA; SIRS

ère

R. Phillip Dellinger
Jean M. Carlet
Henry Masur
Herwig Gerlach
Thierry Calandra
Jonathan Cohen

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

R. Phillip Dellinger
Mitchell M. Levy
Jean M. Carlet
Julian Bion
Margaret M. Parker
Roman Jaeschke
Konrad Reinhart

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

Figure 1. Mean Annual Mortality in Patients With Severe Sepsis

JAMA April 2, 2014 Volume 311, Number 13

Research

Original Investi

Mortality
Critically Ill

Andrew Rhodes
Gary Phillips
Richard Beale
Maurizio Cecconi
Jean Daniel Chiche
Daniel De Backer
Jigeeshu Divatia

Kirsi-Maija Kaukonen, MD,
Rinaldo Bellomo, MD, PhD

Table 2 Surviving Sepsis Campaign bundle compliance and associated hospital mortality for patients enrolled into the IMPReSS study

Detail

3-h bundle compliance (all patients, n = 1794)	
Measurement of lactate	1002 (55.9)
Obtain blood cultures	
Administer broad-spectrum antibiotics	
Administer 30 mL of fluid	
Repeat the lactate measurement	1077 (60.0)
Application of vasopressors for hypotension	1479 (82.4)
Measurement of central venous oxygen saturation	
Full bundle	90 (10.9)
Hospital mortality for 3-h bundle compliance	67/340 (19.7)
Hospital mortality for 3-h bundle non-compliance	443/1454 (30.5)*
6-h bundle compliance (all patients, n = 1794)	
Repeat the lactate measurement	1077 (60.0)
Application of vasopressors for hypotension	1479 (82.4)
Measurement of central venous oxygen saturation	
Full bundle	90 (10.9)
Hospital mortality for 6-h bundle compliance	143/637 (22.4)
Hospital mortality for 6-h bundle non-compliance	367/1157 (31.7)*
6-h bundle compliance (for only patients with persistent hypotension (MAP <65 mmHg) and/or hyperlactataemia (>4 mmol/L) after volume administration (n = 824))	
Repeat the lactate measurement	228 (27.7)
Application of vasopressors for hypotension	824 (100)
Measurement of central venous oxygen saturation	152 (18.4)
Full bundle	90 (10.9)
Hospital mortality for 6-h bundle compliance	25/90 (27.8)
Hospital mortality for 6-h bundle non-compliance	261/734 (35.6)

All numbers are presented as n (%) unless otherwise stated
* Represents a p value of ≤0.0001 by the Fishers exact test for the mortality of bundle compliance versus non-compliance



CrossMark

Volume 311, Number 13

Among bundles

International

Among

67/340 (19.7)
443/1454
(30.5)*

12

Hospital mortality for 3-h bundle compliance
Hospital mortality for 3-h bundle non-compliance

Hospital mortality for 6-h bundle compliance

Hospital mortality for 6-h bundle non-compliance

143/637 (22.4)
367/1157
(31.7)*

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GUIDELINES

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012

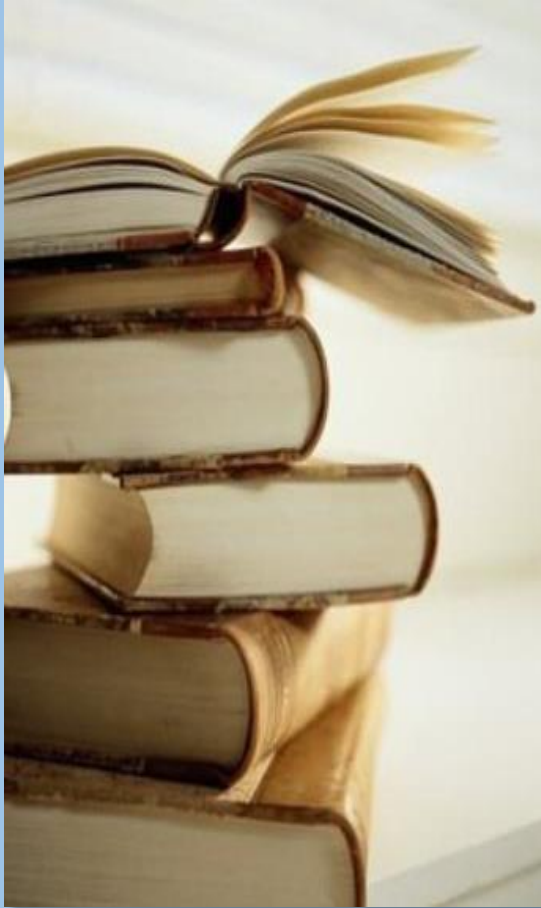
CONFERENCE REPORTS AND EXPERT PANEL

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

Andrew Rhodes^{1*}, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵, Ric

Rangel-Fau

berg, et al., 1998



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Meilleure comparabilité des études





qSOFA



GCS < 15



FR ≥22/min



PAS ≤ 100 mmHg

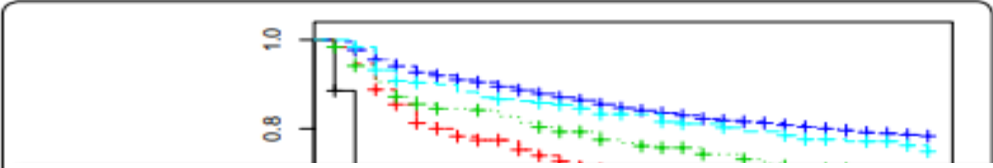
Intensive DOI 10.1 **Table 3 Multivariate analysis of factors associated with sepsis-associated encephalopathy**

OR SMART-COP: A Tool for Predicting the Need for Intensive Respiratory or Vasopressor Support in Community-Acquired Pneumonia

Clinical Infectious Diseases 2008;47:375–84

Patrick G. P. Charles,^{1,3} Rory Wolfe,⁴ Michael Whitby,⁷ Michael J. Fine,^{14,15} Andrew J. Fuller,⁹ Robert Stirling,¹⁰ Alistair A. Wright,¹¹ Julio A. Ramirez,¹⁶ Keryn J. Christiansen,¹² Grant W. Waterer,¹³ Robert J. Pierce,² John G. Armstrong,⁸ Tony M. Korman,⁵ Peter Holmes,⁶ D. Scott Obrosky,¹⁵ Paula Peyrani,¹⁶ Barbara Johnson,⁷ Michelle Hooy,¹⁰ the Australian Community-Acquired Pneumonia Study Collaboration,⁶ and M. Lindsay Grayson^{1,3,4}

Departments of ¹Infectious Diseases and ²Respiratory and Sleep Medicine, Austin Health, Heidelberg, ³Department of Medicine, University of Melbourne, Parkville, ⁴Department of Epidemiology and Preventive Medicine, Monash University, and Departments of ⁵Infectious Diseases and ⁶Respiratory Medicine, Monash Medical Centre, Clayton, Departments of ⁷Infectious Diseases and ⁸Respiratory Medicine, Princess Alexandra Hospital, Woolloongabba, Departments of ⁹Infectious Diseases and ¹⁰Respiratory Medicine, The Alfred Hospital, Prahran, ¹¹West Gippsland Hospital, Warragul, and ¹²Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine, and ¹³Department of Respiratory Medicine, Royal Perth Hospital, Perth, Australia; ¹⁴Division of General Internal Medicine, University of Pittsburgh, and ¹⁵Center for Healthcare Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; and ¹⁶Division of Infectious Diseases, University of Louisville, Louisville, Kentucky



The SMARTCOP study reported that in young adults, the RR threshold that was associated with an increased risk of critical care was **25/min**, while it was **30/min** in patients above **50 years** of age

Fig. 1 Kaplan–Meier’s survival estimates of patients according to the severity of encephalopathy at ICU admission

qSOFA peut remplacer le SIRS?

qSOFA

Specific (96.1%) but insensitive (29.7%)

SDMV

median of 5 hours

Mortalité (30j)

	Sensitivity [% (95% CI)]	Specificity [% (95% CI)]
qSOFA ≥ 2	27	49.1 (46.0–52.3)
SIRS ≥ 2	65.3 (53.1–75.9)	49.1 (46.0–52.3)

ICU transfer or death

SIRS

less specific (61.1%) but more sensitive (80.3%)
17 hours

Williams JM, Greenslade JH, McKenzie JV, et al. Systemic inflammatory response syndrome insights from the emergency department. *Crit Care Med*. 2015;43(3):58-64.

Churpek MM, Snyder A, Han X, et al. qSOFA, SIRS, and early warning scores for detecting clinical deterioration in infected patients outside the ICU. *Am J Respir Crit Care Med*. 2017;45(10): 1677-1682.

Eur J Clin Microbiol Infect Dis



Prognostic accuracy of SIRS criteria, qSOFA score and GYM score for 30-day mortality in older non-severely dependent patients

In a cohort of emergency department patients with suspected infection

Prédiction tardive de la détérioration clinique

Received: 6 June 2017 / Accepted: 12 July 2017
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Conclusion: In this observational cohort study, qSOFA failed to identify two thirds of the patients admitted to an ED with severe sepsis. Further, qSOFA failed to be a risk stratification tool as the sensitivity to predict 7-day and 30-day mortality was low. The sensitivity was poorer than the other warning scores already in use at the study site, RETTS-triage and the SIRS criteria.

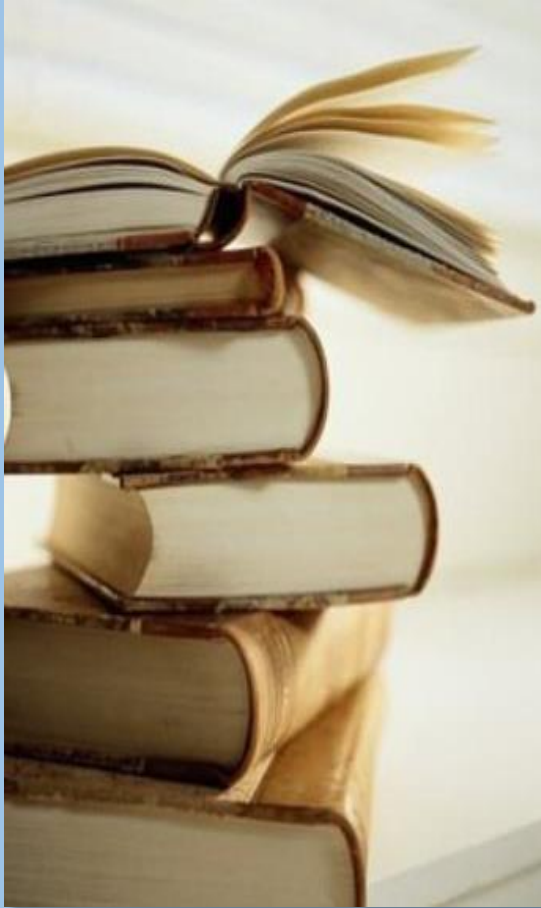


symptoms or clinical signs suggesting an infection ($n = 1535$) were prospectively included in the study from January 1



Table 5 Sensitivity, Specificity, and Positive (PPV) and Negative Predictive Values (NPV) for 30-day mortality by different stratification tools in the Emergency Department ($n = 68$ cases of deaths within 30 days among 1535 patients)

Stratification tool	Ability to identify those who died <i>n</i> (% of 68 cases)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Severe sepsis	19 (27.9%)	0.29 (0.18-0.41)	0.94 (0.92-0.95)	0.18 (0.12-0.24)	0.96 (0.95-0.97)
SIRS ≥ 2	42 (61.8%)	0.64 (0.51-0.75)	0.55 (0.53-0.58)	0.06 (0.05-0.07)	0.97 (0.96-0.98)
SIRS ≥ 2 (without leucocytes)	32 (45.6%)	0.48 (0.36-0.61)	0.70 (0.68-0.72)	0.07 (0.05-0.08)	0.97 (0.96-0.97)
qSOFA ≥ 2	8 (11.9%)	0.13 (0.05-0.25)	0.96 (0.95-0.97)	0.14 (0.07-0.23)	0.96 (0.96-0.96)
Red triage	14 (20.2%)	0.21 (0.12-0.32)	0.94 (0.92-0.95)	0.13 (0.08-0.19)	0.96 (0.96-0.96)
Orange triage	31 (45.6%)	0.46 (0.22-0.58)	0.61 (0.58-0.63)	0.05 (0.04-0.07)	0.96 (0.95-0.97)
\geq Orange triage	45 (66.1%)	0.66 (0.54-0.77)	0.54 (0.52-0.57)	0.06 (0.05-0.07)	0.97 (0.96-0.97)



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qSOFA et SOFA

Meilleure comparabilité des études



Retards potentiels dans l'identification précoce et le traitement

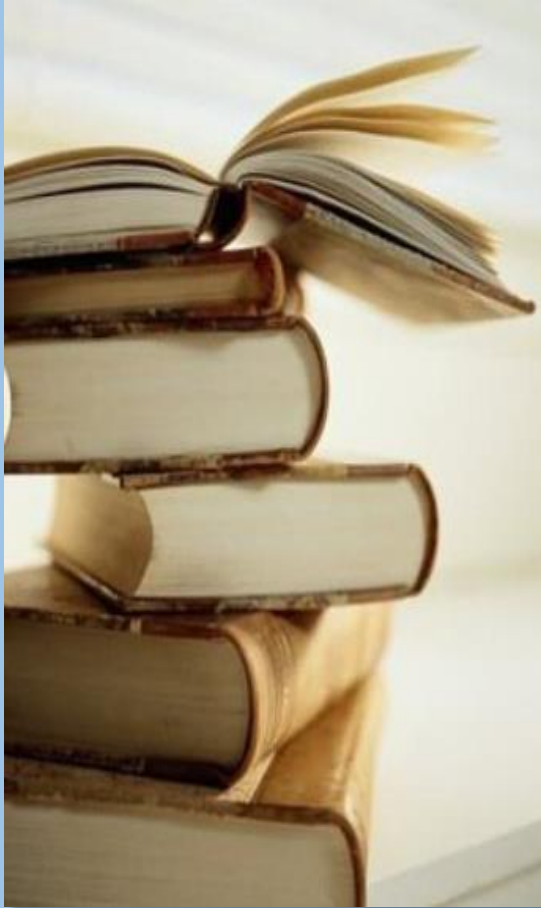
Simpson SQ. New sepsis criteria: a change we should not make. Chest 2016; 149(5):1117–8.

Cortes-Puch I, Hartog CS. Opening the debate on the new sepsis definition change is not necessarily progress: revision of the sepsis definition should be based on new scientific insights. Am J Respir Crit Care Med 2016;194(1):16–8.

Le calcul du score SOFA doit inclure des mesures biologiques.

Coûts associés + temps (Pc)

Ni qSOFA ni le SOFA ne permettent d'identifier l'infection



La définition du sepsis

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qSOFA

qSOFA et SOFA

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Comparabilité avec les anciennes études

Travaux

1992

SEPSIS 1-2

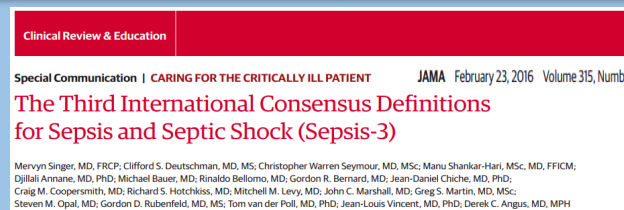
2002

2016

SEPSIS 3

1^{ère} définitions
consensuelles

Ajoutés bibliothèque
de codage



*The International Classification
of Diseases Coding library*

ansi

Centers for M &
M & S

aujourd'hui les anciennes définitions du sepsis et de
travaux à conserver l'ancienne terminologie

Townsend SR, Rivers E et al. Definitions for sepsis and septic shock. JAMA 2016;316(4):457-8.

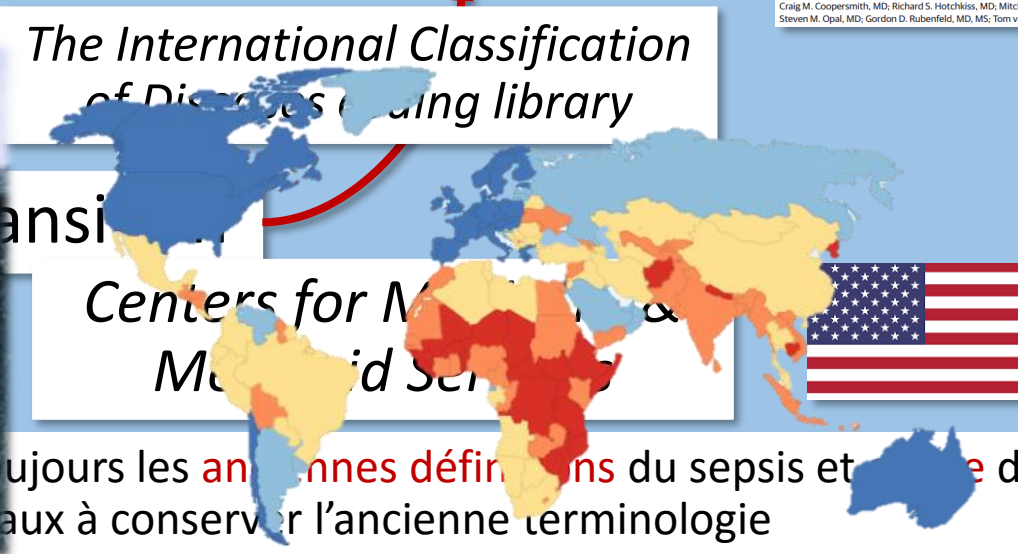


Table 3 Availability of equipment to implement the surviving sepsis campaign guidelines

Table 5 Possibility to implement the surviving sepsis campaign guidelines

		African countries	High-income countries	P-value
Respondents	n	263	44	
Possibility to implement the SSC guidelines in entirety	n (%)	15 (5.7)	36 (81.8)	<0.001*
<i>Percentage of implementable recommendations/suggestions</i>	(%)			
Possibility to implement all Grade 1 recommendations	n (%)	15 (5.7)		<0.001*
<i>Percentage of implementable Grade 1 recommendations</i>	(%)	80.8 (63.5 to 88.5)		
Possibility to implement all Grade 1A and 1B recommendations	n (%)	30 (11.4)		<0.001*
<i>Percentage of implementable Grade 1A and 1B recommendations</i>	(%)	87.5 (70.8 to 95.8)		
Possibility to implement all Grade 1C and 1D recommendations	n (%)	26 (9.9)		<0.001*
<i>Percentage of implementable Grade 1C and 1D recommendations</i>	(%)	71.4 (57.1 to 89.3)		
Possibility to implement all Grade 2 recommendations	n (%)	4 (1.5)		<0.001*
<i>Percentage of implementable Grade 2 recommendations</i>	(%)	57.1 (38.1 to 81)		
Possibility to implement all sepsis resuscitation bundles	n (%)	43 (16.3)		<0.001*
<i>Bundle element "Lactate"</i>	n (%)	64 (24.3)		
<i>Bundle element "Cultures"</i>	n (%)	188 (71.5)		
<i>Bundle element "Antibiotics"</i>	n (%)	204 (77.6)		
<i>Bundle element "Hypotension"</i>	n (%)	238 (90.5)		
<i>Bundle element "CVP/ScvO2"</i>	n (%)	70 (26.6)		
Possibility to implement all sepsis management bundles	n (%)	12 (4.6)		0.03*
<i>Bundle element "Steroids"</i>	n (%)	252 (95.8)		<0.001*
<i>Bundle element "rhAPC"</i>	n (%)	15 (5.7)		<0.001*
<i>Bundle element "Glucose"</i>	n (%)	221 (84)		0.004*
<i>Bundle element "Plateau Pressure"</i>	n (%)	182 (69.2)		<0.001*

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

System	<0.001*
Respiration	<0.001*
PaO ₂ /FIO ₂ , mm Hg (kPa)	<0.001*
Coagulation	<0.001*
Platelets, ×10 ³ /μL	<0.001*
Liver	<0.001*
Bilirubin, mg/dL (μmol/L)	<0.001*
Cardiovascular	<0.001*
Central nervous system	0.03*
Glasgow Coma Scale score ^c	<0.001*
Renal	0.17
Creatinine, mg/dL (μmol/L)	<0.001*
Urine output, mL/d	<0.001*

Count

- Low i
- Low e
- Upper
- High
- High

Year: 20
Source: 1

^a Organ failure group according to SOFA score. Scores were the highest at absolute temperature, pH, prothrombin time, absolute values and percentages of completed responses.

Impact sur le traitement

Nouvelles recommandations basées sur ces nouvelles définitions

EDITORIAL

New Definition of Sepsis: Continuing Evolution

Edward Abraham, MD

Surviving Sepsis Campaign Responds to Sepsis-3

March 1, 2016

Done

July 23, 2016 Volume 315, Number 8

the opinions of the authors and JAMA
of the American Medical Association

Conclusion

Once hospitals have adequately prepared for change, sepsis team leaders should reinforce the message that the new definitions do not change the primary focus of early sepsis identification and initiation of timely treatment in the management of this vulnerable patient population.

Les **nouvelles définitions** ne doivent pas **modifier l'objectif principal** qui est **l'identification précoce** du sepsis et **l'initiation d'un traitement rapide** dans la gestion de ces patients vulnérables

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

Définition plus proche de la physiopathologie du sepsis

Critères simples et facile à retenir

Le risque de **minimiser la gravité du sepsis**

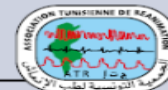
Le risque d'anéantir les efforts déployés depuis plusieurs décennies dans le cadre de la **Surviving Sepsis Campaign**

MERCI DE VOTRE ATTENTION



SOCIÉTÉ TUNISIENNE DE
PATHOLOGIE INFECTIEUSE

ASSOCIATION TUNISIENNE
DE RÉANIMATION (ATR)



5
èmes

RENCONTRES EN INFECTIOLOGIE