Sepsi e shock settico

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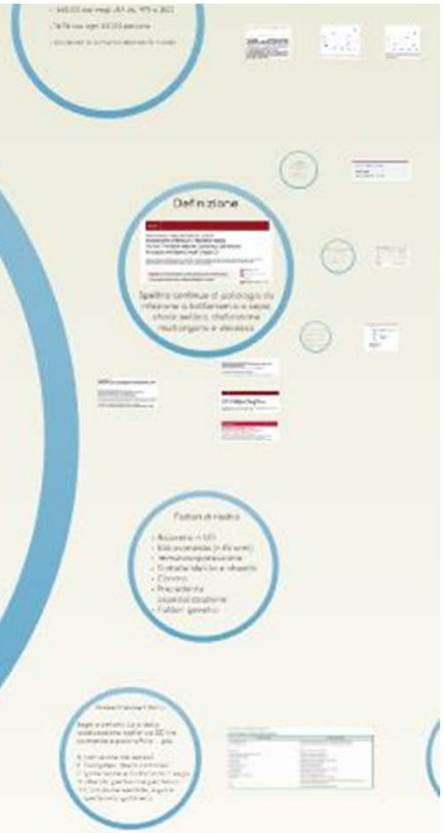
Di cosa parliamo?

Epidemiologia
Definizione
Fattori di Rischio
Presentazione Clinica
Diagnosi
Prognosi



Epidemiologia

- 1.665.000 casi negli USA dal 1979 al 2000
- 13/78 casi ogni 100.000 persone
- incidenza in aumento, mortalità in calo

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Epidemiology of Sepsis in the United States from 1979 through 2000

Greg S. Martin, M.D., David M. Mannino, M.D., Stephanie Eaton, M.D., and Marc Moss, M.D.

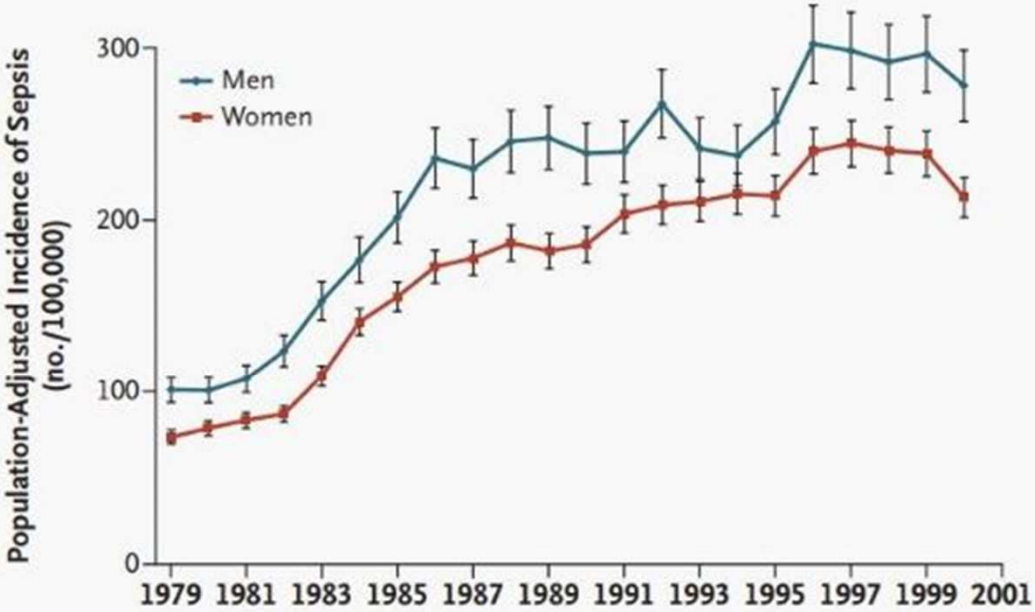


Figure 1. Population-Adjusted Incidence of Sepsis, According to Sex, 1979–2000.
Points represent the annual incidence rate, and I bars the standard error.

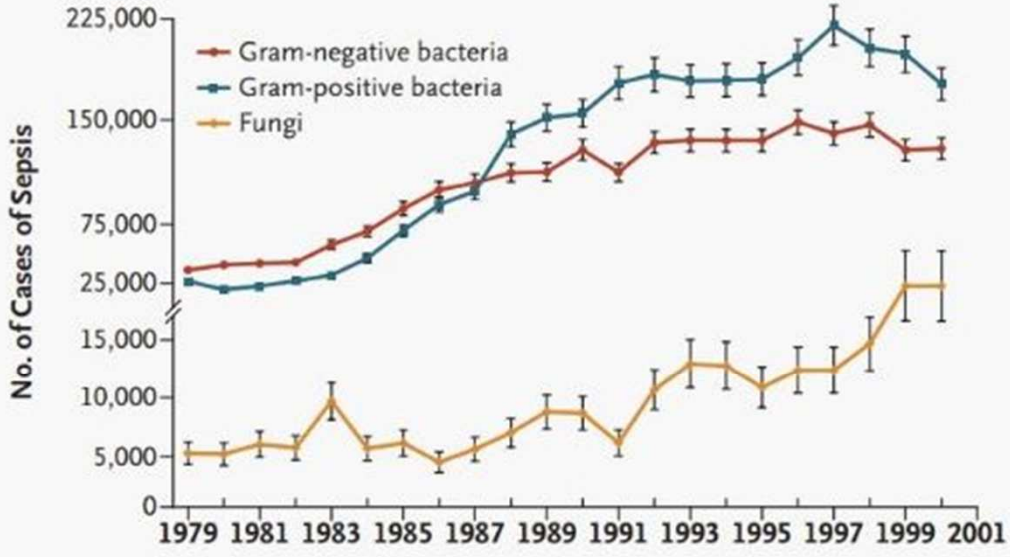


Figure 3. Numbers of Cases of Sepsis in the United States, According to the Causative Organism, 1979–2000.

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

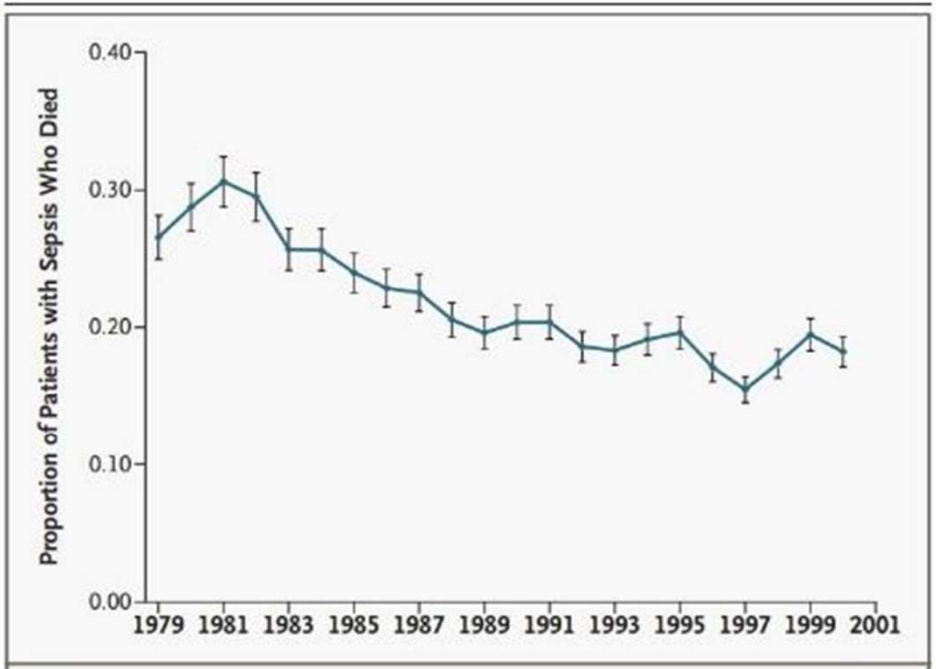
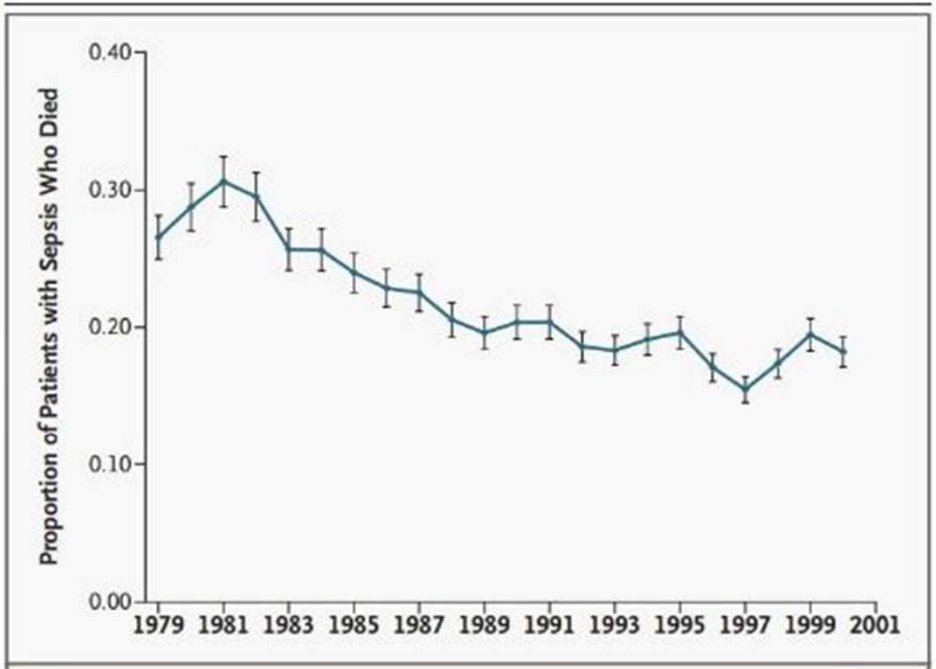


Figure 4. Overall In-Hospital Mortality Rate among Patients Hospitalized for Sepsis, 1979–2000.

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.



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

Derek C. Angus, MD, MPH, FCCM; Walter T. Linde-Zwirble; Jeffrey Lidicker, MA; Gilles Clermont, MD; Joseph Carcillo, MD; Michael R. Pinsky, MD, FCCM

Objective: To determine the incidence, cost, and outcome of severe sepsis in the United States.

Design: Observational cohort study.

Setting: All nonfederal hospitals (n = 847) in seven U.S. states.

Patients: All patients (n = 192,980) meeting criteria for severe sepsis based on the International Classification of Diseases, Ninth Revision, Clinical Modification.

Interventions: None.

Measurements and Main Results: We linked all 1995 state hospital discharge records (n = 6,621,559) from seven large states with population and hospital data from the U.S. Census, the Centers for Disease Control, the Health Care Financing Administration, and the American Hospital Association. We defined severe sepsis as documented infection and acute organ dysfunction using criteria based on the International Classification of Diseases, Ninth Revision, Clinical Modification. We validated these criteria against prospective clinical and physiologic criteria in a subset of five hospitals. We generated national age- and gender-adjusted estimates of incidence, cost, and outcome. We identified 192,980 cases, yielding national estimates of 751,000 cases (3.0 cases per 1,000 population and 2.26 cases per 100 hospital discharges), of whom 383,000 (51.1%) received intensive care and an additional 130,000 (17.3%) were ventilated in an intermediate care unit or cared for in a coronary care unit. Incidence increased >100-fold with age (0.2/1,000 in children to 26.2/1,000 in those >85 yrs old). Mortality was 28.6%, or 215,000 deaths nationally, and also increased with age, from 10% in children to 38.4% in those >85 yrs old. Women had lower age-specific incidence and mortality, but the difference in mortality was explained by differences in underlying disease and the site of infection. The average costs per case were $22,100, with annual total costs of $16.7 billion nationally. Costs were higher in infants, nonsurvivors, intensive care unit patients, surgical patients, and patients with more organ failure. The incidence was projected to increase by 1.5% per annum.

Conclusions: Severe sepsis is a common, expensive, and frequently fatal condition, with as many deaths annually as those from acute myocardial infarction. It is especially common in the elderly and is likely to increase substantially as the U.S. population ages. (Crit Care Med 2001; 29:1303–1310)

KEY WORDS: sepsis; severe sepsis; sepsis syndrome; organ failure; intensive care; outcome; resource use; mortality; elderly; epidemiology

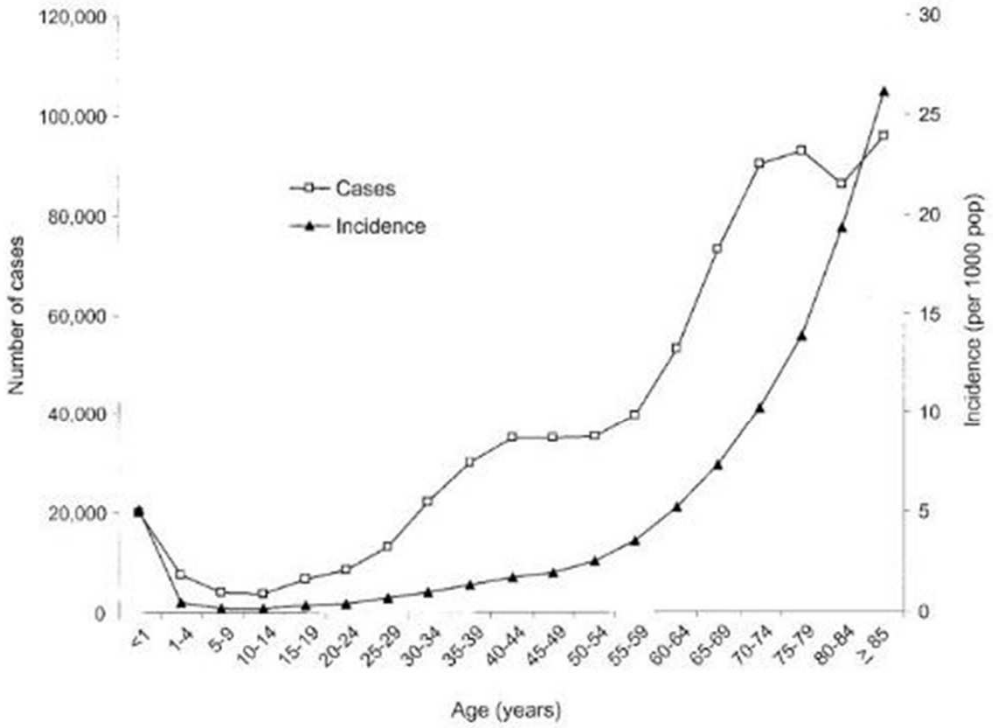


Figure 1. National age-specific number and incidence of cases of severe sepsis. National estimates are generated from the seven-state cohort using state and national age- and gender-specific population estimates from the National Center for Health Statistics and the U.S. Census. *pop*, population.

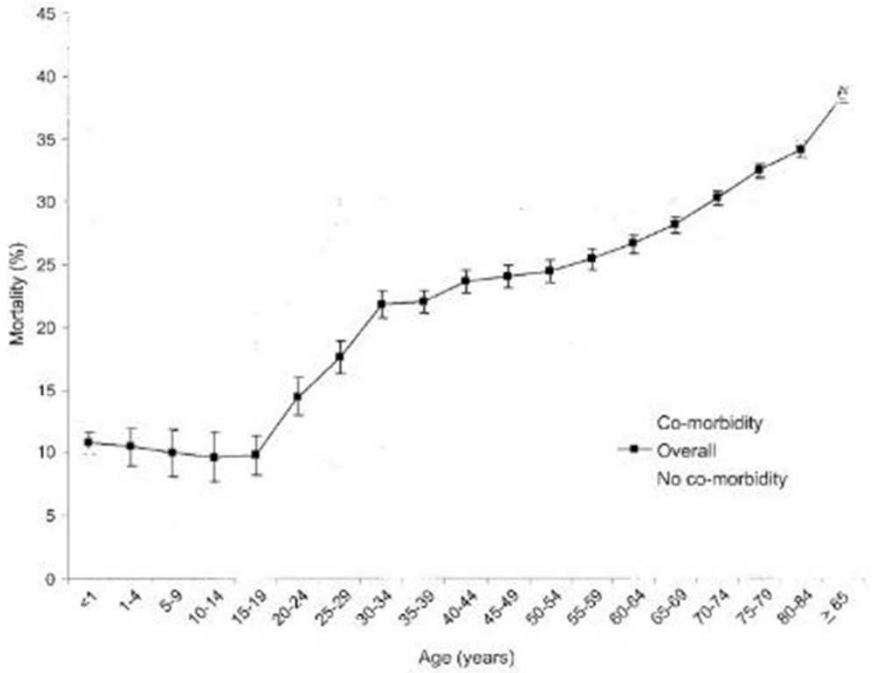


Figure 3. National age-specific mortality rates for all cases of severe sepsis and for those with and without underlying comorbidity. Comorbidity is defined as a Charlson-Deyo score (23) >0. National estimates are generated from the seven-state cohort using state and national age- and gender-specific population estimates from the National Center for Health Statistics and the U.S. Census. Error bars represent 95% confidence intervals.

Definizione

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Assessment of Clinical Criteria for Sepsis
For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Theodore J. Iwashyna, MD, PhD; Frank M. Brunkhorst, MD; Thomas D. Rea, MD, MPH; Ariel Scherag, PhD; Gordon Rubenfeld, MD, MSc; Jeremy M. Kahn, MD, MSc; Manu Shankar-Hari, MD, MSc; Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Gabriel J. Escobar, MD; Derek C. Angus, MD, MPH

IMPORTANCE The Third International Consensus Definitions Task Force defined sepsis as "life-threatening organ dysfunction due to a dysregulated host response to infection." The performance of clinical criteria for this sepsis definition is unknown.

Editorial page 757

Author Audio Interviews at jama.com

Related articles pages 775 and

Spettro continuo di patologia da infezione a batteriemia a sepsi, shock settico, disfunzione multiorgano e decesso

Infezione
Invasione di tessuti corporei normalmente sterili da parte di batteri patogeni

Batteriemia
Presenza di batteri nel torrente ematico

Sepsi

"Disfunzione multiorgano causata da disregolazione della risposta infiammatoria alla infezione"

Disfunzione multiorgano è definita dalla aumentodi almeno due punti al SOFA score che comporta mortalità di almeno il 10%

Infezione: insieme di segni e sintomi, parametri e valutazioni cliniche e laboratoristiche. Non linee guida, non definizioni chiare che la definiscono.

Riconoscimento precoce:

rezi

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg

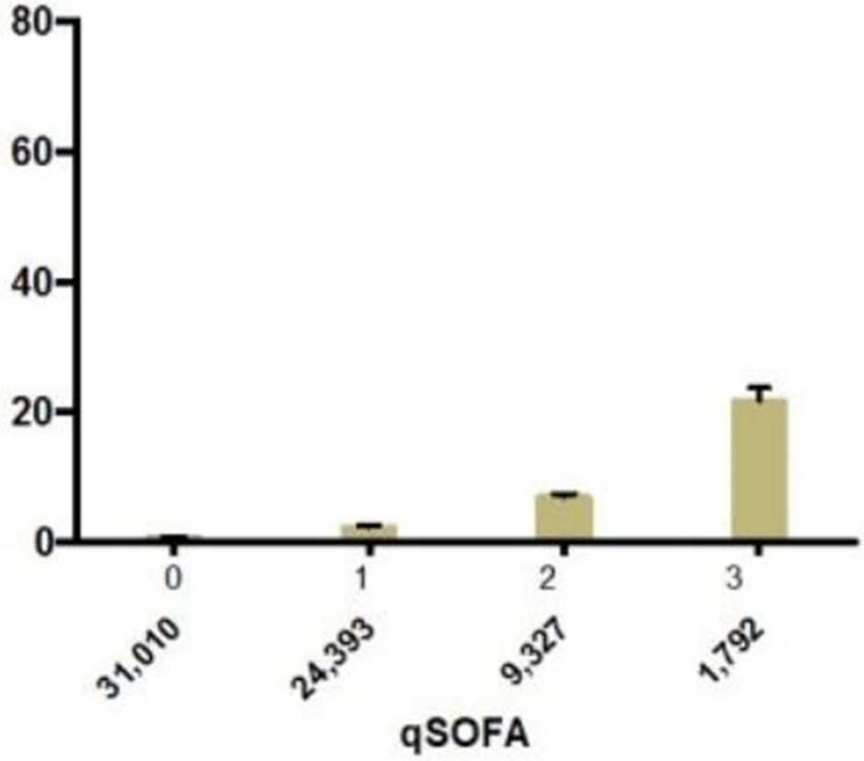
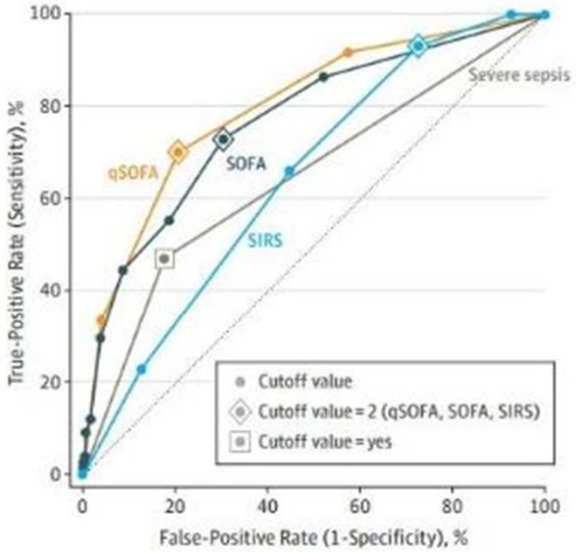

80
60
40
20
0
0
1
2
3
31,010
24,393
9,327
1,792
qSOFA

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).

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

	Score				
System	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.

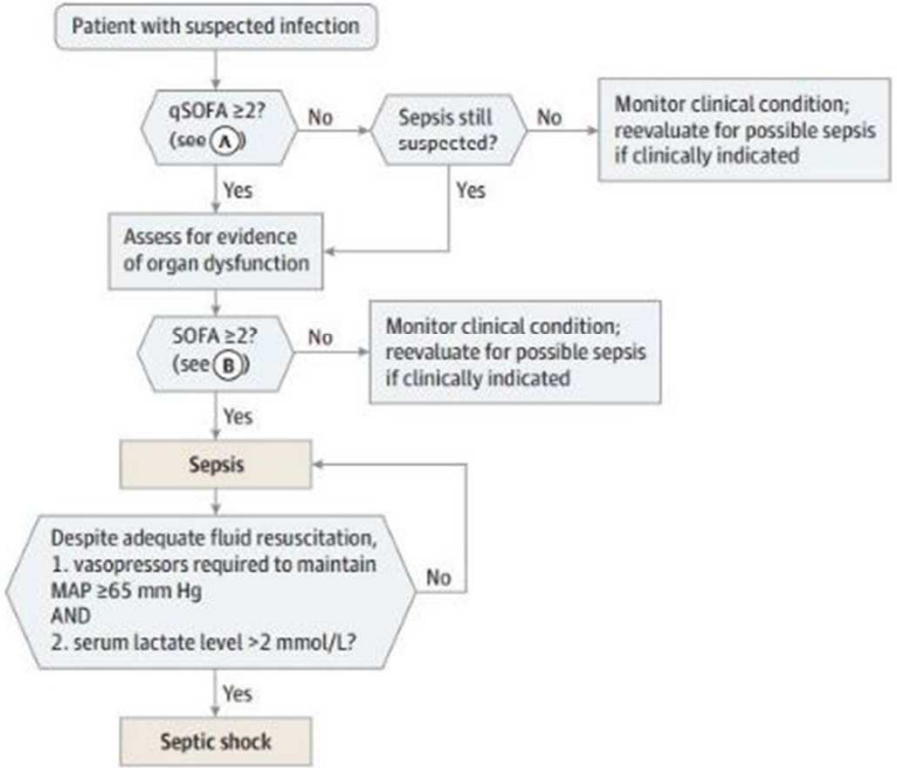
Shock settico

Un tipo di shock distributivo o vasodilatatorio.

Si ha quando la sepsi causa alterazioni circolatorie, metaboliche e cellulari in grado di aumentare significativamente la mortalità. (10 --> 40%)

Clinicamente: Criteri sepsi più necessità di vasopressori nonostante adeguato riempimento volemico per ottenere pressione arteriosa media di 65 mmHg e che presentano valori di lattato di almeno 2 mmol/L (18 mg/dL)

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



Fattori di rischio

- Ricovero in UTI
- Età avanzata (> 65 anni)
- Immunosoppressione
- Diabete Mellito e obesità
- Cancro
- Precedente ospedalizzazione
- Fattori genetici

Presentazione Clinica

Segni e sintomi: tipici della localizzazione batterica! DD tra polmonite e pielonefrite..... più:

A: ostruzione vie aeree?
B: Tachipnea, desaturazione?
C: Ipotensione e Tachicardia + segni di alterata perfusione periferica
D: Confusione mentale, sopore
E: ipertermia, ipotermia

rezi

Initial evaluation of common sources of sepsis

Suspected site	Symptoms/signs*
Upper respiratory tract	Pharyngeal inflammation plus exudate ± swelling and lymphadenopathy
Lower respiratory tract	Productive cough, pleuritic chest pain, consolidative auscultatory findings
Urinary tract	Urgency, dysuria, loin, or back pain
Vascular catheters: arterial, central venous	Redness or drainage at insertion site
Indwelling pleural catheter	Redness or drainage at insertion site
Wound or burn	Inflammation, edema, erythema, discharge of pus
Skin/soft tissue	Erythema, edema, lymphangitis
Central nervous system	Signs of meningeal irritation
Gastrointestinal	Abdominal pain, distension, diarrhea, and vomiting
Intra-abdominal	Specific abdominal symptoms/signs
Peritoneal dialysis (PD) catheter	Cloudy PD fluid, abdominal pain
Genital tract	Women: Low abdominal pain, vaginal discharge Men: Dysuria, frequency, urgency, urge incontinence, cloudy urine, prostatic tenderness
Bone	Pain, warmth, swelling, decreased use
Joint	Pain, warmth, swelling, decreased range of motion

Indagini diagnostiche:

- Leucocitosi vs leucopenia
- Piastrine
- Glicemia
- Ipossiemia
- Creatinina
- Iperbilirubinemia
- Incremento dei tempi di coagulazione
- Lattato
- PCR
- Procalcitonina?
- Emocolture?
- Imaging?


Accuracy of procal
patients: systema

Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis

Benjamin M P Tang, Guy D Eslick, Jonathan C Craig, Anthony S McLean

Lancet Infect Dis 2007; 7: 210–17

Department of Intensive Care Medicine, Nepean Hospital, Penrith, New South Wales, Australia (B M P Tang MD, A S McLean MD); School of Public Health, University of Sydney, Sydney, New South Wales (B M P Tang, G D Eslick PhD, J C Craig MD); and Department of Medicine, University of Sydney, Nepean Hospital, Penrith (G D Eslick)

Procalcitonin is widely reported as a useful biochemical marker to differentiate sepsis from other non-infectious causes of systemic inflammatory response syndrome. In this systematic review, we estimated the diagnostic accuracy of procalcitonin in sepsis diagnosis in critically ill patients. 18 studies were included in the review. Overall, the diagnostic performance of procalcitonin was low, with mean values of both sensitivity and specificity being 71% (95% CI 67–76) and an area under the summary receiver operator characteristic curve of 0·78 (95% CI 0·73–0·83). Studies were grouped into phase 2 studies (n=14) and phase 3 studies (n=4) by use of Sackett and Haynes' classification. Phase 2 studies had a low pooled diagnostic odds ratio of 7·79 (95% CI 5·86–10·35). Phase 3 studies showed significant heterogeneity because of variability in sample size (meta-regression coefficient –0·592, p=0·017), with diagnostic performance upwardly biased in smaller studies, but moving towards a null effect in larger studies. Procalcitonin cannot reliably differentiate sepsis from other non-infectious causes of systemic inflammatory response syndrome in critically ill adult patients. The findings from this study do not lend support to the widespread use of the procalcitonin test in critical care settings

Serial Procalcitonin Predicts Mortality in Severe Sepsis Patients: Results From the Multicenter Procalcitonin MOnitoring SEpsis (MOSES) Study

Philipp Schuetz, MD, MPH[1]; Robert Birkhahn, MD[2]; Robert Sherwin, MD[3]; Alan E. Jones, MD[4]; Adam Singer, MD[5]; Jeffrey A. Kline, MD[6]; Michael S. Runyon, MD, MPH[6]; Wesley H. Self, MD[7]; D. Mark Courtney, MD[8]; Richard M. Nowak, MD[9]; David F. Gaieski, MD[10]; Stefan Ebmeyer, MD[11]; Sascha Johannes, PhD[11]; Jan C. Wiemer, PhD[11]; Andrej Schwabe, PhD[11]; Nathan I. Shapiro, MD, MPH[12]

MAJOR ARTICLE

Comparison of 2 Blood Culture Media Shows Significant Differences in Bacterial Recovery for Patients on Antimicrobial Therapy

Rebecca Zadroga,[1,2] David N. Williams,[2,3] Richard Gottschall,[4] Kevan Hanson,[4] Vickie Nordberg,[4] Marcia Deike,[4] Mike Kuskowski,[5] Lisa Carlson,[6] David P. Nicolau,[7] Christina Sutherland,[7] and Glen T. Hansen[2,4,8]

[1]Veterans Affairs Medical Center, [2]Department of Infectious Disease, University of Minnesota, [3]Department of Infectious Disease and [4]Department of Microbiology, Hennepin County Medical Center, [5]Geriatric Research, Education and Clinical Center, Minneapolis VA Medical Center, University of Minnesota, and [6]Department of Pharmacy, Hennepin County Medical Center, Minneapolis, Minnesota; [7]Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, Connecticut; and [8]Department of Pathology and Laboratory Medicine, University of Minnesota, Minneapolis

Background. Antimicrobial removal devices in blood culture media are designed to remove antibiotics from the blood culture solution, thereby facilitating bacterial growth. How well these devices function clinically has not been established.

Methods. All blood drawn for culture from adult inpatients and emergency department visitors in a level I trauma center was placed in paired BACTEC Plus and BacT/Alert FAN culture media and studied simultaneously, consecutively, and prospectively between 1 February and 30 September 2011. All cultures were processed per standard laboratory protocols.

Results. Of 9395 total cultures collected, 1219 (13%) were positive, 831 were included, and 524 (33%) contained pathogens. BACTEC had a 4.5-hour faster detection time ($P < .0001$), and isolated exclusively 182 of 524 (35%; $P < .001$) pathogens, 136 of 345 (39%) of the gram-positive cocci ($P < .001$), 48 of 175 (27%; $P = .02$) of the gram-negative rods, 101 of 195 (52%) of *Staphylococcus aureus* ($P < .001$), and 59 of 120 (49%; $P = .004$) septic events. If active antibiotics had been dosed 0–4 or 4–48 hours prior to culture collection, the odds of that culture growing in BACTEC were 4.8- and 5.2-fold greater, respectively, than of growing in BacT/Alert ($P < .0001$). Both were equivalent in the recovery of yeast and when no antimicrobials were dosed.

Conclusions. BACTEC media has faster time to detection and increased bacterial recovery over the BacT/Alert media in the following categories: overall growth, pathogens, septic events, gram-positive cocci, gram-negative rods, *Staphylococcus aureus*, and cultures where antimicrobials were dosed up to 48 hours before culture collection.

Keywords. Blood cultures; BACTEC; BacT/Alert; septicemia; antibiotic removal device.

Diagnosi: Medica

Prognosi: Paziente e Medico

- caretteristiche cliniche e risposta alla infezione
- tipo di infezione
- sede infezione
- timing riconoscimento
- corretto supporto emodinamico e respiratorio
- corretta terapia antibiotica

Cosa succede?

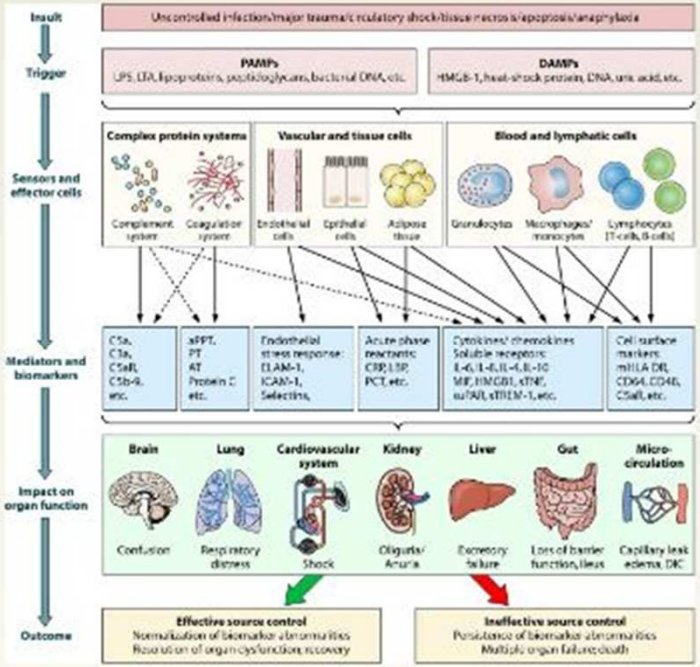
La risposta infiammatoria ha l'obiettivo di **controllare la sede di infezione** ed **iniziare i processi riparativi** via l'attivazione di cellule deputate alla risposta immunitaria circolanti e residenti attivate e modulate da mediatori chimici.

Proinfiammatoria

TNF alfa, Il-1, IL-2, IL-6, IL-8, IL-10, platelet activating factor, interferon

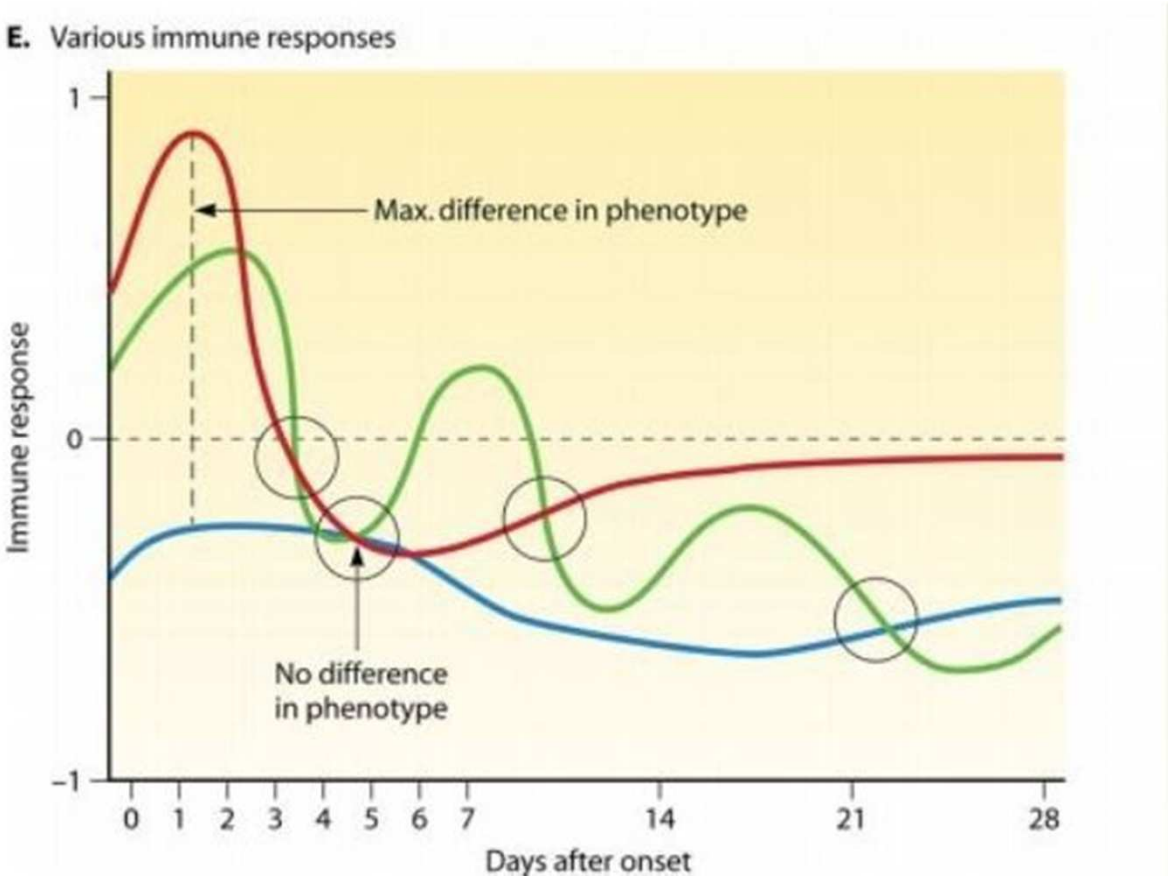
Peptidoglicano, acido lipotecoico, enterotossina B staffilococcica, Tossina sindrome shock tossico, esotossina A dello seudomonas, proteina M streptococco gurppo A)

Iperpiressia, vasodilatazione, aumento permeabilità tissutale, secrezione ormoni dello stress (aumento gluconeogenesi e lipolisi), attività procoagulativo ed anticoagulativa (disfunzione piastrine, CID))



Infiammazione magligna intravascolare:

- mediatori della risposta infiammatoria;
- mediatori con effetto autocrino o paracrino diventano endocrini, coninvolto il sistema
- incontrollata


E. Various immune responses
1
0
−1
Immune response
Max. difference in phenotype
No difference
in phenotype
0 1 2 3 4 5 6 7 14 21 28
Days after onset

Trama vascolare sistemica:

- **Prostaciclina, NO e vasopressina**: vasodilatazione sistemica
- Perdita volume intravascolare da III spazio
- Disfunzione cardiaca: ridotta FE
- Iporesponsività vascolare: ridotta capacità di centralizzare il flusso

Disfunzione endoteliale + intrappolamento macrofagi e distruzione barriera emato-alveolare: ARDS

Compromessa barriera GI: traslocazione batterica e tossine.

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2017, Article ID 4076368, 13 pages
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Review Article

Involvement of Mitoc
Septic Cardiomyopath

Arthur Durand,[1] Thibaul
Raphael Favory,[1] and Sel

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Correspondence should be address

Received 19 May 2017; Revised 11

Sepsis is defined as a life-threate
leading cause of death worldwide,
to as septic cardiomyopathy, is
outcomes. Recent research has inc
septic cardiomyopathy. The purp
research directions.

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2017, Article ID 4076348, 13 pages
https://doi.org/10.1155/2017/4076348

Review Article

Involvement of Mitochondrial Disorders in Septic Cardiomyopathy

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[2]*Département de Physiologie, CHU Martinique, Faculté de Médecine, Université des Antilles, 97200 Fort de France, France*
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Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. It remains a leading cause of death worldwide, despite the development of various therapeutic strategies. Cardiac dysfunction, also referred to as septic cardiomyopathy, is a frequent and well-described complication of sepsis and associated with worse clinical outcomes. Recent research has increased our understanding of the role of mitochondrial dysfunction in the pathophysiology of septic cardiomyopathy. The purpose of this review is to present this evidence as a coherent whole and to highlight future research directions.

Sepsis-associated encephalopathy and its differential diagnosis

Emanuele Iacobone, MD; Juliette Bailly-Salin, MD; Andrea Polito, MD; Diane Friedman, MD; Robert D. Stevens, MD; Tarek Sharshar, MD, PhD

Sepsis is often complicated by an acute and reversible deterioration of mental status, which is associated with increased mortality and is consistent with delirium but can also be revealed by a focal neurologic sign. Sepsis-associated encephalopathy is accompanied by abnormalities of electroencephalogram and somatosensory-evoked potentials, increased in biomarkers of brain injury (i.e., neuron-specific enolase, S-100 β-protein) and, frequently, by neuroradiological abnormalities, notably leukoencephalopathy. Its mechanism is highly complex, resulting from both inflammatory and noninflammatory processes that affect all brain cells and induce blood-brain barrier breakdown, dysfunction of intracellular metabolism, brain cell death, and brain injuries. Its diagnosis relies essentially on neurologic examination that can lead one to perform specific neurologic tests. Electroencephalography is required in the presence of seizure; neuroimaging in the presence of seizure, focal neurologic signs or suspicion of cerebral infection; and both when encephalopathy remains unexplained. In practice, cerebrospinal fluid analysis should be performed if there is any doubt of meningitis. Hepatic, uremic, or respiratory encephalopathy, metabolic disturbances, drug overdose, withdrawal of sedatives or opioids, alcohol withdrawal delirium, and Wernicke's encephalopathy are the main differential diagnoses of sepsis-associated encephalopathy. Patient management is based mainly on controlling infection, organ system failure, and metabolic homeostasis, at the same time avoiding neurotoxic drugs. (Crit Care Med 2009; 37[Suppl.]:S331–S336)

Key Words: sepsis; encephalopathy; delirium; blood brain barrier; neuroimaging

Come lo tratto?

A, B, C!

Assicura e stabilizza le vie aeree,
assicura adeguati scambi respiratori (pump or lung failure?),
reperisci accesso venoso: esami, emocolture e fluidoterapia insieme a terapia antibiotica

Intensive Care Med (2017) 43:304–377
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

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

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LA GESTIONE DELLA SEPSI NELL'ADULTO IN PRONTO SOCCORSO E MEDICINA D'URGENZA IN ITALIA:

LE RACCOMANDAZIONI DELLA CONSENSUS SIMEU

Gruppo di lavoro

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Elaborazione: Alessio Bertini, Andrea Fabbri, Anna Maria Brambilla, Elisa Pontoni, Fabio Causin, Fiammetta Pagnozzi, Francesca Innocenti, Franco Aprà, Germana Ruggiano, Giuseppe Giannazzo, Irene Di Paco, Mario Calci, Maurizio Zanobetti, Renzo Camaiori, Riccardo Pini, Rodolfo Sbrojavacca, Savino Russo, Silvia Musci

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Riempimento volemico

30 ml/Kg nelle prime 3 ore
Boli rapidi di 500 ml alla volta, controllando per sovraccarico e responsività.
Che tipo di liquidi?

Conosci le soluzioni e guarda l'emogas!




The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

The SAFE Study Investigators*

Table 3. **Primary and Secondary Outcomes.***

Outcome	Albumin Group	Saline Group	Relative Risk (95% CI)	Absolute Difference (95% CI)	P Value
Status at 28 days — no./total no. (%)					
Dead	726/3473 (20.9)	729/3460 (21.1)	0.99 (0.91 to 1.09)		0.87
Alive in ICU	111/3473 (3.2)	87/3460 (2.5)	1.27 (0.96 to 1.68)		0.09
Alive in hospital†	793/3473 (22.8)	848/3460 (24.5)	0.93 (0.86 to 1.01)		0.10
Length of stay in ICU — days	6.5±6.6	6.2±6.2		0.24 (−0.06 to 0.54)	0.44
Length of stay in hospital — days†	15.3±9.6	15.6±9.6		−0.24 (−0.70 to 0.21)	0.30
Duration of mechanical ventilation — days	4.5±6.1	4.3±5.7		0.19 (−0.08 to 0.47)	0.74
Duration of renal-replacement therapy — days	0.48±2.28	0.39±2.0		0.09 (−0.0 to 0.19)	0.41
New organ failure — no. (%)‡					0.85§
No failure	1397 (52.7)	1424 (53.3)			
1 organ	795 (30.0)	796 (29.8)			
2 organs	369 (13.9)	361 (13.5)			
3 organs	68 (2.6)	75 (2.8)			
4 organs	18 (0.7)	17 (0.6)			
5 organs	2 (0.1)	0			
Death within 28 days according to subgroup — no./total no. (%)					
Patients with trauma	81/596 (13.6)	59/590 (10.0)	1.36 (0.99 to 1.86)		0.06
Patients with severe sepsis	185/603 (30.7)	217/615 (35.3)	0.87 (0.74 to 1.02)		0.09
Patients with acute respiratory distress syndrome	24/61 (39.3)	28/66 (42.4)	0.93 (0.61 to 1.41)		0.72

* Plus–minus values are means ±SD. CI denotes confidence interval, and ICU intensive care unit.
† The data include the numbers of patients in the ICU or the length of stay in the ICU.
‡ Data were available for 2649 patients in the albumin group and 2673 patients in the saline group. New organ failure was defined as a Sequential Organ-Failure Assessment score[13] of 0, 1, or 2 in any individual organ system at baseline, followed by an increase in the score to 3 or 4 in the same system.
§ The P value pertains to the comparison between the albumin and saline groups in the numbers of patients who had no new organ failure or new failure of one, two, three, four, or five organs.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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Gudmundur Klemenzson, M.D., Anders Åneman, M.D., Ph.D.,
Kristian R. Madsen, M.D., Morten H. Møller, M.D., Ph.D., Jeanie M. Elkjær, M.D.,
Lone M. Poulsen, M.D., Asger Bendtsen, M.D., M.P.H., Robert Winding, M.D.,
Morten Steensen, M.D., Pawel Berezowicz, M.D., Ph.D., Peter Søe-Jensen, M.D.,
Morten Bestle, M.D., Ph.D., Kristian Strand, M.D., Ph.D., Jørgen Wiis, M.D.,
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Frederik Mondrup, M.D., Frank C. Pott, M.D., D.M.Sci., Thea P. Møller, M.D.,
Per Winkel, M.D., D.M.Sci., and Jørn Wetterslev, M.D., Ph.D.,
for the 6S Trial Group and the Scandinavian Critical Care Trials Group*

Table 3. **Primary and Secondary Outcomes.***

Outcome	HES 130/0.42 (N=398)	Ringer's Acetate (N=400)	Relative Risk (95% CI)	P Value
Primary outcome				
Dead or dependent on dialysis at day 90 — no. (%)	202 (51)	173 (43)	1.17 (1.01–1.36)	0.03
Dead at day 90 — no. (%)	201 (51)	172 (43)	1.17 (1.01–1.36)	0.03
Dependent on dialysis at day 90 — no. (%)	1 (0.25)	1 (0.25)	—	1.00
Secondary outcome measures				
Dead at day 28 — no. (%)	154 (39)	144 (36)	1.08 (0.90–1.28)	0.43
Severe bleeding — no. (%)†	38 (10)	25 (6)	1.52 (0.94–2.48)	0.09
Severe allergic reaction — no. (%)†	1 (0.25)	0	—	0.32
SOFA score at day 5 — median (interquartile range)	6 (2–11)	6 (0–10)	—	0.64
Use of renal-replacement therapy — no. (%)‡	87 (22)	65 (16)	1.35 (1.01–1.80)	0.04
Use of renal-replacement therapy or renal SOFA score ≥3 — no. (%)§	129 (32)	108 (27)	1.20 (0.97–1.48)	0.10
Doubling of plasma creatinine level — no. (%)†	148 (41)	127 (35)	1.18 (0.98–1.43)	0.08
Acidosis — no. (%)†¶	307 (77)	312 (78)	0.99 (0.92–1.06)	0.72
Alive without renal-replacement therapy — mean % of days‖	91	93	—	0.048
Use of mechanical ventilation — no. (%)†	325 (82)	321 (80)	1.02 (0.95–1.09)	0.61
Alive without mechanical ventilation — mean % of days‖	62	65	—	0.28
Alive and out of hospital — mean % of days‖	29	34	—	0.048

- 30 ml/kg: ordine di grandezza! sovraccarico fluidi è pericoloso come deplezione!

- Colloidi: aumentano rischio di insufficienza renale acuta, emorragie, aumentano mortalità.

FALSO: proteggono da edema per maggiore pressione oncotica
FALSO: rapporto 1:3= miglior riempimento, dimostrato che rapporto 1:1.
Non beneficio, rischi!

- Soluzioni bilanciate vs NaCl: migliora sopravvivenza?

- Bicarbonato: se pH < 7.1 o < 7.2 e presenza di danno renale. 1-2 mEq/kg

- NaHCO3 1.4% --> 500/1000 cc.
- NaHCO3 8.4% --> 1-2 ml/kg

- Monitoraggio! -->

MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

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Inferior Vena Cava Collapsibility Index is a Valuable and Non-Invasive Index for Elevated General Heart End-Diastolic Volume Index Estimation in Septic Shock Patients

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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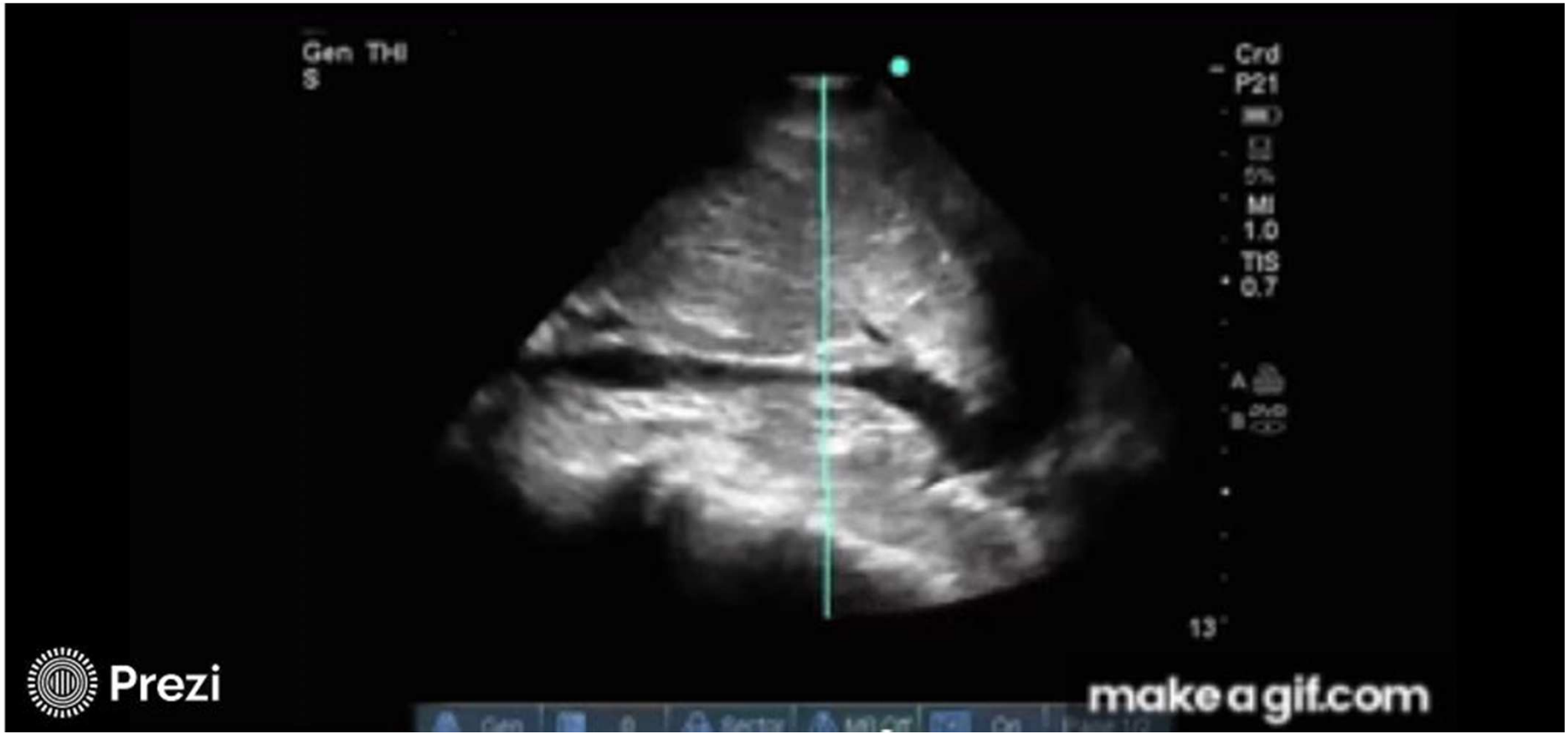
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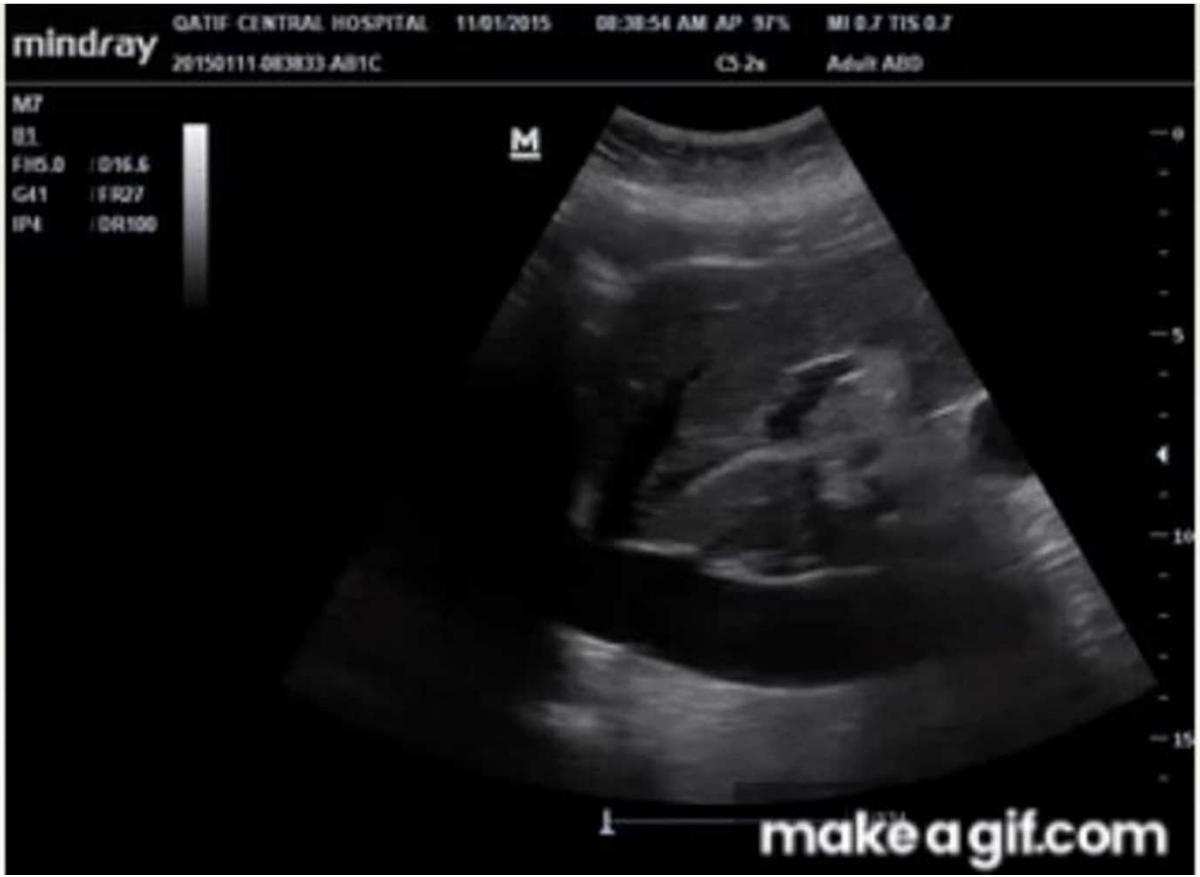
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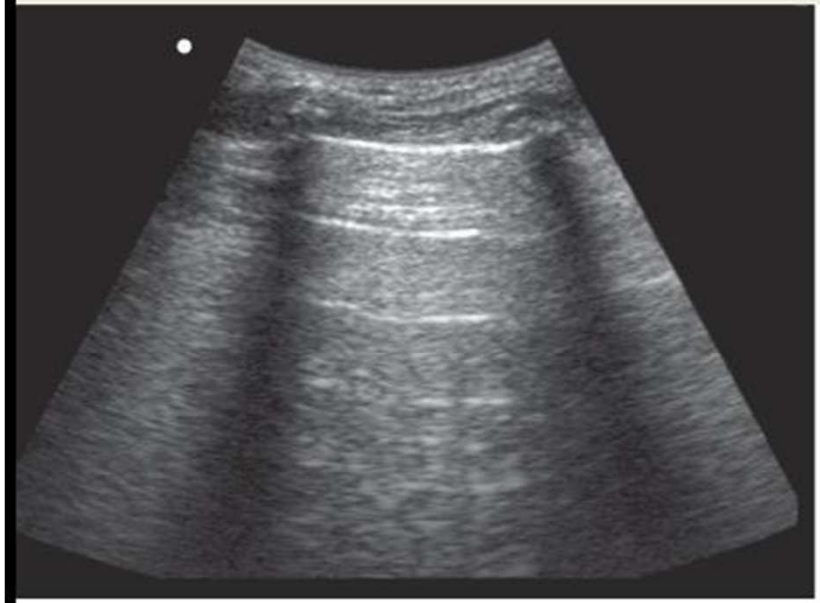
J Clin Monit Comput
DOI 10.1007/s10877-014-9582-6

ORIGINAL RESEARCH

Accuracy of ultrasound B-lines score and E/Ea ratio to estimate extravascular lung water and its variations in patients with acute respiratory distress syndrome

Benoît Bataille · Guillaume Rao · Pierre Cocquet · Michel Mora · Bruno Masson · Jean Ginot · Stein Silva · Pierre-Etienne Moussot

Received: 26 November 2013 / Accepted: 7 May 2014



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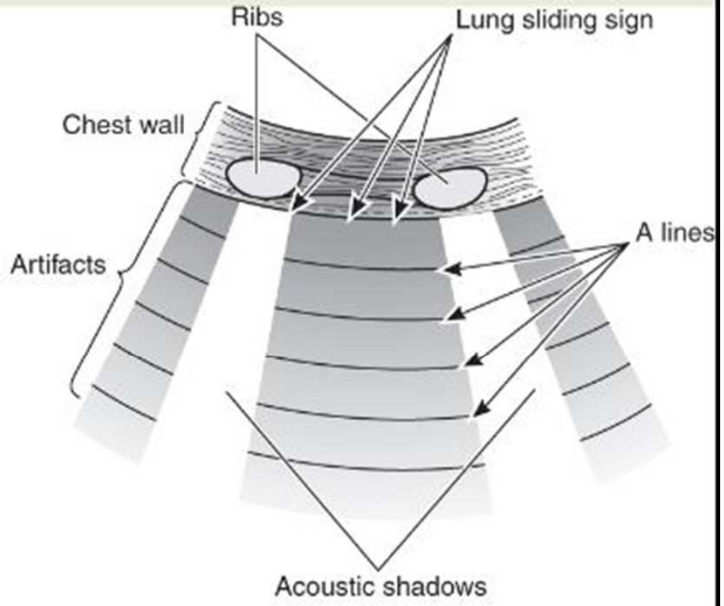

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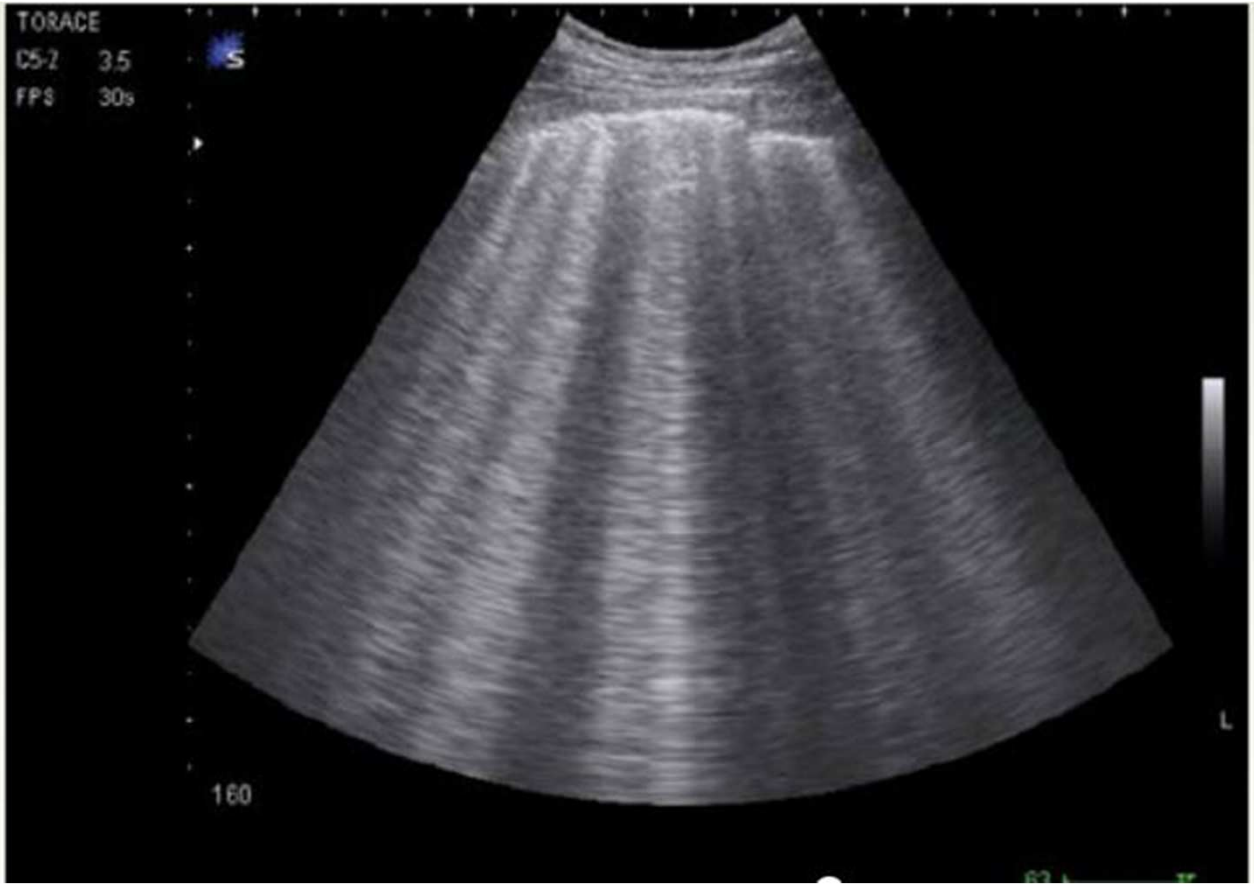
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L

Vasopressori e inotropi

Vasopressore di scelta: Noradrenalina

Dopamina: sconsigliato

Dobutamina: può avere indicazione.

Noradrenalina: 8-12 mcg/min come dose iniziale; mantenimento: 2/4 mcg/min. max 35/100 mcg/min.
Vena periferica: ok antecubitale del braccio, stesse complicanze che in vena centrale.


RESEARCH

Early versus delaye
norepinephrine in


Sepsis/Infection

Dopamine therapy in
on survival?

Thierry Boulain MD*, Isabelle
Dalila Benzekri-Lefevre MD, Ma

Prezi

Bai et al. Critical Care 2014, 18:532
http://ccforum.com/content/18/5/532

CRITICAL CARE

RESEARCH Open Access

Early versus delayed administration of norepinephrine in patients with septic shock

Xiaowu Bai, Wenkui Yu*, Wu Ji, Zhiliang Lin, Shanjun Tan, Kaipeng Duan, Yi Dong, Lin Xu and Ning Li*

Rachoin and Dellinger *Critical Care* 2014, **18**:691
http://ccforum.com/content/18/6/691

CRITICAL CARE

COMMENTARY

Timing of norepinephrine in septic patients: NOT too little too late

Jean-Sebastien Rachoin[1,2] and Richard P Dellinger[1,3,4*]

See related research by Bai *et al.*, http://ccforum.com/content/18/5/532

Journal of Critical Care (2009) **24**, 575–582

ELSEVIER

Journal of Critical Care

Sepsis/Infection

Dopamine therapy in septic shock: Detrimental effect on survival?

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RESEARCH ARTICLE

Vasopressors for the Treatment of Septic Shock: Systematic Review and Meta-Analysis

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Farmaci IC:

Dose da somministrare in 1 h / concentrazione del farmaco = velocità pompa in ml/h

- 10 mcg/min= 600 mcg/h
- 1 fiala da 2 mg in 50 cc: 2 mg=2000 mcg/50 ml= 40 mcg/ml

600 mcg/h/40 mcg/ml=15 ml/h

Agente addizionale

pochi dati di letteratura su optimum

++ **Shock distributivo**:
Vasopressina, dubbia utilità

++ **Shock cardiogeno**: Dobutamina, complessa gestione, solo se evidenza di insufficienza ventricolare

Quale obiettivo?

The NEW ENGLAND JOURNAL of MEDICINE

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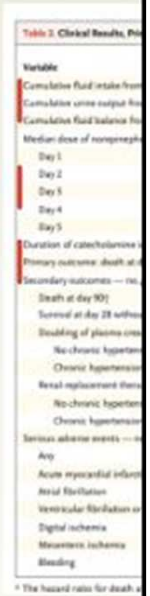
High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., Soizic Gergaud, M.D., Nicolas Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., Marie Conrad, M.D., René Robert, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guitton, M.D., Ph.D., Fabienne Tamion, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., Antoine Vieillard-Baron, M.D., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., Jean-Damien Ricard, M.D., Ph.D., Fabien Hervé, M.D., Damien du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Jean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D., for the SEPSISPAM Investigators*



Monitoraggio

- MAP (2*DIA + SIS)/3
- Urina: > 0.5 ml/kg/h
- Stato mentale
- SpO2
- ScvO2 > 70%
- PVC 8-12 mmHg
- Clearance lattato

Intensive Care Med (2015)
DOI 10.1007/s00134-015-3

Wan-Jie Gu
Zhongheng Zhang
Jan Bakker

**Early lactate clearan
therapy in patients
a meta-analysis with
sequential analysis
of randomized contr**

Accepted: 8 June 2015
Published online: 8 July 20

W.-J. Gu and Z. Zhang cont
the work.

Electronic supplementary
The online version of this
(doi:10.1007/s00134-015-3
supplementary material, wh
to authorized users.

Intensive Care Med (2015) 41:1862–1863
DOI 10.1007/s00134-015-3955-2

LETTER

Wan-Jie Gu
Zhongheng Zhang
Jan Bakker

Early lactate clearance-guided therapy in patients with sepsis: a meta-analysis with trial sequential analysis of randomized controlled trials

Accepted: 8 June 2015
Published online: 8 July 2015

W.-J. Gu and Z. Zhang contribute equally to the work.

Electronic supplementary material
The online version of this article (doi:10.1007/s00134-015-3955-2) contains supplementary material, which is available to authorized users.

the potential to be such a promising goal for quantitative resuscitation. We performed a meta-analysis of randomized controlled trials (RCTs) to evaluate the effect of early lactate clearance-guided therapy on mortality and other outcomes in patients with sepsis.

We searched PubMed, Embase, and Cochrane Central Register of Controlled Trials to identify RCTs that evaluated the effect of early lactate clearance-guided therapy on clinical outcomes in adults with sepsis. The search terms used were "lactate clearance", and "sepsis", or "severe sepsis" or "septic shock". We used the Cochrane collaboration tool to assess risk of bias, and the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach to evaluate the quality of evidence. The primary outcome was all-cause mortality. Secondary outcomes included length event proportion obtained from the results of the meta-analysis, and a relative risk reduction of 20 % in all-causes mortality, using standard software TSA version 0.9 Beta (http://www.ctu.dk/tsa).

Four RCTs enrolling 547 patients were included in the meta-analysis [2–5]. The main characteristics of the four included RCTs are presented in Table 1 in the Electronic Supplementary Material (ESM). Assessment of the risk of bias is summarized in Table 2 (ESM). Overall, two RCTs were categorized as at lower risk of bias [2, 3], and two as at unclear risk of bias [4, 5]. Data on primary outcome were provided in all four trials (547 patients) [2–5]. Early lactate clearance-guided therapy was associated with a reduction in mortality (RR 0.65, 95 % CI 0.49–0.85, $p = 0.002$, $I^2 = 0$ %, Fig. 1). TSA showed that 34.5 % of the required information size of 1586 patients were accrued.

Antibioticoterapia

Entro la prima ora dal contatto medico
DI routine preceduta da emocolture e colturali specifici

Ampio spettro ragionata:

- paziente: allergie, funzionalità renale, pregresse infezioni, stato immunitario
- focus infettivo: polmonite vs colecistite vs IVU
- germi sospettati
-

Target mirata, PCT guidata

Empiric Antibiotic Treatment Reduces Mortality in Severe Sepsis and Septic Shock From the First Hour: Results From a Guideline-Based Performance Improvement Program*

Ricard Ferrer, MD, PhD[1]; Ignacio Martin-Loeches, MD, PhD[2]; Gary Phillips, MAS[3]; Tiffany M. Osborn, MD, MPH[4]; Sean Townsend, MD[5]; R. Phillip Dellinger, MD, FCCP, FCCM[6]; Antonio Artigas, MD, PhD[2]; Christa Schorr, RN, MSN[6]; Mitchell M. Levy, MD, FCCP, FCCM[7]

Caratteristiche paziente -- > sospetto patogeno

MRSA

-
- Pregressa colonizzazione e/o infezione da MRSA (negli ultimi 12 mesi)
- Emodialisi e dialisi peritoneale
- Portatore di CVC e cateteri vascolari a permanenza
- Multipli cicli di terapia antibiotica (es: almeno 5-10 giorni negli ultimi 30-90 gg, in particolare
- con florochinolonici e cefalosporine)
- Residente in long-term care facility o carcere o ricovero negli ultimi 12 mesi
- Contatto stretto con persone colonizzate da MRSA
- Immunodepressi

ESBL

- Pregressa colonizzazione e/o infezione da ESBL (negli ultimi 12 mesi)
- Prolungata ospedalizzazione (mediana di 10 giorni, in particolare in UTI, RSA, hospice ed in reparti ad alta endemia)
- Multipli cicli di terapia antibiotica (almeno 5 giorni negli ultimi 30 gg in particolare con fluorochinolonici, cefalosporine)
- Catetere vescicale a permanenza
- PEG

Pseudomonas Aeruginosa

- Pregressa colonizzazione e/o infezione da P. aeruginosa (negli ultimi 12 mesi)
- Multipli cicli di terapia antibiotica (almeno 5 giorni negli ultimi 30 in particolare con FQ)
- Anatomia polmonare sovvertita con infezioni ricorrenti (es: bronchiectasie)
- Fibrosi cistica
- Prolungato utilizzo della terapia steroidea (> 6 settimane)
- Diabete mellito non controllato/ scompenso diabetico e/o piede diabetico
- Catetere vescicale a permanenza
- Età avanzata (> 80 anni)

-
- Immunocor
  chemiotera
  midollo,
- diabete me
  cronica, ins
- Portatore
  (catetere p
  centrale)
- Nutrizione
- Pancreatit
- Recente in
  sopratutta
- Prolungato
  ad ampio s
- Prolungato
  particolare
- Recente in
  multi-sito

rezi

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ni 12 mesi)
iotica (almeno
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nchiectasie)

rapia

lato/
iede diabetico
anenza

rezi

Funghi

- Immunocompromissione (neutropenia, chemioterapia, trapianto di organo o di midollo,
- diabete mellito, insufficienza epatica cronica, insufficienza renale cronica)
- Portatore di device vascolari invasivi (catetere per emodialisi; catetere venoso centrale)
- Nutrizione parenterale totale
- Pancreatite necrotizzante
- Recente intervento di chirurgia maggiore, sopratutto addominale
- Prolungata somministrazione di antibiotici ad ampio spettro
- Prolungato ricovero in ospedale (in particolare in TI)
- Recente infezione fungina e colonizzazione multi-sito

Caratteristiche antibiotico

- Idrosolubili vs liposolubili (beta-lattamici vs macrolidi e fluorochinolonici
- Tempo dipendenti vs Concentrazione dipendenti (betalattamici e macrolidi vs aminoglicosidi e fluorochinolonici
- Sede di azione
- Spettro di azione
- Eliminazione

Antibiotici: quale?

Anaerobi: Metronidazolo, Carbapenemi, Betalattamici/Betalattamasi inibitore.

MRSA: Vancomicina, Daptomicina, Linezolid

ESBL: Carbapenemi

Pseudomonas: PiP/Taz, Ceftazidime, FLuorochinoloni

Intracellulari: Macrolidi, FLuorochinoloni

Schema terapia antibiotica empirica:

FR per MRSA:
- Vancomicina 2 mg in IC in 24/h secondo funzione renale

+

FR per Pseudomonas:
- Ceftazidime 6 g in IC in 24h opp Pip/Taz 18 g in IC in 24h

no FR per Pseudomonas:
- Ceftriaxone 2 g/24 h;

De-escalation

Ridurre lo spettro appena antibiogramma è disponibile: terapia mirata. No trials definitivi

Durata media: 7-10 giorni.

Maggiore in: focus settici non drenabili, scarsa risposta clinica, endocardite, osteomielite, immunocompromissione, infezione da funghi

Procalcitonina?

Antimicrobial Stewardship

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On completion of this article, readers should be able to: (1) describe the goals of antimicrobial stewardship and discuss why there is an increasing need for antimicrobial stewardship programs; (2) identify stewardship techniques that can be used in a variety of hospital settings by different health care practitioners; and (3) list steps for starting a stewardship program and identify potential barriers to implementation.

Antimicrobial resistance is increasing; however, antimicrobial drug development is slowing. Now more than ever before, antimicrobial stewardship is of the utmost importance as a way to optimize the use of antimicrobials to prevent the development of resistance and improve patient outcomes. This review describes the why, what, who, how, when, and where of antimicrobial stewardship. Techniques of stewardship are summarized, and a plan for implementation of a stewardship program is outlined.

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siderably, and our options for treating increasingly resistant infections are becoming more and more limited. This review aims to describe the why, what, who, how, when, and where of antimicrobial stewardship.

Tens of thousands of Americans die of infections caused by antibiotic-resistant pathogens every year. Every day, patients die of bacterial infections for which no active agents are available. Yet since 1998 only 10 new antibiotics have

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Procalcitonin-guided diagnosis and antibiotic stewardship revisited

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Abstract

Several controlled clinical studies have evaluated the potential of the infection biomarker procalcitonin (PCT) to improve the diagnostic work-up of patients with bacterial infections and its influence on decisions regarding antibiotic therapy. Most research has focused on lower respiratory tract infections and critically ill sepsis patients. A clinical utility for PCT has also been found for patients with urinary tract infections, postoperative infections, meningitis, and patients with acute heart failure with possible superinfection (i.e., pneumonia). In these indications, PCT levels measured on hospital admission were found to substantially reduce the initiation of antibiotic treatment in low-risk situations (i.e., bronchitis, chronic obstructive pulmonary disease exacerbation). For more severe infections (i.e., pneumonia, sepsis), antibiotic stewardship by monitoring of PCT kinetics resulted in shorter antibiotic treatment durations with early cessation of therapy. Importantly, these strategies appear to be safe without increasing the risk for mortality, recurrent infections, or treatment failures. PCT kinetics also proved to have prognostic value correlating with disease severity (i.e., pancreatitis, abdominal infection) and resolution of illness (i.e., sepsis). Although promising findings have been published in these different types of infections, there are a number of limitations regarding PCT, including suboptimal sensitivity and/or specificity, which makes a careful interpretation of PCT in the clinical context mandatory. This narrative review aims to update clinicians on the strengths and limitations of PCT for patient management, focusing on research conducted within the last 4 years.

Keywords: Procalcitonin, Pneumonia, Respiratory tract infection, Sepsis, Antibiotic stewardship

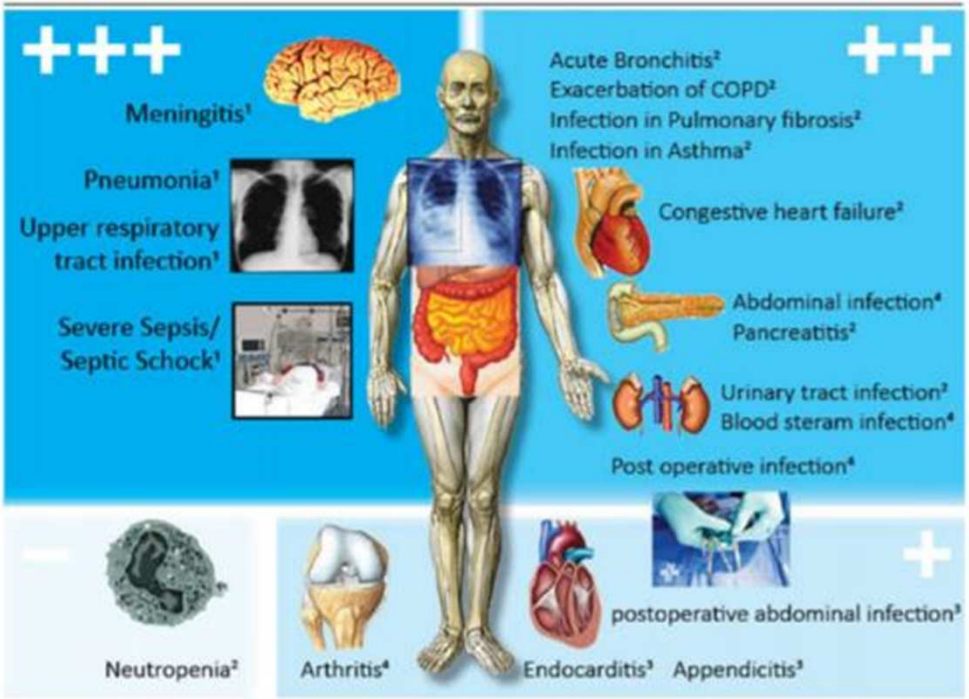

Fig. 1 Summary of evidence regarding procalcitonin (PCT) for diagnosis and antibiotic stewardship in organ-related infections. While for some infections, intervention studies have investigated benefit and harm of using PCT for diagnosis and antibiotic stewardship (*left side*), for other infections only results from diagnostic (observation) studies are available (*right side*). +: moderate evidence in favor of PCT; ++: good evidence in favor of PCT; +++: strong evidence in favor of PCT; – no evidence in favor of PCT

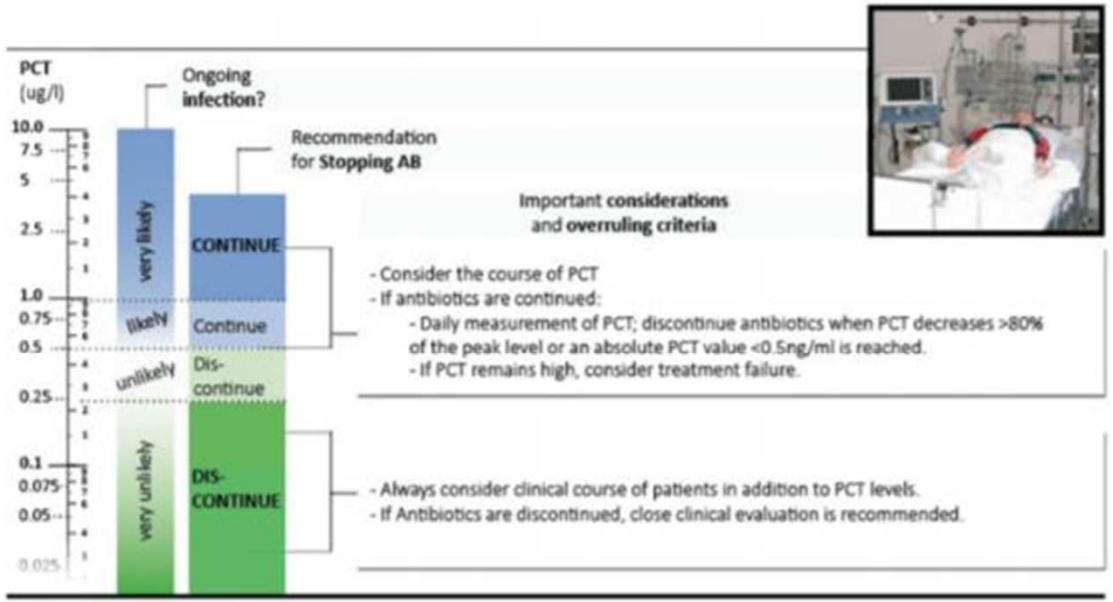

Fig. 3 Procalcitonin (PCT) algorithm in patients with sepsis in the intensive care unit (ICU). In critically ill patients in the ICU, cut-offs are higher and initial empiric antibiotic therapy should be encouraged in all patients with suspicion of sepsis. PCT cut-offs are helpful in the subsequent days after admission to shorten the course of antibiotic therapy in patients with clinical improvement

Terapia di supporto:

- Corticosteroidi: 200 mg/die. Solo casi selezionati, non rispondenti alla tp
- Trasfusione di GRC: solo se Hb < 7 in assenza di ulteriori patologie o sintomatologia
- Trasfusione di piastrine: se < 10.000 o < 20.000 in alto rischio di sanguinamento.
- Insulino terapia se almeno 2 determinazioni > 180 mg/dL

Terapia di supporto:

- Profilassi antitromboembolica con EBPM/ meccanica (Enoxaparina 4000 ui/2000 ui - Fondaparinux 2.5/1.5, Parnaparina 4250 ui)
- Profilassi anti ulcera GI da stress in alto rischio (Antistaminici H2 vs IPP: Ranitidina 300 mg/die)
- Nutrizione enterale via SNG o SND nei primi giorni. Sconsigliato l'uso di nutrizione parenterale nei primi 7 giorni se possibile nutrizione enterale