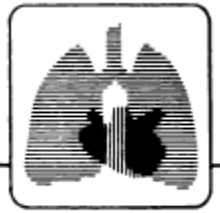
Prevenire, contrastare e gestire la sepsi: un approccio multidisciplinare.

Le nuove definizioni di sepsi:epidemiologia secondo i dati GIVITI

Paolo Malacarne

Rianimazione Pisa

Sepsis 1: 1992 (34 esperti)



accp/sccm consensus conference

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

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:

Roger C. Bone, M.D., F.C.C.P., Chairman
Robert A. Balk, M.D., F.C.C.P.
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R. Phillip Dellinger, M.D., F.C.C.P.
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William A. Knaus, M.D.
Roland M. H. Schein, M.D.
William J. Sibbald, M.D., F.C.C.P.

Figure 1. The Systemic Inflammatory Response Syndrome (SIRS).[8]

Two or more of the following:

- Temperature >38° C or <36° C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min or $PaCO_2$<32 torr
- WBC >12,000 cell/mm^3, <4,000 cells/mm^3, or >10% immature (band) forms

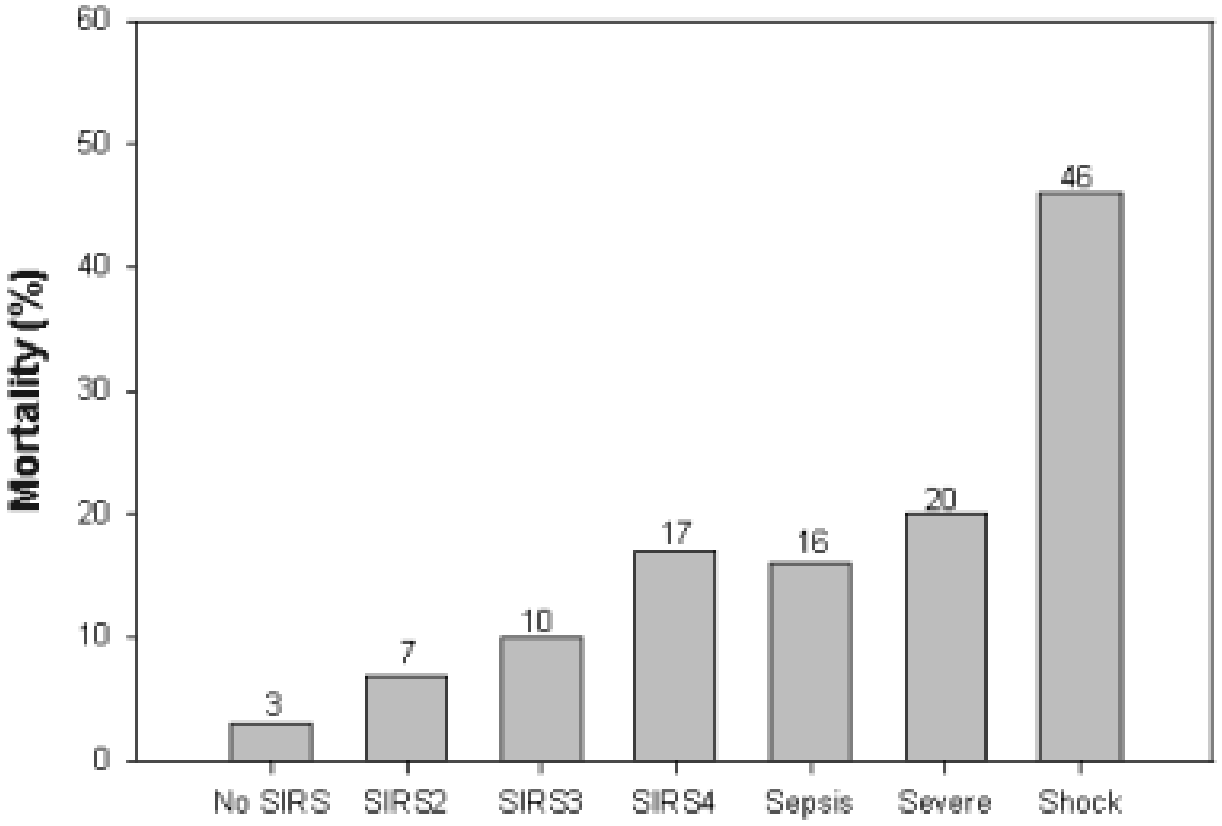
Sepsis 1 1992

Table 1 – Sepsis, SIRS, and MODS: Defining the terms[12]

Term	Definition
Systemic inflammatory response syndrome (SIRS)	Response is manifested by 2 or more of the following conditions: • Temperature > 38°C (100.4°F) or < 36°C (96.8°F) • Heart rate > 90 beats per minute • Respiration rate > 20 breaths per minute or $Paco_2$ < 32 mm Hg • White blood cell count > 12,000/μL, < 4000/μL, or > 10% immature (band) forms
Sepsis	Systemic response to an infection defined by 2 or more SIRS criteria as a result of an infection
Severe sepsis	Sepsis associated with organ dysfunction, hypoperfusion or hypotension
Septic shock	Sepsis-induced hypotension despite adequate fluid resuscitation along with presence of perfusion abnormalities
Multiple organ dysfunction syndrome (MODS)	Presence of altered organ dysfunction in an acutely ill patient

	1991 Consensus Definitions	2015 Consensus Definitions
SIRS (Systemic Inflammatory Response Syndrome)	Due o più tra i seguenti criteri: 1) T° corporea > 38°C o < 36°C 2) Frequenza cardiaca > 90 bpm 3) Frequenza respiratoria > 20 atti/min o paCO2 < 32 mmHg 4) Leucociti > 12.000/mm3 o Leucociti < 4000/mm3 o forme immature > 10%	---
Sepsi	SIRS + Infezione	Infezione + delta SOFA ≥ 2
Sepsi grave	Sepsi + insufficienza d'organo, ipoperfusione o ipotensione (pressione sistolica < 90 mmHg o una riduzione ≥ 40 mmhg rispetto ai valori di partenza in assenza di altre potenziali cause di ipotensione). L'ipoperfusione può includere ma non è limitata a, acidosi lattica, alterazione dello stato di coscienza e oliguria.	---
Shock settico	Shock indotto da sepsi nonostante adeguato riempimento volemico associate alla presenza di alterazioni della perfusione che possono includere, ma non sono limitate a, acidosi lattica, alterazione dello stato di coscienza e oliguria.	Sepsi associata a: 1. Necessità di impiego di vasopressori per mantenere MAP ≥ 65 mmHg e 2. Lattato sierico ≥ 2 mmol/l

Clinical progression from SIRS to sepsis and septic shock (Rangel-Frausto MS et al JAMA 1995; 11: 117-23)



Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.

Table 1. Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.*

Sepsis (documented or suspected infection plus ≥1 of the following)†
General variables
Fever (core temperature, >38.3°C)
Hypothermia (core temperature, <36°C)
Elevated heart rate (>90 beats per min or >2 SD above the upper limit of the normal range for age)
Tachypnea
Altered mental status
Substantial edema or positive fluid balance (>20 ml/kg of body weight over a 24-hr period)
Hyperglycemia (plasma glucose, >120 mg/dl [6.7 mmol/liter]) in the absence of diabetes
Inflammatory variables
Leukocytosis (white-cell count, >12,000/mm^3)
Leukopenia (white-cell count, <4000/mm^3)
Normal white-cell count with >10% immature forms
Elevated plasma C-reactive protein (>2 SD above the upper limit of the normal range)
Elevated plasma procalcitonin (>2 SD above the upper limit of the normal range)
Hemodynamic variables
Arterial hypotension (systolic pressure, <90 mm Hg; mean arterial pressure, <70 mm Hg; or decrease in systolic pressure of >40 mm Hg in adults or to >2 SD below the lower limit of the normal range for age)
Elevated mixed venous oxygen saturation (>70%)‡
Elevated cardiac index (>3.5 liters/min/square meter of body-surface area)§
Organ-dysfunction variables
Arterial hypoxemia (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, <300)
Acute oliguria (urine output, <0.5 ml/kg/hr or 45 ml/hr for at least 2 hr)
Increase in creatinine level of >0.5 mg/dl (>44 μmol/liter)
Coagulation abnormalities (international normalized ratio, >1.5; or activated partial-thromboplastin time, >60 sec)
Paralytic ileus (absence of bowel sounds)
Thrombocytopenia (platelet count, <100,000/mm^3)
Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 μmol/liter])
Tissue-perfusion variables
Hyperlactatemia (lactate, >1 mmol/liter)
Decreased capillary refill or mottling
Severe sepsis (sepsis plus organ dysfunction)
Septic shock (sepsis plus either hypotension [refractory to intravenous fluids] or hyperlactatemia)¶

ORIGINAL ARTICLE

Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M., D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.

conclusioni

- La necessità di avere 2 o più criteri di SIRS per definire “sepsi grave” esclude 1 paziente su 8 (12,1%) che presenta infezione, disfunzione d’organo e elevata mortalità e fallisce nel definire un “transition point” nel rischio di morte”

SEPSIS 3’

ne Third International
onsensus Definitions for Sepsis
nd Septic Shock
CCM, ESICM taskforce

MA. 2016;315(8):801-810

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, MI
Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD;
g S. Martin, MD, MSc;
D, PhD; Derek C. Angus, M

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; André 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 Interview at jama.com
Related articles pages 775 and

Research

Original Investigation | CARING FOR THE CR

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

IMPORTANCE Septic shock currently refers to a state of acute circulatory failure associated with infection. Emerging biological insights and reported variation in epidemiology challenge the validity of this definition.

Editorial page 757
Author Audio Interview at jama.com
Related articles pages 762 and

Sequential (Sepsis-Related) Organ Function Assessment (SOFA) Score.[a]

System / Score	0	1	2	3	4
Respiration: PaO_2/FiO_2, mmHg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation: Platelets x $10^3/\mu L$	≥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); Urine output, mL/day	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440); <500	>5.0 (440); <200

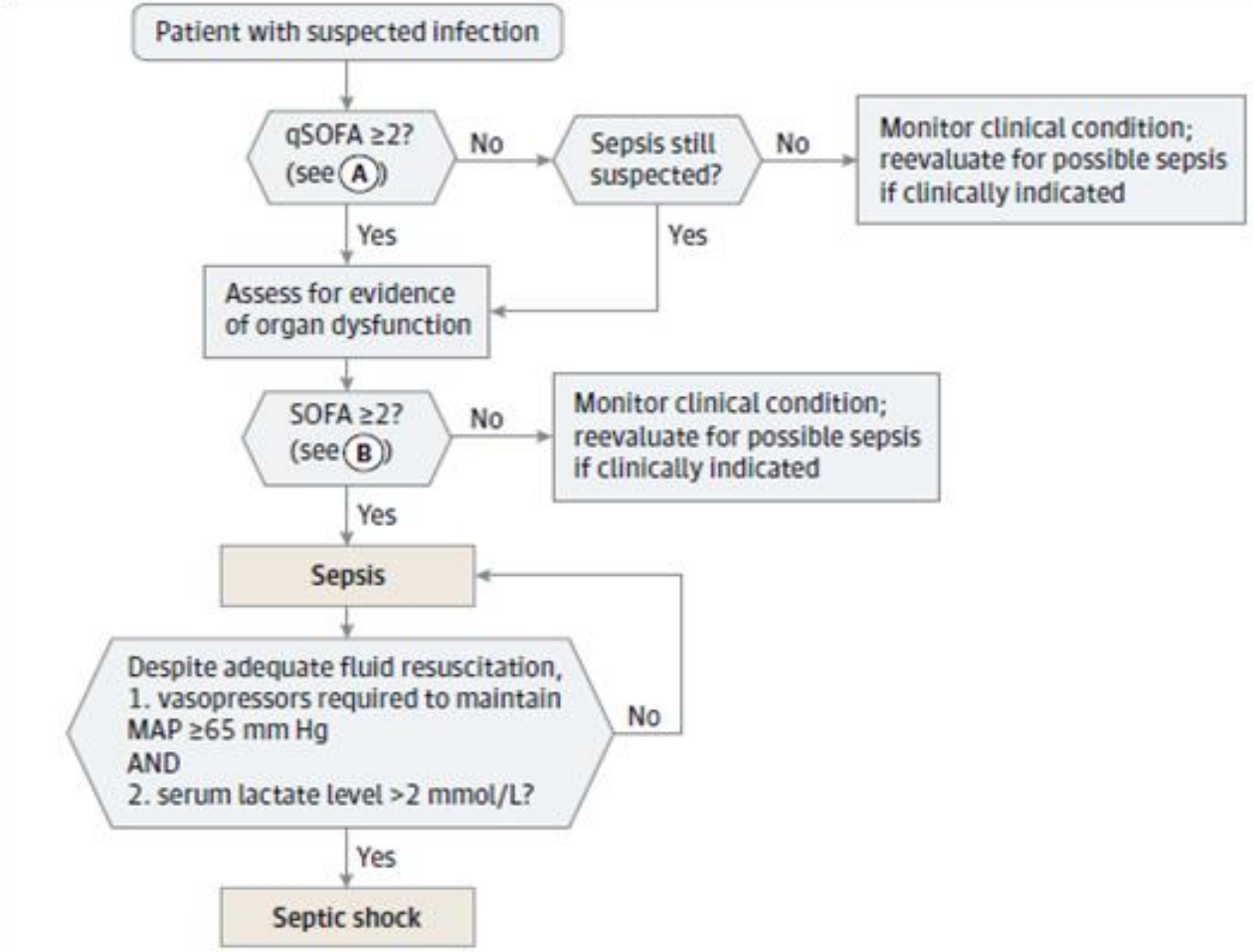
Figure 2. Abbreviations: PaO_2/FiO_2, partial pressure of oxygen/fraction of inspired oxygen. a) Adapted from Vincent et al[3]; b) Catecholamine doss in μg/kg/min, >1 hour; c) Glasgow Coma Scale scores range from 3-15 (3 minimum,15 normal).

	OLD	NEW
SEPSIS	SIRS + Suspected Infection	**SUSPECTED/DOCUMENTED INFECTION** + **2 or 3 on qSOFA** (HAT): **H**ypotension (SBP ≤100 mmHg) **A**MS (GCS ≤13) **T**achypnea (≥22/min) OR Rise in SOFA score by 2 or more
SEVERE SEPSIS	Sepsis + SBP <90 mmHg or MAP < 65 mmHg lactate > 2.0 mmol/L INR >1.5 or a PTT >60 s Bilirubin >34 µmol/L Urine output <0.5 mL/kg/h for 2 h Creatinine >177 µmol/L Platelets <100 ×109/L SpO2 <90% on room air	———
SEPTIC SHOCK	SEPSIS + HYPOTENSION after adequate fluid resuscitation	**SEPSIS** + **VASOPRESSORS needed for MAP >65 mmHg** + **LACTATE >2 mmol/L** after adequate fluid resuscitation

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.


Patient with suspected infection
qSOFA ≥2? (see A)
No
Sepsis still suspected?
No
Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Yes
Yes
Assess for evidence of organ dysfunction
SOFA ≥2? (see B)
No
Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Yes
Sepsis
Despite adequate fluid resuscitation,
1. vasopressors required to maintain MAP ≥65 mm Hg
AND
2. serum lactate level >2 mmol/L?
No
Yes
Septic shock

Sepsis 3: quali vantaggi ipotizzati

- Predittore di mortalità e di «ICU-LoS»
- Offrono maggiore consistenza per studi epidemiologici e trial clinici (maggiore specificità)
- Facilitano il riconoscimento precoce e il trattamento tempestivo dei malati con sepsi (SOFA) o a rischio di sviluppo di sepsi (qSOFA)

Epidemiologia GIVITI

Sepsi severa 2016 vs Sepsi 2017

953 vs 984 pazienti

Nessuna differenza per età, comorbidità, stato chirurgico, provenienza

Gravità alla ammissione

- SOFA: 6,8 (7_{mediana}) vs 6,6 (6)
- SAPS 2: 42,9 (41) vs 42,9 (41)

Epidemiologia GIVITI

Sepsi severa 2016 vs Sepsi 2017

Degenza pre-T.I.: 7,2 gg. (1) vs 7,0 (1)gg.
Degenza in T.I.: 13,3 (8) vs 12,8 (7)

% mortalità in T.I.: 19,7 vs 19,2
% mortalità in H.: 30,8 vs 33,1
Timing mortalità H: 18,5 (12)$_{gg}$ vs 18,8 (10)

Ipotesi di conclusioni

- I nuovi criteri ci hanno permesso di fare una diagnosi più precoce ammettendo malati con “sepsi” che con i precedenti criteri diagnostici rimanevano in corsia e arrivavano in T.I. più tardi ?
- Abbiamo riocverato malati con “sepsi” e minor “S.O.F.A.” ?
- Quale impatto sulla mortalità?

Epidemiologia GIVITI

Shock settico in ammissione: 3328 vs 3026

Nessuna differenza per età, comorbidità, provenienza, stato chirurgico

Gravità alla ammissione

SOFA : 11,3 (11$_{\text{mediana}}$) vs 11,5 (11)

SAPS 2: 59 (57) vs 59,9 (58)

Epidemiologia GIVITI

Shock settico alla ammissione

Degenza pre T.I.: 6,6 (1) vs 6,1 (1)

Degenza in T.I.: 10,6 (6) vs 10,0 (6)

% mortalità in T.I.: 44,8 vs 45,5

% mortalità in H.: 53,6 vs 53,6

Timing mortalità H: 16,1 (9) vs 15,6 (9)

Ipotesi di conclusioni

- Miglior predizione di mortalità e di lunghezza della degenza ?
- Riduzione della mortalità grazie ad una diagnosi più precoce ?