Riconoscimento precoce e gestione clinica della sepsi urinaria: ruolo dell'intensivista

La Gestione Multidisciplinare delle Infezioni Complicate delle Vie Urinarie nel Terzo Millennio

Ferrara, 5 Maggio 2017

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Paz di aa 71

- ✓ Fumatore (da 50aa!); iperteso; diabetico. Nel 2006 IMA NSTEMI postero-laterale. Nel 2015 IMA NSTEMI con PTCA dell'IVA e Cdx con stent medicati; impiantato PM per blocco AV III°
- ✓ Ictus cerebri 3 mesi prima
- ✓ Seguito dall'urologia per CA uroteliale vescicale ad alto grado non infiltrante
- ✓ Giunge in PS da Cento (19/10) per litiasi ureterale; presenta da 2 gg febbre con brivido (39.5) e dolore addominale.

  PA:130/80 mmHg; FC: 93 bpm; SpO_2 94% (aa); WBC 3.70; PLT 89.000; creat: 3.7 mg/dl. Dopo 2 h: PA: 90/60 mmHg

  EGA: pH 7.44; $PaCO_2$: 20 mmHg; PaO_2 69 mmHg; HCO_3^-:13.6 mmol/l; BE: -10 mmol/l; Lattato: 6.1 mmol/l.
- ✓ Ricovero in Clinica Medica: tachipnoico con SpO2 93% in aa. PA: 100/80, FC 70 bpm.
- ✓ Nefrostomia urgente per rottura di bacinetto renale da calcolo ostruttivo (Radiologia Interventistica).

- ✓ Il paz. rientra in reparto ma successivamente veniamo chiamati in consulenza…..
- ✓ Ricovero in TI: assopito ma risvegliabile; anurico; marezzato arti inferiori; Contrazione degli accessori alla ventilazione; PA 90/50 mmHg; FC 67 bpm (da PM!) SpO_2 93% (FiO_2: 50%); FR: 24; creat: 5.3; PLT 79.000.
- ✓ Grave agitazione psicomotoria, grave acidosi, grave insuff. respiratoria: intubato e ventilato fino al 4/11!
- ✓ Un po' di storia infettivologica (!): Tazocin x 3 gg e poi Merrem e Diflucan

  24/10: Emocolture: Staph. Haem. e C. Albicans

  25/10: BASP: Sten. Maltophilia (sens. Bactrim) e C. Albicans

  28/10: Urinocolture: C. Albicans

  29/10: emocolture: Enterococcus Gallinarum e Sten. Maltophilia

  Procalcitonina: > 100 (19 e 20/10/16); 66.7 (22/10); 33 (24/10)… 2.2 (4/11)
- ✓ Insuff. Renale acuta (5 sedute dialitiche)
- ✓ DIMESSO IN DATA 5/11 IN DISCRETE CONDIZIONI DOPO 16 gg DI TERAPIA INTENSIVA (sospesa la terapia ATB)

Problemi clinici riscontrati

Shock settico di origine urinaria

Insufficienza respiratoria, cardiocircolatoria e renale…

The ACADEMIA study

Kause J et al Resuscitation 2004; 62: 275-82

Incidenza di anomalie fisiologiche antecedenti eventi primari (arresto cardiaco, morte o ricovero di emergenza in ICU).

Studio multi-centrico, prospettico, osservazionale in 3 giorni consecutivi, condotto in 90 ospedali: 69 in UK, 19 in Australia + 2 Nuova Zelanda (ANZ).

The ACADEMIA study

Kause J et al Resuscitation 2004; 62: 275-82

Eventi Primari	UK	ANZ
Morti	255 (52%)	53 (35%)
Arresto cardiaco	115 (24%)	26 (17%)
ICU di emergenza	118 (24%)	71 (47%)

Nel 60% degli eventi primari

almeno una anomalia fisiologica

documentata nelle 24 ore precedenti

The ACADEMIA study

Kause J et al Resuscitation 2004; 62: 275-82

Antecedenti (da -24h a -15')		UK	ANZ	
Dispnea	31%	16,3	14,8	33%
RR <5 o >36		14,7	18,5	
HR < 40 o > 140		11,7	14,8	
SAP < 90 mm Hg		31,1	31,5	
GCS ridotto di 2 punti		26,2	20,4	

Ipotensione, FR + dispnea e GCS ridotto sono i maggiori antecedenti di un evento maggiore… o meglio che diventerà maggiore se non interveniamo!!!

Modified Early Warning Score

	3	2	1	0	1	2	3
PA sist	<70	71-80	81-100	101-199		>200	
FC		<40	41-50	51-100	101-110	111-129	>130
FR		<9		9-14	15-20	21-29	>=30
T °C		<35		35-38.4		>=38.5	
AVPU				Alert	reagisce	reagisce	Non reagisce
					Voce	Pain	Unresponsive

Cut-off >4

Subbe CP et al Q J Med 2001; 94: 521-526

Le alterazioni di maggior entità riguardano la ***frequenza respiratoria***, parametro cruciale nell'identificazione del paziente a rischio

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

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

EDITORIAL

New Definitions for Sepsis and Septic Shock
Continuing Evolution but With Much Still to Be Done

Edward Abraham, MD

Vecchia definizione….

Sepsis : infection + SIRS

Severe sepsis : sepsis + sepsis -induced organ dysfunction or tissue hypoperfusion

Septic shock : sepsis -induced hypotension persisting despite adequate fluid resusciation

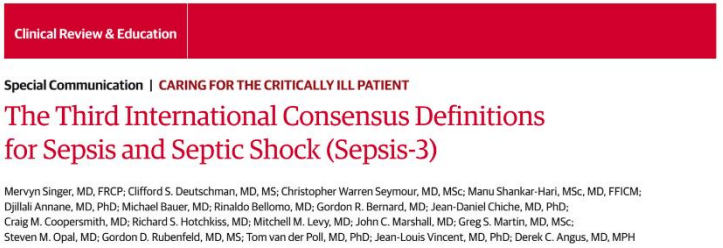
Figure 1. The Systemic Inflammatory Response Syndrome (SIRS).[8]

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

According to the new definitions, sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection clinically characterized by an acute change of 2 points or greater in the SOFA score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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.

OBJECTIVE To evaluate the validity of clinical criteria to identify patients with suspected infection who are at risk of sepsis.

DESIGN, SETTINGS, AND POPULATION Among 1.3 million electronic health record encounters from January 1, 2010, to December 31, 2012, at 12 hospitals in southwestern Pennsylvania, we identified those with suspected infection in whom to compare criteria. Confirmatory analyses were performed in 4 data sets of 706 399 out-of-hospital and hospital encounters at 165 US and non-US hospitals ranging from January 1, 2008, until December 31, 2013.

Editorial page 757

Author Audio Interview at jama.com

Related articles pages 775 and 801

Supplemental content at jama.com

Table 1. Variables for Candidate Sepsis Criteria Among Encounters With Suspected Infection

Systemic Inflammatory Response Syndrome (SIRS) Criteria (Range, 0-4 Criteria)	Sequential [Sepsis-related] Organ Failure Assessment (SOFA) (Range, 0-24 Points)	Logistic Organ Dysfunction System (LODS) (Range, 0-22 Points)[a]	Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Range, 0-3 Points)
Respiratory rate, breaths per minute	Pao_2/Fio_2 ratio	Pao_2/Fio_2 ratio	Respiratory rate, breaths per minute
White blood cell count, 10^9/L	Glasgow Coma Scale score	Glasgow Coma Scale score	Glasgow Coma Scale score
Bands, %	Mean arterial pressure, mm Hg	Systolic blood pressure, mm Hg	Systolic blood pressure, mm Hg
Heart rate, beats per minute	Administration of vasopressors with type/dose/rate of infusion	Heart rate, beats per minute	
Temperature, °C	Serum creatinine, mg/dL, or urine output, mL/d	Serum creatinine, mg/dL	
Arterial carbon dioxide tension, mm Hg	Bilirubin, mg/dL	Bilirubin, mg/dL	
	Platelet count, 10^9/L	Platelet count, 10^9/L	
		White blood cell count, 10^9/L	
		Urine output, L/d	
		Serum urea, mmol/L	
		Prothrombin time, % of standard	

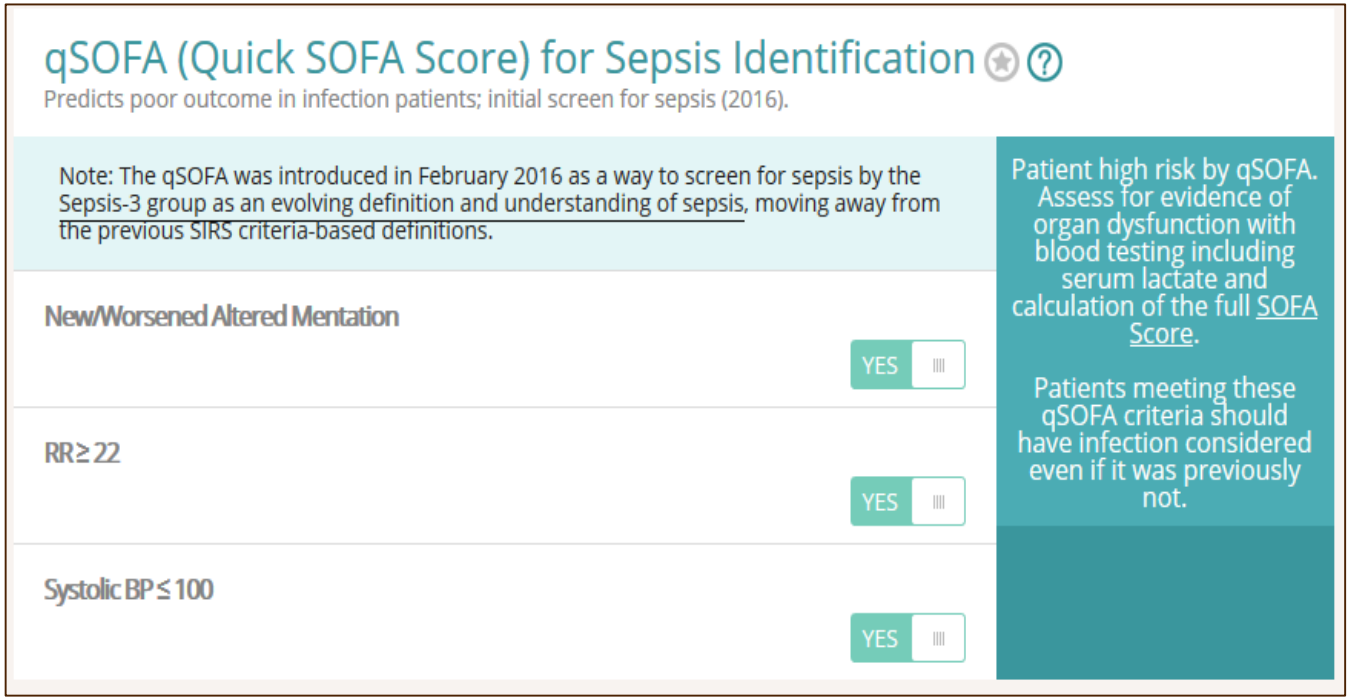
Abbreviation: Fio_2, fraction of inspired oxygen.

[a] Measurement units for LODS variables per original descripti Le Gall et al.[9]

Il vincitore è???

SOFA score

- ✓ Because SOFA is better known and simpler than LODS, the task force recommends using a change in baseline of SOFA > 2.
- ✓ The baseline SOFA score should be assumed to be zero unless the patient is known to have preexisting organ dysfunction



The consensus document also introduces a bedside index, called **qSOFA**, which is proposed to help identify patients with **suspected infection** who are being treated **outside of critical care units** and likely to develop complications of sepsis.

The qSOFA requires at least **2 of the 3 risk variables**

Shock settico

Subset of sepsis in which circulatory, cellular, and metabolic abnormalities are associated with greater risk of mortality than sepsis alone

Criteri clinici

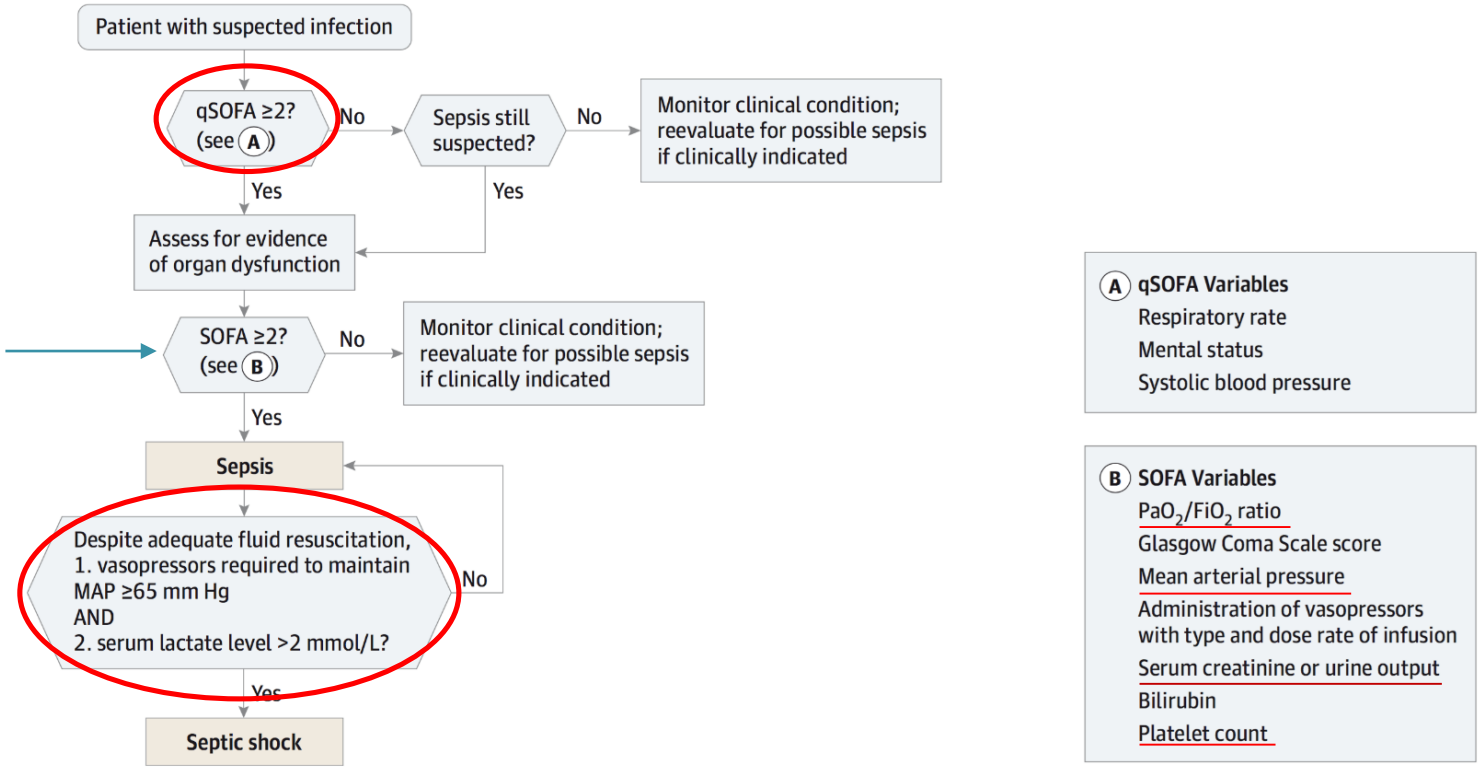
Sepsis with fluid-unresponsive hypotension

Need for vasopressors to maintain mean arterial pressure > 65 mmHg

Serum lactate level > 2 mmol/L

JAMA 2016;315(8):775-787

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



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

PS Cento: PA:130/80 mmHg; FC: 93 bpm; SpO_2 94% (aa); WBC 3.70; ***PLT 89.000****;* ***creat: 3.7 mg/dl****.*

Dopo 2 h: PA: 90/60 mmHg; *EGA: pH 7.44; $PaCO_2$: 20 mmHg;* ***PaO_2 69 mmHg****; HCO_3^-:13.6 mmol/l; BE: -10 mmol/l: Lattato:* ***6.1 mmol/l***

Shock settico: criteri clinici

3 possibilità:

VASOPRESSORE + LAT >2 mmol/L → Mortalità più alta (42,3%)

Rispetto a:

LAT > 2 mmol/L alone or + hypotention,

vasopressore e LAC < 2 mmol/L

JAMA 2016;315(8):775-787

D. ANTIMICROBIAL THERAPY

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 h for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade applies to both conditions).

2. We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage) (strong recommendation, moderate quality of evidence).

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

Come evitare

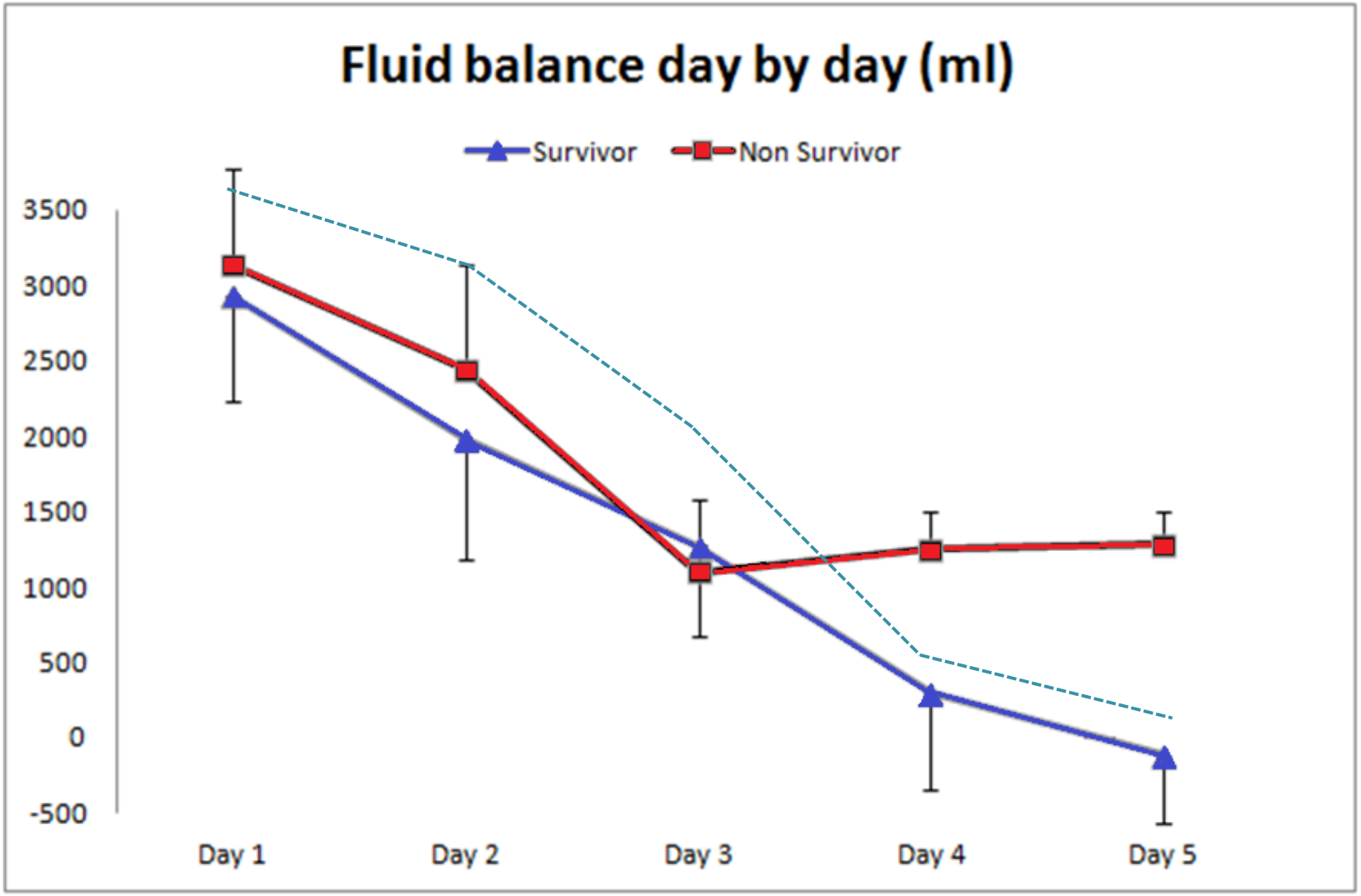
VASOPRESSORE + LAT >2 mmol/L → Mortalità più alta (42,3%)

JAMA 2016;315(8):775-787

Fluidoterapia

TEMPESTIVITÀ E APPROPRIATEZZA DELLA TERAPIA SOMMINISTRATA NELLE PRIME 3 ORE (GOLDEN HOURS) DALLO SVILUPPO DELLA SEPSI DETERMINA L' OUTCOME FINALE

Early Goals-directed therapy: EGDT
(E. Rivers et al. 2001)



Abdominal Sepsis Study (AbSeS), promosso dall'ESICM. Studio di tipo prospettico osservazionale, svolto fra Gennaio e Luglio 2016.

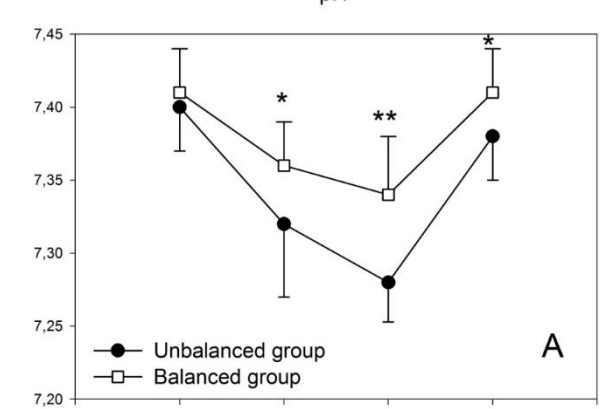
Volta et al. Journal of Inflammation 2013, 10:29
http://www.journal-inflammation.com/content/10/1/29

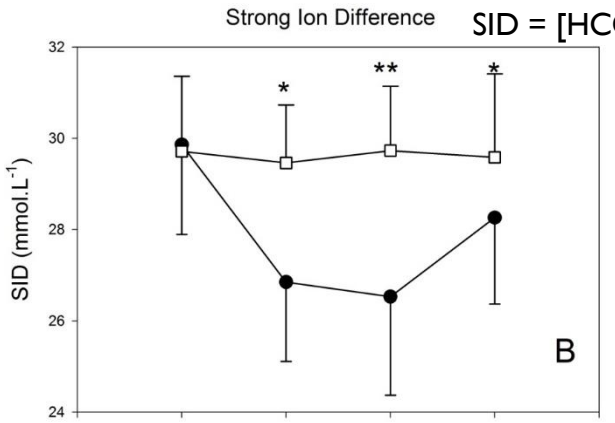
JOURNAL OF INFLAMMATION

RESEARCH Open Access

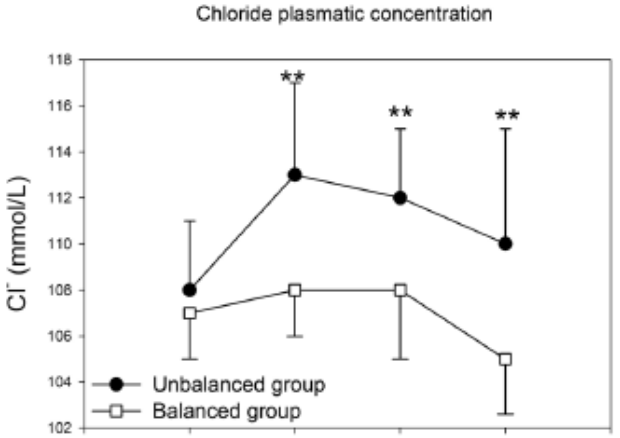
Effects of two different strategies of fluid administration on inflammatory mediators, plasma electrolytes and acid/base disorders in patients undergoing major abdominal surgery: a randomized double blind study

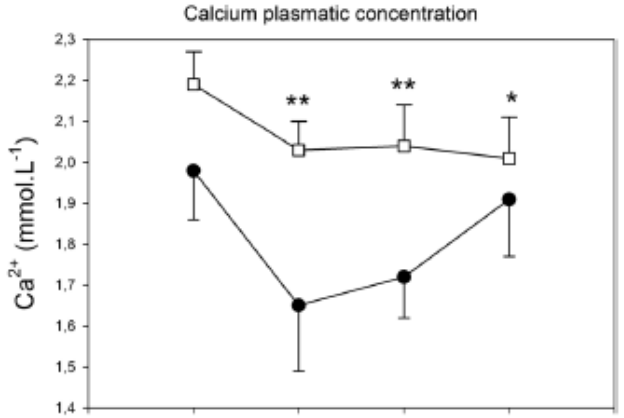
Carlo Alberto Volta[1*], Alessandro Trentini[2], Lucia Farabegoli[1], Maria Cristina Manfrinato[2], Valentina Alvisi[1], Franco Dallocchio[2], Elisabetta Marangoni[1], Raffaele Alvisi[1] and Tiziana Bellini[2]

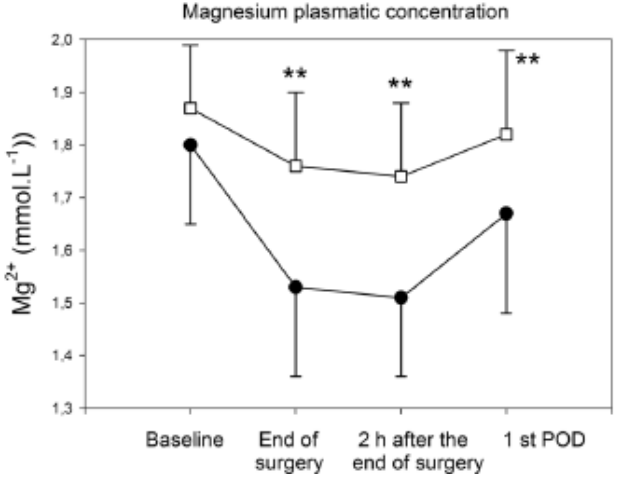




SID = $[HCO_3^-]+[Alb^-]+[Pi^-]$







Acidosi ipercloremica

"Hypercloremic acidosis was associated with higher mortality and postoperative morbidity in patients undergoing open abdominal surgery"

[Kellum; Ann Surg, 2012]

- Acidosi intramucosa (tratto gastrointestinale)
- Prolungamento svuotamento gastrico
- Ileo paralitico e diminuita contrattilità musclatura
- Edema del tratto gastrintestinale e edema anastomotico
- Aumento della pressione addominale (perfusione renale)
- Riduzione flusso spancnico
- vasocostrizione renale
- aumento delle resistenze vascolari renali (approx. 35%)
- diminuzione GFR (approx. 20%), riduzione della diuresi
- soppressione attività della renina (NaCl and not $NaHCO_3$)
- riduzione della pressione arteriosa

PRELIMINARY
COMMUNICATION

Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

Conclusion The implementation of a chloride-restrictive strategy in a tertiary ICU was associated with a significant decrease in the incidence of AKI and use of RRT.

Table 3. Incidence of Acute Kidney Injury Stratified by Risk, Injury, Failure, Loss, and End-Stage (RIFLE) Serum Creatinine Criteria

	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class			
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65 (8.4) [6.4-10.0]	<.001

[a] The control period was from February 18 through August 17, 2008, and the intervention period was from February 18 through August 17, 2009.

In conclusione:

- La valutazione di un paziente potenzialmente critico come quello con urosepsi può essere basata sui parametri vitali. I più importanti da considerare sono presenti in un semplice score, qSOFA (frequenza respiratoria, pressione sistolica e alterazione dello stato mentale)
- Principale obiettivo del trattamento di questi pazienti è il source controll, la terapia antibiotica e la fuidoterapia MOLTO precoce.
- La diagnosi precoce è la chiave per ottenere una diminuzione della mortalità.
- La assenza di precocità non ci da il tempo affinchè gli antibiotici facciano il loro «lavoro».

Results

Among ICU encounters in the validation cohort (n= 7932 with suspected infection, of whom 16% died), the predictive validity for in-hospital mortality was lower for SIRS (AUROC 0,64) and qSOFA (AUROC 0,66) vs SOFA (AUROC 0,74) or LODS (AUROC 0,75)

Among non-ICU encounters in the validation cohort (n=66.522 with suspected infection, of whom 3% died), qSOFA had predictive validity (AUROC 0,81) that was greater than SOFA (AUROC 0,79) and SIRS (AUROC 0,76)