

14. ULUSAL ACİL TIP KONGRESİ

5TH

19-22 Nisan 2018 Kaya Palazzo Golf Resort Otel

INTERCONTINENTAL EMERGENCY MEDICINE CONGRESS
INTERNATIONAL CRITICAL CARE AND EMERGENCY MEDICINE CONGRESS



Sepsis update for the last year

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COI

- Nothing to disclose

Plan of presentation

- A brief discussion of sepsis definition
- Evaluation of guidelines
- Some selected papers from 2017-2018

Sepsis definition; 1993

- **Sepsis:** SIRS + **proven** infection
- **Severe sepsis:** Sepsis + organ dysfunction, hypoperfusion abnormality, or sepsis-induced hypotension
 - (Hypoperfusion abnormalities include lactic acidosis, oliguria, and acute alteration of mental status).
- **Septic shock:** Sepsis + circulatory failure
 - (systolic <90 mmHg, mean arterial pressure <65 mmHg, or a drop in systolic blood pressure of >40 mmHg from baseline after adequate fluid resuscitation).

(Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest. 1992;101(6):1644–55).

Sepsis definition; SSC 2003 guideline:

- Sepsis: *Probable or documented* infection+ systemic manifestations
- Severe Sepsis: Same with 1993 (*SOFA score is used first time to define organ dysfunction*)
- Septic shock: Same with 1993
- Search for a staging system for Sepsis; *PIRO classification*
- 2008- 2012: 2nd and 3rd editions...

(Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. Intensive Care Med. 2003;29(4):530–8)

Table 1. Diagnostic criteria for sepsis

Infection, ^a documented or suspected, and some of the following: ^b
General variables
Fever (core temperature $>38.3^{\circ}\text{C}$)
Hypothermia (core temperature $<36^{\circ}\text{C}$)
Heart rate $>90\text{ min}^{-1}$ or $>2\text{ SD}$ above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance ($>20\text{ mL/kg}$ over 24 hrs)
Hyperglycemia (plasma glucose $>120\text{ mg/dL}$ or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count $>12,000\text{ }\mu\text{L}^{-1}$)
Leukopenia (WBC count $<4000\text{ }\mu\text{L}^{-1}$)
Normal WBC count with $>10\%$ immature forms
Plasma C-reactive protein $>2\text{ SD}$ above the normal value
Plasma procalcitonin $>2\text{ SD}$ above the normal value
Hemodynamic variables
Arterial hypotension ^b (SBP $<90\text{ mm Hg}$, MAP <70 , or an SBP decrease $>40\text{ mm Hg}$ in adults or $<2\text{ SD}$ below normal for age)
$\text{SvO}_2 >70\%$ ^b
Cardiac index $>3.5\text{ L}\cdot\text{min}^{-1}\cdot\text{M}^{-23}$
Organ dysfunction variables
Arterial hypoxemia ($\text{PaO}_2/\text{FiO}_2 <300$)
Acute oliguria (urine output $<0.5\text{ mL}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ or 45 mmol/L for at least 2 hrs)
Creatinine increase $>0.5\text{ mg/dL}$
Coagulation abnormalities (INR >1.5 or aPTT $>60\text{ secs}$)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count $<100,000\text{ }\mu\text{L}^{-1}$)
Hyperbilirubinemia (plasma total bilirubin $>4\text{ mg/dL}$ or 70 mmol/L)
Tissue perfusion variables
Hyperlactatemia ($>1\text{ mmol/L}$)
Decreased capillary refill or mottling

WBC, white blood cell; SBP, systolic blood pressure; MAP, mean arterial blood pressure; SvO_2 , mixed venous oxygen saturation; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

^aInfection defined as a pathologic process induced by a microorganism; ^b SvO_2 sat $>70\%$ is normal in children (normally, 75–80%), and CI 3.5–5.5 is normal in children; therefore, NEITHER should be used as signs of sepsis in newborns or children; ^cdiagnostic criteria for sepsis in the pediatric population are signs and symptoms of inflammation plus infection with hyper- or hypothermia (rectal temperature >38.5 or $<35^{\circ}\text{C}$), tachycardia (may be absent in hypothermic patients), and at least one of the following indications of altered organ function: altered mental status, hypoxemia, increased serum lactate level, or bounding pulses.

(Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. Intensive Care Med. 2003;29(4):530–8)

2016; The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

- Simple infection with signs and symptoms of the inflammatory response but without organ dysfunction, formerly defined as sepsis, is now defined as *infection*.
- *Sepsis*: Suspected/documentated infection + evidence of organ dysfunction (SOFA score ≥ 2) (*Previous severe sepsis*).
- *Septic Shock*: Infection + hypotension (MAP < 65 mmHg or systolic < 90 mmHg) and are receiving vasopressors and with a lactate > 2 mmol/L.
- *SIRS*: No longer used...

(The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Singer M et al. JAMA. 2016)

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.

(The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Singer M et al. JAMA. 2016)

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥ 22 /min

Altered mentation

Systolic blood pressure ≤ 100 mm Hg

- Simple initial bedside criteria to identify adult patients with suspected infection who are likely to have poor outcomes...
- Do not require laboratory tests and can be assessed quickly and repeatedly.

(The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Singer M et al. JAMA. 2016)

Box 2 Three-hour and 6-hour sepsis bundles

Within 3 hours of presentation:

- ▶ Measure lactate
- ▶ Obtain blood cultures
- ▶ Bolus 30 mL/kg crystalloid for hypotension of lactate ≥ 4 mmol/L

Within 6 hours of presentation:

- ▶ If persistent hypotension (mean arterial pressure ≤ 65 mm Hg) despite adequate volume resuscitation, consider addition of vasopressors
- ▶ Frequently re-assess volume status and tissue perfusion for those with persistent hypotension and/or initial lactate ≥ 4 mmol/L
- ▶ Normalization of lactate

- The 2016 guideline update continues to emphasize initial resuscitation with a 30 mL/kg crystalloid bolus within the first 3 hours of presentation.
- After this initial bolus, resuscitation should be guided by either a 'repeat focused exam including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings' or two of the following: CVP, superior vena cava oxygenation saturation (ScvO₂), bedside cardiac ultrasound for dynamic assessment of fluid responsiveness.

- Recommendations for **vasoactive medications** are similar to the 2012 guidelines.
- The 2016 guidelines recommend administering **empiric broad-spectrum antimicrobials** that cover all likely pathogens, including bacteria and potentially viruses/fungi (depending on the risk factors of the patient).

- **Corticosteroids** should empirically be administered (hydrocortisone 200 mg intravenous daily in divided bolus doses) in patients in septic shock **only if** vasopressor therapy and fluid resuscitation fail to achieve hemodynamic stability.
- **No clear consensus** on the optimal initiation timing and total duration of steroid treatment

- No significant changes to use of **blood products**.
- **Mechanical ventilation:** prone position for patient with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 150 mm Hg (previously recommended $\text{PaO}_2/\text{FiO}_2 \leq 100$ mm Hg).

- Sedation, glucose control, renal replacement therapy and bicarbonate therapy remain essentially unchanged from 2012.
- All patients should receive DVT prophylaxis.

- Early enteral nutrition should be given in patients with sepsis or septic shock.
- The 2016 guidelines include **a new recommendation** to avoid routine monitoring of gastric residuals, instead measuring them only in patients who demonstrate feeding intolerance or who are considered to be at high risk of aspiration.
- Also **new** to the 2016 guidelines is a suggestion to use prokinetic agents and place feeding tubes in a postpyloric position in patients with feeding intolerance.



The influence of a change in septic shock definitions on intensive care epidemiology and outcome: comparison of sepsis-2 and sepsis-3 definitions

Rob G. H. Driessen, Marcel C. G. van de Poll, Marianne F. Mol, Walther N. K. A. van Mook & Ronny M. Schnabel

- Study population; older **ICU** patients with a high malignancy rate.
- Patients classified according to **Sepsis-3 criteria** **had a higher ICU mortality** than patients meeting sepsis-2 criteria.
- Lactate levels ≥ 6 mmol/L were associated with increased mortality, but lower levels also had a high mortality rate...

ORIGINAL ARTICLE

Time to Treatment and Mortality
during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D.,
Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D.,
Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H.,
Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

- More rapid complementation of 3-hour bundle of sepsis care and rapid antibiotherapy, but not rapid completion of initial **fluid bolus**, were associated with lower in-hospital mortality.
- Smaller and non-teaching hospitals had a higher rate of bundle completion within 3 hours!!!

RESEARCH

Open Access



Performance of the quick Sequential (sepsis-related) Organ Failure Assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis

Jae-Uk Song^{1†}, Cheol Kyung Sin^{2†}, Hye Kyeong Park³, Sung Ryul Shim⁴ and Jonghoo Lee^{5*}

- Non-ICU setting, qSOFA scores recorded **mostly in ED**.
- No difference for predicting in-hospital mortality and ICU admission
- **qSOFA is better than SIRS** criteria for early detection of acute organ dysfunction.
- qSOFA; high specificity but poor sensitivity for predicting in-hospital mortality, acute organ dysfunction and ICU admission
- SIRS criteria; high sensitivity but insufficient specificity for in-hospital mortality.

ORIGINAL RESEARCH

Open Access



Poor performance of quick-SOFA (qSOFA) score in predicting severe sepsis and mortality – a prospective study of patients admitted with infection to the emergency department

Åsa Askim^{1,3,9†}, Florentin Moser^{2†}, Lise T. Gustad^{3,8,9}, Helga Stene¹⁰, Maren Gundersen¹⁰, Bjørn Olav Åsvold^{4,6,9}, Jostein Dale², Lars Petter Bjørnsen², Jan Kristian Damås^{5,7,9} and Erik Solligård^{1,2,3,9}

- Patients aged >16 y.o. admitted to **ED** with symptoms and signs of **infection**
- All clinical data were measured upon arrival to the ED
- **qSOFA** had **poor sensitivity** for detecting severe sepsis, 7-day and 30-day mortality in patients admitted with infection to an ED
- SIRS criteria were better, but not perfect.

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

Yonathan Freund, MD, PhD; Najla Lemachatti, MD; Evguenia Krastinova, MD, PhD; Marie Van Laer, MD; Yann-Erick Claessens, MD, PhD; Aurélie Avondo, MD; Céline Occelli, 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

- Adult patients admitted to ED with suspected infection, 30 EDs
- qSOFA was better from SIRS and Sepsis-3 (=SOFA) criteria for predicting in-hospital death, ICU admission and ICU stay>72 hours.
- Lactate level>2 mmol/L added no value to qSOFA.

ORIGINAL ARTICLE

Quick Sepsis-related Organ Failure Assessment, Systemic Inflammatory Response Syndrome, and Early Warning Scores for Detecting Clinical Deterioration in Infected Patients outside the Intensive Care Unit

Matthew M. Churpek^{1,2}, Ashley Snyder¹, Xuan Han¹, Sarah Sokol³, Natasha Pettit³, Michael D. Howell^{1,2}, and Dana P. Edelson^{1,2}

¹Department of Medicine, ²Center for Healthcare Delivery Science and Innovation, and ³Department of Pharmacy, University of Chicago, Chicago, Illinois

- All patients admitted to **ED or hospital wards** with **suspected infection**
- **qSOFA** was more accurate **than SIRS** for predicting in-hospital mortality and ICU transfer in both ward and ED patients
- **NEWS** (National Early Warning Score) was better from both of qSOFA and SIRS for predicting adverse outcomes in both ward and ED patients

*Am J Respir Crit Care Med. 2017 Apr 1;195(7):906-911.

Quick SOFA Scores Predict Mortality in Adult Emergency Department Patients With and Without Suspected Infection



Adam J. Singer, MD*; Jennifer Ng, MD; Henry C. Thode, Jr, PhD; Rory Spiegel, MD; Scott Weingart, MD

*Corresponding Author. E-mail: adam.singer@stonybrook.edu.

- **qSOFA** scores were associated with inpatient mortality, admission, ICU admission, and hospital length of stay in adult **ED patients** likely to be admitted both **with and without suspected infection** and may be **useful** in predicting outcomes.

*Annals of Emergency Medicine Volume 69, no. 4 : April 2017

- The data about the selection SIRS or qSOFA in ED to predict septic shock is confusing...

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD

- Sepsis + hypotension, adults
- Limited resources (Africa), lack of mechanical ventilation
- Patients are mostly young, malnourished and HIV+
- Early resuscitation with IV fluids and vasopressors increased in-hospital mortality!
- Rapid IV fluid may predispose to **pulmonary edema** and respiratory failure, conferring high mortality in the absence of ventilator support...

Higher Fluid Balance Increases the Risk of Death From Sepsis: Results From a Large International Audit*

Yasser Sakr, MD, PhD¹; Paolo Nahuel Rubatto Birri, MD¹; Katarzyna Kotfis, MD, PhD²; Rahul Nanchal, MD³; Bhagyesh Shah, MBBS, DA, IDCCM⁴; Stefan Kluge, MD⁵; Mary E. Schroeder, MD⁶; John C. Marshall, MD⁷; Jean-Louis Vincent, MD, PhD, FCCM⁸; on behalf of the Intensive Care Over Nations Investigators

- Multicenter, **ICU** patients.
- The cumulative fluid balances in the first 24 hours, 3 days, and 7 days of the ICU stay were calculated.
- The cumulative fluid intake was similar in survivors and nonsurvivors. However, fluid output was significantly less in nonsurvivors leading to a **more positive fluid balance** in these patients.

* Crit Care Med. 2017 Mar;45(3):386-394

The Use of Ultrasound in Caring for Patients with Sepsis



Laurent Guérin, MD^{a,b},
Antoine Vieillard-Baron, MD, PhD^{a,b,c,*}

KEYWORDS

- Critical care echocardiography • Hemodynamic monitoring • Septic shock
- Septic cardiomyopathy

KEY POINTS

- Echocardiography is essential for hemodynamic management of patients with septic shock.
- Echocardiography provides an independent evaluation of every mechanism involved in sepsis: hypovolemia, right and left cardiac dysfunction, and persistent vasoplegia.
- Septic cardiomyopathy is a constant phenomenon during septic shock, but may be masked by profound vasoplegia. Repeated echocardiography could unmask left ventricular (LV) systolic failure caused by sepsis after correction of LV afterload by norepinephrine.
- Dobutamine is the first-line therapy in septic cardiomyopathy when LV systolic dysfunction is associated with clinical and biochemical markers of uncontrolled shock.
- Fluid responsiveness can be predicted by respiratory variation in the collapsibility index of the superior vena cava in patients fully adapted to mechanical ventilation by transesophageal echocardiography.



BET 3: In septic patients requiring fluid resuscitation can the bedside lung ultrasound be used to assess the pulmonary fluid status?

Alain Judith and Maude St-Onge

Emerg Med J 2017 34: 419-422
doi: 10.1136/emmermed-2017-206808.3

Clinical bottom line

In patients presenting to the emergency department with severe sepsis requiring fluid resuscitation the use of lung ultrasound for determining the pulmonary fluid status remains unknown. The current data supporting this practice is missing. A coming prospective observational study will better document this clinical question by measuring the effect of fluid bolus with lung ultrasound in children diagnosed with sepsis.

SEVERE SEPSIS BUNDLES
ENDPOINTS/TARGETS FOR RESUSCITATION
3 & 6 HOUR TARGETS Rev. 9/8/15

START (Time) _____ (ED/Sepsis triage time or Inpatient time symptoms evident)
 First vital sign (HR) is usually a reliable time when pt. entered facility
 Search for source, source control, antibiotics, volume resuscitation

3-Hour Goal Time _____

6-Hour Goal Time _____

Resuscitation Bundle: 3-Hour Bundle Goal
To be accomplished as soon as possible but at least within 3 hours

Time Met	Indicator	Initials
	Serum lactate: Measured	
	Blood cultures: Obtained prior to antibiotic administration.	
	Antibiotics: Broad-spectrum antibiotics administered within 3 hrs. ED or within 1 hr. ICU admit	
	Fluids (for any hypotension or lactate ≥ 4 mmol/L): Deliver an initial minimum of 30 mL/kg of crystalloid.	

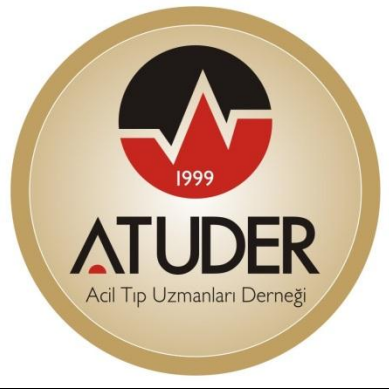
Resuscitation Bundle: 6-Hour Bundle Goal
To be accomplished as soon as possible but at least within 6 hours

Time Met	Indicator	Initials
	Vasopressors For hypotension not responding to initial fluid resuscitation (30 mL/kg within 3 hrs.) to maintain mean arterial pressure (MAP) ≥ 65 and SBP >90 mm Hg.	
	Re-measure lactate if initial lactate elevated (> 2 mmol/L)	
	For persistent hypotension after fluids (30 mL/kg) OR lactate ≥ 4 mmol/L reassess volume status and tissue perfusion by using one of the following strategies	
	Strategy A: Repeat focused exam (after initial fluid resuscitation) by licensed independent practitioner (MD/Nurse Practitioner) including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings. • Provider to use Sepsis PowerNote Template for structured documentation	
	OR	
	Strategy B: Reassessment using two of the following	
	Measure CVP (goal 8-12 mmHg / fluids)	
	Measure ScvO₂ (goal $\geq 70\%$ / blood if HCT < 30 or inotropes if appropriate)	
	Bedside cardiovascular ultrasound (echo)	
	Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge	

*Refer to Surviving Sepsis Guidelines for more complete information

Summary...

- Sepsis-3 criteria are better to predict high-risk patients in ICU environment
- The data about the selection SIRS, SOFA or qSOFA in ED to predict septic shock and poor outcome is confusing...
- There is a lack of evidence about using bedside lung ultrasound for guiding fluid therapy in sepsis patients.



EPAT

Emergency Physicians Association of Turkey

THANKS...



SonoSchool

