Sepsis 3.0

Dr. Halit Aytar

Ankara Keçiören Eğitim ve Araştırma Hastanesi

12. ULUSAL ACİL TIP KONGRESİ

SUENO DELUXE OTEL
ANTALYA
19-22 MAYIS 2016

ATUDER
1999
Acil Tıp Uzmanları Derneği

12.ULUSAL ACİLTIP KONGRESİ

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Sepsis 3.0 *Anahtar Kavramlar*

- Enfeksiyon nedenli ölümlerde #1
  - Erken teşhis, uygun tedavi
- Non-koroner YBÜ ölüm nedenlerinde #1
  - Sepsis %30-50 mortalite
- Enfeksiyon / Sepsis
  - Bozulmuş konak yanıtı
  - Organ disfonksiyonu

Sepsis 3.0 *Anahtar Kavramlar*

- Sepsis kaynaklı organ disfonksiyonu gizli olabilir.
  - Enfeksiyon saptanması!
  - Enfeksiyon saptanmamış olması!

- Açıklanamayan organ disfonksiyonu
  - Altta yatan enfeksiyon?

Sepsis 3.0 *Anahtar Kavramlar*

- Bozulmuş sistemik konak yanıtı olmaksızın bölgesel enfeksiyonlar kaynaklı organ disfonksiyonu gelişebilir.

Chest

Volume 101, Issue 6, June 1992, Pages 1644–1655

ACCP/SCCM Consensus Conference

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

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

Sepsis Sınıflanması (1991 Konsensusu)

- SIRS
  - A >38 / <36
  - Kalp Hızı >90/dk
  - Solunum sayısı >20/dk / PCO_2<32
  - WBC >12.000/mm^3 / <4.000/mm^3 / Bant >10%
- Sepsis = SIRS + Enfeksiyon
- Ciddi Sepsis: Sepsis + Organ Disfonksiyonu, Hipoperfüzyon / Hipotansiyon
- Septik Şok : Ciddi Sepsis + Sıvı Tedavisine yanıtsızlık

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

- Tek merkezli randomize çalışma
- Mart 1997 – Mart 2000 arasında başvuran ağır sepsis ve septik şoktaki hastalar
  - (SIRS kriterlerini karşılayan + sıvı puşesine rağmen SKB < 90 mmHg veya laktat > 4mmol/L)

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

- Gruplar:
  - 1. Erken hedefe yönelik tedavi grubu: Acil serviste en az 6 saatlik hedefe yönelik tedavi:
    - CVP'yi 8-12 arasında tutacak şekilde 30'ar dakika arayla 500 cc sıvı bolusu
    - İdrar çıkışı > 0.5 cc/kg/s
    - MAP > 65 üzerinde tutacak şekilde vazopressör tedavi
    - SVO2 < %70 ise Htc'i %30'un üzerinde tutacak şekilde ES replasmanı
    - CVP, MAP ve Htc düzeltildikten sonra SVO2<%70 ise dobutamin infuzyonu
  - 2. Standart tedavi grubu (kontrol): Acil serviste santral venöz kateterizasyon ve klinisyenin yaklaşımına göre tedavi (antibiyotik uygulamadan önce kültürlerin alınması, uygun hemodinamik destek, YBÜ konsültasyonu)

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

TABLE 3. KAPLAN–MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	[illegible]	[illegible]	0.46 (0.21–1.03)	0.06
Patients with septic shock			0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (21.0)	12/117 (10.3)	—	0.02
Multiorgan failure	26/119 (21.8)	19/117 (16.2)	—	0.27

*CI denotes confidence interval. Dashes indicate that the relative risk is not applicable.

†Percentages were calculated by the Kaplan–Meier product-limit method.

‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

Special Articles

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

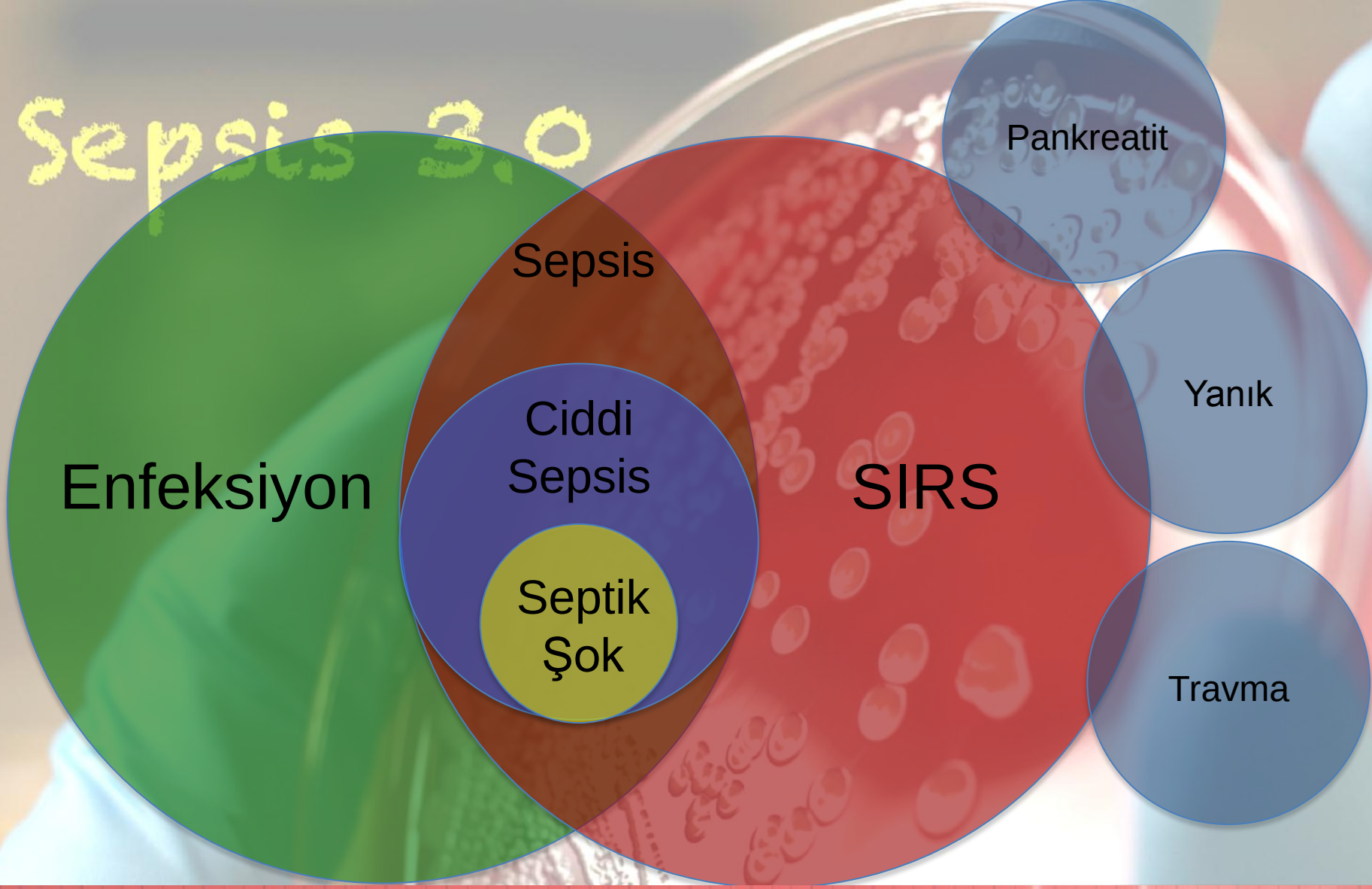
Mitchell M. Levy, MD, FCCP; Mitchell P. Fink, MD, FCCP; John C. Marshall, MD; Edward Abraham, MD; Derek Angus, MD, MPH, FCCP; Deborah Cook, MD, FCCP; Jonathan Cohen, MD; Steven M. Opal, MD; Jean-Louis Vincent, MD, FCCP, PhD; Graham Ramsay, MD; For the International Sepsis Definitions Conference

- Tanı kriterleri listesi genişledi
- Alternatif tanımlar geliştirmek için yeterli kanıta dayalı çalışma yok

Sepsis 3.0 *Neden Yeni Tanımlama*

- Basit enfeksiyon? / Sepsis?

- Enfeksiyon
  - organ disfonksiyonu veya ölüm olmadan tanımak


Sepsis 3.0
Enfeksiyon
Sepsis
Ciddi Sepsis
Septik Şok
SIRS
Pankreatit
Yanık
Travma

The NEW ENGLAND JOURNAL of MEDICINE

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.

- Avusturalya ve Yeni Zellandada
- 172 YBÜ
- 109,663 Hasta
- Retrospektif

Sepsis 3.0

Ciddi Sepsis

SIRS +	SIRS -
87.9%	12.1%

8 Hastanın 1 tanesi atlanıyor

Sepsis 3.0

Sonuç olarak
≥2 SIRS Kriteri
Sepsis için
Sensitivitesi ve
spesifisitesi
düşük

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

ProCESS

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

- Birleşmiş Devletler
- 3 grup
  - EHYT
  - Protokole dayalı standart tedavi
  - Olağan tedavi

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

ProCESS

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

RESULTS

We enrolled 1341 patients, of whom 439 were randomly assigned to protocol-based EGDT, 446 to protocol-based standard therapy, and 456 to usual care. Resuscitation strategies differed significantly with respect to the monitoring of central venous pressure and oxygen and the use of intravenous fluids, vasopressors, inotropes, and blood transfusions. By 60 days, there were 92 deaths in the protocol-based EGDT group (21.0%), 81 in the protocol-based standard-therapy group (18.2%), and 86 in the usual-care group (18.9%) (relative risk with protocol-based therapy vs. usual care, 1.04; 95% confidence interval [CI], 0.82 to 1.31; P=0.83; relative risk with protocol-based EGDT vs. protocol-based standard therapy, 1.15; 95% CI, 0.88 to 1.51; P=0.31). There were no significant differences in 90-day mortality, 1-year mortality, or the need for organ support.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

ARISE

- Avustralya ve Yeni Zellanda
- 2 grup
  - Protokole dayalı EHYT
  - Olağan tedavi

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

ARISE

RESULTS

Of the 1600 enrolled patients, 796 were assigned to the EGDT group and 804 to the usual-care group. Primary outcome data were available for more than 99% of the patients. Patients in the EGDT group received a larger mean (±SD) volume of intravenous fluids in the first 6 hours after randomization than did those in the usual-care group (1964±1415 ml vs. 1713±1401 ml) and were more likely to receive vasopressor infusions (66.6% vs. 57.8%), red-cell transfusions (13.6% vs. 7.0%), and dobutamine (15.4% vs. 2.6%) (P<0.001 for all comparisons). At 90 days after randomization, 147 deaths had occurred in the EGDT group and 150 had occurred in the usual-care group, for rates of death of 18.6% and 18.8%, respectively (absolute risk difference with EGDT vs. usual care, −0.3 percentage points; 95% confidence interval, −4.1 to 3.6; P=0.90). There was no significant difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

ProMISe

- İngiltere
- 2 grup
  - Protokole dayalı EHYT
  - Olağan tedavi

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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ProMISe

RESULTS

We enrolled 1260 patients, with 630 assigned to EGDT and 630 to usual care. By 90 days, 184 of 623 patients (29.5%) in the EGDT group and 181 of 620 patients (29.2%) in the usual-care group had died (relative risk in the EGDT group, 1.01; 95% confidence interval [CI], 0.85 to 1.20; P=0.90), for an absolute risk reduction in the EGDT group of −0.3 percentage points (95% CI, −5.4 to 4.7). Increased treatment intensity in the EGDT group was indicated by increased use of intravenous fluids, vasoactive drugs, and red-cell transfusions and reflected by significantly worse organ-failure scores, more days receiving advanced cardiovascular support, and longer stays in the intensive care unit. There were no significant differences in any other secondary outcomes, including health-related quality of life, or in rates of serious adverse events. On average, EGDT increased costs, and the probability that it was cost-effective was below 20%.

Sepsis Hasta Yönetiminde Esneklik

Hastaların
-Sıvı desteği
-Uygun antibiyotik
- Destek Tedavisi (erken kritik bakım ve resüsitasyon)

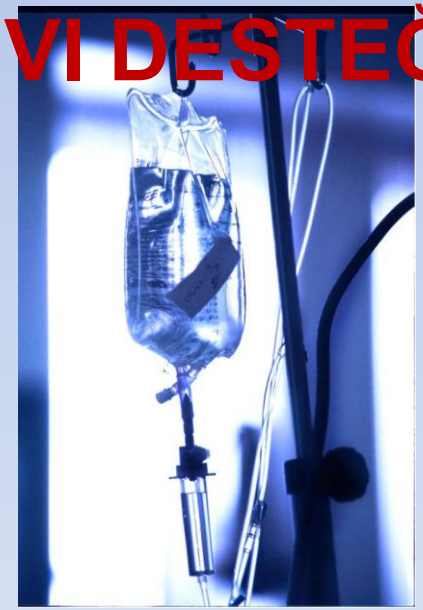
İHTİYACI VARKEN

-CVP
-SCVO2
monitorizasyonuna ihtiyacı YOK

ERKEN

TANI

SIVI DESTEĞİ



ANTİBİYOTİK

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JAMA The Journal of the American Medical Association

February 23, 2016, Vol 315, No. 8 >

Special Communication | February 23, 2016

CARING FOR THE CRITICALLY ILL PATIENT

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

Mervyn Singer, MD, FRCP[1]; Clifford S. Deutschman, MD, MS[2]; Christopher Warren Seymour, MD, MSc[3]; Manu Shankar-Hari, MSc, MD, FFICM[4]; Djillali Annane, MD, PhD[5]; Michael Bauer, MD[6]; Rinaldo Bellomo, MD[7]; Gordon R. Bernard, MD[8]; Jean-Daniel Chiche, MD, PhD[9]; Craig M. Coopersmith, MD[10]; Richard S. Hotchkiss, MD[11]; Mitchell M. Levy, MD[12]; John C. Marshall, MD[13]; Greg S. Martin, MD, MSc[14]; Steven M. Opal, MD[12]; Gordon D. Rubenfeld, MD, MS[15,16]; Tom van der Poll, MD, PhD[17]; Jean-Louis Vincent, MD, PhD[18]; Derek C. Angus, MD, MPH[19,20]

Sepsis 3.0

- Sepsis; Enfeksiyona karşı geliştirilen düzensiz bir konak yanıtı nedeniyle hayatı tehdit eden organ disfonksiyonu olarak tanımlanır.
- Organ disfonksiyonu ➔ SOFA skoru ≥2
- Septik Şok; dirençli hipovolemi veya hipovoleminin olmadığı durumlarda MAP > 65 mmHg olması için vazopressör desteği gerektiren ve laktat seviyesi > 2mmol/L olan hastalar

Sepsis 3.0

SOFA Skoru

SOFA skoru	0	1	2	3	4
Solunum PaO_2/FiO_2	>400	≤400	≤300	≤200	≤100
Koagulasyon Trombosit $10^3/mm^3$	>150	≤150	≤100	≤50	≤20
Karaciğer Billurubin mg/dl Billurubin mol/l	 <1.2 <20	 1.2-1.9 20-32	 2.0-5.9 33-101	 6.0-11.9 102-204	 >12 >204
Kardiovasküler Hipotansiyon	Yok	MAP<70	Dopa≤5 Dobu	Dopa>5 Epi≤0.1 Nor≤0.1	Dopa>15 Epi>0.1 Nor>0.1
Merkezi sinir sistemi Glasgow koma skoru	15	13-14	10-12	6-9	<6
Renal Kreatinin (mg/dl) Kreatinin (µmol/l) İdrar çıkışı (ml/gün)	 <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

Sepsis 3.0

qSOFA

- **qSOFA**
  - Hipotansiyon ≤ 100 mmHg 1 puan
  - Bilinç bozukluğu GKS ≤ 13 1 puan
  - Takipne ≥22/dk 1 puan

Sepsis 3.0

- Hastaların %73-90'ında qSOFA<2
  - mortalite %1-24 olarak belirlenmiş.
- ***YBÜ'de de SIRS'a göre hastane içi mortaliteyi öngördürmede daha başarılı olarak belirlenmiş.***
- YBÜ dışındaki grupta hastane içi mortalite; qSOFA>2 olan hastalarda qSOFA<2 olanlara göre3-14 kat daha fazla olarak izlenmiş.

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

RESULTS In the primary cohort, 148 907 encounters had suspected infection (n = 74 453 derivation; n = 74 454 validation), of whom 6347 (4%) died. Among ICU encounters in the validation cohort (n = 7932 with suspected infection, of whom 1289 [16%] died), the predictive validity for in-hospital mortality was lower for SIRS (AUROC = 0.64; 95% CI, 0.62-0.66) and qSOFA (AUROC = 0.66; 95% CI, 0.64-0.68) vs SOFA (AUROC = 0.74; 95% CI, 0.73-0.76; $P < .001$ for both) or LODS (AUROC = 0.75; 95% CI, 0.73-0.76; $P < .001$ for both). Among non-ICU encounters in the validation cohort (n = 66 522 with suspected infection, of whom 1886 [3%] died), qSOFA had predictive validity (AUROC = 0.81; 95% CI, 0.80-0.82) that was greater than SOFA (AUROC = 0.79; 95% CI, 0.78-0.80; $P < .001$) and SIRS (AUROC = 0.76; 95% CI, 0.75-0.77; $P < .001$). Relative to qSOFA scores lower than 2, encounters with qSOFA scores of 2 or higher had a 3- to 14-fold increase in hospital mortality across baseline risk deciles. Findings were similar in external data sets and for the secondary outcome.

Sepsis 3.0

- Sepsis
  - Şüpheli/Tanılı infeksiyon

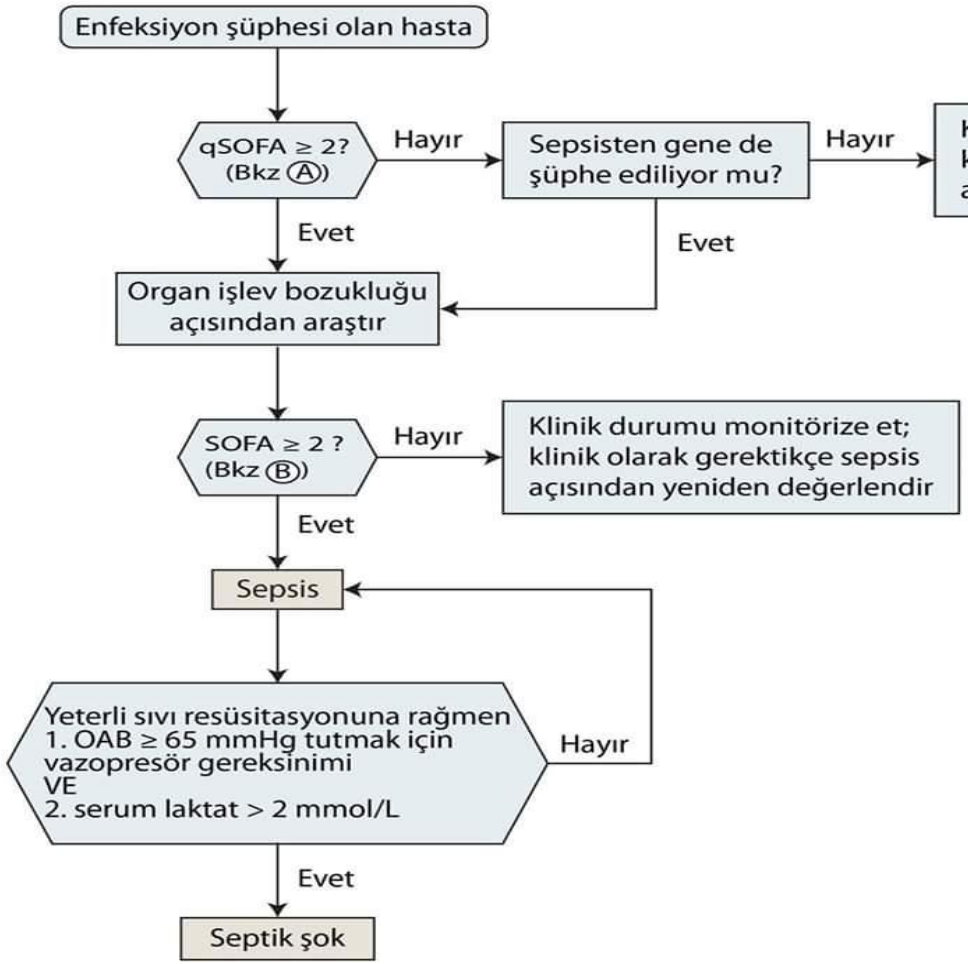
    +

  - >2 qSOFA kriteri:
- Ciddi Sepsis Tanımı kaldırıldı.

Sepsis 3.0

- Septik Şok
  - Sepsis
    +
  - MAP>65 mmHg için Vazopressör ihtiyacı
    +
  - Laktat > 2mmol/L

Sepsis 3.0



Ⓐ qSOFA değişkenleri
- Soluk sayısı
- Şuur durumu
- Sistolik kan basıncı

Ⓑ Sofa değişkenleri
- PaO2/FiO2 oranı
- Glasgow koma skoru
- Ortalama arter basıncı
- Vazopresör uygulaması, tip ve uygulama dozu ile birlikte
- Serum kreatinin düzeyi veya idrar miktarı
- Bilirübin
- Trombosit sayısı

- Teşekkürler