Enfeksiyon Hastalıklarının Tedavi Sürecinde Steroid Kullanımı

SEPSİS

Dr. Adalet ALTUNSOY
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji
SBÜ Ankara Bilkent Şehir Hastanesi

KLİMİK, 15.03.2023

Sunum Planı

- Giriş
- Sepsiste adrenal yetmezlik
- Sepsiste kortikosteroid kullanımı ile ilgili literatürün gözden geçirilmesi
- Rehberler ne diyor
- Sonuçlar

Sepsis

- Yaygın
- Mortalite oranı yüksek (%35-45)
- Hastanede yatış süresi uzun
- Pahalı

- **Tedavinin hızı ve uygunluğu yaşamsal**
- **Rehberler eşliğinde tedavi**
- **Standardize edilmiş tedavi**

Sepsis

- Klinik bir sendrom
- Konağın enfeksiyona karşı disregüle yanıtı sonucu oluşur ve hayatı tehdit eder;
  - Fizyolojik,
  - Biyolojik,
  - Biyokimyasal bozukluklarla gider
- Sepsis ve septik şok nedeni ile her yıl dünyada milyonlarca insan etkilenmektedir

Sepsis Rehberleri

2002

2002 SSC initated between ESICM, SCCM & ISF

Declaration Barcelona

2004

2004 Adult Guidelines

2005 working with IHI to create first set of performance improvement bundles.
2008 SSC independent of industry funding and ISF no longer a partner

2006

2010

2010 Data published on 15,000 patients from SSC database demonstrating 20% RRR for death.
2013 sepsis metrics adopted by New York state, USA.

2008 Adult Guidelines

2012

2012 Adult Guidelines

2014 Data published on 30,000 patients from SSC database demonstrating 25% RRR for death.

2014

2018

2017 Data from New York state published on 100,000 patients with 15.2% RRR for death.
2018 Hour-one bundle released.

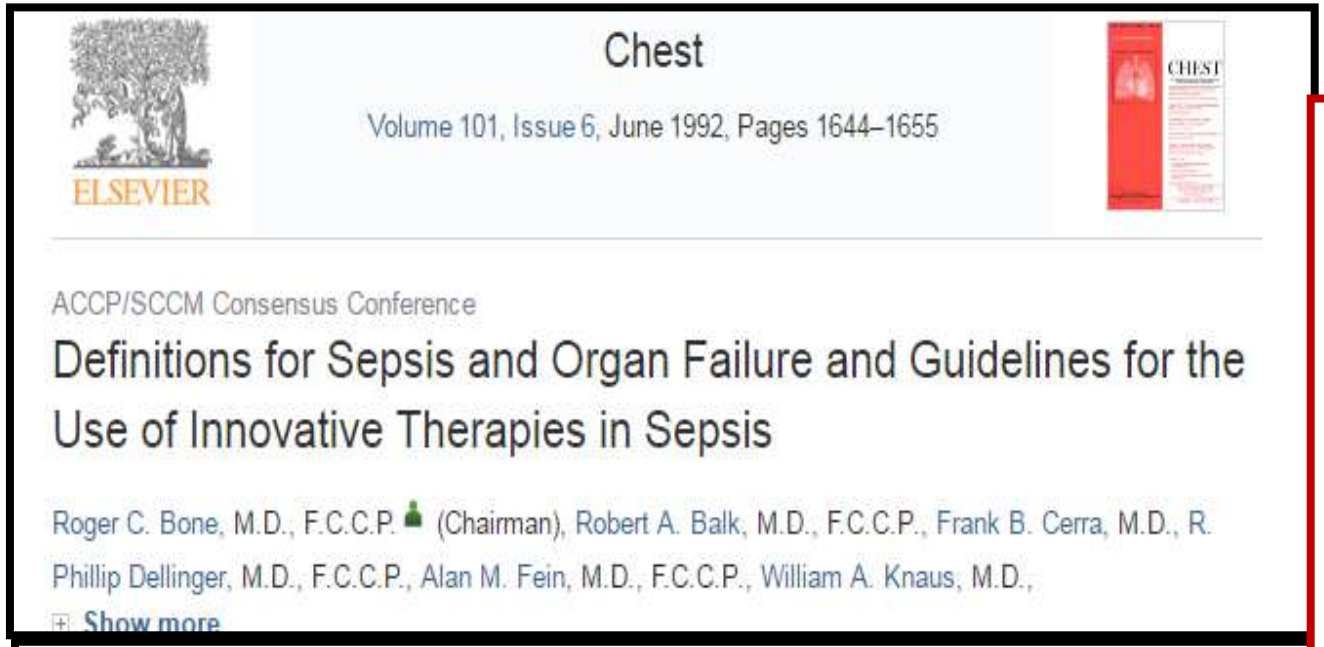
2016 Adult Guidelines

2021

2021 Adult Guidelines

2018 Sepsis research priorities published
2020 SSC COVID-19 Guidelines

2022



Chest

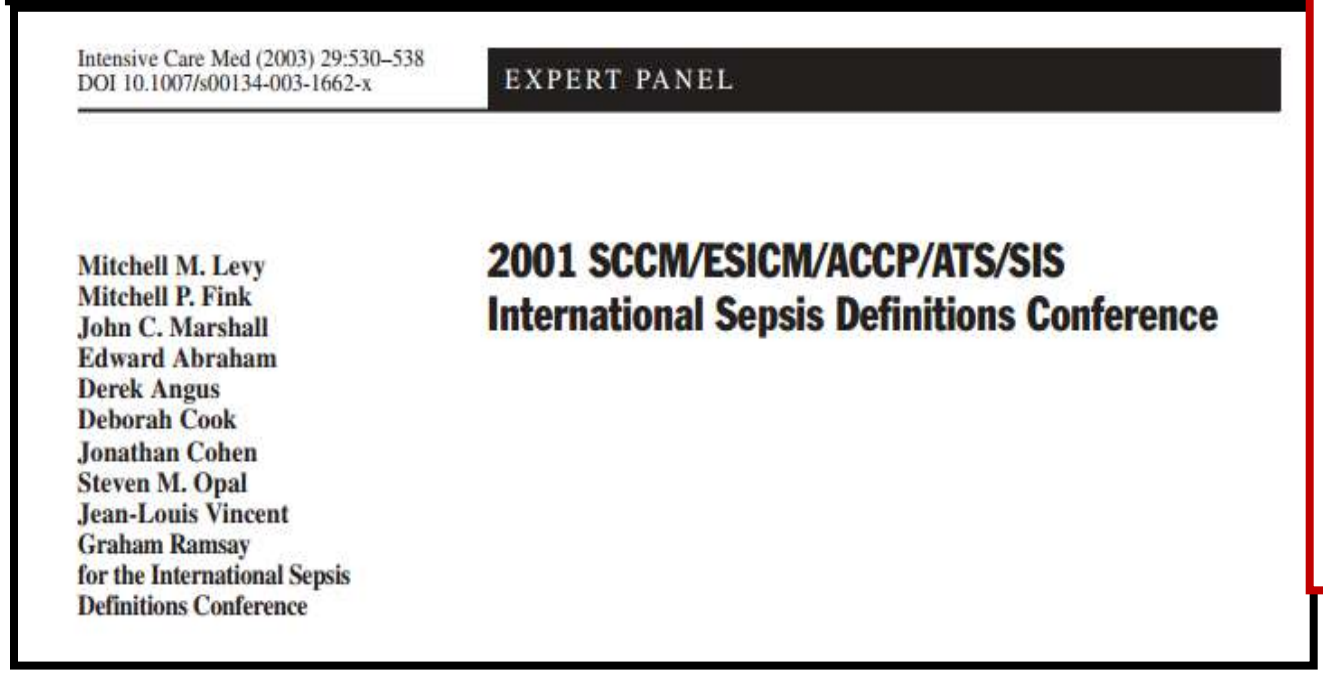
Volume 101, Issue 6, June 1992, Pages 1644–1655

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.,

Show more



Intensive Care Med (2003) 29:530–538
DOI 10.1007/s00134-003-1662-x

EXPERT PANEL

Mitchell M. Levy
Mitchell P. Fink
John C. Marshall
Edward Abraham
Derek Angus
Deborah Cook
Jonathan Cohen
Steven M. Opal
Jean-Louis Vincent
Graham Ramsay
for the International Sepsis Definitions Conference

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

- Sepsis tanımı
- SIRS
- Ciddi Sepsis

Intensive Care Med (2008) 34:17–60
DOI 10.1007/s00134-007-0934-2

SPECIAL ARTICLE

R. Phillip Dellinger
Mitchell M. Levy
Jean M. Carlet
Julian Bion
Margaret M. Parker
Roman Jaeschke
Konrad Reinhart
Derek C. Angus
Christian Brun-Buisson
Richard Beale
Thierry Calandra
Jean-Francois Dhainaut
Herwig Gerlach
Maurene Harvey
John J. Marini
John Marshall
Marco Ranieri
Graham Ramsay
Jonathan Sevransky
B. Taylor Thompson
Sean Townsend
Jeffrey S. Vender
Janice L. Zimmerman
Jean-Louis Vincent

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Surviving Sepsis Campaign

Special Articles

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

Ciddi Sepsis ve Septik Şok Yönetimi

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.

EXPOSURES Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score, systemic inflammatory response syndrome (SIRS) criteria, Logistic Organ Dysfunction System (LODS) score, and a new model derived using multivariable logistic regression in a split sample, the quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) score (range, 0-3 points, with 1 point each for systolic hypotension [≤100 mm Hg], tachypnea [≥22/min], or altered mentation).

MAIN OUTCOMES AND MEASURES For construct validity, pairwise agreement was assessed. For predictive validity, the discrimination for outcomes (primary: in-hospital mortality; secondary: in-hospital mortality or intensive care unit [ICU] length of stay ≥3 days) more common in sepsis than uncomplicated infection was determined. Results were expressed as the fold change in outcome over deciles of baseline risk of death and area under the receiver operating characteristic curve (AUROC).

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.

CONCLUSIONS AND RELEVANCE Among ICU encounters with suspected infection, the predictive validity for in-hospital mortality of SOFA was not significantly different than the more complex LODS but was statistically greater than SIRS and qSOFA, supporting its use in clinical criteria for sepsis. Among encounters with suspected infection outside of the ICU, the predictive validity for in-hospital mortality of qSOFA was statistically greater than SOFA and SIRS, supporting its use as a prompt to consider possible sepsis.

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288
Corrected on May 24, 2016.

Editorial page 757
Author Audio Interview at jama.com
Related articles pages 775 and 801
Supplemental content at jama.com

Author Affiliations: Author affiliations are listed at the end of this article.
Corresponding Author: Christopher W. Seymour, MD, MSc, Departments of Critical Care Medicine and Emergency Medicine, University of Pittsburgh School of Medicine, Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center, 3550 Terrace St, Scaife Hall, Ste 639, Pittsburgh, PA 15261 (seymourcw@upmc.edu).

Sepsis-3

Seymour CW, Liu VX, Iwashyna TJ et al.
Assessment of Clinical Criteria for Sepsis
For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)
JAMA 2016; 315: 762-774

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

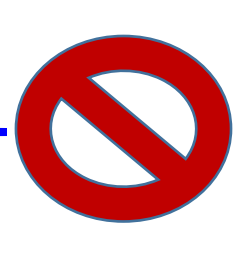
Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

- **SCCM (Kritik Bakım Derneği)**
- **ESICM (Avrupa Yoğun Bakım Derneği)**

Sepsis-3

"Konağın infeksiyona karşı
düzensiz yanıtına
bağlı organ disfonksiyonu"

sepsis sendromu,
septisemi
ciddi sepsis



Organ Disfonksiyonu:
Toplam SOFA skorunda ≥ 2
akut değişim

Singer M et al. JAMA 2016

2021 Rehberi
Sepsis Tanısı

Intensive Care Med (2021) 47:1181–1247
https://doi.org/10.1007/s00134-021-06506-y

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Laura Evans[1*], Andrew Rhodes[2], Waleed Alhazzani[3], Massimo Antonelli[4], Craig M. Coopersmith[5],

PICO Question	2021 Recommendation	Recommendation Strength and Quality	Change from 2016
In acutely ill patients should we use qSOFA criteria to screen for the presence of sepsis?	**We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock.**	Strong, moderate-quality evidence	New recommendation

Intensive Care Med (2021) 47:1181–1247
https://doi.org/10.1007/s00134-021-06506-y

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Laura Evans[1*], Andrew Rhodes[2], Waleed Alhazzani[3], Massimo Antonelli[4], Craig M. Coopersmith[5],

- 93 öneri..
- Kapiller dolum zamanı
- Empirik MRSA tedavisi
- Empirik fungal tedavi
- Periferik vazopressör kullanımı
- Levosimendan
- HFNC ve NIV
- ECMO kullanımı
- Post-YB takip

Sepsiste Tedavi Gelişimi

Önerilen Ana Tedavi:
Kaynak kontrolü
Antibiyotikler
Resüsitasyon
Destek tedavisi

Steroid

MORTALİTE

Steroid yok
Sıkı glisemik kontrol
İmmünnutrisyon

Endotoksin antogonistleri
LPS/LPS reseptör antogonistleri
anti-TNF
NSAID
Nitrik Oksit Sentetaz İnhibitörleri
Doku Faktörü Yolak İnhibitörleri
anti-TLR4

Steroid
Esnek glisemik kontrol
İmmünnutrisyon?
Steroid verilmeli mi?

Önerilen Ana Tedavi:
Kaynak kontrolü
Daha çok antibiyotik
Daha hızlı resüsitasyon
Daha iyi destek tedavisi

Genel olarak bakım süreci iyileşmiştir

Sepsiste Steroid Tedavisi Gerekliliği…

- Kritik hastalıklarda şoka katkıda bulunabilecek mutlak veya rölatif adrenal yetmezlik durumu indüklenir
- Mortalite gibi klinik olarak anlamlı sonuçları iyileştirmek amacıyla,
- Değişmiş hipotalamik-hipofiz-adrenal (HPA) ekseninde dengeyi yeniden sağlamak amaçlanır
- Sepsis hastalarına glukokortikoidlerin uygulanmasıyla ilgili en büyük zorluk, fayda görme olasılığı yüksek olan hastaların seçilmesidir..

Sepsiste Adrenal Yetmezlik

- HPA aktivasyon
  - Sirküle olan kortizol düzeyinde artış
- HPA'da bozulma
  - Adrenokortikal hiporesponsivite
- Glukokortikoid direnci

Sepsiste Adrenal Yetmezlik

- **HPA Aktivasyon**
  - Sirküle olan kortizol düzeyinde artış
  - 5-24 mcg/dL---------40-50 mcg/dL
  - Kortizolün, Kortizol bağlayan globulin(KBG) ve albümina bağlanması azalır
  - Kortizolün glikokortikoid reseptör afinitesi artar
  - Periferde prekürsörlerin kortizole dönüşümü artar

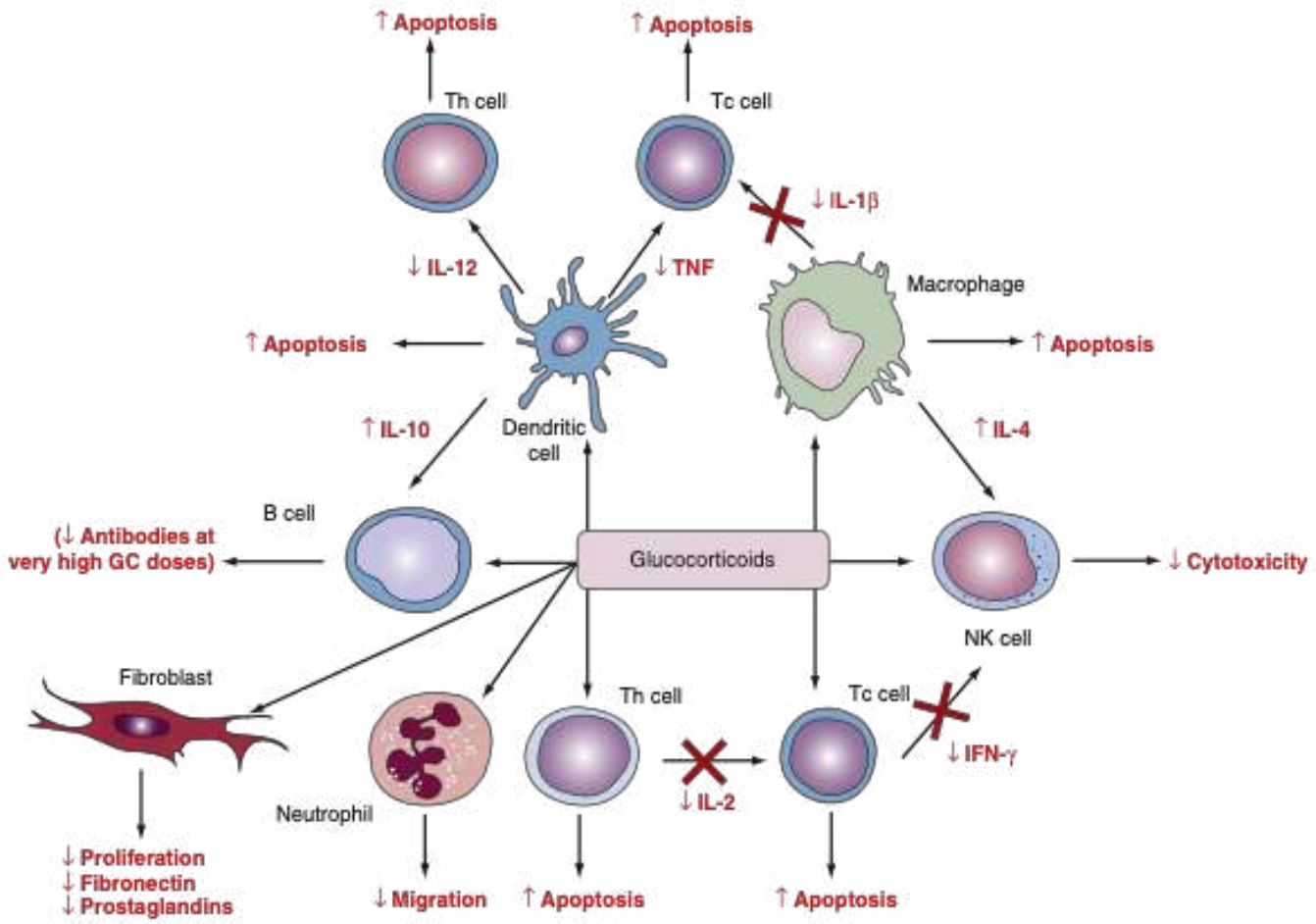
Kritik Hastalık İlişkili Adrenal Yetmezlik (CIRCI)

- Absolut adrenal yetmezlik <%3

- **Rölatif adrenal yetmezlik** (suboptimal kortizol üretimi)—Daha sık kritik hastalarda
  - Kortizol düzeyi normal?
  - ACTH cevabı?
    - Plazma kortizol <10 mcg/dL
    - ACTH stimülasyon testine cevap olarak 1 saatte<9 mcg/dL değişiklik

İmmun Sistem Üzerine Etkileri

Güçlü anti-enflamatuar ve immünosupresif etki



- **İnflamatuar hücrelerin** aktivasyonu, proliferasyonunu, farklılaşmasını ve migrasyonunu **azaltır**
- **Apopitozu arttırır** (Sitokinler aracılığıyla) (Özellikle immatür ve aktif **T hücreleri**)

Kelley's Textbook Rheumatology 2020

Kime verelim?

Septik şoklu erişkin hastalarda başlangıç tedavisinin bir parçası olarak intravenöz glukokortikoid tedavisinin rutin olarak kullanılmaması önerilmektedir….

- Dirençli şoku olan hastalarda
- Hem yeterli sıvı resüsitasyonu hem de vazopresör uygulamasını takiben bir saatten fazla sistolik kan basıncı <90 mmHg olması

- Vaka bazında glukokortikoid tedavisi kullanılabilir

Etkinlik???

Yüksek doz GK

mortaliteyi azaltır

-Düşük doz GK şoku hızlı döndürür

-Vazoprösör ihtiyacını azaltır

-Mortaliteye etkisi yok

Yararlıdır…

Clinical Trial > JAMA. 2002 Aug 21;288(7):862-71. doi: 10.1001/jama.288.7.862.

Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock

Djillali Annane [1], Véronique Sébille, Claire Charpentier, Pierre-Edouard Bollaert, Bruno François, Jean-Michel Korach, Gilles Capellier, Yves Cohen, Elie Azoulay, Gilles Troché, Philippe Chaumet-Riffaud, Eric Bellissant

- French trial 2002
- 300 hasta
- Vazopresör ihtiyacı olan septik şok
- Plasebo& hidrokortizon 50 mg iv X4 + fludrocortizon 50 mcg/gün oral
- 8.saatte tedavi başlangıcı—7 gün kullanım

- 28 günlük mortaliteyi azaltıyor (%55 & %61)
- Şoku hızlı döndürür (%57 & %40)

Yararlıdır…

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and E. Bellissant, for the CRICS-TRIGGERSEP Network*

APROCCHHS Çalışması..2018

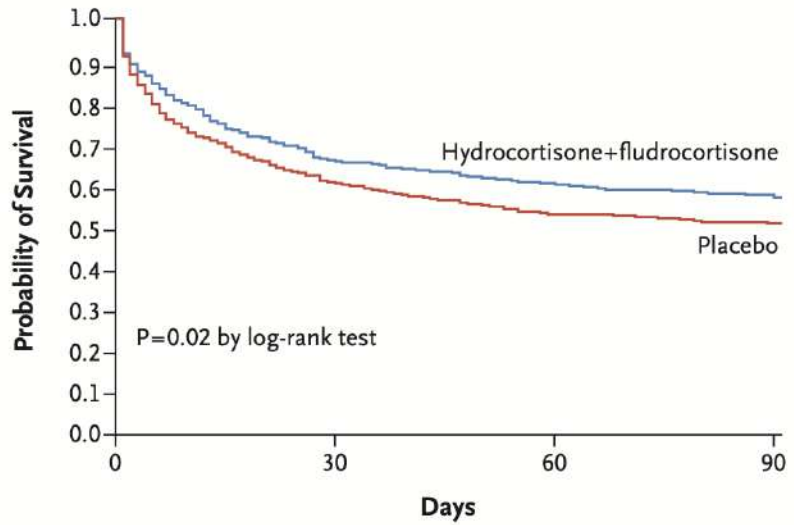
- Çok merkezli, Septik şoklu vazopresör ihtiyacı olan 1241 hasta (cerrahi ve dahili)
- RKÇ (Plasebo & hidrokortizon 200 mg/gün qd + fludrokortizon 50 mcg/gün
- 7 günde azaltılarak kesildi
- 90 günlük mortaliteyi azaltıyor (%43 & %49)
- 180 günlük mortaliteyi azaltıyor (%47 & %53)
- Vazopresör ihtiyacı olmayan gün sayısı arttı (17 &15 gün)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

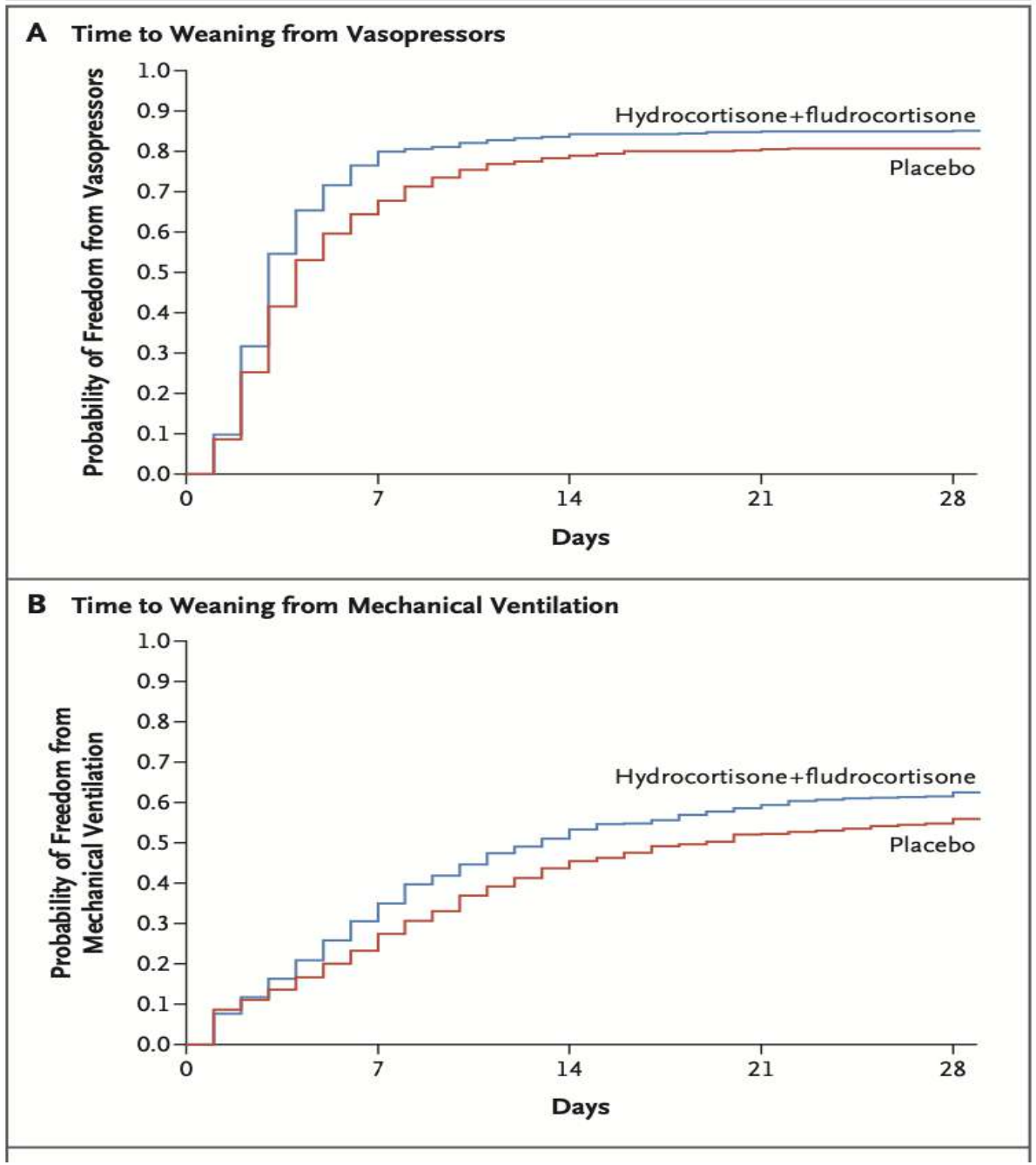
D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and E. Bellissant, for the CRICS-TRIGGERSEP Network*



No. at Risk				
Hydrocortisone+ fludrocortisone	614	405	372	353
Placebo	627	381	333	319

Figure 1. 90-Day Survival Distributions.

Shown are survival curves from randomization up to 90 days. The survival rate was significantly higher in the hydrocortisone-plus-fludrocortisone group than in the placebo group.



Yararlıdır…

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Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

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- YB'dan taburculuk arttı (%35 & &41)
- Hastaneden taburculuk arttı (%39 & 45)
- Organ yetmezliğinin olmadığı gün sayısında artış (14 & 12 gün)

- Süperenfeksiyon ve nörolojik tabloda değişiklik yok
- Hiperglisemi oranları arttı (%89 & 83)

Mortaliteyi azaltmıyor..

Hydrocortisone Therapy for Patients with Septic Shock

Charles L. Sprung, M.D., Djillali Annane, M.D., Ph.D., Didier Keh, M.D., Rui Moreno, M.D., Ph.D., Mervyn Singer, M.D., F.R.C.P., Klaus Freivogel, Ph.D., Yoram G. Weiss, M.D., Julie Benbenishty, R.N., Armin Kalenka, M.D., Helmuth Forst, M.D., Ph.D., Pierre-Francois Laterre, M.D., Konrad Reinhart, M.D., Brian H. Cuthbertson, M.D., Didier Payen, M.D., Ph.D., and Josef Briegel, M.D., Ph.D., for the CORTICUS Study Group*

CORTİCUS çalışması

- 2008, septik şoklu 499 hasta
- Hidrokortizon 50 mg X4 & plasebo, 5 gün
- Şokta hızlı cevap (3.3 & 5.8 gün)
- 28 günlük mortalitede fark yok

Mortaliteyi azaltmıyor..

Randomized Controlled Trial > JAMA. 2016 Nov 1;316(17):1775-1785.
doi: 10.1001/jama.2016.14799.

Effect of Hydrocortisone on Development of Shock Among Patients With Severe Sepsis: The HYPRESS Randomized Clinical Trial

HYPRESS çalışması, 2016

- Ciddi sepsisli 353 hasta
- Hidrokortizon & plasebo

- Septik şoka ilerleme ve mortalitede fark yok
- Hiperglisemi
- Infeksiyon oranlarında artış
- Kas zayıflığı

Mortaliteyi azaltmıyor..


The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MARCH 1, 2018 VOL. 378 NO. 9

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

- ADRENAL çalışması
- 2018, çok merkezli 3800 hasta
- MV+ septik şokta
- Sürekli hidrokortizon **infüzyonu 200 mg/gün, 7 gün**

- MV süresi kısaldı
- Kan transfüzyon ihtiyacı azaldı

Mortaliteyi azaltmıyor..


The NEW ENGLAND JOURNAL of MEDICINE
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Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

- 28 ve 90 günlük mortalitede
- Toplamda MV de kalınan süre
- Şok tekrarlama oranı
- Renal replasman tedavi ihtiyacı
- Infeksiyon sıklığında
- Hiperglisemi ve hipernatremi

Değişiklik yok…

Metaanalizler

Seven-Day Profile Publication | Published: 14 May 2018

Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis

Sofie Louise Rygård, Ethan Butler, Anders Granholm, Morten Hylander Møller, Jeremy Cohen, Simon Finfer, Anders Perner, John Myburgh, Balasubramanian Venkatesh & Anthony Delaney

Intensive Care Medicine 4

Corticosteroids in Sepsis: An Updated Systematic Review and Meta-Analysis

Bram Rochwerg [1 2], Simon J Oczkowski [1], Reed A C Siemieniuk [2], Thomas Agoritsas [2 3 4], Emilie Belley-Cote [1 2], Frédérick D'Aragon [5], Erick Duan [1 2], Shane English [6 7], Kira Gossack-Keenan [1], Mashari Alghuroba [1], Wojciech Szczeklik [1 8], Kusum Menon [9], Waleed Alhazzani [1 2], Jonathan Sevransky [10], Per Olav Vandvik [11], Djillali Annane [12], Gordon Guyatt [1 2]

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Intensive Care Medicine **44**, 1003–1016 (2018) | Cite this article

- 2018, 22 çalışma, 7297 hasta
- Mortaliteye etkisi yok
- Şok süresi kısalıyor
- Steroid alan grupta yan etki daha fazla (hipernatremi, hiperglisemi)

Corticosteroids in Sepsis: An Updated Systematic Review and Meta-Analysis

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RAPID RECOMMENDATIONS

Corticosteroid therapy for sepsis: a clinical practice guideline

Francois Lamontagne,[1 2] Bram Rochwerg,[3 4] Lyubov Lytvyn,[4] Gordon H Guyatt,[4] Morten Hylander Møller,[5] Djillali Annane,[6] Michelle E Kho,[7] Neill K J Adhikari,[8 9] Flavia Machado,[10 11] Per O Vandvik,[12 13] Peter Dodek,[14] Rebecca Leboeuf,[15] Matthias Briel,[4 16] Madiha Hashmi,[17] Julie Camsooksai,[18] Manu Shankar-Hari,[19 20] Mahder Kinfe Baraki,[21] Karie Fugate,[22] Shunjie Chua,[23] Christophe Marti,[24] Dian Cohen,[25] Edouard Botton,[26] Thomas Agoritsas,[4 27] Reed A C Siemieniuk[4]

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- Mortaliteyi azaltır mı?
- İyileşmeye katkısı var mı?

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DATA SOURCES

NUMBER OF TRIALS 42

Use this information to gauge how similar your patients' conditions are to those of people studied in the trials

NUMBER OF PATIENTS 10 194

TRIAL CHARACTERISTICS

Type of corticosteroid

Hydrocortisone	25	6037
Hydrocortisone and Fludrocortisone	2	1541
Methylprednisone and Prednisone	11	1426
Dexamethasone	5	333

Corticosteroid dose and duration:

Long course and low dose	35	8427
Short course and high dose	7	910

PATIENT CHARACTERISTICS

Patient subtype:

Septic Shock	24	6305
Sepsis without shock	7	1167
Sepsis and CAP	5	763
Sepsis and ARDS	4	311

Setting

All included trials took place in hospitalised patients including emergency department, ward and intensive care unit.

MEAN AGE at baseline

SEX % women

CONTROL GROUP 1-month mortality %

FUNDING — 2 trials were funded by steroid industry

PREREGISTRATION — 14 trials were publicly preregistered

PATIENT PARTNERSHIP — No trials reported patient involvement

- 42 RKÇ.
- Sepsis tanılı 10.194 hasta
- Kadın hasta %38. 9, Yaş ortalaması 49.5

- Dahil edilen 42 çalışmadan 24'ü septik şoku olan hastalar
- Katılımcıların% 32'sinin medyanı ilk ay içinde kaybedildi
- Sepsisin kaynağı en sık pulmoner enfeksiyonlar (medyan %44) ve abdominal enfeksiyonlar (medyan %17).

Hasta Popülasyonu

People with sepsis

SOFA score of at least 2

✔ Recommendation applies to:

- Adults and children
- Any infectious source
  - Intra abdominal infections
  - Pneumonia
- Patients with and without shock

✘ Recommendation does **not** apply to:

- Patients with pre-existing adrenal insufficiency
- Non-infectious causes of shock
  - Anaphylactic
  - Cardiogenic
  - Hypovolaemic
- Neonates
- Pregnant women

Comparison

Corticosteroid therapy

Intravenous corticosteroids plus usual care

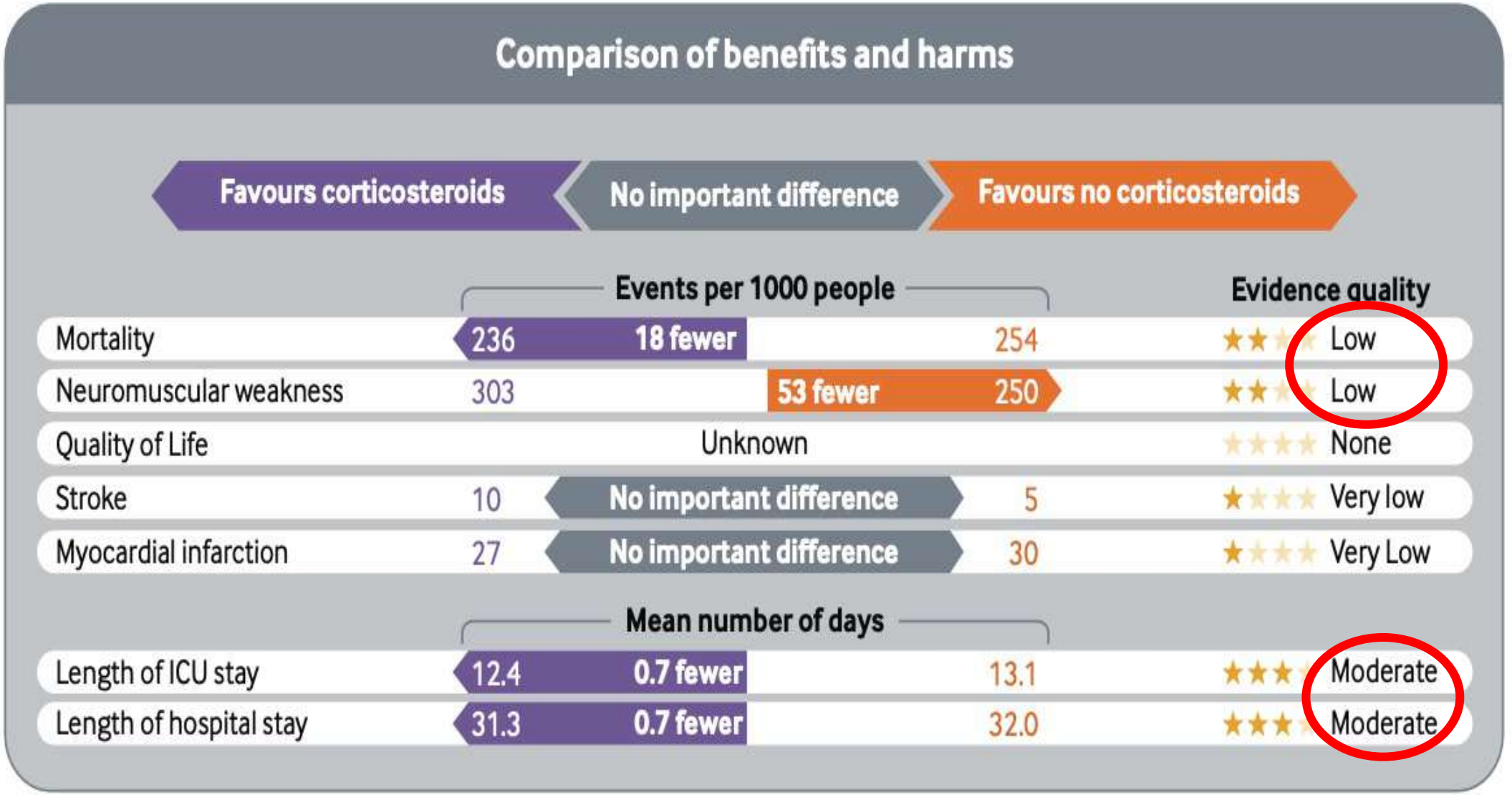
or

No corticosteroid therapy

Usual care only

Corticosteroids		No corticosteroids	
Strong	**Weak**	Weak	Strong

We suggest corticosteroid therapy rather than no corticosteroid therapy.
Either option is reasonable.


Comparison of benefits and harms
Favours corticosteroids
No important difference
Favours no corticosteroids
Events per 1000 people
Evidence quality
Mortality
236
18 fewer
254
Low
Neuromuscular weakness
303
53 fewer
250
Low
Quality of Life
Unknown
None
Stroke
10
No important difference
5
Very low
Myocardial infarction
27
No important difference
30
Very Low
Mean number of days
Length of ICU stay
12.4
0.7 fewer
13.1
Moderate
Length of hospital stay
31.3
0.7 fewer
32.0
Moderate

Sonuçlar…

- Kortikosteroidler YBÜ ve hastanede kalış süresini azaltabilir (orta düzey kanıt)
- Organ fonksiyonunu artırır ve şoku tersine çevirir (düşük düzey kanıt)
- Nöromüsküler zayıflık riskini az miktarda artırabilirler
- Hiperglisemi, hipernatremi

Pratik hususlar

- Optimal kortikosteroid ilaç, doz ve tedavi süresi belirsizdir
- İnfüzyon veya intermitant bolus şeklinde verilebilir
- Hidrokortizon, RKÇ'lerde en çokkullanılan kortikosteroiddir ve bu nedenle makul bir seçimdir
- Kortikosteroidler arasındaki farklar, eğer varsa, muhtemelen küçüktür; deksametazon, metilprednizolon ve prednizolon da incelenmiş ve benzer sonuçlar elde edilmiştir
- Fludrokortizon gibi ek mineralokortikoid aktiviteye sahip bir ajan eklemek yararlı olabilir, ancak bu oldukça spekülatiftir
- Na, K, glukoz düzey takibi yapılmalı

Pratik hususlar

- Hidrokortizon (< 400 mg/gün bölünmüş dozlarda)
- Fludrokortizon tedavisine gerek yok (Grade 2C)
- 5-7 gün uygulama

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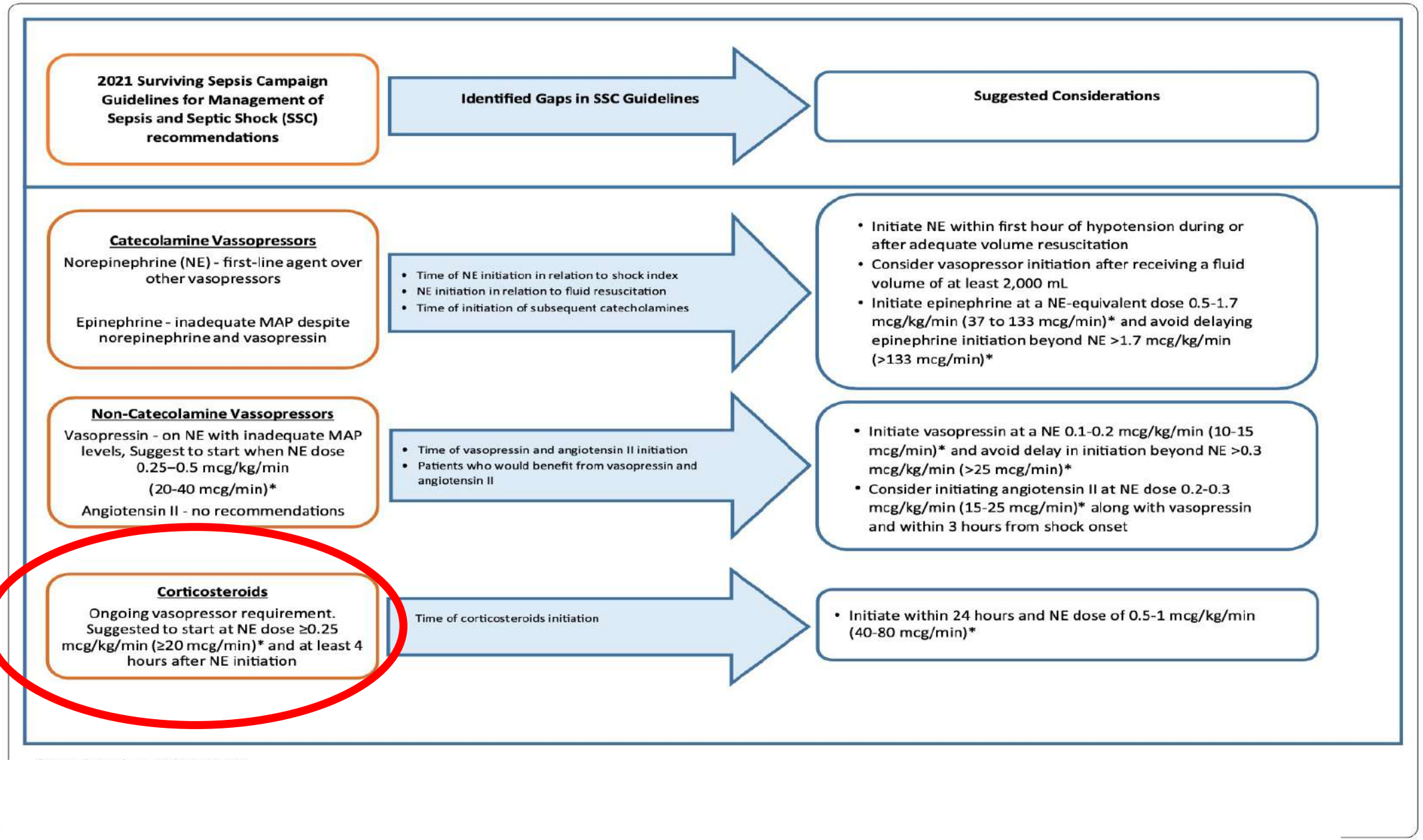
- Mortaliteyi azaltır mı?
- İyileşmeye katkısı var mı?

- **Yeni kanıtlara göre zayıf öneri**
- **Hasta değerleri ve kliniğine göre karar verilir….**

Rehberler ne diyor?..

	Recommendation regarding corticosteroid use		
Society	In sepsis	In septic shock	Other situations
"Surviving Sepsis" for SCCM and ESICM, 2016[7]	Against	In favour for hypotension refractory to fluid resuscitation and vasopressor	History of adrenal insufficiency or corticosteroid use
CIRCI guidelines for SCCM and ESICM, 2018[12 13]	Against	In favour for shock not responsive to fluid and at least moderate dose vasopressor	Acute respiratory distress syndrome Community acquired pneumonia Bacterial meningitis History of adrenal insufficiency or corticosteroid use
CAEP, 2008[14]	Against	In favour for haemodynamically unstable patients not responsive to fluid resuscitation and vasopressor	
NICE, 2017[15]	Not mentioned	Not mentioned	Not mentioned
JSICM, 2018[16]	Against	In favour for shock not responsive to initial fluid resuscitation and	

2021 Sepsis Rehberi



Sonuç olarak…

- Sepsiste relatif adrenal yetmezlik (kritik hastalık ilişkili kortikosteroid yetmezliği) sıklıkla gelişir
- Sepsis ve septik şok gelişen hastalarda iv glukokortikoid tedavisi rutin önerilmez (Grade 2B)
- Refrakter septik şoku olan hastalarda hasta bazlı yaklaşım önemli
- Şokun daha hızlı rezolüsyonunu sağlar
- Mortalite üzerine etkisi yoktur
- Ciddi hastalıktaki yarar > Orta şiddetteki hastalık
- Hipernatremi, hiperglisemi, nöromüsküler zayıflık

Sonuç olarak…

- Hidrokortizon (< 400 mg/gün bölünmüş dozlarda)
- Fludrokortizon tedavisine gerek yok (Grade 2C)
- 5-7 gün uygulama