

Sepsis

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| Giriş

Sepsis, enfeksiyona karşı düzensiz bir konak yanıtının neden olduğu, hayatı tehdit eden organ disfonksiyonudur (1). Septik şok ve sepsis, her yıl dünyada milyonlarca insanı etkiler ve etkilediği kişilerin üçte biri ile altında birinin ölümüne neden olan önemli bir sağlık sorunlarıdır (2). Erken teşhis ve enfeksiyondan sonraki ilk saatlerde uygun yönetim sonuçları iyileştirir (3).

Bu bölümdeki tavsiyeler, hastane ortamında septik şoklu veya sepsisli erişkin hastalara bakan klinisyene rehberlik etmeyi amaçlamaktadır.

| Tarama ve Erken Tedavi

Sepsis tarama araçları, sepsisin erken teşhisini desteklemek için tasarlanmıştır ve manuel yöntemlerden veya elektronik sağlık kaydının (EHR) otomatik kullanımından oluşur(4). Sepsis taraması için sistemik inflamatuar yanıt sendromu (SIRS) kriterleri, hayatı belirtiler, enfeksiyon belirtileri, hızlı sıralı organ yetmezliği skoru (qSOFA) veya sıralı organ yetmezliği değerlendirmesi (SOFA) kriterleri gibi çeşitli klinik değişkenler ve araçlar kullanılır (5).

Tarama araçları, yatan hasta servisleri, acil servisler veya yoğun bakım üniteleri gibi çeşitli konumlardaki hastaları hedef alabilir (6). Sepsis tarama araçlarının duyarlılık ve özgüllüklerinde geniş farklılıklar olsa da, zamanında müdahale için sepsisi erken tanımlamanın önemli bir bileşenidirler.

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| Kaynaklar

1. Michael D. Howell, MD, MPH, Andrew M. Davis, MD, MPH Management of Sepsis and Septic Shock JAMA. 2017;317(8):847-848. doi:10.1001/jama.2017.0131
2. Lakshmikanth CL, Jacob SP, Chaithra VH, de Castro-FariaNeto HC, Marathe GK. Sepsis: in search of cure. Inflamm Res. 2016 Aug;65(8):587-602. doi: 10.1007/s00011-016-0937-y.
3. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign Guidelines Committee Including the Pediatric Subgroup. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013; 41(2):580-637.
4. Alberto L, Marshall AP, Walker R et al (2017) Screening for sepsis in general hospitalized patients: a systematic review. J Hosp Infect 96(4):305–315
5. Schorr C, Odden A, Evans L et al (2016) Implementation of a multicenter performance improvement program for early detection and treatment of severe sepsis in general medical-surgical wards. J Hosp Med 11(S1):S32-S39
6. Warttig S, Alderson P, Evans DJ et al (2018) Automated monitoring compared to standard care for the early detection of sepsis in critically ill patients. Cochrane Database oSyste Rev. 6(6):CD012404-CD
7. Singer M, Deutschman CS2, Seymour CW, ShankarHari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. (12) The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).JAMA. 2016 Feb 23;315(8):801-10. doi: 10.1001/jama.2016.0287.
8. Vincent J-L, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. Lancet. 2013; 381(9868):774–775. (PubMed: 23472921) <http://adelaideemergencyphysicians.com/2016/02/sepsis-3-0-andthe-quick-sofa/>
9. Yaklışık Çakır E, Özkoçak Turan I. Yoğun bakım ünitesinde laktat ve mortalite. Ahi Evran Med J. 2022;6(2):115-120. DOI:10.46332/aemj.960131
10. Chebl RB, Tamim H, Dagher GA, Sadat M, Al Enezi F, Arabi YM. Serum Lactate as an Independent Predictor of In-Hospital Mortality in Intensive Care Patients. J Intensive Care Med. 2020;35(11):1257-1264.
11. Levy MM, Dellinger RP, Townsend SR et al (2010) The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Intensive Care Med 36(2):222–231
12. Fleischmann-Struzek C, Mellhammar L, Rose N et al (2020) Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med 46(8):1552–1562
13. Levy B (2006) Lactate and shock state: the metabolic view. Curr Opin Crit Care 12(4):315–321
14. Lewis SR, Pritchard MW, Evans DJ et al (2018) Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev 8:CD000567
15. Levy MM, Dellinger RP, Townsend SR et al (2010) The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Intensive Care Med 36(2):222–231
16. Fleischmann-Struzek C, Mellhammar L, Rose N et al (2020) Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med 46(8):1552–1562
17. Cherpanath TG, Hirsch A, Geerts BF et al (2016) Predicting fluid responsiveness by passive leg raising: a systematic review and meta-analysis of 23 clinical trials. Crit Care Med 44(5):981–991

18. Misango D, Pattnaik R, Baker T et al (2017) Haemodynamic assessment and support in sepsis and septic shock in resource-limited settings. *Trans R Soc Trop Med Hyg* 111(11):483–489
19. Hernandez G, Ospina-Tascon GA, Damiani LP et al (2019) Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK Randomized Clinical Trial. *JAMA* 321(7):654–664
20. Andrews B, Semler MW, Muchemwa L et al (2017) Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: a randomized clinical trial. *JAMA* 318(13):1233–1240
21. Asfar P, Meziani F, Hamel JF et al (2014) High versus low blood-pressure target in patients with septic shock. *N Engl J Med* 370(17):1583–1593
22. Hylands M, Moller MH, Asfar P et al (2017) A systematic review of vasopressor blood pressure targets in critically ill adults with hypotension. *Can J Anaesth* 64(7):703–715
23. Lamontagne F, Meade MO, Hebert PC et al (2016) Higher versus lower blood pressure targets for vasopressor therapy in shock: a multicentre pilot randomized controlled trial. *Intensive Care Med* 42(4):542–550
24. Groenland CNL, Termorshuizen F, Rietdijk WJR et al (2019) Emergency department to ICU time is associated with hospital mortality: a registry analysis of 14,788 patients from six University Hospitals in The Netherlands. *Crit Care Med* 47(11):1564–1571
25. Ferrer R, Artigas A, Suarez D et al (2009) Effectiveness of treatments for severe sepsis: a prospective, multicenter, observational study. *Am J Respir Crit Care Med* 180(9):861–866
26. Heffner AC, Horton JM, Marchick MR et al (2010) Etiology of illness in patients with severe sepsis admitted to the hospital from the emergency department. *Clin Infect Dis* 50(6):814–820
27. Ferrer R, Artigas A, Suarez D et al (2009) Effectiveness of treatments for severe sepsis: a prospective, multicenter, observational study. *Am J Respir Crit Care Med* 180(9):861–866
28. Baggs J, Jernigan JA, Halpin AL et al (2018) Risk of subsequent sepsis within 90 days after a hospital stay by type of antibiotic exposure. *Clin Infect Dis* 66(7):1004–1012
29. Seymour CW, Gesten F, Prescott HC et al (2017) Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med* 376(23):2235–2244
30. Alam N, Oskam E, Stassen PM et al (2018) Prehospital antibiotics in the ambulance for sepsis: a multicentre, open label, randomised trial. *Lancet Respir Med* 6(1):40–50
31. Peng F, Chang W, Xie JF et al (2019) Ineffectiveness of procalcitonin-guided antibiotic therapy in severely critically ill patients: a meta-analysis. *Int J Infect Dis* 85:158–166
32. Wacker C, Prkno A, Brunkhorst FM et al (2013) Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. *Lancet Infect Dis* 13(5):426–435
33. Vincent JL, Sakr Y, Singer M, et al (2020) Prevalence and outcomes of infection among patients in intensive care units in 2017. *JAMA* 323(15):1478–1487
34. Jernigan JA, Hatfield KM, Wolford H et al (2020) Multidrug-resistant bacterial infections in U.S. hospitalized patients, 2012–2017. *N Engl J Med* 382(14):1309–1319
35. Aliberti S, Reyes LF, Faverio P et al (2016) Global initiative for meticillinresistant *Staphylococcus aureus* pneumonia (GLIMP): an international, observational cohort study. *Lancet Infect Dis* 16(12):1364–1376
36. Rhodes A, Evans LE, Alhazzani W et al (2017) Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 45(3):486–552
37. Kollef M, Micek S, Hampton N et al (2012) Septic shock attributed to *Candida* infection: importance of empiric therapy and source control. *Clin Infect Dis* 54(12):1739–1746
38. Timsit JF, Azoulay E, Schwebel C et al (2016) Empirical micafungin treatment and survival without invasive fungal infection in adults with ICU-acquired sepsis, candida colonization, and multiple organ failure: the EMPIRICUS Randomized Clinical Trial. *JAMA* 316(15):1555–1564

39. Freifeld AG, Bow EJ, Sepkowitz KA et al (2011) Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. *Clin Infect Dis* 52(4):e56-93
40. Vincent JL, Sakr Y, Singer M, et al (2020) Prevalence and outcomes of infection among patients in intensive care units in 2017. *JAMA* 323(15):1478–1487
41. Cantan B, Luyt CE, Martin-Loeches I (2019) Influenza infections and emergent viral infections in intensive care unit. *Semin Respir Crit Care Med* 40(4):488–497
42. Wiersinga WJ, Rhodes A, Cheng AC et al (2020) Pathophysiology, transmission, diagnosis, and treatment of Coronavirus Disease 2019 (COVID-19): a review. *JAMA* 324(8):782–793
43. Lin GL, McGinley JP, Drysdale SB et al (2018) Epidemiology and immune pathogenesis of viral sepsis. *Front Immunol* 9:2147
44. Goncalves-Pereira J, Povoa P (2011) Antibiotics in critically ill patients: a systematic review of the pharmacokinetics of beta-lactams. *Crit Care* 15(5):R206
45. Roberts JA, Abdul-Aziz MH, Davis JS et al (2016) Continuous versus intermittent beta-lactam infusion in severe sepsis. A meta-analysis of individual patient data from randomized trials. *Am J Respir Crit Care Med* 194(6):681–691
46. Roberts JA, Abdul-Aziz MH, Lipman J et al (2014) Individualised antibiotic dosing for patients who are critically ill: challenges and potential solutions. *Lancet Infect Dis* 14(6):498–509
47. Gregoire N, Marchand S, Ferrandiere M et al (2019) Population pharmacokinetics of daptomycin in critically ill patients with various degrees of renal impairment. *J Antimicrob Chemother* 74(1):117–125
48. Ulldemolins M, Roberts JA, Rello J et al (2011) The effects of hypoalbuminaemia on optimizing antibacterial dosing in critically ill patients. *Clin Pharmacokinet* 50(2):99–110
49. Choi G, Gomersall CD, Tian Q et al (2009) Principles of antibacterial dosing in continuous renal replacement therapy. *Crit Care Med* 37(7):2268–2282
50. Bougle A, Dujardin O, Lepere V et al (2019) PHARMECMO: Therapeutic drug monitoring and adequacy of current dosing regimens of antibiotics in patients on Extracorporeal Life Support. *Anaesth Crit Care Pain Med* 38(5):493–497
51. Rhodes A, Evans LE, Alhazzani W et al (2017) Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 45(3):486–552
52. Jimenez MF, Marshall JC, International Sepsis F (2001) Source control in the management of sepsis. *Intensive Care Med* 27(Suppl 1):S49–62
53. Martinez ML, Ferrer R, Torrents E et al (2017) Impact of Source Control in Patients With Severe Sepsis and Septic Shock. *Crit Care Med* 45(1):11–19
54. Azuhata T, Kinoshita K, Kawano D et al (2014) Time from admission to initiation of surgery for source control is a critical determinant of survival in patients with gastrointestinal perforation with associated septic shock. *Crit Care* 18(3):R87
55. Bloos F, Thomas-Ruddel D, Ruddel H et al (2014) Impact of compliance with infection management guidelines on outcome in patients with severe sepsis: a prospective observational multi-center study. *Crit Care* 18(2):R42
56. Mermel LA, Allon M, Bouza E et al (2009) Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 49(1):1–45
57. Arulkumaran N, Routledge M, Schlebusch S et al (2020) Antimicrobial-associated harm in critical care: a narrative review. *Intensive Care Med* 46(2):225–235
58. Tabah A, Bassetti M, Kollef MH et al (2020) Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group (ESGCIP). *Intensive Care Med* 46(2):245–265

59. Pugh R, Grant C, Cooke RP et al (2015) Short-course versus prolongedcourse antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev 8:CD007577
60. Chastre J, Wolff M, Fagon JY et al (2003) Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. *JAMA* 290(19):2588–2598
61. van Engelen TSR, Wiersinga WJ, Scicluna BP et al (2018) Biomarkers in Sepsis. *Crit Care Clin* 34(1):139–152
62. Lewis SR, Pritchard MW, Evans DJ et al (2018) Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev 8:CD000567
63. Awad S, Allison SP, Lobo DN (2008) The history of 0.9% saline. *Clin Nutr* 27(2):179–188
64. Semler MW, Wanderer JP, Ehrenfeld JM et al (2017) Balanced crystalloids versus saline in the intensive care unit. The SALT Randomized Trial. *Am J Respir Crit Care Med* 195(10):1362–1372
65. Brown RM, Wang L, Coston TD et al (2019) Balanced crystalloids versus saline in sepsis. A secondary analysis of the SMART clinical trial. *Am J Respir Crit Care Med* 200(12):1487–1495
66. Caironi P, Tognoni G, Gattinoni L (2014) Albumin replacement in severe sepsis or septic shock. *N Engl J Med* 371(1):84
67. Martin GS, Bassett P (2019) Crystalloids vs. colloids for fluid resuscitation in the Intensive Care Unit: a systematic review and meta-analysis. *J Crit Care* 50:144–154
68. Rochwerg B, Alhazzani W, Sindi A et al (2014) Fluid resuscitation in sepsis: a systematic review and network meta-analysis. *Ann Intern Med* 161(5):347–355
69. Avni T, Lador A, Lev S et al (2015) Vasopressors for the treatment of septic shock: systematic review and meta-analysis. *PLoS One* 10(8):e0129305
70. Gordon AC, Mason AJ, Thirunavukkarasu N et al (2016) Effect of early vasopressin vs norepinephrine on kidney failure in patients with septic shock: the VANISH randomized clinical trial. *JAMA* 316(5):509–518
71. Liu ZM, Chen J, Kou Q et al (2018) Terlipressin versus norepinephrine as infusion in patients with septic shock: a multicentre, randomised, double-blinded trial. *Intensive Care Med* 44(11):1816–1825
72. Avni T, Lador A, Lev S et al (2015) Vasopressors for the treatment of septic shock: systematic review and meta-analysis. *PLoS One* 10(8):e0129305
73. De Backer D, Creteur J, Silva E et al (2003) Effects of dopamine, norepinephrine, and epinephrine on the splanchnic circulation in septic shock: which is best? *Crit Care Med* 31(6):1659–1667
74. Landry DW, Levin HR, Gallant EM et al (1997) Vasopressin deficiency contributes to the vaso-dilation of septic shock. *Circulation* 95(5):1122–1125
75. Dunser MW, Mayr AJ, Tur A et al (2003) Ischemic skin lesions as a complication of continuous vasopressin infusion in catecholamineresistant vasodilatory shock: incidence and risk factors. *Crit Care Med* 31(5):1394–1398
76. Russell JA, Walley KR, Singer J et al (2008) Vasopressin versus norepinephrine infusion in patients with septic shock. *N Engl J Med* 358(9):877–887
77. Ukor IF, Walley KR (2019) Vasopressin in Vasodilatory Shock. *Crit Care Clin* 35(2):247–261
78. Gamper G, Havel C, Arrich J et al (2016) Vasopressors for hypotensive shock. Cochrane Database Syst Rev 2:CD0037709
79. Akinaga J, Lima V, Kiguti LR et al (2013) Differential phosphorylation, desensitization, and internalization of alpha1A-adrenoceptors activated by norepinephrine and oxymetazoline. *Mol Pharmacol* 83(4):870–881
80. Belletti A, Benedetto U, Biondi-Zocca G et al (2017) The effect of vasoactive drugs on mortality in patients with severe sepsis and septic shock. A network meta-analysis of randomized trials. *J Crit Care* 37:91–98

81. Russell JA, Vincent JL, Kjolby AL et al (2017) Selepressin, a novel selective vasopressin V1A agonist, is an effective substitute for norepinephrine in a phase IIa randomized, placebo-controlled trial in septic shock patients. *Crit Care* 21(1):213
82. Chawla LS, Busse L, Brasha-Mitchell E et al (2014) Intravenous angiotensin II for the treatment of high-output shock (ATHOS trial): a pilot study. *Crit Care* 18(5):534
83. Bhattacharjee S, Soni KD, Maitra S et al (2017) Levosimendan does not provide mortality benefit over dobutamine in adult patients with septic shock: a meta-analysis of randomized controlled trials. *J Clin Anesth* 39:67–72
84. Delaney A, Finnis M, Bellomo R et al (2020) Initiation of vasopressor infusions via peripheral versus central access in patients with early septic shock: a retrospective cohort study. *Emerg Med Australas* 32(2):210–219
85. Rivers E, Nguyen B, Havstad S et al (2001) Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 345(19):1368–1377
86. Girardis M, Busani S, Damiani E et al (2016) Effect of Conservative vs conventional oxygen therapy on mortality among patients in an intensive care unit: the oxygen-ICU randomized clinical trial. *JAMA* 316(15):1583–1589
87. Mauri T, Turrini C, Eronia N et al (2017) Physiologic effects of high-flow nasal cannula in acute hypoxic respiratory failure. *Am J Respir Crit Care Med* 195(9):1207–1215
88. Demoule A, Chevret S, Carlucci A et al (2016) Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. *Intensive Care Med* 42(1):82–92
89. Brower RG, Matthay MA, Acute Respiratory Distress Syndrome N et al (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 342(18):1301–1308
90. Serpa Neto A, Cardoso SO, Manetta JA et al (2012) Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. *JAMA* 308(16):1651–1659
91. Rygård SL, Butler E, Granholm A et al (2018) Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med* 44(7):1003–1016
92. Zhou F, Peng Z, Murugan R et al (2013) Blood purification and mortality in sepsis: a meta-analysis of randomized trials. *Crit Care Med* 41(9):2209–2220
93. Hirano Y, Miyoshi Y, Kondo Y et al (2019) Liberal versus restrictive red blood cell transfusion strategy in sepsis or septic shock: a systematic review and meta-analysis of randomized trials. *Crit Care* 23(1):262
94. Madsen MB, Hjortrup PB, Hansen MB et al (2017) Immunoglobulin G for patients with necrotising soft tissue infection (INSTINCT): a randomised, blinded, placebo-controlled trial. *Intensive Care Med* 43(11):1585–1593
95. D'Silva KM, Mehta R, Mitchell M, et al (2021) Proton pump inhibitor use and risk for recurrent Clostridioides difficile infection: a systematic review and meta-analysis. *Clin Microbiol Infect*
96. Arabi YM, Al-Hameed F, Burns KEA et al (2019) Adjunctive intermittent pneumatic compression for venous thromboprophylaxis. *N Engl J Med* 380(14):1305–1315
97. Barbar SD, Clere-Jehl R, Bourredjem A et al (2018) Timing of renal replacement therapy in patients with acute kidney injury and sepsis. *N Engl J Med* 379(15):1431–1442
98. The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* 2009;360(13):1283–1297
99. Putzu A, Daems AM, Lopez-Delgado JC et al (2019) The effect of vitamin c on clinical outcome in critically ill patients: a systematic review with meta-analysis of randomized controlled trials. *Crit Care Med* 47(6):774–783

100. Jaber S, Paugam C, Futier E et al (2018) Sodium bicarbonate therapy for patients with severe metabolic acidosis in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial. *Lancet* 392(10141):31–40
101. Reignier J, Boisramé-Helms J, Brisard L et al (2018) Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet* 391(10116):133–143
102. Ma J, Chi S, Buettner B et al (2019) Early palliative care consultation in the medical ICU: a cluster randomized crossover trial. *Crit Care Med* 47(12):1707–1715
103. Bell CM, Brener SS, Gunraj N et al (2011) Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA* 306:840–84