

BÖLÜM

8

SEPSİS

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GİRİŞ

Sepsis eski Yunanca'daki yazılışı ile "σηψις", hayvansal ya da bitkisel organik maddelerin bakteriler tarafından yıkılması anlamına gelmektedir. Sepsis kelimesi Homer'un şiirlerinde, "çürüdüm" anlamına gelen "sepo" "σηπω" şeklinde geçmektedir. Hipokrat tarafından ise MÖ 460-370 yıllarında "ağ örgüsünün bozulması, ayrışması" anlamına gelen "sepidon" "σηπεδω" kelimesi ile ifade edilmiştir. Sepsis "σηψις" kelimesi 2700 yıldan beri anlamı değişmeden kullanılmaya devam etmiş olup Galen, Aristotales, Plutarch tarafından Hipokrates'in kullandığı anlamıyla kullanılmıştır (1,4).

Sepsis yoğun bakım ünitelerinde en önemli mortalite nedeni olup son yıllarda insidasındaki anlamlı artışla dikkatleri çekmektedir. Sepsis ilişkili mortalite risk faktörleri, merkezin büyülüğü ve gelişmişliğine bağlı olarak değişmekte birlikte, günümüzde yüksek maliyeti ile en pahalı sağlık hizmeti olmuştur (3). Gelişmiş teknolojilerin kullanıldığı yoğun bakımlarda hastaların daha uzun süre kalmaları, artan yaşlı nüfus, malign hastalıkların kendilerinin ve agresif tedavilerinin yarattığı immun baskılanma, artan transplantasyon uygulamaları ve ilişkili immünsüpresiflerin kullanımı, invaziv

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Tablo 3. Dünya Sağlık Örgütü'nün yayınladığı yeni antibiyotiklere acilen ihtiyaç duyulan öncelikli patojenler listesi(2017)

Öncelik 1: KRİTİK

- *Acinetobacter baumannii*, karbapenem dirençli
- *Pseudomonas aeruginosa*, karbapenem dirençli
- *Enterobacteriaceae*, karbapenem dirençli, GSBL üreten

Öncelik 2: YÜKSEK

- *Enterococcus faecium*, vankomisine dirençli
- MRSA, VISA ve VRSA
- *Helicobacter pylori*, klaritromisin dirençli
- *Campylobacter spp.*, florokinolon duyarlı olmayan
- *Salmonella*, florokinolon duyarlı olmayan
- *Neisseria gonorrhoeae*, sefatosporine dirençli, florokinolon duyarlı olmayan

Öncelik 3: ORTA

- *Streptococcus pneumoniae*, penisiline duyarlı olmayan
- *Haemophilus influenzae*, ampisiline dirençli
- *Shigella spp.*, florokinolon duyarlı olmayan

KAYNAKLAR

1. Johnson GB, Brunn GJ, Samstein B, Platt JL. New insight into the pathogenesis of sepsis and the sepsis syndrome. *Surgery*. 2005; 137: 393-5.
2. Geroulanos S, Douka ET. Historical perspective of the Word "sepsis". *Intensive Care Med*. 2006; 32: 2077.
3. Gul F, Arslantaş MK, Cinel I, Kumar A. Changing Definition of Sepsis. *Turk J Anaesthesiol Reanim*. 2017; 45: 129-38.
4. Funk DJ, Parrillo JE and Kumar A. Sepsis and septic shock: a history. *Crit Care Clin* 2009; 125(1): 83–101.
5. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med*. 2003; 348: 1546-54.
6. Fleischmann C, Scherag A, Adhikari NK, et al. Assessment of global incidence and mortality of hospital-treated Sepsis. Current estimates and limitations. *Am J Respir Crit Care Med*. 2016;193:259–72.
7. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. *Crit Care Med*. 2007;35:1284–9.
8. Gaieski DF, Edwards JM, Kallan MJ, Carr BG. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med*. 2013;41:1167–74.
9. Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/ Society of Critical Care Medicine consensus conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med*. 1992;20:864–74.
10. Levy MM, Dellinger RP, Townsend SR, Linde-Zwirble WT, Marshall JC, Bion J, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Intensive Care Med* 2010; 38: 367-74
11. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med* 2003; 348: 1546-54.
12. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/SIS international Sepsis definitions conference. *Intensive Care Med*. 2003; 29:530–8.
13. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for Sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315:775–87.

14. Song JU, Sin CK, Park HK, Shim SR, Lee J. 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. *Critical Care.* 2018; 22:28.
15. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for Sepsis and septic shock (Sepsis-3). *JAMA.* 2016;315:801–10.
16. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the working group on Sepsis-related problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996;22:707–10.
17. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis campaign: international guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med.* 2017;43:304–77.
18. Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for change. *Lancet.* 2013;381:774–5.
19. Kaukonen KM, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic inflammatory response syndrome criteria in defining severe sepsis. *N Engl J Med.* 2015;372:1629–38.
20. 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;315:762–74.
21. Arai T, Kumasaka K, Nagata K, et al. Prediction of blood culture results by measuring procalcitonin levels and other inflammatory biomarkers. *Am J Emerg Med.* 2014; 32: 330-3.
22. Huang AM, Newton D, Kunapuli A, et al. Impact of rapid organism identification via matrix-assisted laser desorption/ionization time-of-flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia. *Clin Infect Dis.* 2013; 57: 1237-45.
23. Becker KL, Snider R, Nylen ES. Procalcitonin in sepsis and systemic inflammation: a harmful biomarker and a therapeutic target. *Br J Pharmacol.* 2010; 159: 253-64.
24. de Azevedo JR, Torres OJ, Beraldi RA, Ribas CA, Malafaia O. Prognostic evaluation of severe sepsis and septic shock: Procalcitonin clearance vs Delta Sequential Organ Failure Assessment. *J Crit Care.* 2015; 30: 219.e9-12.
25. Hochreiter M, Kohler T, Schweiger AM, Keck FS, Bein B, von Spiegel T, et al. Procalcitonin to guide duration of antibiotic therapy in intensive care patients: a randomized prospective controlled trial. *Crit Care.* 2009; 13: R83.
26. Wacker C, Prkno A, Brunkhorst FM, et al. Procalcitonin as a diagnostic marker for sepsis: a system review and meta-analysis. *Lancet Infect Dis.* 2013;12:70323–7.
27. Faix J.D. Biomarkers of sepsis. *Crit Rev Clin Lab Sci.* 2013; 50(1): 23–36.
28. Christaki E, Anyfanti P, Opal SM. Immunomodulatory therapy for sepsis: an update. *Expert Rev Anti Infect Ther.* 2011;9:1013–33.
29. Dolin HH, Papadimos TJ, Stepkowski S, et al. A Novel Combination of Biomarkers to Herald the Onset of Sepsis Prior to the Manifestation of Symptoms. *Shock.* 2018; Apr; 49(4): 364–370.
30. Chi H, Barry SP, Roth RJ, et al. Dynamic regulation of pro- and anti-inflammatory cytokines by MAPK phosphatase 1 (MKP-1) in innate immune responses. *Proc Natl Acad Sci U S A.* 2006; 103 7:2274–2279.
31. Yucel T, Memiş D, Karamanlioglu B, Süt N, Yuksel M. The prognostic value of atrial and brain natriuretic peptides, troponin I and C-reactive protein in patients with sepsis. *Exp Clin Cardiol.* 2008 Winter;13(4):183-8.
32. Avolio M, Diamante P, Modolo ML, et al. Direct molecular detection of pathogens in blood as specific rule-in diagnostic biomarker in patients with presumed sepsis: our experience on a heterogeneous cohort of patients with signs of infective systemic inflammatory response syndrome. *Shock.* 2014; 42 2:86–92.
33. Cho SY, Choi JH. Biomarkers of sepsis. *Infect Chemother.* 2014; 46 1:1–12.
34. Jones AE, Puskarich MA. Is lactate the “Holy Grail” of biomarkers for sepsis prognosis? *Crit Care Med.* 2009;37(5):1812–1813.
35. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med.* 2004;32(8):1637–1642.
36. Trzeciak S, Dellinger RP, Chansky ME, et al. Serum lactate as a predictor of mortality in patients with infection. *Intensive Care Med.* 2007;33 (6):970–977.

37. Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. *Ann Emerg Med.* 2005;45(5):524-528.
38. Jansen TC, van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med.* 2010;182(6):752-761.
39. Rhee C, Murphy MV, Li L, et al. Lactate Testing in Suspected Sepsis: Trends and Predictors of Failure to Measure Levels. *Crit Care Med.* 2015; Aug; 43(8): 1669-1676.
40. Jones AE. Lactate Clearance for Assessing Response to Resuscitation in Severe Sepsis. *Acad Emerg Med.* 2013; Aug; 20(8): 844-847.
41. Hernández, G., Ospina-Tascón, G. A., Damiani, L. P., Estenssoro, E., 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.
42. The initial resuscitation of septic shock. Cinel I, Kasapoğlu US, Gul F, Dellinger RP. *Journal of Critical Care.* 2020; 57:108-117
43. Cinel I, Opal S. Molecular biology of inflammation and sepsis: a primer. *Crit Care Med.* 2009 Jan;37(1):291-304.
44. Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., et al. (2021). Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive care medicine*, 47(11), 1181-1247.
45. Rhodes, A., Evans, L. E., Alhazzani, W., Levy, M. M., et al. (2017). Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Intensive care medicine*, 43, 304-377.
46. Scheeren TWL, Bakker J, De Backer D, et al. Current use of vasopressors in septic shock. *Ann Intensive Care.* 2019; 9: 20.
47. Early Goal-Directed Therapy Collaborative Group of Zhejiang Province The effect of early goal-directed therapy on treatment of critical patients with severe sepsis/septic shock: a multi-center, prospective, randomized, controlled study (in Chinese) *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue.* 2010;6:331-334.
48. Levy MM, Dellinger RP, Townsend SR, Surviving Sepsis Campaign et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Crit Care Med.* 2010;38:367-374.
49. Caironi, Pietro, Gianni Tognoni, Serge Masson, Roberto Fumagalli, Antonio Pesenti, Marilena Romero, Caterina Fanizza et al. "Albumin replacement in patients with severe sepsis or septic shock." *New England Journal of Medicine* 370, no. 15 (2014): 1412-1421.
50. Ueyama H, Kiyonaka S. Predicting the Need for Fluid Therapy—Does Fluid Responsiveness Work? *J Intensive Care* 2017;5:34.
51. Leisman DE, Doerfler ME, Schneider SM, et al. Predictors, Prevalence and Outcomes of Early Crystallloid Responsiveness Among Initially Hypotensive Patients With Sepsis and Septic Shock. *Critical Care Medicine.* 2018;46(2) 189-98.
52. Jones AE, Shapiro NI, Trzeciak S, Emergency MEDICINE SHOCK RESEARCH NETWORK (EMShockNet) Investigators et al. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. *JAMA.* 2010;303:739-746.
53. Jansen TC, van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med.* 2010;182:752-761.
54. Levy MM, Evans LE, Rhodes A . The Surviving Sepsis Campaign Bundle: 2018 update. *Intensive Care Med.* 2018; 44:925-928.
55. Van Dujin PJ, Bonten MJM. Antibiotic rotation strategies to reduce antimicrobial resistance in Gram-negative bacteria in European intensive care units: study protocol for a cluster-randomized crossover controlled trial. *Trials.* 2014; 15: 277.
56. E. Tacconelli (Infectious Diseases, DZIF Center, Tübingen University, Germany) and N. Magrini (WHO, EMP Department). Global Priority List Of Antibiotic-Resistant Bacteria to Guide Research, Discovery, and Development Of New Antibiotics. WHO. 2015.

57. Yesilbag Z, Karadeniz A, Basaran S, Kaya FO, et al. Nosocomial infections and risk factors in intensive care unit of a university hospital. *J Clin Exp Invest* 2015;6:233-9. 3.
58. Taş SŞ, Kahveci K. Uzun Süreli Yoğun Bakım Ünitesi ve Palyatif Bakım Merkezinde Hastane Enfeksiyonlarının Sürveyansı; 3 Yıllık Analiz. *J Contemp Med* 2018;8:55-59.
59. Otto GP, Sossdorff M, Claus RA, et al. The late phase of sepsis is characterized by an increased microbiological burden and death rate. *Crit Care*. 2011;15:R183.
60. Kollef KE, Schramm GE, Wills AR, et al. Predictors of 30-day mortality and hospital costs in patients with ventilator-associated pneumonia attributed to potentially antibiotic-resistant gram-negative bacteria. *Chest*. 2008;134(2):281–287.
61. Bassetti M, Peghin M, Vena A, Giacobbe DR. Treatment of Infections Due to MDR Gram-Negative Bacteria. *Front Med (Lausanne)*. 2019; 6: 74.
62. Zhao, S., Wu, Y., Dai, Z., Chen, Y., Zhou, X., & Zhao, J. (2022). Risk factors for antibiotic resistance and mortality in patients with bloodstream infection of Escherichia coli. *European Journal of Clinical Microbiology & Infectious Diseases*, 41(5), 713-721.
63. Rhee, C., Kadri, S. S., Dekker, J. P., Danner, R. L., et al., & CDC Prevention Epicenters Program. (2020). Prevalence of antibiotic-resistant pathogens in culture-proven sepsis and outcomes associated with inadequate and broad-spectrum empiric antibiotic use. *JAMA Network Open*, 3(4), e202899-e202899.
64. Paul, M., Carrara, E., Retamar, P., Tängdén, T., et al. (2022). European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine). *Clinical Microbiology and Infection*, 28(4), 521-547.
65. Bassetti, M., Echols, R., Matsunaga, Y., Ariyasu, M., et al. (2021). Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial. *The Lancet Infectious Diseases*, 21(2), 226-240.
66. Sader HS, Farrell DJ, Flamm RK, Jones RN. Antimicrobial susceptibility of Gram-negative organisms isolated from patients hospitalized in intensive care units in United States and European hospitals (2009-2011). *Diagn Microbiol Infect Dis* 2014;78:443-8.