

Bölüm 15

HEPATOSELLÜLER KARSİNOM; GÖRÜNTÜLEME BULGULARI, LI-RADS ve EVRELEME

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GİRİŞ

Hepatosellüler karsinom (HCC), hepatositlerden kaynaklanan bir tümördür. Primer karaciğer tümörlerinin en yaygın olanıdır ve vakaların %75-85'ini oluşturur (1).

1.EPİDEMİYOLOJİ VE ETYOLOJİ

HCC, global insidans açısından meme, akciğer, kolorektal, prostat, serviks ve mide kanserinden sonra yedinci sıradadır. Mortalite açısından her iki cinsiyet için üçüncü sıradadır ve insidans ve mortalite oranları kadınlara göre erkeklerde 2-3 kat daha yüksektir (2).

HCC'nin başlıca risk faktörleri şunlardır: karaciğer sirozlu ve kronik hepatit; kronik hepatit B virüsü (HBV) enfeksiyonu (hepatit D virüsü veya olmadan), kronik alkol kullanımıdır (1,3,4). Obezite, diabetes mellitus, metabolik sendromun artan yaygınlığı ile non alkolik steatohepatitis (NASH) sonucuna yol açarak, HCC etyolojisinde yer almaktır. Dünya'da bölgelere göre farklılıklar bulunmaktadır. Başlıca risk faktörleri bölgeden bölgeye farklılık gösterir. Yüksek riskli HCC bölgelerinde (Çin, Doğu Afrika gibi), ana belirleyiciler kronik HBV enfeksiyonu ve aflatoksin maruziyeti, diğer ülkelerde (Japonya, Mısır gibi) ise HCV enfeksiyonu daha baskın neden olabilir (1). 2020'de Avrupa ve Kuzey Amerika'da alkol tüketimi tüm HCC vakalarının %22'sini oluşturur (5). HCC'lerin büyük çoğunluğu sirozlu veya kronik hepatit B enfeksiyonu olan hastalarda teşhis edilir, bu nedenle bu grplarda tümörü erken aşamada tespit etmek için yakın takip gereklidir. Ancak HCC kronik Hepatit B enfeksiyonunda siroz gelişmeden önce de karşımıza çıkabilir (6). Pediatric yaş grubunda ise; HBV biliyer atrezi, primer sklerozan kolanjit, Fanconi sendromu, kalitsal tirozinemi ve glikojen depo

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KAYNAKÇA:

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424.
2. Global Cancer Observatory. (2 Temmuz 2023 tarihinde <http://globocan.iarc.fr/Default.aspx> adresinden ulaşılmıştır.)
3. Jiang Y, Han Q, Zhao H, et al. The Mechanisms of HBV-Induced Hepatocellular Carcinoma. *J Hepatocell Carcinoma.* 2021;8:435–450. [PMC free article] [PubMed] [Google Scholar]
4. Khatun M, Ray R, Ray RB. Hepatitis C virus associated hepatocellular carcinoma. *Adv Cancer Res.* 2021;149:103–142. [PubMed] [Google Scholar]
5. Rumgay, H.; Shield, K.; Charvat, H.; et al. Global burden of cancer in 2020 attributable to alcohol consumption: A population-based study. *Lancet Oncol.* 2021, 22, 1071–1080. [Google Scholar] [CrossRef]
6. Tang, A, Hallouch, O, Chernyak, at al. Epidemiology of hepatocellular carcinoma: target population for surveillance and diagnosis. *Abdominal Radiology (NY).* 2018, 43(1), 13–25.
7. Marrero, J.A.; Kulik, L.M.; Sirlin, C.B et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2018, 68, 723–750. [Google Scholar] [CrossRef]
8. Galle, P.R.; Forner, A.; Llovet, J.M.; et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J. Hepatol.* 2018, 69, 182–236. [Google Scholar] [CrossRef]
9. Omata, M.; Cheng, A.-L.; Kokudo, N. et al. Asia–Pacific clinical practice guidelines on the management of hepatocellular carcinoma: A 2017 update. *Hepatol. Int.* 2017, 11, 317–370. [Google Scholar] [CrossRef]
10. Masch, W.R.; Kampalath, R.; Parikh, N et al. Imaging of treatment response during systemic therapy for hepatocellular carcinoma. *Abdom. Radiol.* 2021, 46, 3625–3633. [Google Scholar] [CrossRef]
11. Chartampilas E, Rafailidis V, Georgopoulou V et al. Current Imaging Diagnosis of Hepatocellular Carcinoma. *Cancers.* 2022; 14(16):3997. <https://doi.org/10.3390/cancers14163997>
12. Sparchez Z, Craciun R, Caraiani C, et al. Ultrasound or Sectional Imaging Techniques as Screening Tools for Hepatocellular Carcinoma: Fall Forward or Move Forward? *Journal of Clinical Medicine.* 2021; 10(5):903. <https://doi.org/10.3390/jcm10050903>
13. Tanaka, H. Current role of ultrasound in the diagnosis of hepatocellular carcinoma. *J. Med. Ultrason.* 2020, 47, 239–255. [Google Scholar] [CrossRef]
14. Heimbach, J.K.; Kulik, L.M.; Finn, R.S.; et al AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology* 2018, 67, 358–380. [Google Scholar] [CrossRef] [PubMed][Green Version]
15. European Association for the Study of the Liver; European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol.* 2018;69:182–236. [PubMed] [Google Scholar][Ref list]
16. Kokudo N, Takemura N, Hasegawa K, et al. Clinical practice guidelines for hepatocellular carcinoma: The Japan Society of Hepatology 2017 (4th JSH-HCC guidelines) 2019 update. *Hepatol. Res.* 2019, 49, 1109–1113. [Google Scholar] [CrossRef]

17. Omata M, Cheng A.-L., Kokudo N, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: A 2017 update. *Hepatol. Int.* 2017; 11, 317–370. [Google Scholar] [CrossRef] [Green Version]
18. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann. Oncol.* 2018; 29, iv238–iv255. [Google Scholar] [CrossRef]
19. Rapaccini GL, Pompili M, Caturelli E, et al. Hepatocellular carcinomas <2 cm in diameter complicating cirrhosis: ultrasound and clinical features in 153 consecutive patients. *Liver Int.* 2004 Apr;24(2):124-30. doi: 10.1111/j.1478-3231.2004.0903.x. PMID: 15078476.
20. Yu NC, Chaudhari V, Raman SS, et al. CT and MRI improve detection of hepatocellular carcinoma, compared with ultrasound alone, in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2011; 9: 161–167. doi: 10.1016/j.cgh.2010.09.017.
21. Guarneri V, Loggi E, Serra C, et al. Diagnostic performance of PIVKA-II in patients with hepatocellular carcinoma. *J Hepatol.* 2020;73:S631–S632.
22. Mohamed AA, Ghanem HM, Kamal MM, et al. Dickkopf-1 and β-catenin as biomarkers for early diagnosis of hepato-cellular carcinoma. *CCTR.* 2020;16(2):136–144. [Crossref], [Google Scholar]
23. Shaker MK, Attia FM, Hassan AA, et al. Evaluation of golgi protein 73 (GP73) as a potential biomarkers for hepatocellular carcinoma. *Clin Lab.* 2020;66(8). [PubMed], [Web of Science °], [Google Scholar] doi: 10.7754/Clin.Lab.2020.190911. PMID: 32776730.
24. Sun B, Huang Z, Wang B, et al. Significance of glycan-3 (GPC3) expression in hepatocellular cancer diagnosis. *Med Sci Monit.* 2017;23:850–855. [Crossref], [PubMed], [Web of Science °], [Google Scholar]
25. Prorok PC, Marcus PM. Cancer screening trials: nuts and bolts. *Semin Oncol.* 2010 Jun;37(3):216–23. doi: 10.1053/j.seminoncol.2010.05.009. PMID: 20709206; PMCID: PMC2923646. 26).
26. Marelli C. Preliminary experience with NC100100, a new ultrasound contrast agent for intravenous injection. *Eur Radiol.* 1999;9:S343–S346346.
27. Numata K, Luo W, Morimoto M, et al. Contrast enhanced ultrasound of hepatocellular carcinoma. *World J Radiol.* 2010;2:68–82.
28. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part I. Development, growth, and spread: key pathologic and imaging aspects. *Radiology.* 2014;272:635–654. [PMC free article] [PubMed] [Google Scholar] [Ref list].
29. Lim JH, Choi D, Kim SH, et al. Detection of hepatocellular carcinoma: value of adding delayed phase imaging to dual-phase helical CT. *AJR Am J Roentgenol* 2002;179(1):67–73. Crossref, Medline, Google Scholar.
30. Chernyak V, Fowler KJ, Kamaya A, et al. Liver Imaging Reporting and Data System (LI-RADS) Version 2018: Imaging of Hepatocellular Carcinoma in At-Risk Patients. *Radiology.* 2018 Dec;289(3):816-830. doi: 10.1148/radiol.2018181494. Epub 2018 Sep 25. PMID: 30251931; PMCID: PMC6677371.
31. Kondo T, Fujiwara K, Nakagawa M, et al. The efficacy of contrast-enhanced computed tomography on the management of gastroesophageal varices in patients with hepatocellular carcinoma. *Sci Rep.* 2022 Dec 1;12(1):20726. doi: 10.1038/s41598-022-25350-8. PMID: 36456830; PMCID: PMC9715668.

32. Chan LWC, Wong SCC, Cho WCS, et al. Primary Tumor Radiomic Model for Identifying Extrahepatic Metastasis of Hepatocellular Carcinoma Based on Contrast Enhanced Computed Tomography. *Diagnostics*. 2023; 13(1):102. <https://doi.org/10.3390/diagnostics13010102>
33. Rimola J, Forner A, Tremosini S, et al. Non-invasive diagnosis of hepatocellular carcinoma ≤ 2 cm in cirrhosis. Diagnostic accuracy assessing fat, capsule and signal intensity at dynamic MRI. *J Hepatol*. 2012 Jun;56(6):1317-23. doi: 10.1016/j.jhep.2012.01.004. Epub 2012 Feb 4. PMID: 22314420
34. Kudo M, Matsui O, Izumi N, et al. Liver Cancer Study Group of Japan Surveillance and diagnostic algorithm for hepatocellular carcinoma proposed by the Liver Cancer Study Group of Japan: 2014 update. *Oncology*. 2014;87(Suppl 1):7–21. [PubMed] [Google Scholar] [Ref list]
35. Saito K, Kotake F, Ito N, et al. Gd-EOB-DTPA enhanced MRI for hepatocellular carcinoma: quantitative evaluation of tumor enhancement in hepatobiliary phase. *Magn Reson Med Sci* 2005;4(1):1–9.
36. Kitao A, Zen Y, Matsui O, et al. Hepatocellular carcinoma: signal intensity at gadoxetic acid-enhanced MR Imaging--correlation with molecular transporters and histopathologic features. *Radiology*. 2010 Sep;256(3):817-26. doi: 10.1148/radiol.10092214. Epub 2010 Jul 27. PMID: 20663969.
37. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma. Part II. Extracellular agents, hepatobiliary agents, and ancillary imaging features. *Radiology* 2014; 273:30–50.
38. Ringe KI, Husarik DB, Sirlin CB, et al. Gadoxetate disodium-enhanced MRI of the liver: part 1, protocol optimization and lesion appearance in the noncirrhotic liver. *AJR Am J Roentgenol* 2010; 195:13–28.
39. Ichikawa S, Goshima S. Clinical Significance of Liver MR Imaging. *Magn Reson Med Sci*. 2023 Apr 1;22(2):157-175. doi: 10.2463/mrms.rev.2022-0100. Epub 2023 Feb 1. PMID: 36725068; PMCID: PMC10086396
40. Bae JS, Kim JH, Lee DH, et al. Hepatobiliary phase of gadoxetic acid-enhanced MRI in patients with HCC: prognostic features before resection, ablation, or TACE. *Eur Radiol*. 2021;31(6):3627–3637. doi: 10.1007/s00330-020-07499-w. [PubMed] [CrossRef] [Google Scholar]
41. Kang TW, Rhim H, Lee J, et al. Magnetic resonance imaging with gadoxetic acid for local tumour progression after radiofrequency ablation in patients with hepatocellular carcinoma. *Eur Radiol*. 2016;26(10):3437–3446. doi: 10.1007/s00330-015-4190-5. [PubMed] [CrossRef] [Google Scholar]
42. <https://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf>
43. Vauthey JN, Klimstra D, Blumgart LH. A simplified staging system for hepatocellular carcinomas. *Gastroenterology* 1995;108(2):617–618. [PubMed] [Google Scholar] [Ref list]
44. Pons F, Varela M, Llovet JM. Staging systems in hepatocellular carcinoma. *HPB (Oxford)*. 2005;7(1):35–41. doi: 10.1080/13651820410024058. PMID: 18333159; PMCID: PMC2023920
45. Llovet JM, Bru C, Bruix J: Prognosis of hepatocellular carcinoma: the BCLC staging classification. *Semin Liver Dis* 1999;19: 329–338

46. Bruix J, Sherman M; Practice Guidelines Committee, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma. *Hepatology* 2005;42(5):1208–1236. [PubMed] [Google Scholar] [Ref list]
47. Kim BK, Kim SU, Park JY, et al. Applicability of BCLC stage for prognostic stratification in comparison with other staging systems: single centre experience from long-term clinical outcomes of 1717 treatment-naïve patients with hepatocellular carcinoma. *Liver Int* 2012;32(7):1120–1127. [PubMed] [Google Scholar] [Ref list]
48. Pomfret EA, Washburn K, Wald C, et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. *Liver Transpl* 2010;16(3):262–278. [PubMed] [Google Scholar] [Ref list]
49. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2018;68(2):723–750. doi: 10.1002/hep.29913. [PubMed] [CrossRef] [Google Scholar]
50. Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. *J Hepatol*. 2022;76(3):681–693. doi: 10.1016/j.jhep.2021.11.018. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
51. Nault J-C, Sutter O, Nahon P, et al. Percutaneous treatment of hepatocellular carcinoma: State of the art and innovations. *J Hepatol* 2018;68:783–97. 10.1016/j.jhep.2017.10.004. [PubMed] [CrossRef] [Google Scholar] [Ref list]
52. Ferrer-Fàbrega J, Forner A, Liccioni A, et al. Prospective validation of ab initio liver transplantation in hepatocellular carcinoma upon detection of risk factors for recurrence after resection. *Hepatology* 2016;63:839–49. 10.1002/hep.28339. [PubMed] [CrossRef] [Google Scholar] [Ref list]
53. Pompili M, Saviano A, de Matthaeis N, et al. Long-term effectiveness of resection and radiofrequency ablation for single hepatocellular carcinoma ≤3 cm. Results of a multicenter Italian survey. *J Hepatol* 2013;59:89–97. 10.1016/j.jhep.2013.03.009. [PubMed] [CrossRef] [Google Scholar] Eğer transplantasyon
54. Forner A, Gilabert M, Bruix J, et al. Heterogeneity of intermediate-stage HCC necessitates personalized management including surgery. *Nat Rev Clin Oncol* 2014;12:10–10. 10.1038/nrclinonc.2014.122-c2. [PubMed] [CrossRef] [Google Scholar] [Ref list]
55. Raoul J-L, Forner A, Bolondi L, et al. Updated use of TACE for hepatocellular carcinoma treatment: How and when to use it based on clinical evidence. *Cancer Treat Rev* 2019;Jan;72:28–36. 10.1016/j.ctrv.2018.11.002. [PubMed] [CrossRef] [Google Scholar] [Ref list].
56. Galle PR, Tovoli F, Foerster F, et al. The treatment of intermediate stage tumours beyond TACE: From surgery to systemic therapy. *J Hepatol* 2017;67:173–83. 10.1016/j.jhep.2017.03.007. [PubMed] [CrossRef] [Google Scholar] [Ref list]
57. Kim TH, Woo S, Joo I, et al. LI-RADS treatment response algorithm for detecting incomplete necrosis in hepatocellular carcinoma after locoregional treatment: a systematic review and meta-analysis using individual patient data. *Abdom Radiol (NY)* 2021; 46:3717–3728. [PMC free article] [PubMed] [Google Scholar] [Ref list]