



## BÖLÜM 17

# Primer Karaciğer Kanseri

Hakan CANBAZ<sup>1</sup>

### Giriş

Vücutta gelişen orijinal veya ilk tümör olarak tanımlanmaktadır (1). Kansere dönüşen kontrolsüz hücre çoğalmasının vücutta ilk olarak başladığı yer primer kanser odağı olarak tanımlanmaktadır. Primer karaciğer kanserleri, hepatositler ve safra yolu epiteli hücreleri başta olmak üzere karaciğerin yapısında bulunan diğer dokulara (damar, sinir, lenfatik, yağ ve bağ dokusu) ait hücrelerin malign tümörlerini de içermektedir.

Dünya Sağlık Örgütü'nün (WHO) 2020 yılı verilerine göre karaciğer kanserleri her iki cinsiyet ve tüm yaş gruplarında yeni olgular bakımından %4,7'lik oranla (905.677 olgu) tüm kanserler içinde altıncı sırada, kansere bağlı ölümlerde ise %8,3'lük oranla (830.180 ölüm) üçüncü sırada yer almaktadır. Hastalığın insidansı 9,5/100000, mortalitesi 8,7/100000'dır. Erkeklerde kadınlara göre daha fazla oranda (E/K: 14,1/5,2) görülmektedir. Dünyadaki hastaların %72,5'i, mortalitenin %73,3'ü Asya kıtasında görülmektedir (2).

### Primer Karaciğer Kanseri Tipleri

Karaciğerin yapısını oluşturan tüm hücre gruplarından kanser gelişebilmektedir. Karaciğer kütleinin %60-80'ini hepatositler oluşturmaktadır (3), yapısında hepatositlerin yanı sıra safra yolu epiteli hücreleri ve mezenkimal hücreler de bulunmaktadır. Primer karaciğer kanserlerinin en sık görülenleri, hepatositlerden köken alan hepatoselüler kanser (HSK) (%75-85) ve kolanjiositlerden köken alan intrahepatik kolanjiokarsinom (İKK) (%10-15) olmakla birlikte az oranda diğer kanser tipleri de görülmektedir (4, 5).

Sirotik karaciğerlerdeki ve nonsirotik kronik karaciğer hastalıklarındaki displastik odaklar ve displastik nodüller prekanseröz lezyonları içermektedir. Displastik nodüller histomorfolojik olarak düşük ve yüksek dereceli şeklinde sınıflanmaktadır (6). Yüksek dereceli displastik nodüller HSK'nin öncüsü olarak kabul edilmektedir (7). Kanser gelişmiş olan nodül ve hepatositlerde histopatolojik olarak farklılıklar görülebilmektedir, bunlar

<sup>1</sup> Prof. Dr., Mersin Üniversitesi Tıp Fakültesi Genel Cerrahi AD., canbazhakan@yahoo.com

fazla görülenlerdir. Tanıda temel olarak çok kesitli görüntüleme yöntemlerinden (BT ve MRG) yararlanılmaktadır. Hastaların tedavisinin planlanmasında kullanılmak üzere türetilmiş çok sayıda skorlama ve evreleme sistemi bulunmaktadır. Cerrahi rezeksiyon ve karaciğer transplantasyonu hastalara uygulanacak başlıca küratif tedavi seçenekleridir. Primer karaciğer kanserli hastaların tedavi yönetimi geniş kapsamlı multidisipliner ekip değerlendirmesi ile yapılmalıdır.

## Kaynaklar

1. NIH, National Cancer Institute (2021). NCI Dictionary. (21/11/2021 tarihinde <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/primary-cancer> adresinden ulaşılmıştır).
2. World Health Organization. Liver Factsheet. Globocan <https://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf> (2020)
3. Stanger BZ. Cellular homeostasis and repair in the mammalian liver. *Annu Rev Physiol.* 2015;77:179–200.
4. Torbenson, M.S., Ng, I.O.L, Park, Y.N., et al. (2019). Hepatocellular carcinoma. In: WHO Classification of Tumours Editorial Board, editor. *Digestive system tumours. WHO classification of tumours series.* (5th ed., pp 229-39). Lyon: International Agency for Research on Cancer.
5. Thomas-London, W., Petrick, J.L., McGlynn, K.A. (2018). Liver cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. *Cancer Epidemiology and Prevention.* (4th ed. pp 635-660). Oxford University Press.
6. Jiang K, Al-Diffalha S, Centeno BA. Primary Liver Cancers—Part 1: Histopathology, Differential Diagnoses, and Risk Stratification. *Cancer Control.* 2018;25:1–26.
7. Ferrell LD, Crawford JM, Dhillon AP, et al. Proposal for standardized criteria for the diagnosis of benign, borderline, and malignant hepatocellular lesions arising in chronic advanced liver disease. *Am J Surg Pathol.* 1993;17(11):1113-1123.
8. Kim H, Jang M, Park YN. Histopathological Variants of Hepatocellular Carcinomas: an Update According to the 5th Edition of the WHO Classification of Digestive System Tumors. *J Liver Cancer.* 2020;20(1):17-24.
9. Nagtegaal ID, Odze RD, Klimstra D, et al. The 2019 WHO classification of tumours of the digestive system. *Histopathology.* 2020;76:182–188.
10. Zen Y, Adsay NV, Bardadin K, et al. Biliary intraepithelial neoplasia: an international interobserver agreement study and proposal for diagnostic criteria. *Mod Pathol.* 2007;20(6):701-709.
11. Yeh MM. Pathology of combined hepatocellular-cholangiocarcinoma. *J Gastroenterol Hepatol.* 2010;25(9):1485-1492.
12. Panqueva L, del Pilar R. Diagnosis and Differential Diagnosis Problems with Histological Variants of Benign Liver Neoplasms. *Rev Col Gastroenterol.* 2015;116-124.
13. Torbenson MS. Morphologic Subtypes of Hepatocellular Carcinoma. *Gastroenterol Clin North Am.* 2017;46:365–391.
14. Cardinale V, Bragazzi MC, Carpino G, et al. Intrahepatic cholangiocarcinoma: review and update. *Hepatoma Res.* 2018;4:20.
15. Joo I, Lee JM, Yoon JH. Imaging Diagnosis of Intrahepatic and Perihilar Cholangiocarcinoma: Recent Advances and Challenges. *Radiology.* 2018;288:7–13.
16. Massarweh NN, El-Serag HB. Epidemiology of Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *Cancer Control.* 2017;24(3):1–11.
17. M, Cheng AL, Kokudo N, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int.* 2017;11(4):317-370.
18. de Martel C, Maucourt-Boulch D, Plummer M, et al. World-wide relative contribution of hepatitis B and C viruses in hepatocellular carcinoma. *Hepatology.* 2015;62:1190–1200.
19. Thiele M, Gluud LL, Fiella AD, et al. Large variations in risk of hepatocellular carcinoma and mortality in treatment naive hepatitis B patients: systematic review with metaanalyses. *PLoS One.* 2014;9(9):e107177.
20. Welzel TM, Graubard BI, El-Serag HB, et al. Risk factors for intrahepatic and extrahepatic cholangiocarcinoma in the United States: a population-based case-control study. *Clin Gastroenterol Hepatol.* 2007;5(10):1221-1228.
21. Palmer WC, Patel T. Are common factors involved in the pathogenesis of primary liver cancers? A meta-analysis of risk factors for intrahepatic cholangiocarcinoma. *J Hepatol.* 2012;57(1):69-76.
22. Singh S, Singh PP, Singh AG, et al. Antidiabetic medications and the risk of hepatocellular cancer: a systematic review and meta-analysis. *Am J Gastroenterol.* 2013;108(6):881-891.
23. Mejia JC, Pasko J. Primary Liver Cancers: Intrahepatic Cholangiocarcinoma and Hepatocellular Carcinoma. *Surg Clin North Am.* 2020;100(3):535-549.
24. Buettner S, van Vugt JL, IJzermans JN, et al. Intrahepatic cholangiocarcinoma: current perspectives. *Onco Targets Ther.* 2017;10:1131-1142.
25. Clark T, Maximin S, Meier J, et al. Hepatocellular Carcinoma: Review of Epidemiology, Screening, Imaging Diagnosis, Response Assessment, and Treatment. *Curr Probl Diagn Radiol.* 2015;44(6):479-86.
26. Anderson CD, Rice MH, Pinson CW, et al. Fluorodeoxyglucose PET imaging in the evaluation of gallbladder carcinoma and cholangiocarcinoma. *J Gastrointest Surg.* 2004;8(1):90–97.
27. Bruix J, Sherman M. American Association for the Study of Liver D. Management of hepatocellular carcinoma.

- noma: An update. *Hepatology*. 2011;53(3):1020–1022.
28. Saini S. Imaging of the hepatobiliary tract. *N Engl J Med*. 1997;336:1889–1894.
  29. Valls C, Guma A, Puig I, et al. Intrahepatic peripheral cholangiocarcinoma: CT evaluation. *Abdom Imaging*. 2000;25:490–496.
  30. Murakami T, Nakamura H, Tsuda K, et al. Contrast enhanced MR imaging of intrahepatic cholangiocarcinoma: pathologic correlation study. *J Magn Reson Imaging*. 1995;5:165–170.
  31. Chung YE, Kim MJ, Park YN, et al. Varying appearances of cholangiocarcinoma: radiologic-pathologic correlation. *RadioGraphics*. 2009;29(3):683–700.
  32. Shah A, Tang A, Santillan C, Sirlin C. Cirrhotic liver: what's that nodule? the LI-RADS approach. *J Magn Reson Imaging*. 2016;43(2):281–294.
  33. Weber S, Ribero D, O'Reilly E, et al. Intrahepatic cholangiocarcinoma: expert consensus statement. *HPB (Oxford)*. 2015;17(8):669–680.
  34. Vitale A, Farinati F, Finotti M, et al. Associazione Italiana per lo Studio del Fegato (AISF) HCC Special Interest Group, and Italian Liver Cancer (ITA.LI.CA) Study Group 11, Overview of Prognostic Systems for Hepatocellular Carcinoma and ITA.LI.CA External Validation of MESH and CNLC Classifications. *Cancers*. 2021;13:1673.
  35. Llovet JM, Brú C, Bruix J. Prognosis of Hepatocellular Carcinoma: The BCLC Staging Classification. *Semin Liver Dis*. 1999;19:329–338.
  36. Kumar Y, Sharma P, Bhatt N, et al. Transarterial therapies for hepatocellular carcinoma: a comprehensive review with current updates and future directions. *Asian Pacific journal of cancer prevention: Asian Pac J Cancer Prev*. 2016;17:473–478.
  37. Farinati F, Vitale A, Spolverato G, et al. Development and Validation of a New Prognostic System for Patients with Hepatocellular Carcinoma. *PLoS Med*. 2016;13:e1002006.
  38. Liu PH, Hsu CY, Hsia CY, et al. Proposal and Validation of a New Model to Estimate Survival for Hepatocellular Carcinoma Patients. *Eur J Cancer*. 2016;63:25–33.
  39. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med*. 1996;334(11):693–699.
  40. Pugh RN, Murray-Lyon IM, Dawson JL, et al. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973;60:646–649.
  41. Zhou J, Sun H, Wang Z, et al. Guidelines for the Diagnosis and Treatment of Hepatocellular Carcinoma (2019 Edition). *Liver Cancer*. 2020;9:682–720.
  42. Lee AJ, Chun YS. Intrahepatic cholangiocarcinoma: the AJCC/UICC 8th edition updates. *Chin Clin Oncol*. 2018;7(5):52.
  43. Forner A, Llovet JM, Bruix J. Hepatocellular carcinoma. *Lancet*. 2012;379(9822):1245–1255.
  44. Saraswat VA, Pandey G, Shetty S. Treatment algorithms for managing hepatocellular carcinoma *J Clin Exp Hepatol*. 2014;3(3):S80–9.
  45. Ishizaki Y, Kawasaki S. The evolution of liver transplantation for hepatocellular carcinoma (past, present, and future). *J Gastroenterol*. 2008;43:18–26.
  46. Adam R, Bhangui P, Vibert E, et al. Resection or transplantation for early hepatocellular carcinoma in a cirrhotic liver: does size define the best oncological strategy? *Ann Surg*. 2012;256(6):883–891.
  47. Qi X, Zhao Y, Li H, et al. Management of hepatocellular carcinoma: an overview of major findings from meta-analyses. *Oncotarget*. 2016;7(23):34703–34751.
  48. Vogel A, Martinelli E; ESMO Guidelines Committee. Updated treatment recommendations for hepatocellular carcinoma (HCC) from the ESMO Clinical Practice Guidelines. *Annals of Oncology*, 2021;32(6):801–805.
  49. Proneth A, Zeman F, Schlitt HJ, et al. Is resection or transplantation the ideal treatment in patients with hepatocellular carcinoma in cirrhosis if both are possible? A systematic review and metaanalysis. *Ann Surg Oncol*. 2014;21(9):3096–3107.
  50. Morise Z, Kawabe N, Tomishige H, et al. Recent advances in the surgical treatment of hepatocellular carcinoma. *World J Gastroenterol*. 2014;20(39):14381–14392.
  51. Bosetti C, Levi F, Boffetta P, et al. Trends in Mortality from Hepatocellular Carcinoma in Europe, 1980–2004. *Hepatology*. 2008;48:137–145.
  52. Pinter M, Trauner M, Peck-Radosavljevic M, et al. Cancer and liver cirrhosis: implications on prognosis and management. *ESMO Open*. 2016;1(2):e000042.
  53. Dodson RM, Weiss MJ, Cosgrove D, et al. Intrahepatic cholangiocarcinoma: management options and emerging therapies. *J Am Coll Surg*. 2013;217:736–750.e4.
  54. Zhang H, Yang T, Wu M et al. Intrahepatic cholangiocarcinoma: Epidemiology, risk factors, diagnosis and surgical management. *Cancer Lett*. 2016;379(2):198–205.
  55. Farges O, Fuks D, Le Treut YP, et al. AJCC 7th edition of TNM staging accurately discriminates outcomes of patients with resectable intrahepatic cholangiocarcinoma: by the AFC-IHCC-2009 study group. *Cancer*. 2011;117:2170–2177.
  56. Spolverato G, Kim Y, Alexandrescu S, et al. Management and outcomes of patients with recurrent intrahepatic cholangiocarcinoma following previous curative-intent surgical resection. *Ann Surg Oncol*. 2016;23:235–243.