

GERİATRİ VE PRİMER KARACİĞER MALİGNİTELERİ

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GİRİŞ

İleri yaşlarda beklentiği üzere maligniteler daha fazla görülmektedir. Malignitelerin yaklaşık %50 si geriatrik populasyonda görülmekte ve hastaların %70'inde mortal olarak seyretmektedir(2). Ülkemizde kanser önemli bir halk sağlığı problemi olarak değerlendirilmektedir. Beklenen yaşam süresinin artması da önemli bir etkendir. Türkiye İstatistik Kurumu (TÜİK) verilerine göre 2023 yılında toplumun yaklaşık yüzde 10'un ve 2050 yılına kadar da yaklaşık %20' sinin 65 yaş ve üzerinde olacağı tahmin edilmektedir (3).

Yaşlı hasta grubunda, genç hasta grubuna göre kullanılan standart kemoterapi düzeyleri ve standartları da farklılık göstermektedir. Standardize tedavi planının olmaması, artmış toksisite riski, tıbbi tedaviye ulaşım problemleri gibi farklı sorunlar ana nedenler arasında sayılmaktadır(4).

Yaşlılarda en sık tanı konulan kanserlerden birisi olan ve hepatoselüler kanser(HCC)'in sıklığı gittikçe artmaktadır. HCC günümüzde erkek hastalar arasında kansere bağlı en sık ikinci ölüm nedenidir(3-5).

HCC genellikle orta - ileri yaşta ve çoğu zaman siroz ile birlikte görülmektedir. İleride insidansının daha fazla artması beklenmektedir. Bu durumun farklı nedenleri mevcuttur. Özellikle HCV karaciğer hasarı ve karaciğer sirozu oluşumuna HBV 'den daha sık neden olmaktadır. HBV için aşılamanın ve kronik hepatit B ile hepatit C'de antiviral tedavinin orta vadede iyileştirici olduğu, ileri dönemde ise karaciğer sirozu oluşumunu ve HCC gelişimini geçiktirdiği kabul edilmektedir.

Önümüzdeki yıllarda, özellikle gelişmekte olan ülkelerde yaşlı popülasyonun artması, kanser tarama programlarına ulaşımın azlığı veya olmaması, kanser ve kanser ilişkili mortalitenin artacağı öngörüsüne neden olmaktadır(6). Ülkemizdeki kanser verileri gelişmekte olan ülkelerle benzerlik göstermektedir.

Son yıllarda HCC tedavisinde yeni cerrahi tekniklerin geliştirilmesi, yeni ablatif yöntemlerin başarıyla uygulanması mortalite oranlarının düşürülmesi прогноз açısından önemlidir. En uygun tedavi stratejisi, erken tanı, karaciğer fonksiyon düzeyleri, hasta performans durumu, tümör özelliklerini ve eşlik eden komorbid hastalıklar gibi çeşitli faktörlere göre düzenlenmelidir.

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KAYNAKLAR

1. Kondo K, Chijiwa K, Funagayama M, Kai M, Otani K, Ohuchida J. Hepatic resection is justified for elderly patients with hepatocellular carcinoma. *World J Surg.* 2008;32(10):2223–2229.
2. Ries EM, Kosary CL, Hankey BF, et al. SEER Cancer Statistics Review: 1975-2000. National Cancer Institute, Bethesda, MD.
3. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65(2): 87–108.
4. Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *N Engl J Med.* 1999 Dec 30;341(27):2061–7. doi: 10.1056/NEJM199912303412706. PMID: 10615079.
5. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65(2): 87–108.
6. World Cancer Report 2014.
7. Kew M. Clinical, pathologic, and etiologic heterogeneity in hepatocellular carcinoma: evidence from southern Africa. *Hepatology* 1981;1:366–9.
8. Jiang Z, Jhunjhunwala S, Liu J, Haverty PM, Kennemer MI, Guan Y, Lee W, Carnevali P, Stinson J, Johnson S, Diao J, Yeung S, Jubb A, Ye W, Wu TD, Kapadia SB, de Sauvage FJ, Gentleman RC, Stern HM, Seshagiri S, Pant KP, Modrusan Z, Ballinger DG, Zhang Z. The effects of hepatitis B virus integration into the genomes of hepatocellular carcinoma patients. *Genome Res* 2012; 22: 593–601
9. Blum H, Moradpour D. Viral pathogenesis of hepatocellular carcinoma. *J Gastroenterol Hepatol* 2002;17:S413–20.
10. Taura N, Hamasaki K, Nakao K, Ichikawa T, Nishimura D, Goto T, Fukuta M, Kawashimo H, Miyaaki H, Fujimoto M, Kusumoto K, Motoyoshi Y, Shibata H, Inokuchi K, Eguchi K. Aging of patients with hepatitis C virus-associated hepatocellular carcinoma: long-term trends in Japan. *Oncol Rep.* 2006 Oct;16(4):837–43.
11. George SL, Bacon BR, Brunt EM, et al. Clinical, virologic, histologic, and biochemical outcomes after successful HCV therapy: a 5-year follow-up of 150 patients. *Hepatology* 2009;49:729–38.
12. Ioannou G, Splan M, Weiss N, et al. Incidence and predictors of hepatocellular carcinoma in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2007;5:938–45.
13. Hart, C. L., Morrison, D. S., Batty, G. D., Mitchell, R. J. & Smith, G. D. Effect of body mass index and alcohol consumption on liver disease: analysis of data from two prospective cohort studies. *BMJ* 340, c1240 (2010).
14. Liu, Y. L. et al. TM6SF2 rs58542926 influences hepatic fibrosis progression in patients with non-alcoholic fatty liver disease. *Nat. Commun.* 5, 4309 (2014)
15. Llovet, J.M., Willoughby, C.E., Singal, A.G. et al. Nonalcoholic steatohepatitis-related hepatocellular carcinoma: pathogenesis and treatment. *Nat Rev Gastroenterol Hepatol* 20, 487–503 (2023).
16. Huang, D. Q. et al. Hepatocellular carcinoma incidence in alcohol-associated cirrhosis: systematic review and meta-analysis. *Clin. Gastroenterol. Hepatol.*
17. Hagström, H. et al. Risk of cancer in biopsy-proven alcohol-related liver disease: a population-based cohort study of 3,410 persons. *Clin. Gastroenterol. Hepatol.*
18. Jepsen, P., Ott, P., Andersen, P. K., Sørensen, H. T. & Vilstrup, H. Risk for hepatocellular carcinoma in patients with alcoholic cirrhosis: a Danish nationwide cohort study. *Ann. Intern. Med.* 156, 841–847 (2012).
19. Ganne-Carrié, N. et al. Estimate of hepatocellular carcinoma incidence in patients with alcoholic cirrhosis. *J. Hepatol.* 69, 1274–1283 (2018)
20. Lin, C. W. et al. Heavy alcohol consumption increases the incidence of hepatocellular carcinoma in hepatitis B virus-related cirrhosis. *J. Hepatol.* 58, 730–735 (2013).
21. Huang, D.Q., Mathurin, P., Cortez-Pinto, H. et al. Global epidemiology of alcohol-associated cirrhosis and HCC: trends, projections and risk factors. *Nat Rev Gastroenterol Hepatol* 20, 37–49 (2023).
22. Wogan G. Aflatoxin exposure as a risk factor in the etiology of hepatocellular carcinoma. New York: Churchill Livingstone; 1997.
23. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. *Gastroenterology.* 2004 Nov;127
24. Kew M. Pathogenesis of hepatocellular carcinoma in hereditary hemochromatosis: occurrence in non-cirrhotic patients. *Hepatology* 1990;11:1806–7.
25. Walshe JM, Waldenstrom E, Sams V, Nordlinder H, Westermark K. Abdominal malignancies in patients with Wilson's disease. *Q J Med* 2003;96:637–662.
26. Polio J, Enriquez R, Chow A, et al. Hepatocellular carcinoma in wilson's disease. case report and review of the literature. *J Clin Gastroenterol* 1989;11:220–4.
27. El-Serag H, Richardson P, Everhart J. The role of diabetes in hepatocellular carcinoma: a case-control study among United States veterans. *Am J Gastroenterol* 2001;96:2462–7.
28. Oishi K, Itamoto T, Kohashi T, Matsugu Y, Nakahara H, Kitamoto M. Safety of hepatectomy for elderly patients with hepatocellular carcinoma. *World J Gastroenterol.* 2014;20(41):15028–15036
29. Isokawa O, Suda T, Aoyagi Y, Kawai H, Yokota T, Takahashi T, Tsukada K, Shimizu T, Mori S, Abe Y, Suzuki Y, Nomoto M, Mita Y, Yanagi M, Igarashi H, Asakura H. Reduction of telomeric repeats as a possible predictor for development of hepatocellular carcinoma: convenient evaluation by slot-blot analysis. *Hepatology.* 1999 Aug;30(2):408–12.
30. Honda T, Miyaaki H, Ichikawa T, et al. Clinical characteristics of hepatocellular carcinoma in elderly patients. *Oncol Lett.* 2011;2(5):851–854.
31. Cohen MJ, Bloom AI, Barak O, et al. Trans-arterial chemo-embolization is safe and effective for very elderly patients with hepatocellular carcinoma. *World J Gastroenterol.* 2013;19(16):2521–2528.
32. Van der Poorten D, Milner KL, Hui J, et al. Visceral fat: A key mediator of steatohepatitis in metabolic liver disease. *Hepatology.* 2008;48(2):449–457.
33. Reddy SK, Barbas AS, Turley RS, et al. Major liver resection in elderly patients: a multi-institutional analysis. *J Am Coll Surg.* 2011;212(5):787–795.
34. Nishikawa H, Kimura T, Kita R, Osaki Y. Treatment for hepatocellular carcinoma in elderly patients: a literature review. *J Cancer.* 2013;4(8):635–643.
35. Efremidis S, Hytioglu P. The multistep process of hepatocarcinogenesis in cirrhosis with imaging correlation. *Eur Radiol.* 2002;12:753–64.
36. Bruix J, Sherman M. Management of hepatocellular carcinoma. *Hepatology* 2005;42(5):1208–1236.

37. Luca A, Milazzo M, Caruso S, et al. Hepatic nodules detected in cirrhotic patients using high-performance multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI): radiological-pathological correlation on explanted livers. *J Hepatol* 2007;46:S37.
38. Ryder SD. Guidelines for the diagnosis and treatment of hepatocellular carcinoma (HCC) in adults. *Gut* 2003;52 Suppl 3(iii1-8).
39. Caturelli E, Biasini E, Bartolucci F, Facciorusso D, Decembrino F, Attino V, Bisceglia M. Diagnosis of hepatocellular carcinoma complicating liver cirrhosis: utility of repeat ultrasound-guided biopsy after unsuccessful first sampling. *Cardiovasc Intervent Radiol* 2002;25(4):295-299.
40. Rapaccini GL, Pompili M, Caturelli E, Anti M, Aliotta A, Cedrone A, Amadei E, et al. Focal ultrasound lesions in liver cirrhosis diagnosed as regenerating nodules by fine-needle biopsy. Follow-up of 12 cases. *Dig Dis Sci* 1990;35(4):422-427.
41. Mor E, Kaspa RT, Sheiner P, Schwartz M. Treatment of hepatocellular carcinoma associated with cirrhosis in the era of liver transplantation. *Ann Intern Med* 1998;129(8):643-653.
42. Cedrone A, Covino M, Caturelli E, Pompili M, Lorenzelli G, Villani MR, Valle D, et al. Utility of alpha-fetoprotein (AFP) in the screening of patients with virus-related chronic liver disease: does different viral etiology influence AFP levels in HCC? A study in 350 western patients. *Hepatogastroenterology* 2000;47(36):1654-1658.
43. Chaïbi P, Magné N, Breton S, Chebib A, Watson S, Duron JJ, Hannoun L, Lefranc JP, Piette F, Menegaux F, Spano JP. Influence of geriatric consultation with comprehensive geriatric assessment on final therapeutic decision in elderly cancer patients. *Crit Rev Oncol Hematol*. 2011 Sep;79(3):302-7.
44. Thornton RH, Covey A, Petre EN, et al. A comparison of outcomes from treating hepatocellular carcinoma by hepatic artery embolization in patients younger or older than 70 years. *Cancer*. 2009;115(21):5000-5006.
45. Mirici-Cappa F, Gramenzi A, Santi V, et al. Treatments for hepatocellular carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. *Gut*. 2010;59(3):387-396.
46. Hilgard P, Hamami M, Fouly AE, et al. Radioembolization with yttrium-90 glass microspheres in hepatocellular carcinoma: European experience on safety and long-term survival. *Hepatology*. 2010;52(5):1741-1749.
47. Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med*. 2008;359(4):378-390.
48. Di Costanzo GG, Tortora R, De Luca MD, et al. Impact of age on toxicity and efficacy of sorafenib-targeted therapy in cirrhotic patients with hepatocellular carcinoma. *Med Oncol*. 2013;30(1):446.
49. Iavarone M, Cabibbo G, Piscaglia F, et al. Field-practice study of sorafenib therapy for hepatocellular carcinoma: A prospective multicenter study in Italy. *Hepatology*. 2011;54(6):2055-2063.
50. Sato M, Tateishi R, Yasunaga H, et al. Mortality and morbidity of hepatectomy, radiofrequency ablation, and embolization for hepatocellular carcinoma: a national survey of 54,145 patients. *J Gastroenterol*. 2012;47(10):1125-1133.
- 51)Keswani RN, Ahmed A, Keeffe EB. Older age and liver transplantation: A review. *Liver Transpl*. 2004;10(8):957-967
- 52) Keswani RN, Ahmed A, Keeffe EB. Older age and liver transplantation: A review. *Liver Transpl*. 2004;10(8):957-967
- 53) Cescon M, Grazi GL, Del Gaudio M, et al. Outcome of right hepatectomies in patients older than 70 years. *Arch Surg*. 2003;138(5):547-552
- 54) Liver EA for the S of the, Cancer EO for R and T of. EASL-EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol*. 2012;56(4):908-943.
- 55) Ishizawa T, Mise Y, Aoki T, et al. Surgical technique: new advances for expanding indications and increasing safety in liver resection for HCC. *J Hepatobiliary Pancrat Sci*. 2010;17(4):389-393
- 56) Nanashima A, Abo T, Nonaka T, et al. Prognosis of patients with hepatocellular carcinoma after hepatic resection: Are elderly patients suitable for surgery? *J Surg Oncol*. 2011;104(3):284-291.
- 57) Ferrero A, Viganò L, Polastri R, et al. Hepatectomy as treatment of choice for hepatocellular carcinoma in elderly cirrhotic patients. *World J Surg*. 2005;29(9):1101-1105
- 58) Yamada S, Shimada M, Miyake H, et al. Outcome of hepatectomy in super-elderly patients with hepatocellular carcinoma. *Hepatol Res*. 2012;42(5):454-458.
- 59) Liver EA for the S of the, Cancer EO for R and T of. EASL-EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol*. 2012;56(4):908-943
- 60) López-Plaza B, Loria-Kohen V, González-Rodríguez LG, Fernández-Cruz E. Alimentación y estilo de vida en la prevención del cáncer [Diet and lifestyle in cancer prevention]. *Nutr Hosp*. 2022 Sep 1;39(Spec No3):74-77.