

35. BÖLÜM

HEPATOSELÜLER KANSERDE GERİATRİK HASTA YÖNETİMİ

Tahir YERLİKAYA¹

GİRİŞ

Hepatoselüler karsinom (HCC) dünya genelinde yaygınlığı giderek artmakta ve kansere bağlı ölümlerin en sık üçüncü nedeni haline gelmektedir (1-2). 2012 itibarıyle, dünya genelinde 14 milyondan fazla HCC vakası var iken bu sayının önumüzdeki yirmi yıl içinde 22 milyona çıkması beklenmektedir (3). HCC'li hastaların ortalama medyan yaşı 63'tür (medyan tanı yaşı 56 ile 74 arasındadır (4). HCC'nin insidansı 65-69 yaşlarındaki kişilerde % 8 ve 70 yaş ve üzerindeki kişilerde % 3 artmıştır (5-6). HCC yaşlı yetişkinlerde giderek artmaktadır, özellikle Avrupa ve ABD'de geç başlangıçlı HCC'nin hepatit, karaciğer yağlanması ve komorbiditelerin yaşlanma ile ilişkili olabileceği belirtilmektedir (4). HCC, primer karaciğer malignitelerinin % 90'ından fazlasını oluşturur ve çoğu hepatit ve / veya sirozlu hastalarda görülür (2).

Amerika Birleşik Devletleri'nde, Hepatit C virüsü (HCV) enfeksiyonu, HC-C'nin en yaygın nedeni iken gelişmekte olan ülkelerde ve Asya'da, Hepatit B virüsü (HBV) enfeksiyonu en yaygın sebebidir (2-7). HBV ve HCV için etkili tedavilere rağmen, HCC riski tamamen ortadan kaldırılamamıştır ve HCC, kriptojenik siroz, obezite, insülin direnci, hiperlipidemi ve non-alkolik yağlı karaciğer hastalığında (NAFLD) artış gibi risk faktörleri nedeniyle görülmeye devam etmektedir (2-8-9). Yaşlılarda HCC'nin yaygınlığı ve artan insidansı göz önüne alındığında, geriatrik populasyonda HCC'yi tedavi ederken ortaya çıkan sorunlar ve tedavi yönetimi önemlidir. Birçok klinik çalışmada yaşlı hastalar dışlanmıştır ancak birkaç retrospektif ve meta-analizlerde genç hastalar ile seçilmiş yaşlı hastalarda benzer yaklaşımların tedavide aynı etkinlikte olduğu gösterilmiş

¹ Uzm. Dr., Sağlık Bilimleri Üniversitesi Antalya Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği
drtahiryerlikaya@gmail.com

bildirilen sonuçlar açısından yaşlı yetişkinlerin alt grup analizlerine odaklanması önemlidir.

SONUÇ

Genel olarak, HCC tanılı ve iyi performans durumuna sahip yaşlı yetişkinler, bir çok tedavi seçeneğine sahip; cerrahi, transplant, lokal ablatif tedaviler ve sistemik tedavi dahil olmak üzere standart tedavileri tolerasyonları iyi olup ve bu tedaviler yararlı görülmektedir. Geriatrik tarama araçları ve CGA'nın ileriye dönük olarak araştırılması ve klinik araştırmalara dahil edilmesi gereklidir, böylece yaşlı hastalarda zinde, kırılgan veya zayıf olup olmadıklarına bakılmaksızın sonuçları ve güvenliği nasıl tahmin edeceğimizi daha iyi anlayabiliriz. Bu tür klinik deneyimler ve araştırmalar, HCC'li artan yaşlı yetişkin nüfus için en iyi desteği optimize etmek ve kişiselleştirmek için gereklidir.

KAYNAKLAR

- Waller LP, Deshpande V, Pyrsopoulos N. Hepatocellular carcinoma: a comprehensive review. *World J Hepatol* 2015;7:2648–63.
- Forner A, Reig M, Bruix J. Hepatocellular carcinoma. *Lancet* 2018;391:1301–14.
- Ghouri YA, Mian I, Rowe JH. Review of hepatocellular carcinoma: epidemiology, etiology, and carcinogenesis. *J Carcinog* 2017;16(1).
- Yang JD, Altekruse SF, Nguyen MH, et al. Impact of country of birth on age at the time of diagnosis of hepatocellular carcinoma in the United States. *Cancer* 2017;123:81–9.
- Ryerson AB, Eheman CR, Altekruse SF, et al. Annual report to the nation on the status of cancer, 1975–2012, featuring the increasing incidence of liver cancer. *Cancer* 2016;122:1312–37.
- SEER: Surveillance, Epidemiology, and End Results Program Incidence-SEER 9 Regs Research Data with Delay-Adjustment, Malignant Only. Sub (1975–2014) bkatrina/rita population adjustmentN. 2017 Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Surveillance Systems Branch; Nov. 2016.
- Lok AS, McMahon BJ. Chronic hepatitis B. *Hepatology* 2007;45:507–39.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018;68:7–30.
- Su TH, Tseng TC, Kao JH. HCC risk in patients with HBV-related cirrhosis receiving nucleos(t)ide analogues therapy: is HCC prevented or delayed? *Hepatology* 2018;67:1634–5.
- 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;59:387–96.
- Wilson GC, Quillin 3rd RC, Wima K, et al. Is liver transplantation safe and effective in elderly (≥ 70 years) recipients? A case-controlled analysis. *HPB (Oxford)* 2014;16:1088–94.
- Soto-Perez-de-Celis E, Li D, Yuan Y, et al. Functional versus chronological age: geriatric assessments to guide decision making in older patients with cancer. *Lancet Oncol* 2018;19:e305–16.
- Loh KP, Soto-Perez-de-Celis E, Hsu T, et al. What every oncologist should know about geriatric assessment for older patients with Cancer: young international society of geriatric oncology position paper. *J.Oncol Pract* 2018;14:85–94.

14. Hamaker ME, Wildes TM, Rostoft S. Time to stop saying geriatric assessment is too time consuming. *J Clin Oncol* 2017;35:2871–4.
15. Jolly TA, Deal AM, Nyrop KA, et al. Geriatric assessment-identified deficits in older cancer patients with normal performance status. *Oncologist* 2015;20:379–85.
16. Hamaker ME, Schiphorst AH, ten Bokkel Huinink D, et al. The effect of a geriatric evaluation on treatment decisions for older cancer patients—a systematic review. *Acta Oncol* 2014;53:289–96.
17. Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *J Clin Oncol* 2011;29:3457–65.
18. Clinical Practice Guidelines EASL. Management of hepatocellular carcinoma. *J Hepatol* 2018;69:182–236.
19. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2018;29:iv238–55.
20. Kudo M, Chung H, Osaki Y. Prognostic staging system for hepatocellular carcinoma (CLIP score): its value and limitations, and a proposal for a new staging system, the Japan integrated staging score (JIS score). *J Gastroenterol* 2003;38:207–15.
21. Mizuguchi T, Kawamoto M, Meguro M, et al. Impact of aging on morbidity and mortality after liver resection: a systematic review and meta-analysis. *Surg Today* 2015;45:259–70.
22. Ni JY, Liu SS, Xu LF, et al. Transarterial chemoembolization combined with percutaneous radiofrequency ablation versus TACE and PRFA monotherapy in the treatment for hepatocellular carcinoma: a meta-analysis. *J Cancer Res Clin Oncol* 2013;139:653–9.
23. Tan E, Sandroussi C. Liver resection in elderly patients over the age of 70 with primary liver cancer: a retrospective analysis. *J Clin Oncol* 2019;37:e15647.
24. Keswani RN, Ahmed A, Keeffe EB. Older age and liver transplantation: a review. *Liver Transpl*, 2004;10:957–67.
25. Egeli T, Unek T, Agalar C, et al. Survival outcomes after liver transplantation in elderly patients: a single-center retrospective analysis. *Transplant Proc* 2019;51:1143–6.
26. Levy MF, Somasundar PS, Jennings LW, et al. The elderly liver transplant recipient: a call for caution. *Ann Surg* 2001;233:107–13.
27. Gomez Gavara C, Esposito F, Gurusamy K, et al. Liver transplantation in elderly patients: a systematic review and first meta-analysis. *HPB (Oxford)* 2019;21:14–25.
28. McCaughey GW, Munn SR. Liver transplantation in Australia and New Zealand. *Liver Transplant* 2016;22:830–8.
29. Cucchetti A, Piscaglia F, Cescon M, et al. Cost-effectiveness of hepatic resection versus percutaneous radiofrequency ablation for early hepatocellular carcinoma. *J Hepatol* 2013;59:300–7.
30. Bertot LC, Sato M, Tateishi R, et al. Mortality and complication rates of percutaneous ablative techniques for the treatment of liver tumors: a systematic review. *Eur Radiol* 2011;21:2584–96.
31. Majumdar A, Roccarina D, Thorburn D, et al. Management of people with early- or very early-stage hepatocellular carcinoma: an attempted network meta-analysis. *Cochrane Database Syst Rev* 2017;3:CD011650.
32. Facciorusso A, DiMaso M, Muscatiello N. Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: a systematic review and meta-analysis. *Int J Hyperthermia* 2016;32:339–44.
33. Hung AK, Guy J. Hepatocellular carcinoma in the elderly: meta-analysis and systematic literature review. *World J Gastroenterol* 2015;21:12197–210.
34. Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. *Lancet* 2002;359:1734–9.
35. Tsouchatzis EA, Fatouros E, O’Beirne J, et al. Transarterial chemoembolization and bland embolization for hepatocellular carcinoma. *World J Gastroenterol* 2014;20: 3069–77.

36. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology* 2002;35:1164–71.
37. Vilgrain V, Pereira H, Assenat E, et al. Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial. *Lancet Oncol* 2017;18:1624–36.
38. Teraoka Y, Kimura T, Aikata H, et al. Clinical outcomes of stereotactic body radiotherapy for elderly patients with hepatocellular carcinoma. *Hepatol Res* 2018;48:193–204.
39. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 noninferiority trial. *Lancet* 2018;391:1163–73.
40. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2017;389:56–66.
41. Abou-Alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in patients with advanced and progressing hepatocellular carcinoma. *N Engl J Med* 2018;379:54–63.
42. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (checkmate 040): an open-label, non-comparative, phase ½ dose escalation and expansion trial. *Lancet* 2017;389:2492–502.
43. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (keynote-224): a nonrandomised, open-label phase 2 trial. *Lancet Oncol* 2018;19:940–52.
44. Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med* 2008;359:378–90.
45. Montella L, Addeo R, Cennamo G, et al. Sorafenib in elderly patients with advanced hepatocellular carcinoma: a case series. *Oncology* 2013;84:265–72.
46. Edeline J, Crouzet L, Le Sourd S, et al. Sorafenib use in elderly patients with hepatocellular carcinoma: caution about use of platelet aggregation inhibitors. *Cancer Chemother Pharmacol* 2015;75:215–9.
47. Arora SP, Ketchum NS, Gelfond J, et al. Comparative efficacy and safety of sorafenib in elderly versus non-elderly patients with advanced hepatocellular carcinoma (HCC) with varying liver dysfunction. *J Clin Oncol* 2018;36:430.
48. Wilhelm SM, Dumas J, Adnane L, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. *Int J Cancer* 2011;129:245–55.
49. Yakes FM, Chen J, Tan J, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. *Mol Cancer Ther* 2011;10:2298308.
50. Guo L, Zhang H, Chen B. Nivolumab as programmed Death-1 (PD-1) inhibitor for targeted immunotherapy in tumor. *J Cancer* 2017;8:410–6.
51. Finn RS, Ryoo B-Y, Merle P, et al. Results of KEYNOTE-240: phase 3 study of pembrolizumab (pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC). *J Clin Oncol* 2019;37:4004.
52. Chen CL, Pan QZ, Zhao JJ, et al. PD-L1 expression as a predictive biomarker for cytokine-induced killer cell immunotherapy in patients with hepatocellular carcinoma. *Oncoimmunology* 2016;5:e1176653.
53. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased alpha-fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2019;20:282–96.