



BÖLÜM 17

Kolorektal ve Nöroendokrin Olmayan Karaciğer Metastatik Tümörleri

Serdar ŞENOL ¹

ÖZET

Karaciğer solid organ tümörlerinin birincil metastaz bölgelerinden biridir. Eşlik eden ekstrahepatik hastalık nedeniyle metastatik karaciğer hastalığı olan hastaların çoğunluğu küratif cerrahi için aday olamazlar. Kolorektal ya da nöroendokrin kanser karaciğer metastazlarında hepatektomi kabul edilmiş bir tedavi seçeneğidir.

Kolorektal, nöroendokrin olmayan karaciğer metastatik tümörleri (NCRNNLM) için cerrahinin endikasyonları ve prognozu, nadir olması nedeniyle tartışılmaya devam etmektedir. Biyolojik davranış hastalığın primerine bağlı olarak değişir.

Kolorektal ve nöroendokrin karaciğer metastazları olan hastalarda hepatektomi ile uzamış sağkalım kanıtının artmasıyla birlikte, Schwartz ve arkadaşları ilk olarak NCRNNLM'yi sınıflandırdı ve 1995'te literatürleri gözden geçirdi. Takiben Harrison ve arkadaşları tarafından 1997'de geniş bir kohort çalışmasında prognoz analizi yapıldı.

NCRNNLM için zor olan hangi hastaların cerrahiden fayda göreceğinin belirlenebilmesidir.

Mide Kanseri Karaciğer Metastazı

Semptomların nonspesifik olması ve geç bulgu vermesi nedeniyle çoğu mide kanseri başvuru sırasında lokal ileri ve metastatik evrede tanı alır (1,2). Hastaların 3% ile 5%'inde karaciğer metastazları senkron olarak tespit edilir (3,4). Küratif cerrahi sonrası metakron olarak tespit edilen

hastalık 37%'e varan sıklıktadır (5). Evre IV mide kanserinde güncel tek tedavi önerisi sistemik kemoterapidir (6). Ancak güncel moleküler tedavi rejimlerine rağmen prognoz tatmin edici olmayıp medyan toplam sağkalım (OS) 13,8 aydır (7,8).

Japon Mide Kanseri kılavuzlarının son revizyonunda, soliter karaciğer metastazı olan hasta

¹ Uzm Dr. Serdar ŞENOL, SBÜ Samsun Eğitim ve Araştırma Hastanesi, Gastroenteroloji Cerrahisi
serdarardaduru@gmail.com

KAYNAKLAR

- Schwartz SI. Hepatic resection for noncolorectal nonneuroendocrine metastases. *World J Surg.* 1995;19(1):72-5.
- Harrison LE, Brennan MF, Newman E, et al. Hepatic resection for noncolorectal, nonneuroendocrine metastases: a fifteen-year experience with ninety-six patients. *Surgery.* 1997;121(6):625-32.
- Shah MA, Kelsen DP. Gastric cancer: a primer on the epidemiology and biology of the disease and an overview of the medical management of advanced disease. *J Natl Compr Canc Netw.* 2010;8(4):437-47.
- Saiura A, Umekita N, Inoue S, et al. Clinicopathological features and outcome of hepatic resection for liver metastasis from gastric cancer. *Hepatogastroenterology.* 2002;49(46):1062-5.
- D'Angelica M, Gonen M, Brennan MF, et al. Patterns of initial recurrence in completely resected gastric adenocarcinoma. *Ann Surg.* 2004;240(5):808-16.
- Ajani, J.A, D'Amico TA, Almhanna K, et al. Gastric Cancer, Version 3.2016; Clinical Practice Guidelines in Oncology. *J. Natl. Compr. Cancer Netw.* 2016;14(10):1286-1312.
- Bang Y.J, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): A phase 3, open-label, randomised controlled trial. *Lancet.* 2010;376(9742):687-97.
- Smyth E.C, Verheij M, Allum W, et al. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann. Oncol.* 2016;27(suppl 5):v38-v49.
- Kodera Y, Fujitani K, Fukushima N, et al. Surgical resection of hepatic metastasis from gastric cancer: A review and new recommendation in the Japanese gastric cancer treatment guidelines. *Gastric Cancer.* 2014;17(2):206-12.
- Tiberio G, Ministrini S, Gardini A, et al. Factors influencing survival after hepatectomy for metastases from gastric cancer. *Eur J Surg Oncol.* 2016;42(8):1229-35.
- Sakamoto Y, Ohyama S, Yamamoto J, et al. Surgical resection of liver metastases of gastric cancer: an analysis of a 17-year experience with 22 patients. *Surgery.* 2003;133(5):507-11.
- Marte G, Tufo A, Steccanella F, et al. Efficacy of surgery for the treatment of gastric cancer liver metastases: A systematic review of the literature and meta-analysis of prognostic factors. *J Clin Med.* 2021;10(5):1141
- Schmidt B, Look-Hong N, Maduekwe UN, et al. Noncurative Gastrectomy for Gastric Adenocarcinoma Should only be Performed in Highly Selected Patients. *Ann Surg Oncol.* 2013;20(11):3512-8.
- Ambiru S, Miyazaki M, Ito H, et al. Benefits and limits of hepatic resection for gastric metastases. *Am J Surg.* 2001;181(3):279-83.
- Viganò L, Vellone M, Ferrero A, et al. Liver resection for gastric cancer metastases. *Hepatogastroenterology.* 2013;60(123):557-62.
- Baek HU, Kim SB, Cho EH, et al. Hepatic Resection for Hepatic Metastases from Gastric Adenocarcinoma. *J Gastric Cancer.* 2013;13(2):86-92.
- Sakamoto Y, Sano T, Shimada K, et al. Favorable indications for hepatectomy in patients with liver metastasis from gastric cancer. *J Surg Oncol.* 2007;95(7):534-9.
- Cui JK, Liu M, Shang XK. Hepatectomy for Liver Metastasis of Gastric Cancer: A Meta-Analysis. *Surg Innov.* 2019;26(6):692-697.
- Tatsubayashi T, Tanizawa Y, Miki Y, et al. Treatment outcomes of hepatectomy for liver metastases of gastric cancer diagnosed using contrast-enhanced magnetic resonance imaging. *Gastric Cancer.* 2017;20(2):387-93.
- Montagnani F, Crivelli F, Aprile G, et al. Long-term survival after liver metastasectomy in gastric cancer: Systematic review and meta-analysis of prognostic factors. *Cancer Treat Rev.* 2018;69:11-20.
- Morgagni P, Solaini L, Framarini M, et al. Conversion surgery for gastric cancer: A cohort study from a western center. *Int J Surg.* 2018;53:360-65.
- Cheon SH, Rha SY, Jeung HC, et al. Survival benefit of combined curative resection of the stomach (D2 resection) and liver in gastric cancer patients with liver metastases. *Ann Oncol.* 2008;19(6):1146-53.
- Fujitani K, Yang HK, Mizusawa J, et al. Gastrectomy plus chemotherapy versus chemotherapy alone for advanced gastric cancer with a single non-curable factor (REGATTA): A phase 3, randomised controlled trial. *Lancet Oncol.* 2016;17(3):309-18.
- Al-Batran SE, Homann N, Pauligk C, et al. Effect of Neoadjuvant Chemotherapy Followed by Surgical Resection on Survival in Patients With Limited Metastatic Gastric or Gastroesophageal Junction Cancer. *JAMA Oncol.* 2017;3(9):1237-44.
- Al-Batran SE, Hartmann JT, Hofheinz R, et al. Biweekly fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) for patients with metastatic adenocarcinoma of the stomach or esophagogastric junction: A phase II trial of the Arbeitsgemeinschaft Internistische Onkologie. *Ann Oncol.* 2008;19(11):1882-7.
- Salati M, Valeri N, Spallanzani A, et al. Oligometastatic gastric cancer: An emerging clinical entity with distinct therapeutic implications. *Eur J Surg Oncol.* 2019;45(8):1479-82.
- Han, DS, Suh YS, Kong SH, et al. Outcomes of surgery aiming at curative resection in good responder to induction chemotherapy for gastric cancer with distant metastases. *J. Surg. Oncol.* 2012;107: 511-16.
- Kinoshita J, Fushida S, Tsukada T, et al. Efficacy of conversion gastrectomy following docetaxel, cisplatin, and S-1 therapy in potentially resectable stage IV gastric cancer. *Eur. J. Surg. Oncol.* 2015; 41: 1354-60.
- Sato Y, Ohnuma H, Nobuoka T, et al. Conversion therapy for inoperable advanced gastric cancer patients by docetaxel, cisplatin, and S-1 (DCS) chemotherapy: A multi-institutional retrospective study. *Gastric Cancer.* 2017; 20: 517-26.
- Yamaguchi K, Yoshida K, Tanahashi T, et al. The long-term survival of stage IV gastric cancer patients with conversion therapy. *Gastric Cancer.* 2017; 21: 315-23.
- National Comprehensive Cancer Network. Breast Cancer (Version 5.2020). Available at: <http://www.nccn.org/>

- professionals/physician_gls/pdf/breast.pdf
32. Berman AT, Thukral AD, Hwang WT, et al. Incidence and patterns of distant metastases for patients with early stage breast cancer after breast conservation treatment. *Clinical breast cancer*. 2013;13(2):88-94.
 33. Singletary SE, Walsh G, Vauthey JN, et al. A role for curative surgery in the treatment of selected patients with metastatic breast cancer. *Oncologist*. 2003;8(3):241-51.
 34. Campos SM, Guastalla JP, Subar M, et al. A comparative study of exemestane versus anastrozole in patients with postmenopausal breast cancer with visceral metastases. *Clin Breast Cancer*. 2009;9(1):39-44.
 35. Crump M, Gluck S, Tu D, et al. Randomized trial of high dose chemo-therapy with autologous peripheral-blood stem-cell support compared with standard-dose chemotherapy in women with metastatic breast cancer: NCIC MA.16. *J Clin Oncol*. 2008;26(1):37-43.
 36. Pockaj BA, Wasif N, Dueck A, et al. Metastectomy and surgical resection of the primary tumor in patients with stage IV breast cancer. *Ann Surg Oncol*. 2010;17(9):2419-26.
 37. Malassagne B, Goere D, Cherqui D, et al. Surgical treatment of non-colorectal and non-endocrine liver metastases. *Gastroenterol Clin Biol*. 2000;24(12):1177-85.
 38. Salgado R, Denkert C, Campbell C, et al. Tumor-infiltrating lymphocytes and associations with pathological complete response and event-free survival in HER2-positive early-stage breast cancer treated with lapatinib and trastuzumab: a secondary analysis of the NeoALT-TO Trial. *JAMA Oncol*. 2015;1(4):448-54.
 39. Zhang P, Yin Y, Mo H, et al. Better pathologic complete response and relapse-free survival after carboplatin plus paclitaxel compared with epirubicin plus paclitaxel as neoadjuvant chemotherapy for locally advanced triple-negative breast cancer: a randomized phase 2 trial. *Oncotarget*. 2016;7(37):60647-656.
 40. Schoellhammer HF, Hsu F, Vito C, et al. Complete pathologic response of HER2-positive breast cancer liver metastasis with dual anti-HER2 antagonism. *BMC Cancer*. 2014;14:242.
 41. Rastogi S, Gulia S, Bajpai J, et al. Oligometastatic breast cancer: a mini review. *Indian J Med Paediatr Oncol*. 2014;35(3):203-6.
 42. Pagani O, Senkus E, Wood W, et al. International guidelines for management of metastatic breast cancer: can metastatic breast cancer be cured? *J Natl Cancer Inst*. 2010;102(7):456-63.
 43. Adam R, Chiche L, Aloia T, et al. Hepatic resection for noncolorectal nonendocrine liver metastases: analysis of 1,452 patients and development of a prognostic model. *Ann Surg*. 2006;244(4):524-35.
 44. Diaz R, Santaballa A, Munarriz B, et al. Hepatic resection in breast cancer metastases: should it be considered standard treatment? *Breast*. 2004;13(3):254-8.
 45. Pogoda K, Nawińska A, Murawska M, et al. Analysis of pattern, time and risk factors influencing recurrence in triple-negative breast cancer patients. *Med Oncol*. 2013;30(1):388.
 46. Hanrahan EO, Broglio KR, Buzdar AU, et al. Combined modality treatment for isolated recurrences of breast carcinoma: update on 30 years of experience at the University of Texas M.D. Anderson Cancer Center and assessment of prognostic factors. *Cancer*. 2005;104(6):1158-71.
 47. Yoo TG, Cranshaw I, Broom R, et al. Systematic review of early and long-term outcome of liver resection for metastatic breast cancer: is there a survival benefit? *Breast*. 2017;32:162-72.
 48. Chua TC, Saxena A, Liauw W, et al. Hepatic resection for metastatic breast cancer: a systematic review. *Eur J Cancer*. 2011;47(15):2282-90.
 49. Adam R, Aloia T, Krissat J, et al. Is liver resection justified for patients with hepatic metastases from breast cancer? *Ann Surg*. 2006;244(6):897-907.
 50. Lendoire J, Moro M, Andriani O, et al. Liver resection for non-colorectal, nonneuroendocrine metastases: analysis of a multicenter study from Argentina. *HPB (Oxford)*. 2007;9(6):435-9.
 51. Wyld L, Gutteridge E, Pinder SE, et al. Prognostic factors for patients with hepatic metastases from breast cancer. *Br J Cancer*. 2003;89(2):284-90.
 52. Pocard M, Pouillart P, Asselain B, et al. Hepatic resection for breast cancer metastases: results and prognosis (65 cases). *Ann Chir*. 2001 Jun;126(5):413-20.
 53. Ruiz A, Castro-Benitez C, Sebah M, et al. Repeat hepatectomy for breast cancer liver metastases. *Ann Surg Oncol*. 2015;22 Suppl 3:S1057-66.
 54. Duan XF, Dong NN, Zhang T, et al. The prognostic analysis of clinical breast cancer subtypes among patients with liver metastases from breast cancer. *Int J Clin Oncol*. 2013;18(1):26-32.
 55. Chun YS, Mizuno T, Cloyd JM, et al. Hepatic Resection for Breast Cancer Liver Metastases: Impact of Intrinsic Subtypes. *Eur J Surg Oncol*. 2020;46(9): 1588-95.
 56. Rivera K, Jeyerajah DR, Washington K. Hepatectomy, RFA, and Other Liver Directed Therapies for Treatment of Breast Cancer Liver Metastasis: A Systematic Review. *Front Oncol*. 2021;11:643383.
 57. Sundén M, Hermansson C, Taflin H, et al. Surgical treatment of breast cancer liver metastases - A nationwide registry-based case control study. *Eur J Surg Oncol*. 2020;46(6):1006-12.
 58. Lucchese AM, Kalil AN, Ruiz A, et al. Neoadjuvant chemotherapy response influences outcomes in non-colorectal, non-neuroendocrine liver metastases. *Br J Surg*. 2018;105(12):1665-70.
 59. Hoffmann K, Bulut S, Tekbas A, et al. Is hepatic resection for non-colorectal, non-neuroendocrine liver metastases justified? *Ann Surg Oncol*. 2015; 22(Suppl 3): S1083-S92.
 60. Yedibela S, Gohl J, Graz V, et al. Changes in indication and results after resection of hepatic metastases from noncolorectal primary tumors: a single-institutional review. *Ann Surg Oncol*. 2005;12(10):778-85.
 61. Jemal A, Siegel R, Xu J, et al. Cancer statistics. *CA Cancer J Clin*. 2010;60(5):277-300.
 62. Leiter U, Meier F, Schitteck B, et al. The natural course of cutaneous melanoma. *J Surg Oncol*. 2004;86(4):172-8.
 63. Aubin JM, Rekman J, Vandenbroucke-Menu F, et al. Systematic review and meta-analysis of liver resection for metastatic melanoma. *Br J Surg*. 2013;100(9):1138-47.

64. Lane AM, Kim IK, Gragoudas ES. Survival Rates in Patients After Treatment for Metastasis From Uveal Melanoma. *JAMA Ophthalmol*. 2018;136(9):981-86.
65. Carvajal RD, Piperno-neumann S, Kapiteijn E, et al. Selumetinib in Combination With Dacarbazine in Patients With Metastatic Uveal Melanoma: A Phase III, Multicenter, Randomized Trial (SUMIT). *J Clin Oncol*. 2018;36(12):1232-39.
66. Gomez D, Wetherill C, Cheong J, et al. The Liverpool uveal melanoma liver metastases pathway: outcome following liver resection. *J Surg Oncol*. 2014;109(6):542-7.
67. Frenkel S, Nir I, Hendler K, et al. Long-term survival of uveal melanoma patients after surgery for liver metastases. *Br J Ophthalmol*. 2009;93(8):1042-6.
68. Mariani P, Piperno-neumann S, Servois V, et al. Surgical management of liver metastases from uveal melanoma: 16 years' experience at the Institut Curie. *Eur J Surg Oncol*. 2009;35(11):1192-7.
69. Hand F, Doherty S, Gullo G, et al. Metastatic uveal melanoma: A valid indication for liver resection. *J BUON*. 2020;25(2):1161-65.
70. Bacalbasa N, Dima S, Brasoveanu V, et al. Liver resection for ovarian cancer liver metastases as part of cytoreductive surgery is safe and may bring survival benefit. *World J Surg Oncol*. 2015;13:235.
71. Alcarraz C, Mun˘iz J, Mas L, et al. Optimal cytoreduction in advanced ovarian cancer treated with dose-dense paclitaxel and carboplatin followed by interval surgery at the Peruvian National Institute of Neoplastic Diseases. *Rev Peru Med Exp Salud Publica*. 2018;35(1):46-54.
72. Deng K, Yang C, Tan Q, et al. Sites of distant metastases and overall survival in ovarian cancer: A study of 1481 patients. *Gynecol Oncol*. 2018;150:460.
73. Bacalbasa N, Balescu I, Dima S, et al. Hematogenous splenic metastases as an independent negative prognosis factor at the moment of primary cytoreduction in advanced stage epithelial ovarian cancer—a single center experience. *Anticancer Res*. 2015;35:5649.
74. Kato K, Katsuda T, Takeshima N. Cytoreduction of diaphragmatic metastasis from ovarian cancer with involvement of the liver using a ventral liver mobilization technique. *Gynecol Oncol*. 2016;140:577.
75. Brunschwig A. Hepatic lobectomy for metastatic cancer. *Cancer* 1963;16:277-82.
76. Bacalbařa N, Balescu I, Dima S, et al. Long-term Survivors After Liver Resection for Ovarian Cancer Liver Metastases. *Anticancer Res*. 2015;35:6919-23.
77. Bacalbasa N, Dima S, Brasoveanu V, et al. Liver resection for ovarian cancer liver metastases as part of cytoreductive surgery is safe and may bring survival benefit. *World J Surg Oncol*. 2015;13:235.
78. Neumann UP, Fotopoulou C, Schmeding M, et al. Clinical outcome of patients with advanced ovarian cancer after resection of liver metastases. *Anticancer Res*. 2012;32:4517-21.
79. Winter WE, Maxwell GL, Tian C, et al. Tumor residual after surgical cytoreduction in prediction of clinical outcome in stage IV epithelial ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2008;26:83-9.
80. Nakayama K, Nakayama N, Katagiri H, et al. Mechanisms of ovarian cancer metastasis: biochemical pathways. *Int J Mol Sci*. 2012;13:11705-17.
81. Saxena A, Valle SJ, Liauw W, et al. Limited synchronous hepatic resection does not compromise peri-operative outcomes or survival after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *J Surg Oncol*. 2017;115:417-24.
82. O'Neill AC, Somarouthu B, Tirumani SH, et al. Patterns and Prognostic Importance of Hepatic Involvement in Patients with Serous Ovarian Cancer: A Single-Institution Experience with 244 Patients. *Radiology*. 2017;282:160-70.
83. Harries M, Gore M. Part II: chemotherapy for epithelial ovarian cancer-treatment of recurrent disease. *Lancet Oncol*. 2002;3:537-45.
84. Kamel SI, de Jong MC, Schulick RD, et al. The role of liver-directed surgery in patients with hepatic metastasis from a gynecologic primary carcinoma. *World J Surg*. 2011;35:1345-54.
85. Eng OS, Raoof M, Blakely AM, et al. A collaborative surgical approach to upper and lower abdominal cytoreductive surgery in ovarian cancer. *J Surg Oncol*. 2018;118:21.
86. Gallotta V, Ferrandina G, Vizzielli G, et al. Hepatoceliac Lymph Node Involvement in Advanced Ovarian Cancer Patients: Prognostic Role and Clinical Considerations. *Ann Surg Oncol* 2017;24:3413-21.