

MİDE KANSERİNDE MULTİMODAL TEDAVİ YAKLAŞIMLARI VE RADYOTERAPİNİN YERİ

42.
BÖLÜM

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ÖZET

Mide kanseri, kansere bağlı ölüm sebeplerinde en üst sıralarda yer almaktadır. Esas tedavisi cerrahi olmakla beraber takipte hastaların çoğu nüks ve/veya metastaz gelişmesi klinisyenleri preoperatif ve postoperatif tedavi arayışına itmiştir. Eş zamanlı kemoradyoterapinin cerrahiye eklenmesi ile hasta-lıksız ve toplam sağkalımın uzaması, özellikle son 20 yıldır adjuvan kemoradyoterapiyi sıkılıkla kullanılır hale getirmiştir. Son yıllarda kemoterapi çalışmalarında elde edilen başarı ile peroperatif kemoterapi, postoperatif kemoradyoterapiye ciddi bir alternatif olmuştur. Her hasta için optimal tedavi algoritması multidisipliner bir ekip tarafından kişiye özgü şekilde kurgulanmalıdır ve evre olarak T2N0 ve üzeri tüm olgular olası radyoterapi faydalannımı açısından değerlendirilmelidir.

GENEL BAKIŞ

Mide adenokanseri insidansı zaman içerisinde azalıyor olsa da halen dünya genelinde en sık görülen kancer tipleri arasında beşinci ve ölüme en çok sebep olanlar arasında üçüncü sıradaır (1). 1980 yılında görülme sıklığı 100.000 de 11.2 iken, 2017'ye gelindiğinde bu oran 100.000 de 6.6 ya düşmüştür ve düşme eğilimi devam etmektedir (2). Geçmişe oranla antrum ve gövde yerleşimli tümör sıklığının görece azalmasından dolayı proksimal yerleşimli tümörlerin görülme sıklığı artmıştır (3).

Sadece cerrahi yapılan Mukoza ve submuko-za kısıtlı tümörlerde 5 yıllık sağkalım % 90 civarında olsa da nodal tutulum varlığında ve gastrik duvar tutulumunun derinliği arttığında 5 yıllık

sağkalım oranları %10-%30 civarına düşmektedir (4,6). Rekürrens lokorejyonal, peritoneal ya da uzak metastaz şeklinde olabilir (7). Otopsi se-rileri mide kanseri nedeniyle hayatını kaybeden hastalarda %80 oranında lokal nüks gelişliğini ortaya çıkarmıştır (8). Tüm bunlar lokal ve siste-mik kontrol için adjuvan ve neoadjuvan tedavi gerekliliğini özellikle lokal ileri tümörler için or-taya koymaktadır. Cerrahi ile kombine edilecek optimal tedavi konusunda henüz bir konsensus olmamakla beraber adjuvan kemoradyoterapi (KRT), peroperatif kemoterapi (KT), postopera-tif kemoterapi gibi tedavi seçeneklerinden hasta bazında uygun olanı tercih edilmelidir (9,10). Bir sonraki bölümde cerrahi, radyoterapi ve kemo-terapiyi ayrı ayrı ya da kombine şekilde irdele-yen çalışmalar inceleneciktir.

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KAYNAKLAR

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;68:394-424.
2. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD, based on November 2019 SEER data submission, posted to the SEER web site, April 2020. (06.08.2020 tarihinde https://seer.cancer.gov/csr/1975_2017/ adresinden ulaşılmıştır.)
3. Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. *J Natl Cancer Inst*. 2008;100:1184-1187.
4. Endo M, Habu H. Clinical studies of early gastric cancer. *Hepatogastroenterology*. 1990;37:408-41
5. Farley DR, Donohue JH, Nagorney DM, et al. Early gastric cancer. *Br J Surg*. 1992;79:539-542.
6. Cady B, Rossi RL, Silverman ML, et al. Gastric adenocarcinoma. A disease in transition. *Arch Surg*. 1989;124:303-308.
7. D'Angelica M, Gonen M, Brennan MF, et al. Patterns of initial recurrence in completely resected gastric adenocarcinoma. *Annals of Surgery*. 2004; 240: 808-16.
8. Gunderson LL, Sosin H. Adenocarcinoma of the stomach: areas of failure in a reoperation series (second or symptomatic look) clinopathologic correlation and implications for adjuvant therapy. *Int J Radiat Oncol Biol Phys*. 1982;8(1):1-11.
9. Datta J, McMillan MT, Ruffolo L, et al. Multimodality therapy improves survival in resected early stage gastric cancer in the United States. *Ann Surg Oncol*. 2016;23:1-10.
10. Goetze OT, Al-Batran SE, Chevallay M, et al. Multimodal treatment in locally advanced gastric cancer. *Updat Surg*. 2018;70(2):173-9.
11. Krijnen P, den Dulk M, Meershoek-Klein Kranenborg E, et al. Improved survival after resectable non-cardia gastric cancer in The Netherlands: the importance of surgical training and quality control. *Eur J Surg Oncol*. 2009;35:715-720.
12. Takahashi T. A study on preoperative and postoperative telecobalt therapy in gastric cancer. Three year results of Co⁶⁰ irradiation following palliative gastric resection. *Nippon Acta Radiol* 1964;24:129-132.
13. Wieland C, Hymmen U. Mega-volt therapy of malignant stomach neoplasms. *Strahlentherapie*. 1970;140:20-26.
14. Hallissey MT, Dunn JA, Ward LC, et al. The second British Stomach Cancer Group trial of adjuvant radiotherapy or chemotherapy in resectable gastric cancer: five-year follow-up. *Lancet*. 1994;343:1309-1312.
15. Abe M, Takahashi M. Intraoperative radiotherapy: the Japanese experience. *Int J Radiat Oncol Biol Phys*. 1981;7:863-868.
16. Takahashi M, Abe M. Intra-operative radiotherapy for carcinoma of the stomach. *Eur J Surg Oncol*. 1986;12:247-250.
17. Qin HL, Lin CH, Zhang XL. Evaluation of intraoperative radiotherapy for gastric carcinoma with D2 and D3 surgical resection. *World J Gastroenterol*. 2006;12:7033-7.
18. Calvo FA, Aristu JJ, Azinovic I, et al. Intraoperative and external radiotherapy in resected gastric cancer: updated report of a phase II trial. *Int J Radiat Oncol Biol Phys*. 1992;24:729-73.
19. Martinez-Monge R, Calvo FA, Azinovic I, et al. Patterns of failure and long-term results in high-risk resected gastric cancer treated with postoperative radiotherapy with or without intraoperative electron boost. *J Surg Oncol*. 1997;66:24-29.
20. Zhang Q, Tey J, Peng L, et al. Adjuvant chemoradiotherapy with or without intraoperative radiotherapy for the treatment of resectable locally advanced gastric adenocarcinoma. *Radiother Oncol*. 2012;102:51-55.
21. Sakuramoto S, Sasako M, Yamaguchi T, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med*. 2007;357:1810-182.
22. Noh SH, Park SR, Yang HK, et al. Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. *Lancet Oncol*. 2014;15:1389-1396.
23. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med*. 2001;345:725-73.
24. Smalley SR, Benedetti JK, Haller DG, et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. *J Clin Oncol* 2012; 30:2327-3.
25. Songun I, Putter H, Kranenborg EM, et al. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *The Lancet Oncology*. 2010;11: 439-49.
26. Coburn NG, Guller U, Baxter NN, et al. Adjuvant therapy for resected gastric cancer—rapid, yet incomplete adoption following results of intergroup 0116 trial. *International journal of radiation oncology, biology, physics*. 2008;70:1073-80.
27. Lee J, Lim DH, Kim S, et al. Phase III trial comparing capecitabine plus cisplatin versus capecitabine plus cisplatin with concurrent capecitabine radiotherapy in completely resected gastric cancer with D2 lymph node dissection: the ARTIST trial. *J Clin Oncol*. 2012;30:268-273.
28. S.H. Park, D.Y. Zang, B. Han, et al. ARTIST 2: interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC) *J Clin Oncol*, 2019;37:4001.
29. Shchepotin IB, Evans SR, Chorny V, et al. Intensive preoperative radiotherapy with local hyperthermia for the treatment of gastric carcinoma. *Surg Oncol*. 1994;3:37-44.
30. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355:11-20.

31. Al-Batran SE, Homann N, Pauligk C, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. *Lancet.* 2019;393:1948–1957.
32. Stahl M, Walz MK, Riera-Knorrenschild J, et al. Pre-operative chemotherapy versus chemoradiotherapy in locally advanced adenocarcinomas of the oesophagogastric junction (POET): Long-term results of a controlled randomised trial. *Eur J Cancer.* 2017;81:183–190.
33. Reynolds JV, Preston SR, O'Neill B, et al: ICORG 10–14: NEOadjuvant trial in Adenocarcinoma of the oEsophagus and oesophagoGastric junction International Study (Neo-AEGIS). *BMC Cancer.* 2017;17:401.
34. Hoeppner J, Lordick F, Brunner T, et al. ESOPEC: prospective randomized controlled multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (NCT02509286). *BMC Cancer.* 2016;16:503.
35. Ajani JA, Mansfield PF, Janjan N, et al. Multi-institutional trial of preoperative chemoradiotherapy in patients with potentially resectable gastric carcinoma. *J Clin Oncol.* 2004;22:2774–2780.
36. Leong T, Smithers BM, Michael M, et al. TOPGEAR: a randomised phase III trial of perioperative ECF chemotherapy versus preoperative chemoradiation plus perioperative ECF chemotherapy for resectable gastric cancer (an international, intergroup trial of the AGITG/TROG/ EORTC/NCIC CTG). *BMC Cancer.* 2015;15:532.
37. Slagter AE, Jansen EPM, van Laarhoven HWM, et al. CRITICS-II: A multicentre randomised phase II trial of neo-adjuvant chemotherapy followed by surgery versus neo-adjuvant chemotherapy and subsequent chemoradiotherapy followed by surgery versus neo-adjuvant chemoradiotherapy followed by surgery in resectable gastric cancer. *BMC Cancer.* 2018;18:877.
38. Cats A, Jansen EPM, van Grieken NCT, et al. Chemotherapy versus chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS): an international, open-label, randomised phase 3 trial. *Lancet Oncol.* 2018;19:616–628.
39. Repka MC, Salem ME, Unger KR. The role of radiotherapy in the management of gastric cancer. *Am J Hematol Oncology.* 2017;13(5):8–15.
40. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med.* 2012;366:2074–2084.
41. Noordman BJ, BPL W, Lagarde SM, et al. Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial. *BMC Cancer.* 2018;18(1):142.
42. Bedenne L, Mariette C. Comparison of systematic surgery versus surveillance and rescue surgery in operable oesophageal cancer with a complete clinical response to radiochemotherapy (esostate). (14.08.2020 tarihinde <https://clinicaltrials.gov/ct2/show/NCT02551458>. adresinden ulaşılmıştır.)
43. Saikawa Y, Kubota T, Kumagai K, et al. Phase II study of chemoradiotherapy with S-1 and low-dose cisplatin for inoperable advanced gastric cancer. *Int J Radiat Oncol Biol Phys.* 2008;71(1):173–179.
44. Miller C. Carcinoma of thoracic oesophagus and cardia. A review of 405 cases. *Br J Surg.* 1962;49:507–522.
45. Tepper JE, Gunderson LL. Radiation treatment parameters in the adjuvant postoperative therapy of gastric cancer. *Semin Radiat Oncol.* 2002;12:187–195.
46. Chung HT, Lee B, Park E, et al. Can all centers plan intensity-modulated radiotherapy (IMRT) effectively? An external audit of dosimetric comparisons between three-dimensional conformal radiotherapy and IMRT for adjuvant chemoradiation for gastric cancer. *Int J Radiat Oncol Biol Phys.* 2008;71:1167–1174.
47. Trip AK, Nijkamp J, van Tinteren H, et al. IMRT limits nephrotoxicity after chemoradiotherapy for gastric cancer. *Radiother Oncol.* 2014;112:289–294.
48. Stahl M, Walz MK, Stuschke M, Phase III comparison of preoperative chemotherapy compared with chemoradiotherapy in patients with locally advanced adenocarcinoma of the esophagogastric junction. *J Clin Oncol Off J Am Soc Clin Oncol.* 2009;851–56.
49. Oppedijk V, van der Gaast A, van Lanschot JJ, et al. Patterns of recurrence after surgery alone versus preoperative chemoradiotherapy and surgery in the CROSS trials. *J Clin Oncol Off J Am Soc Clin Oncol.* 2014;32:385–391.
50. Nam H, Lim-Do H, Kim S, et al. A new suggestion for the radiation target volume after a subtotal gastrectomy in patients with stomach cancer. *Int J Radiat Oncol Biol Phys.* 2008;71:448–55.
51. Kim TH, Park SR, Ryu KW, et al. Phase 3 trial of postoperative chemotherapy alone versus chemoradiation therapy in stage III–IV gastric cancer treated with R0 gastrectomy and D2 lymph node dissection. *Int J Radiat Oncol Biol Phys.* 2012;84:585–92.
52. Chang JS, Lim JS, Noh SH, et al. Patterns of regional recurrence after curative D2 resection for stage III (N3) gastric cancer: implications for postoperative radiotherapy. *Radiother Oncol J Eur Soc Therap Radiol Oncol.* 2012;104:367–73.
53. Yoon HI, Chang JS, Lim JS, et al. Defining the target volume for post-operative radiotherapy after D2 dissection in gastric cancer by CT-based vessel-guided delineation. *Radiother Oncol J Eur Soc Therap Radiol Oncol.* 2013;108:72–7.