

# BÖLÜM 21

## İNVAZİF MEME KANSERİNDE RADYASYON TEDAVİSİ

EDA BENGİ YILMAZ<sup>1</sup>

### Giriş

Meme kanseri kadınlar arasında en sık görülen kanserdir ve kansere bağlı ölümler arasında akciğer kanserinin ardından ikinci sırada gelmektedir. Amerikan Kanser Derneği 2020 yılı için, 279.100 Amerikalı'nın meme kanseri tanısı alacağı ve 42.690 hastanın da meme kanserine bağlı kaybedilecekleri tahmininde bulunmuştur (1). Ülkemizde de meme kanseri kadınlar arasında görülen kanserler içinde 41.6/100.000 oranı ile ilk sırada yer almaktır olup görülme yaşı giderek düşmektedir (2).

Meme tümörlerinin çoğunun etiyolojisi tam olarak bilinmemekle birlikte çok sayıda risk faktörü tanımlanmıştır. En önemli risk faktörleri: İleri yaş (>50), kadın cinsiyet, ailede meme kanseri öyküsü olması, geç menopoz, erken menarş, ilk doğum yaşının ileri olması, uzatılmış hormon replasman tedavisi uygulanımı, iyi huylu proliferatif meme lezyonları, genetik faktörler (BRCA 1-2 gen mutasyonları gibi), yaşam tarzı ile ilgili faktörler (alkol tüketimi, sigara, gibi) ve göğüs duvarına daha önce radyasyon tedavisi almış olmasıdır (3).

Meme kanserli hastalarda optimal tedavi stratejisini saptamada prognostik faktörler göz önünde bulundurulmalıdır. Önemli prognostik faktörler: Hasta yaşı, tümör boyutu, tutulu aksiller nod sayısı, histolojik grad, lenfovasküler invazyon durumu, östrojen reseptör (ER) ve progesteron reseptör (PR) durumu, HER2-neu (C-erb B2), tümör supressör genler (p53 ve bcl-2) şeklidir. Aksiller lenf nodu durumu (ALN) hastalıksız sağkalım (HSK) ve genel sağkalım (GSK) açısından en önemli prognostik faktördür. Pozitif aksiller lenf nodlarının varlığı, mortaliteyi doğrudan etkileyen, lokal nüks ve uzak metastazın göstergesidir (3,4). Meme kanseri tanısı kesinleştikten sonra hastalığın başlangıçtaki yaygınlığını yani evresini doğru belirlemek tedavi yönetimi açısından ve hastalığın прогнозu ile ilgili tahminde bulunmak açısından çok önemlidir. Evrelemede Amerikan Joint Committee on Cancer (AJCC) TNM evreleme sistemi kullanılmaktadır. Çeşitli kriterler düzenlenen bu evrelemenin 2017 yılında güncellenen son hali kullanılmaktadır (5).

Meme kanseri tedavisi, lokal hastalığın cerrahi, radyoterapi (RT) veya her ikisiyle tedavisini

<sup>1</sup> Dr. Öğr. Üyesi, Mersin Üniversitesi Tıp Fakültesi, bengimd@yahoo.com

PMRT hem göğüs duvarı hem de bölgesel nodlara uygulanmaktadır. Bölgesel nodlar supra/infraklaviküler nodları aynı zamanda IMN'leri kapsamaktadır. Tam aksilla disseksiyonu uygulanmış dışındakilerde aksilla da tedavi alanına eklenmiştir.

## KAYNAKÇA

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7-30.
2. T.C. Sağlık Bakanlığı sağlık istatistikleri yılı 2010. ss.27-8. <http://sbu.saglik.gov.tr/Ekutuphane/kitaplar/saglikistatistikleri2010.pdf>
3. Ünal D, Oğuz A, Taşdemir A. Rate of metastasis in examined lymph nodes as a predictor of extracapsular extension in patients with axillary node-positive breast cancer. J Nippon Med Sch. 2014;81:372-377.
4. Danko ME, Bennett KM, Zhai J, et al. Improved staging in node-positive breast cancer patients using lymph node ratio: results in 1,788 patients with long-term follow-up. J Coll Surg. 2010;210:797-805.
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer Version 6.2020-September 8, 2020
6. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet 2011; 378:1707-1716.
7. Lyman GH, Temin S, Edge SB, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2014;32:1365-1383.
8. FAST Trialists group, Agrawal RK, Alhasso A, et al. First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer). Radiother Oncol. 2011; 100:93.
9. Brunt AM, Haviland JS, Sydenham M, et al. Ten-Year Results of FAST: A Randomized Controlled Trial of 5-Fraction Whole-Breast Radiotherapy for Early Breast Cancer. J Clin Oncol. 2020; 38:3261-3272.
10. Smith BD, Bentzen SM, Correa CR, et al. Fractionation for whole breast irradiation: an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Int J Radiat Oncol Biol Phys. 2011; 81:59.
11. Smith BD, Bellon JR, Blitzblau R, et al. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Pract Radiat Oncol. 2018; 8:145.
12. Hickey BE, James ML, Lehman M, et al. Fraction size in radiation therapy for breast conservation in early breast cancer. Cochrane Database Syst Rev. 2016; 7:CD003860.
13. Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10- year follow-up results of two randomised controlled trials. Lancet Oncol. 2013; 14:1086.
14. Correa C, Harris EE., Leonardi MC, et. al. Accelerated partial breast irradiation: executive summary for the update of an ASTRO evidence-based consensus statement. Pract Radiat Oncol 2016;7:73-79.
15. Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet. 2016;387:229.
16. Antonini N, Jones H, Horiot JC, et al. Effect of age and radiation dose on local control after breast conserving treatment: EORTC trial 22881- 10882. Radiother Oncol. 2007;82:265-271.
17. Bartelink H, Horiot JC, Poortmans P, et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. N Engl J Med. 2001;345:1378-1387.
18. Poortmans PM, Collette S, Kirkove C, et al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015; 373:317-327.
19. Whelan TJ, Olivotto IA, Parulekar WR, et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015; 373:307-316.
20. Galimberti V, Cole BF, Viale G, et al. Axillary dissection versus no axillary dissection in patients with breast cancer and sentinel-node micrometastases (IBCSG 23-01): 10-year follow-up of a randomised, controlled phase 3 trial. Lancet Oncol 2018; 19:1385-1393.
21. Jaggi R, Chadha M, Moni J, et al. Radiation field design in the ACOSOG Z0011 (Alliance) Trial. J Clin Oncol. 2014; 32:3600-3606.
22. Swisher SK, Vila J, Tucker SL, et al. Locoregional Control According to Breast Cancer Subtype and Response to Neoadjuvant Chemotherapy in Bre-

- ast Cancer Patients Undergoing Breast-conserving Therapy. *Ann Surg Oncol* 2016; 23:749-756.
23. Fisher B, Bryant J, Dignam JJ, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. *J Clin Oncol*. 2002; 20:4141-4149.
  24. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol*. 2013; 31:2382-2387.
  25. Ford HT, Coombes RC, Gazet JC, et al. Long-term follow-up of a randomised trial designed to determine the need for irradiation following conservative surgery for the treatment of invasive breast cancer. *Ann Oncol*. 2006; 17:401-408.
  26. van de Water W, Bastiaannet E, Scholten AN, et al. Breast-conserving surgery with or without radiotherapy in older breast patients with early stage breast cancer: a systematic review and meta-analysis. *Ann Surg Oncol*. 2014; 21:786-794.
  27. Vaidya JS, Wenz F, Bulsara M, et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. *Lancet*. 2014; 383:603-613.
  28. Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. *Lancet Oncol*. 2013; 14:1269-1277.
  29. Vaidya JS, Bulsara M, Saunders C, et al. Effect of Delayed Targeted Intraoperative Radiotherapy vs Whole-Breast Radiotherapy on Local Recurrence and Survival: Longterm Results From the TARGIT-A Randomized Clinical Trial in Early Breast Cancer. *JAMA Oncol*. 2020; 6:e200249.
  30. Warren LE, Miller CL, Horick N, et al. The impact of radiation therapy on the risk of lymphedema after treatment for breast cancer: a prospective cohort study. *Int J Radiat Oncol Biol Phys*. 2014; 88:565-571.
  31. Chandra RA, Miller CL, Skolny MN, et al. Radiation therapy risk factors for development of lymphedema in patients treated with regional lymph node irradiation for breast cancer. *Int J Radiat Oncol Biol Phys*. 2015; 91:760-764.
  32. Pierce LJ, Oberman HA, Strawderman MH, Lichter AS. Microscopic extracapsular extension in the axilla: is this an indication for axillary radiotherapy? *Int J Radiat Oncol Biol Phys*. 1995; 33:253-259.
  33. Wang SL, Fang H, Song YW, et al. Hypofractionated versus conventional fractionated postmas-
  - tectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. *Lancet Oncol*. 2019; 20:352-360.
  34. Recht A, Comen EA, Fine RE, et al. Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update. *Pract Radiat Oncol*. 2016; 6:e219.
  35. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005; 366:2087-2106.
  36. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet*. 2014; 383:2127-2135.
  37. Danish Breast Cancer Cooperative Group, Nielsen HM, Overgaard M, et al. Study of failure pattern among high-risk breast cancer patients with or without postmastectomy radiotherapy in addition to adjuvant systemic therapy: long-term results from the Danish Breast Cancer Cooperative Group DBCG 82 b and c randomized studies. *J Clin Oncol*. 2006; 24:2268-2275.
  38. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. *N Engl J Med*. 1997; 337:949.
  39. Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet*. 1999; 353:1641-1648.
  40. Liu J, Mao K, Jiang S, et al. The role of postmastectomy radiotherapy in clinically nodepositive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB. *Oncotarget*. 2016; 7: 24848-24859.
  41. Huang EH, Tucker SL, Strom EA, et al. Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol* 2004; 22:4691-4696.
  42. Buchholz TA, Tucker SL, Masullo L, et al. Predictors of local-regional recurrence after neoadjuvant chemotherapy and mastectomy without radiation. *J Clin Oncol*. 2002; 20:17-23.

43. Ring A, Webb A, Ashley S, et al. Is surgery necessary after complete clinical remission following neoadjuvant chemotherapy for early breast cancer? *J Clin Oncol.* 2003; 21:4540-4545.
44. McGuire SE, Gonzalez-Angulo AM, Huang EH, et al. Postmastectomy radiation improves the outcome of patients with locally advanced breast cancer who achieve a pathologic complete response to neoadjuvant chemotherapy. *Int J Radiat Oncol Biol Phys.* 2007; 68:1004-1009.
45. Thorsen LB, Offersen BV, Danø H, et al. DBCG-IMN: A Population-Based Cohort Study on the Effect of Internal Mammary Node Irradiation in Early Node-Positive Breast Cancer. *J Clin Oncol.* 2016; 34:314-320.
46. Chang JS, Park W, Kim YB, et al. Long-term survival outcomes following internal mammary node irradiation in stage II-III breast cancer: results of a large retrospective study with 12-year follow-up. *Int J Radiat Oncol Biol Phys.* 2013; 86:867-872.
47. Fisher B, Dignam J, Mamounas EP, et al. Sequential methotrexate and fluorouracil for the treatment of node-negative breast cancer patients with estrogen receptor-negative tumors: eight-year results from National Surgical Adjuvant Breast and Bowel Project (NSABP) B-13 and first report of findings from NSABP B-19 comparing methotrexate and fluorouracil with conventional cyclophosphamide, methotrexate, and fluorouracil. *J Clin Oncol.* 1996; 14:1982-1992.
48. Fisher B, Dignam J, Bryant J, et al. Five versus more than five years of tamoxifen therapy for breast cancer patients with negative lymph nodes and estrogen receptor-positive tumors. *J Natl Cancer Inst.* 1996; 88:1529-1542.
49. Dalberg K, Johansson H, Johansson U, Rutqvist LE. A randomized trial of long term adjuvant tamoxifen plus postoperative radiation therapy versus radiation therapy alone for patients with early stage breast carcinoma treated with breast-conserving surgery. Stockholm Breast Cancer Study Group. *Cancer.* 1998; 82:2204-2211.
50. Bellon JR, Come SE, Gelman RS, et al. Sequencing of chemotherapy and radiation therapy in early-stage breast cancer: updated results of a prospective randomized trial. *J Clin Oncol.* 2005; 23:1934-1940.
51. Valakh V, Trombetta MG, Werts ED, et al. Influence of concurrent anastrozole on acute and late side effects of whole breast radiotherapy. *Am J Clin Oncol.* 2011; 34:245-248.
52. Adams MJ, Hardenbergh PH, Constine LS, et al. Radiation-associated cardiovascular disease. *Crit Rev Oncol Hematol.* 2003; 45: 55-75.
53. Ahsan H and Al Neugut. Radiation therapy for breast cancer and increased risk for esophageal carcinoma. *Ann. Intern. Med.* 1998; 128: 114-117.