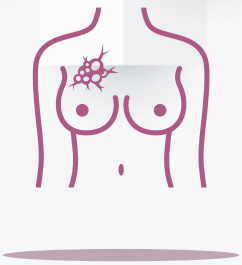

Bölüm 34

Lokal İleri Evre Meme Kanserinde Tedavi

Sezin YÜCE SARI [1] Çağlayan Selenge BEDÜK ESEN [2]

Giriş

Lokal ileri evre meme kanseri evre IIB - IIIC hastalığı kapsamaktadır. Bu evrelerde lokal-bölgesel rekürrens (LBR) riskinin yanı sıra uzak metastaz (UM) riski de yüksektir. Bu nedenle tedavide multimodal tedavi yöntemleri tercih edilmektedir. Tanı anında tüm hastalar öncelikle opere edilebilirlik açısından değerlendirilmelidir. Negatif cerrahi sınır sağlanamayacak, T4 tümörü olan veya inflamatuar meme kanseri olan hastalar ilk aşamada operasyona uygun olmamaktadır. Neoadjuvan (NA) sistemik tedavi (kemoterapi [KT] ve/veya hormonoterapi [HT]) bu hastalarda tümör hacmini küçültüp lokal tedaviye olanak sağlamasının yanında operasyona uygun olan hastalarda da meme koruyucu tedaviyi mümkün kılmakta ve mikrometastazları önleyerek rekürrens riskini azaltmaktadır. Bu tedavinin bir diğer yararı da sistemik tedavi etkinliğinin erken dönemde ve sıklıkla basit bir muayene veya ultrason yöntemi ile test edilmesini sağlamasıdır. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) 2018 meta-analizine dahil edilen 10 adet faz III çalışmada %81 olguya antrasiklin temelli NAKT uygulanmış ve toplam yanıt oranı %69, klinik tam yanıt oranı %28 olarak bildirilmiştir (1). Aynı metaanalizde adjuvan KT verilen hastalara göre NAKT'ye klinik tam yanıt veren olgularda uzak metastazsız sağkalım (UMS) ve kansere spesifik sagkalım (KSS) anlamlı olarak yüksek bulunurken, parsiyel yanıt elde edilen olgularda ise lokal-bölgesel kontrol (LBK) adjuvan KT uygulanan olgulara göre anlamlı olarak yüksek bulunmuştur. Çalışmalarda NAKT sonrası patolojik tam yanıt oranları %13-40 arasında raporlanmakta ve üçlü negatif veya HER2(+) meme kanserinde yanıt oranları daha yüksek bildirilmektedir (2-5).

Tanı anında cerrahiye uygun olan hastalarda ise KT neoadjuvan veya adjuvan olarak uygulanabilmekte ve bu iki KT zamanlaması arasında sağkalım farkı bulunmamaktadır (1, 3). Burada temel hedef, meme koruyucu cerrahi (MKC) olanağının arttırılması ve patolojik lenf nodu (LN) metastazı riskinin düşürülmesidir. kT1-3 N0-1 hastaların dahil edildiği ve neoadjuvan 4 kür doksorubisin ve siklofosfamid (AC) KT'si sonrası cerrahi ile cerrahi sonrası 4 kür AC KT'sinin karşılaştırıldığı National Surgical Adju-

[1] Doç. Dr. Sezin YÜCE SARI, Hacettepe Üniversitesi Tıp Fakültesi Radyasyon Onkolojisi AD., sezin.yuce@hacettepe.edu.tr

[2] Dr. Çağlayan Selenge BEDÜK ESEN, Hacettepe Üniversitesi Tıp Fakültesi Radyasyon Onkolojisi AD., selengebedk@gmail.com

pnomonisi tedavisinde steroid ve antibiyotikler kullanılmaktadır.

Meme kanseri RT'sinde diğer korkulan geç yan etki ikincil kanser riskidir. Surveillance, Epidemiology, and End Results (SEER) verilerinde meme kanseri nedeni ile tedavi edilen ve ikincil kanser geliştiren olguların %3,4'ünde ikincil kanser RT ile ilişkili bulunmuştur (58). Toplam 374.999 hasta verisinin değerlendirildiği bu çalışmada RT uygulanan hastalarda uygulanmayanlara göre daha fazla özefagus, plevra, kemik ve yumuşak doku, melanom, karşı meme, uterus-over ve lösemi olguları gözlenmiştir. Benzer çalışmalarda özellikle ≥1 Gy doz alan hacimlerde ikincil kanser riskinin arttığı gösterilmiştir (59, 60). Tüm bu bilgiler ışığında meme kanseri nedeni ile RT planlanan hastalarda tedavi alanlarının iyi seçilmesi, gereksiz ışınlamalardan kaçınılması ve bu hastaların yaşam boyu geç yan etkiler açısından izlenmesi gerekir.

Kaynaklar

1. Early Breast Cancer Trialists' Collaborative Group. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol. 2018;19(1):27-39.
2. van der Hage JA, van de Velde CJ, Julien JP ve ark. Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902. J Clin Oncol. 2001;19(22):4224-37.
3. Rastogi P, Anderson SJ, Bear H ve ark. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. J Clin Oncol. 2008;26(5):778-85.
4. Cortazar P, Zhang L, Untch M ve ark. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384(9938):164-72.
5. Houssami N, Macaskill P, von Minckwitz G ve ark. Meta-analysis of the association of breast cancer subtype and pathologic complete response to neoadjuvant chemotherapy. Eur J Cancer. 2012;48(18):3342-54.
6. Early Breast Cancer Trialists' Collaborative Group. Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials. Lancet. 2000;355(9217):1757-70.
7. Clarke M, Collins R, Darby S ve ark. 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(9503):2087-106.
8. Early Breast Cancer Trialists' Collaborative Group, McGale P, Taylor C ve ark. 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(9935):2127-35.
9. Hojris I, Overgaard M, Christensen JJ ve ark. Morbidity and mortality of ischaemic heart disease in high-risk breast-cancer patients after adjuvant postmastectomy systemic treatment with or without radiotherapy: analysis of DBCG 82b and 82c randomised trials. Radiotherapy Committee of the Danish Breast Cancer Cooperative Group. Lancet. 1999;354(9188):1425-30.
10. Breast Cancer Version 4.2021-April 28, 2021 2021 [Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
11. Balic M, Thomssen C, Wurstlein R ve ark. St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment. Breast Care (Basel). 2019;14(2):103-10.
12. Mamounas EP, Anderson SJ, Dignam JJ ve ark. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. J Clin Oncol. 2012;30(32):3960-6.
13. McGuire SE, Gonzalez-Angulo AM, Huang EH ve ark. 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(4):1004-9.
14. Buchholz TA, Tucker SL, Masullo L ve ark. Predictors of local-regional recurrence after neoadjuvant chemotherapy and mastectomy without radiation. J Clin Oncol. 2002;20(1):17-23.
15. Huang EH, Tucker SL, Strom EA ve ark. Postmastectomy radiation improves local-regional control and survival for selected patients with locally ad-

vanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. J Clin Oncol. 2004;22(23):4691-9.

16. Garg AK, Strom EA, McNeese MD ve ark. T3 disease at presentation or pathologic involvement of four or more lymph nodes predict for locoregional recurrence in stage II breast cancer treated with neoadjuvant chemotherapy and mastectomy without radiotherapy. Int J Radiat Oncol Biol Phys. 2004;59(1):138-45.
17. Early Breast Cancer Trialists' Collaborative Group, Darby S, McGale P ve ark. 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(9804):1707-16.
18. Danish Breast Cancer Cooperative Group, Nielsen HM, Overgaard M ve ark. 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(15):2268-75.
19. Strom EA, Woodward WA, Katz A ve ark. Clinical investigation: regional nodal failure patterns in breast cancer patients treated with mastectomy without radiotherapy. Int J Radiat Oncol Biol Phys. 2005;63(5):1508-13.
20. Recht A, Comen EA, Fine RE ve ark. Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update. J Clin Oncol. 2016;34(36):4431-42.
21. Hennequin C, Bossard N, Servagi-Vernat S ve ark. Ten-year survival results of a randomized trial of irradiation of internal mammary nodes after mastectomy. Int J Radiat Oncol Biol Phys. 2013;86(5):860-6.
22. Thorsen LB, Offersen BV, Dano H ve ark. 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(4):314-20.
23. Whelan TJ, Olivotto IA, Parulekar WR ve ark. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015;373(4):307-16.
24. Poortmans PM, Collette S, Kirkove C ve ark. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015;373(4):317-27.
25. Poortmans PM, Weltens C, Fortpied C ve ark. Internal mammary and medial supraclavicular lymph node chain irradiation in stage I-III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial. Lancet Oncol. 2020;21(12):1602-10.
26. Budach W, Bolke E, Kammers K ve ark. Adjuvant radiation therapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials- an update. Radiat Oncol. 2015;10:258.
27. Recht A, Gray R, Davidson NE ve ark. Locoregional failure 10 years after mastectomy and adjuvant chemotherapy with or without tamoxifen without irradiation: experience of the Eastern Cooperative Oncology Group. J Clin Oncol. 1999;17(6):1689-700.
28. Rowland JH, Desmond KA, Meyerowitz BE ve ark. Role of breast reconstructive surgery in physical and emotional outcomes among breast cancer survivors. J Natl Cancer Inst. 2000;92(17):1422-9.
29. Parker PA, Youssef A, Walker S ve ark. Short-term and long-term psychosocial adjustment and quality of life in women undergoing different surgical procedures for breast cancer. Ann Surg Oncol. 2007;14(11):3078-89.
30. Thiruchelvam PT, McNeill F, Jallali N ve ark. Post-mastectomy breast reconstruction. BMJ. 2013;347:f5903.
31. Spear SL, Ducic I, Cuoco F ve ark. Effect of obesity on flap and donor-site complications in pedicled TRAM flap breast reconstruction. Plast Reconstr Surg. 2007;119(3):788-95.
32. Albornoz CR, Bach PB, Pusic AL ve ark. The influence of sociodemographic factors and hospital characteristics on the method of breast reconstruction, including microsurgery: a U.S. population-based study. Plast Reconstr Surg. 2012;129(5):1071-9.
33. A national audit of provision and outcomes of mastectomy and breast reconstruction surgery for women in England. Fourth Annual Report 2011. 2011 [Available from: https://digital.nhs.uk/data-and-information/publications/statistical/national-mastectomy-and-breast-reconstruction-audit-annual-report/national-mastectomy-and-breast-reconstruction-audit-fourth-annual-report-2011.
34. Hirsch EM, Seth AK, Dumanian GA ve ark. Outcomes of immediate tissue expander breast reconstruction followed by reconstruction of choice in the setting of postmastectomy radiation therapy. Ann Plast Surg. 2014;72(3):274-8.
35. Hirsch EM, Seth AK, Kim JYS ve ark. Analysis of risk

factors for complications in expander/implant breast reconstruction by stage of reconstruction. Plast Reconstr Surg. 2014;134(5):692e-9e.

36. Gerber B, Krause A, Dieterich M ve ark. The oncological safety of skin sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction: an extended follow-up study. Ann Surg. 2009;249(3):461-8.
37. McCarthy CM, Mehrara BJ, Riedel E ve ark. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. Plast Reconstr Surg. 2008;121(6):1886-92.
38. Hvilsom GB, Holmich LR, Steding-Jessen M ve ark. Delayed breast implant reconstruction: is radiation therapy associated with capsular contracture or reoperations? Ann Plast Surg. 2012;68(3):246-52.
39. Yuce Sari S, Guler OC, Gultekin M ve ark. Radiotherapy After Skin-Sparing Mastectomy and Implant-Based Breast Reconstruction. Clin Breast Cancer. 2019;19(5):e611-e6.
40. Lam TC, Hsieh F, Boyages J. The effects of postmastectomy adjuvant radiotherapy on immediate two-stage prosthetic breast reconstruction: a systematic review. Plast Reconstr Surg. 2013;132(3):511-8.
41. Rogers NE, Allen RJ. Radiation effects on breast reconstruction with the deep inferior epigastric perforator flap. Plast Reconstr Surg. 2002;109(6):1919-24; discussion 25-6.
42. Guerra AB, Metzinger SE, Bidros RS ve ark. Bilateral breast reconstruction with the deep inferior epigastric perforator (DIEP) flap: an experience with 280 flaps. Ann Plast Surg. 2004;52(3):246-52.
43. Selber JC, Kurichi JE, Vega SJ ve ark. Risk factors and complications in free TRAM flap breast reconstruction. Ann Plast Surg. 2006;56(5):492-7.
44. Greco JA, 3rd, Castaldo ET, Nanney LB ve ark. Autologous breast reconstruction: the Vanderbilt experience (1998 to 2005) of independent predictors of displeasing outcomes. J Am Coll Surg. 2008;207(1):49-56.
45. Barry M, Kell MR. Radiotherapy and breast reconstruction: a meta-analysis. Breast Cancer Res Treat. 2011;127(1):15-22.
46. Gurunluoglu R, Gurunluoglu A, Williams SA ve ark. Current trends in breast reconstruction: survey of American Society of Plastic Surgeons 2010. Ann Plast Surg. 2013;70(1):103-10.
47. Kelley BP, Ahmed R, Kidwell KM ve ark. A systematic review of morbidity associated with autologous breast reconstruction before and after exposure to radiotherapy: are current practices ideal? Ann Surg Oncol. 2014;21(5):1732-8.
48. Yang JR, Kuo WL, Yu CC ve ark. Reconstructive outcome analysis of the impact of neoadjuvant chemotherapy on immediate breast reconstruction: a retrospective cross-sectional study. BMC Cancer. 2021;21(1):522.
49. Langstein HN, Cheng MH, Singletary SE ve ark. Breast cancer recurrence after immediate reconstruction: patterns and significance. Plast Reconstr Surg. 2003;111(2):712-20; discussion 21-2.
50. Aristei C, Kaidar-Person O, Tagliaferri L ve ark. The Assisi Think Tank Meeting and Survey of post MAstectomy Radiation Therapy after breast reconstruction: The ATTM-SMART report. Eur J Surg Oncol. 2018;44(4):436-43.
51. Muresan H, Lam G, Cooper BT ve ark. Impact of Evolving Radiation Therapy Techniques on Implant-Based Breast Reconstruction. Plast Reconstr Surg. 2017;139(6):1232e-9e.
52. Kaidar-Person O, Vrou Offersen B, Hol S ve ark. ESTRO ACROP consensus guideline for target volume delineation in the setting of postmastectomy radiation therapy after implant-based immediate reconstruction for early stage breast cancer. Radiother Oncol. 2019;137:159-66.
53. White ATJ, Arthur D, Buchholz T ve ark. Breast Cancer Atlas for Radiation Therapy Planning: Consensus Definitions 2009 [Available from: https://www.nrgoncology.org/Portals/0/Scientific%20Program/CIRO/Atlases. BreastCancerAtlas_corr.pdf?-ver=2018-04-18-144201-270.
54. Marks LB, Yorke ED, Jackson A ve ark. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S10-9.
55. Yan M, Kong W, Kerr A ve ark. The radiation dose tolerance of the brachial plexus: A systematic review and meta-analysis. Clin Transl Radiat Oncol. 2019;18:23-31.
56. Ma J, Li J, Xie J ve ark. Post mastectomy linac IMRT irradiation of chest wall and regional nodes: dosimetry data and acute toxicities. Radiat Oncol. 2013;8:81.
57. Darby SC, Ewertz M, McGale P ve ark. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med. 2013;368(11):987-98.

58. Burt LM, Ying J, Poppe MM ve ark. Risk of secondary malignancies after radiation therapy for breast cancer: Comprehensive results. Breast. 2017;35:122-9.
59. Berrington de Gonzalez A, Gilbert E, Curtis R ve ark. Second solid cancers after radiation therapy: a systematic review of the epidemiologic studies of the radiation dose-response relationship. Int J Radiat Oncol Biol Phys. 2013;86(2):224-33.
60. Stovall M, Weathers R, Kasper C ve ark. Dose reconstruction for therapeutic and diagnostic radiation exposures: use in epidemiological studies. Radiat Res. 2006;166(1 Pt 2):141-57.