

ENDOMETRİUM KANSERİ TEDAVİSİNDE RADYOTERAPİ VE BRAKİTERAPİ

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GİRİŞ

Endometriyum kanseri, uterusun en iç tabakası olan endometriyum kaynaklı bir uterin kanseridir.(1) Endometriyum kanseri (EK), jinekolojik kanserler içinde en sık, tüm kanserler içinde beşinci sıklıkla görülen malignitedir.(2) Endometriyum kanseri, obezite ve yaşam süresinin uzamasıyla birlikte özellikle gelişmekte olan ülkelerde görülmeye sıklığı giderek artan bir eğilim göstermektedir.(3) Olguların yaklaşık %90'ında anormal uterin kanama görüldüğünden çoğunlukla erken evrede tanı konmaktadır.(4) Hastaların %80'i evre I'de tanı almaktadır ve tanı sırasında medyan yaş 63 olarak bildirilmektedir. Sağkalım, hastalık evresiyle orantılı olarak değişmektedir; evre I'de 5 yıllık sağkalım %95 iken lokal ileri olgularda bu oran %68, uzak metastazlı olgularda ise %17'lere düşmektedir.(5,6) Türkiye'de yıllık 3850 yeni vaka bildirilmekte olup uterus korpus kanserlerine bağlı yaklaşık 520 ölüm görülmektedir.(7)

Tanı için genellikle pipelle endometriyal örneklemeye ya da dilatasyon ve küretaj ile endometriyal biyopsi kullanılmaktadır.(8) Endometriyum kanserinin ortaya çıkışındaki en önemli risk faktörleri; obezite, erken menarş, geç menapoz, nulliparite, diyabet, ileri yaş (> 55 yaş) ve tamoksifen kullanımı olduğu gösterilmiştir.(9) Endometriyum kanserinde tedavi genellikle cerrahi olarak uterus, serviks, overler ve fallop tüplerinin çıkartılması; bazen lenf nodu örneklemesi ve/veya lenf nodu diseksiyonunu kapsar.(1)

Endometrium kanserinin evrelemesinde, cerrahi teknik ve adjuvan tedavi yaklaşımlarında son yıllarda değişim yaşanmaktadır. Cerrahi halen esas tedavi olmakla birlikte, hasta popülasyonunun genellikle ≥ 60 yaş olması ve eş zamanlı

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seksiyonu sonrasında RT ile toksisitenin fazla olduğu, bu nedenle BT ve yoğunluk ayarlı RT (YART) teknikleriyle daha az yan etki ve yüksek lokal kontrol sağlanabileceği düşünülmüştür. Yapılan çalışmalarda; yüksek riskli lokal ileri olgularda RT-KT'nin birlikte kullanımı ile sağkalım oranlarının arttığı gösterilmektedir.

EK'de morbiditeyi azaltan minimal invazif cerrahi yaklaşımın ön plana çıkması ve KT'nin artan oranda rutin kullanımı, nüks riskinin azalmalarını sağlamıştır. Adjuvan tedavi modalitelerini iyileştirmek ve moleküler analiz verileri doğrultusunda hedefe yönelik tedavi stratejilerini geliştirmek için yeni çalışmalarla ihtiyaç vardır.

Anahtar Kelimeler: Uterus maligniteleri, endometrium kanseri, tedavi, radyoterapi, brakiterapi.

KAYNAKÇA

1. uptodate.com (2019). Plaxe SC, Mundt AJ. Patient education: Endometrial cancer treatment after surgery (Beyond the Basics) 2019. (14.07.2019 tarihinde <https://www.uptodate.com/contents/endometrial-cancer-treatment-after-surgery-beyond-the-basics> adresinden ulaşılmıştır).
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:359-86.
3. Morice P, Leary A, Creutzberg C, et al. Endometrial cancer. Lancet 2016;387(10023):1094-108.
4. Colombo N, Preti E, Landoni F, et al. ESMO Guidelines Working Group. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(6):33-8.
5. Lee NK, Cheung MK, Shin JY, et al. Prognostic factors for uterine cancer in reproductive-aged women. Obstet Gynecol 2007;109(3):655-62.
6. Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. Int J Gynecol Cancer 2016; 26(1):2-30.
7. Gultekin, M, Kucukyildiz I, Karaca MZ, et al. Trends of Gynecological Cancers in Turkey: Toward Europe or Asia? Int J Gynecol Cancer 2017;27(1):S1-S9.
8. Dijkhuizen FP, Mol BW, Brölmann HA, et al. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 2000;89:1765-72.
9. Grady D, Gebretsadik T, Kerlikowske K, et al. Hormone replacement therapy and endometrial cancer risk: a meta-analysis. Obstet Gynecol 1995;85:304-13.
10. TJOD (2017). Jinekolojik Kanserlerin Yönetimi Kilavuzu: Endometrium Kanseri 2017. (14.07.2019 tarihinde <http://www.trsgo.org/trsgoData/userfiles/file/endometriumkanseri.pdf> adresinden ulaşılmıştır).
11. Steloo E, Nout RA, Osse EM, et al. Improved Risk Assessment by Integrating Molecular and Clinicopathological Factors in Early-stage Endometrial Cancer-Combined Analysis of the PORTEC Cohorts. Clin Cancer Res. 2016;22(16):4215-24.
12. Weiderpass E, Antoine J, Bray FI, et al. Trends in corpus uteri cancer mortality in member states of the European Union. Eur J Cancer 2014;50:1675-84.
13. Creasman WT, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri. FIGO 26th annual report on the results of treatment in gynecological cancer. Int J Gynaecol Obstet 2006;95:105-43.
14. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial.

- PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet 2000;355:1404-11.
- 15. Meyer LA, Bohlke K, Powell MA, et al. Postoperative Radiation Therapy for Endometrial Cancer: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Society for Radiation Oncology EvidenceBased Guideline. J Clin Oncol 2015;33(26):2908-13.
 - 16. Nag S, Erickson B, Parikh S, et al. The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the endometrium. Int J Radiat Oncol Biol Phys 2000;48:779-90.
 - 17. Nout RA, Smit VT, Putter H, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. Lancet 2010;375(9717):816-23.
 - 18. Chino JP, Jones E, Berchuck A, et al. The influence of radiation modality and lymph node dissection on survival in early-stage endometrial cancer. Int J Radiat Oncol Biol Phys 2012; 82(5):1872-9.
 - 19. Lee CM, Szabo A, Shrieve DC, et al. Frequency and effect of adjuvant radiation therapy among women with stage I endometrial adenocarcinoma. JAMA 2006;295(4):389-97.
 - 20. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. Gynecol Oncol 2004;92:744-51.
 - 21. Blake P, Swart AM, Orton J, et al. Adjuvant external beam radiotherapy in the treatment of endometrial cancer (MRC ASTEC and NCIC CTG EN.5 randomised trials): pooled trial results, systematic review, and meta-analysis. Lancet 2009;373:137-46.
 - 22. Johnson N, Cornes P. Survival and recurrent disease after postoperative radiotherapy for early endometrial cancer: systematic review and meta-analysis. BJOG 2007;114:1313-20.23: de Boer SM, Powell ME, Mileskin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. Lancet Oncol 2018;19(3):295-309.
 - 24. Sorbe B, Nordström B, Mäenpää J, et al. Intravaginal brachytherapy in FIGO stage I low-risk endometrial cancer: A controlled randomized study. Int J Gynecol Cancer 2009;19:873-878.
 - 25. Kong, A, Johnson N, Kitchener HC, et al. Adjuvant radiotherapy for stage I endometrial cancer: an updated Cochrane systematic review and meta-analysis. J Natl Cancer Inst 2012; 104(21):1625-34.
 - 26. Kitchener H, Swart AM, Qian Q, et al. Efficacy of systemic pelvic lymphadenectomy in early stage endometrial cancer (MRC ASTEC trial): a randomized controlled trial. Lancet 2009;373:125-136.
 - 27. Greven K, Winter K, Underhill K, et al. Final analysis of RTOG 9708: adjuvant postoperative irradiation combined with cisplatin /paclitaxel chemotherapy following surgery for patients with high-risk endometrial cancer. Gynecol Oncol 2006;103(1):155-159.
 - 28. Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. Gynecol Oncol 2009;112(3):543-552.
 - 29. Randall ME, Filiaci VL, Muss H, et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: A Gynecologic Oncology Group Study. J Clin Oncol 2006;24:36-44.
 - 30. Maggi R, Lissoni A, Spina F, et al. Adjuvant chemotherapy vs radiotherapy in high-risk endometrial carcinoma: Results of a randomised trial. Br J Cancer 2006;95:266-271.
 - 31. Susumu N, Sagae S, Udagawa Y, et al. Randomized phase III trial of pelvic radiotherapy versus cisplatin-based combined chemotherapy in patients with intermediate- and high-risk endometrial cancer: A Japanese Gynecologic Oncology Group study. Gynecol Oncol 2008; 108:226-233.

32. Greven K, Winter K, Underhill K, et al. Radiation Therapy Oncology Group Preliminary analysis of RTOG 9708: Adjuvant postoperative radiotherapy combined with cisplatin/paclitaxel chemotherapy after surgery for patients with high-risk endometrial cancer. *Int J Radiat Oncol Biol Phys* 2004;59(1):168-73.
33. Matei D, Filiaci VL, Randall M, et al. A randomized phase III trial of cisplatin and tumor volume directed irradiation followed by carboplatin and paclitaxel vs. carboplatin and paclitaxel for optimally debulked, advanced endometrial carcinoma. *J Clin Oncol* 2017;35:5505.
34. Yavaş G. Role and Timing of Radiotherapy in High-Risk Endometrial Cancer. *Turk J Oncol* 2017;32(3):123-132.
35. NCCN (2017). NCCN guidelines version 2017 Uterine neoplasms. (14.07.2019 tarihinde https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf adresinden ulaşılmıştır)
36. Klopp A, Smith BD, Alektiar K, et al. The role of postoperative radiation therapy for endometrial cancer: Executive summary of an American Society for Radiation Oncology evidence-based guideline. *Pract Radiat Oncol* 2014;4(3):137-44.
37. Jhingran A, Ramondetta LM, Bodurka DC, et al. A prospective phase II study of chemoradiation followed by adjuvant chemotherapy for FIGO stage I-IIIA (1988) uterine papillary serous carcinoma of the endometrium. *Gynecol Oncol* 2013;129(2):304-9.
38. Viswanathan AN, Macklin EA, Berkowitz R, et al. The importance of chemotherapy and radiation in uterine papillary serous carcinoma. *Gynecol Oncol* 2011;123(3):542-7.
39. Del Carmen MG, Boruta DM, Schorge JO. Recurrent endometrial cancer. *Clin Obstet Gynecol* 2011;54(2):266-77.
40. Fung-Kee-Fung M, Dodge J, Elit L, et al. Follow-up after primary therapy for endometrial cancer: a systematic review. *Gynecol Oncol* 2006;101(3):520-9.
41. Lajer H, Elnegaard S, Christensen RD, et al. Survival after stage IA endometrial cancer; can follow-up be altered? A prospective nationwide Danish survey. *Acta Obstet Gynecol Scand* 2012;91(8):976-82.
42. Lin LL, Grigsby PW, Powell MA, et al. Definitive radiotherapy in the management of isolated vaginal recurrences of endometrial cancer. *Int J Radiat Oncol Biol Phys* 2005;63(2): 500-4.
43. American Cancer Society (2019). Radiation Therapy for Endometrial Cancer. (14.07.2019 tarihinde <https://www.cancer.org/cancer/endometrial-cancer/treating/radiation.html> adresinden ulaşılmıştır).
44. Salani R, Backes FJ, Fung MF, et al. Posttreatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. *Am J Obstet Gynecol* 2011;204(6):466.