

## BÖLÜM 32

### NADİR ENDOMETRİYAL KANSERLER

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#### GİRİŞ

Endometrium kanseri (EK) gelişmiş ülkelerde en sık görülen jinekolojik kanserdir. Kanserlerinin yüzde 90'ından fazlası epitelden kaynaklanan endometriyal, geri kalanların çoğu myometrial kastan veya daha az sıklıkla endometriyalstromadan kaynaklanan mezenkimaldir (1).

Epitelial endometrium kanserleri; 1983 yılında Bokhman tarafından endokrin ve metabolik etkilerine göre tip I ve tip II şeklinde iki alt tip olarak sınıflandırılmıştır. Tip I endometriyal kanserler en sık görülen alt tip olup yaklaşık %65'ini kapsar. Östrojen maruziyeti ile ilişkili ve çoğunlukla endometrioid histolojide düşük derecelidir. Tip I daha iyi прогнозlu olup 5 yıllık sağkalım %85'in üstündedir. Tip II endometriyal kanserler daha kötü прогнозlu olup tüm endometriyal kanserlerin %10-20'sidir ve endometriyal kanserlere bağlı ölümlerin %40'ından sorumlu görülen tümörlerdir (2). Bu sınıflandırma sistemi EK'yi anlamak için yardımcı olmasına rağmen, iki tipten birine tam olarak uymayan bazı histolojik alt tiplerin biyolojik çeşitliliğini veya klinik sonuçlarının çeşitliliğini kapsamamaktadır. Tek başına cerrahiyle tedavi edilecek hastalar ile nüks açısından risk altında olan ve bu nedenle adjuvan tedaviye ihtiyaç duyan hastalar arasında ayırm yapmak büyük bir zorluk olmaya devam etmektedir. Bu yüzden EK için çok sayıda sınıflandırma sistemi geliştirilmiştir.

#### A-MOLEKÜLER SINIFLANDIRMA SİSTEMİ

2013 yılında Kanser Genom Atlas Projesi (TCGA) 370'ten fazla EK'yi karakterize etmek için genomik, transkriptomik ve proteomik analizleri kullanarak farklı prognostik sonuçlara sahip tümör hücresi genomik mimarisine dayalı dört moleküler alt tipi belirledi (3). Bu moleküler alt tipler EK'lerin patogenezi hakkında fikir verirken alt sınıflandırması için de bir yol gösterir.

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Genellikle lokalde nüks eder. Metastatik hastalıktan vaka bildirimlerinde mTOR inhibitörlerin etkin olduğu bildirilmiştir (58).

## SONUÇ

Endometrium kanserlerde sınıflama sistemiyle tek başına cerrahi ile tedavi edilebilecek hastalar ve hem lokal hem de uzak nüks açısından önemli risk altında olan, bu nedenle adjuvan tedaviye ihtiyaç olan hastalar arasında ayrılmaması gerekmektedir.

Evre IV bir hasta için ek tedavi ihtiyacının belirlenmesi daha kolaydır ancak erken evre hastalık için nüks riskine göre adjuvan tedaviye ihtiyaç duyulup duyulmadığını belirlemek birden fazla patolojik özelliklere bağlı olabilir. Mevcut bilgilerimizle henüz yeterli bilgiye sahip değiliz. EK için çok sayıda risk sınıflandırma sistemi, klinik deneylerle veya kurumsal tercihlere dayalı geliştirilmiştir. Bu derlemede nadir görülen endometrium kanser tiplerinin histopatolojik ve immünohistokimyasal özellikleri, прогноз ve güncel yaklaşımları vurgulanmaya çalışılmıştır. Nadir görülen endometrium kanserleri hakkında daha fazla bilgi öğrendikçe tedavi ve izlem şekillerimiz netleşecektir.

## KAYNAKLAR

1. <https://www.cancer.net/cancer-types/uterine-cancer/statistics>.
2. JV B. Two pathogenetic types of endometrial carcinoma.: Gynecol Oncol. 1983;15(1):10..
3. Cancer Genome Atlas Research Network KC, Schultz N, et al. Integrated genomic characterization of endometrial carcinoma. Nature 2013, 497:67.
4. Murali R SR, Weigelt B. Classification of endometrial carcinoma: more than two types. Lancet Oncol. 2014, 15(7):e268-78.
5. Mao TL AL, Ayhan A, Kuo KT, Wu CH, Wang TL, et al. Loss of ARID1A expression correlates with stages of tumor progression in uterine endometrioid carcinoma. Am J Surg Pathol. 2013, 37(9):1342-8.
6. Creutzberg CL L-CA, De Boer SM, et al. Molecular classification of the PORTEC-3 trial for high-risk endometrial cancer: Impact on adjuvant therapy. Ann Oncol 2019, 3-:mdz394.
7. Nout RA SV, 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, 375:816.
8. Church DN SE, Nout RA, et al. Prognostic significance of POLE proofreading mutations in endometrial cancer. J Natl Cancer Inst 2015, 107:402.
9. McAlpine JN CD, Nout RA, et al. Evaluation of treatment effects in patients with endometrial cancer and POLE mutations: An individual patient data meta-analysis. Cancer 2021, 127:2409.
10. Howitt BE SS, Sholl LM, et al. Association of Polymerase e-Mutated and Microsatellite-Instable Endometrial Cancers With Neoantigen Load, Number of Tumor-Infiltrating Lymphocytes, and Expression of PD-1 and PD-L1. JAMA Oncol 2015, 1:1319.
11. Talhouk A DH, Schmidt P, et al. Molecular Subtype Not Immune Response Drives Outcomes in Endometrial Carcinoma. Clin Cancer Res 2019, 25:2537.
12. Reijnen C K-VH, Prinsen CF, et al. Mismatch repair deficiency as a predictive marker for response to adjuvant radiotherapy in endometrial cancer. Gynecol Oncol 2019, 154:124.
13. Jamieson A TE, Huvila J, et al. p53abn Endometrial Cancer: understanding the most aggressive endometrial cancers in the era of molecular classification. Int J Gynecol Cancer 2021, 31:907.

14. Concin N M-GX, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer* 2021, 31:12.
15. Imboden S ND, Ghaderi M, et al. Implementation of the 2021 molecular ESGO/ESTRO/ESP risk groups in endometrial cancer. *Gynecol Oncol* 2021, 162:394.
16. Russo M BJ, Sheldon K, et al. Clonal evolution in paired endometrial intraepithelial neoplasia/atypical hyperplasia and endometrioid adenocarcinoma. *Hum Pathol* 2017, 67:69.
17. Lucas E CH, Molberg K, et al. Mismatch Repair Protein Expression in Endometrioid Intraepithelial Neoplasia/Atypical Hyperplasia: Should We Screen for Lynch Syndrome in Precancerous Lesions? *Int J Gynecol Pathol* 2019, 38:533.
18. Abdulfatah E WE, Sakr S, et al. Molecular classification of endometrial carcinoma applied to endometrial biopsy specimens: Towards early personalized patient management. *Gynecol Oncol* 2019, 154:467.
19. Pecorelli S. Revised FIGO staging for carcinoma of the vulva c, and endometrium. *Int J Gynaecol Obstet*. 2009 May, 2010 -EiIJGO, 108(2):176.
20. James DB MK, Christian W. TNM Classification of Malignant Tumours. 8th Edition. Wiley-Blackwell. UICC. Published, Ltd.p.171-9. bjWS.
21. Singh N HL, Zaino R, et al. Pathologic Prognostic Factors in Endometrial Carcinoma (Other Than Tumor Type and Grade). *Int J Gynecol Pathol* 2019, 1:S93. S.
22. WHO Classification of Tumours Editorial Board. Female Genital Tumours te, IARC, 2020. Vol 4.
23. Ambros RA SM, Zahn CM, Bitter- man P, Kurman RJ. Endometrial intraepithelial carcinoma: a distinctive lesion specifically associated with tumors displaying serous differentiation. *Hum Pathol*. 1995, 26:1260-7.
24. Huang CY TY, Chiang YC, Wang KL, Fu HC, et al. Impact of management on the prognosis of pure uterine papillary serous cancer - a Taiwanese Gynecologic Oncology Group (TGOG) study. *Gynecol Oncol*. 2014, 133:221-8.
25. Growdon WB R-HJ, Cordon A, Gar- rett L, et al. Prognostic determinants in patients with stage I uterine papillary serous carcinoma: a 15-year multi-institutional review. *Int J Gynecol Cancer*. 2012, 22(3):417-24.
26. Leslie KK FV, Mallen AR, et al. Mutated p53 portends improvement in outcomes when bevacizumab is combined with chemotherapy in advanced/recurrent endometrial cancer: An NRG Oncology study. *Gynecol Oncol* 2021, 161:113.
27. Fadare O ZW, Crispens MA, et al. Morphologic and other clinicopathologic features of endometrial clear cell carcinoma: a comprehensive analysis of 50 rigorously classified cases. *Am J Cancer Res* 2013, 3:70.
28. DeLair DF BK, Selenica P, et al. The genetic landscape of endometrial clear cell carcinomas. *J Pathol* 2017, 243:230.
29. Matrai CE PEaELDdm, many mixed endometrial carcinomas show unexpected immunohistochemical staining patterns. *Int J Gynecol Pathol* 37(5):405-413.
30. Rabban JT GC, Malpica A, Matias-Guiu X, et al. Issues in the differential diagnosis of uterine low-grade endometrioid carcinoma, including mixed endometri.
31. Altrabulsi B MA, Deavers MT, et al. Undifferentiated carcinoma of the endometrium. *Am J Surg Pathol* 2005, 29:1316–21.
32. Silva EG DM, Bodurka DC, et al. Association of low-grade endometrioid carcinoma of the uterus and ovary with undifferentiated carcinoma: a new type of dedifferentiated carcinoma? *Int J Gynecol Pathol* 2006, 25:52–8.
33. Ramalingam P MR, Euscher ED, et al. Undifferentiated Carcinoma of the Endometrium: An Expanded Immunohistochemical Analysis Including PAX-8 and Basal-Like Carcinoma Surrogate Markers. *Int J Gynecol Pathol* 2016, 35:410–8.
34. Tessier-Cloutier B SR, Stewart CJR, et al. Frequent loss of claudin-4 expression in dedifferentiated and undifferentiated endometrial carcinomas. *Histopathology* 2018, 73:299–305.
35. Broaddus RR LH, Chen LM, et al. Pathologic features of endometrial carcinoma associated with HNPCC: a comparison with sporadic endometrial carcinoma. *Cancer* 2006, 106:87.
36. Travaglino A RA, Mascolo M, et al. TCGA Molecular Subgroups in Endometrial Undifferentiated/Dedifferentiated Carcinoma. *Pathol Oncol Res* 2020, 26:1411.

37. Gotoh O SY, Takazawa Y, et al. Clinically relevant molecular subtypes and genomic alteration-independent differentiation in gynecologic carcinosarcoma. *Nat Commun* 2019; 10:4965.
38. Cherniack AD SH, Walter V, et al. Integrated Molecular Characterization of Uterine Carcinosarcoma. *Cancer Cell* 2017; 31:411.
39. Sreenan JJ, Hart WR. Carcinosarcomas of the female genital tract. A pathologic study of 29 metastatic tumors: further evidence for the dominant role of the epithelial component and the conversion theory of histogenesis. *Am J Surg Pathol* 1995; 19:666.
40. Powell MA FV, Rose PG, Mannel RS, Hanjani P, Degeest K, et al. Phase II evaluation of paclitaxel and carboplatin in the treatment of carcinosarcoma of the uterus: a Gynecologic Oncology Group study. *J Clin Oncol*. 2010, 28(16):2727-31.
41. McFarland M QC, McCluggage WG. Hormone receptor-negative, thyroid transcription factor 1-positive uterine and ovarian adenocarcinomas: report of a series of mesonephric-like adenocarcinomas. *Histopathology* 2016; 68:1013–20.
42. da Silva EM FD, Sebastiao APM, et al. Mesonephric and mesonephric-like carcinomas of the female genital tract: molecular characterization including cases with mixed histology and matched metastases. *Mod Pathol* 2021; 34:1570–87.
43. Na K, Kim HS. Clinicopathologic and Molecular Characteristics of Mesonephric Adenocarcinoma Arising From the Uterine Body. *Am J Surg Pathol* 2019; 43:12–25.
44. Yano M SD, Katoh T, et al. Coexistence of endometrial mesonephric-like adenocarcinoma and endometrioid carcinoma suggests a Mullerian duct lineage: a case report. *Diagn Pathol* 2019; 14:54.
45. Mirkovic J UaDH-GEC, Surgical Pathology 15 (2022) 301–314. doi.org/10.1016/j.path.2022.02.007.
46. Kolin DL CD, Dong F, et al. A Combined Morphologic and Molecular Approach to Retrospectively Identify KRAS-Mutated Mesonephric-like Adenocarcinomas of the Endometrium. *Am J Surg Pathol* 2019; 43:389–98.
47. Pors J SS, Chiu DS, et al. Clinicopathologic Characteristics of Mesonephric Adenocarcinomas and Mesonephric-like Adenocarcinomas in the Gynecologic Tract: A Multi-institutional Study. *Am J Surg Pathol* 2021; 45:498–506.
48. Paik ES YA, Lee YY, et al. Pulmonary metastasectomy in uterine malignancy: outcomes and prognostic factors. *J Gynecol Oncol* 2015; 26:270–6.
49. Labi FL ES, Di Miscia A, et al. FIGO Stage I endometrial carcinoma: evaluation of lung metastases and follow-up. *Eur J Gynaecol Oncol* 2008; 29:65–6.
50. Abiko K BT, Ogawa M, et al. Minimal deviation mucinous adenocarcinoma ('adenoma malignum') of the uterine corpus. *Pathol Int* 2010; 60:42–7.
51. McCarthy WA MR, Miller K, et al. Gastric- Type Endometrial Adenocarcinoma: Report of Two Cases in Patients From the United States. *Int J Surg Pathol* 2018; 26:377–81.
52. Lokuhetty D WV, Watanabe R. Female genital tumours. 5th edition. Internal Agency for Research on Cancer (IARC), 2020.
53. Wong RW RA, Grondin K, et al. Endometrial Gastric (Gastrointestinal)-type Mucinous Lesions: Report of a Series Illustrating the Spectrum of Benign and Malignant Lesions. *Am J Surg Pathol* 2020; 406–19.
54. Travaglino A RA, Gencarelli A, et al. Endome- trial Gastric-type Carcinoma: An Aggressive and Morphologically Heterogenous New Histotype Arising From Gastric Metaplasia of the Endometrium. *Am J Surg Pathol* 2020; 44:1002–4.
55. Skala SL LC, Udager AM, et al. Molecular characterization of uterine and ovarian tumors with mixed epithelial and germ cell features confirms frequent somatic derivation. *Mod Pathol* 2020; 33:1989–2000.
56. Rawish KR BN, Zheng W, et al. Endometrial Carcinoma With Trophoblastic Components: Clinicopathologic Analysis of a Rare Entity. *Int J Gynecol Pathol* 2018; 37:174–90.
57. Xing D ZG, Pallavajjala A, et al. Lineage-Specific Alterations in Gynecologic Neoplasms with Choriocarcinomatous Differentiation: Implications for Origin and Therapeutics. *Clin Cancer Res* 2019; 25:4516–29.
58. Musella A DFF, Kyriacou AK, Barletta F, Di Matteo FM, Marchetti C, et al. Perivasculär epithelioid cell neoplasm (PEComa) of the uterus: A systematic review. *Int J Surg*. 2015, 19:1–5.