

## Bölüm

11

# Adrenal Bez Tümörlerinin Evrelemesi ve Evrelendirmede Nükleer Tıp Yöntemleri

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## Adrenokortikal Karsinom

### Giriş

Adrenokortikal karsinom (AKK), adrenal korteksten kaynaklanan, yıllık insidanının milyonda 0,7- 2,0 arasında olduğu tahmin edilen nadir görülen bir tümördür. En sık 4. ve 5. dekatlar arasında görülmesine rağmen her yaşıta ortaya çıkabilir (1-3).

AKK'lı hastalarda prognoz genellikle kötüdür. Yapılan çalışmalarda beş yıllık genel sağkalım (GS) %13-80 arasında değişmekle birlikte çoğunlukla %40'ın altındadır (3,4-11). Hastaların tanı anındaki evresi, ana prognostik faktör olup sağ kalımın bağımsız bir prediktif değeri olarak kabul edilmektedir (6-13). Ayrıca hastlığın evresinden başka derece (Weiss skorlama sistemi), Ki 67 düzeyi, aşırı hormon sekresyonu ve cerrahi rezeksiyon sınırı (R0-R2) klinik ve patolojik prognostik faktörler arasında gösterilmektedir (14-17).

### Evreleme

AKK'nin evrelemesi diğer kanser türlerine benzer şekilde “tümör, lenf nodu ve metastaz (TNM)” sınıflandırmasına dayanır. AKK evrelemesi için “Uluslararası Kanser Kontrol Birliği (UICC) ve Dünya Sağlık Örgütü (WHO)” tarafından 2004 yılında ilk kez TNM sınıflandırmasına dayalı Tablo 1'de gösterilen bir evreleme sistemi yayınlanmıştır (18). Bu evreleme sisteminde evre 4 hastalar içerisinde

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de nöroblastomda tutulumu [<sup>I-123</sup>] MIBG sintirafisine benzer şekilde norepinefrin taşıyıcı sistemi ile görüntüleme sağlamaktadır (56,57).

[F-18] FDG, [F-18] F-DOPA ve [Ga-68] Ga-DOTA peptidleri norepinefrin taşıyıcı sistemi dışında nöroblastomda tutulum göstermektedir ve MIBG tutulumu göstermeyen nöroblastom hastalarında kullanılması giderek artmaktadır. MIBG tutulumu göstermeyen nöroblastom hastalarında veya MIBG görüntüleme ile klinik bulgular arasında uyumsuzluğu olan hastaların değerlendirilmesinde kılavuzlar tarafından MIBG sintigrafisine alternatif olarak önerilen tek PET görüntüleme yöntemi [F-18] FDG PET görüntülemesidir (50).

Nöroblastomda tümör dokusu heterojen olduğu için farklı moleküller hedefler ile görüntüleme yöntemleri kullanılmasını gerektirmektedir ancak ekstra radyasyon maruziyeti ve maliyet artışı nedeniyle bu mümkün görünmemektedir. Gelecekte PET/MR, görüntüleme merkezlerinin sayısının artması radyasyon maruziyetini azaltıp daha yüksek çözünürlükte görüntüler sağlayarak hastaların yönetiminde katkı sağlayacağı düşünülmektedir.

## KAYNAKLAR

1. Fassnacht M, Assie G, Baudin E, et al. Adrenocortical carcinomas and malignant phaeochromocytomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2020;31: 1476–1490.
2. Custódio G, Komechen H, Figueiredo FRO, et al. Molecular epidemiology of adrenocortical tumors in southern Brazil. *Molecular and cellular endocrinology.* 2012;351: 44–51.
3. Else T, Kim AC, Sabolch A, et al. Adrenocortical carcinoma. *Endocrine reviews.* 2014;35(2): 282-326.
4. Kerkhofs TM, Verhoeven RH, Van der Zwan JM, et al. Adrenocortical carcinoma: a population-based study on incidence and survival in the Netherlands since 1993. *European Journal of Cancer.* 2013;49(11): 2579-2586.
5. Fassnacht M, Johanssen S, Quinkler M, et al. Limited prognostic value of the 2004 International Union Against Cancer staging classification for adrenocortical carcinoma: proposal for a Revised TNM Classification. *Cancer.* 2009;115(2): 243-250.
6. Assié G, Antoni G, Tissier F, et al. Prognostic parameters of metastatic adrenocortical carcinoma. *The Journal of Clinical Endocrinology & Metabolism.* 2007;92(1): 148-154.
7. Kebebew E, Reiff E, Duh, QY, et al. Extent of disease at presentation and outcome for adrenocortical carcinoma: have we made progress?. *World journal of surgery.* 2006;30(5): 872-878.
8. Bilimoria KY, Shen WT, Elaraj D, et al. Adrenocortical carcinoma in the United States: treatment utilization and prognostic factors. *Cancer: Interdisciplinary International Journal of the American Cancer Society.* 2008;113(11): 3130-3136.

9. Else T, Williams AR, Sabolch A, et al. Adjuvant therapies and patient and tumor characteristics associated with survival of adult patients with adrenocortical carcinoma. *The Journal of Clinical Endocrinology & Metabolism*. 2014;99(2): 455-461.
10. Ayala-Ramirez M, Jasim S, Feng L, et al. Adrenocortical carcinoma: clinical outcomes and prognosis of 330 patients at a tertiary care center. *European journal of endocrinology/European Federation of Endocrine Societies*. 2013;169(6): 891.
11. Icard P, Goudet P, Charpenay C, et al. Adrenocortical carcinomas: surgical trends and results of a 253-patient series from the French Association of Endocrine Surgeons study group. *World journal of surgery*. 2001;25(7): 891-897.
12. Stojadinovic A, Ghossein RA, Hoos A, et al. Adrenocortical carcinoma: clinical, morphologic, and molecular characterization. *Journal of Clinical Oncology*. 2002;20(4): 941-950.
13. Abiven G, Coste J, Groussin L, et al. Clinical and biological features in the prognosis of adrenocortical cancer: poor outcome of cortisol-secreting tumors in a series of 202 consecutive patients. *The Journal of Clinical Endocrinology & Metabolism*. 2006;91(7): 2650-2655.
14. Fassnacht M, Dekkers OM, Else T, et al. European Society of Endocrinology Clinical Practice Guidelines on the management of adrenocortical carcinoma in adults, in collaboration with the European Network for the Study of Adrenal Tumors. *European journal of endocrinology*. 2018;179(4): G1-G46.
15. Owen DH, Patel S, Wei L, et al. Metastatic adrenocortical carcinoma: a single institutional experience. *Hormones and Cancer*. 2019;10(4): 161-167.
16. Papotti M, Libè R, Duregon E, et al. The Weiss score and beyond—histopathology for adrenocortical carcinoma. *Hormones and Cancer*. 2011;2(6): 333-340.
17. Libe R, Borget I, Ronchi CL, et al. Prognostic factors in stage III-IV adrenocortical carcinomas (ACC): an European Network for the Study of Adrenal Tumor (ENSAT) study. *Annals of Oncology*. 2015;26(10): 2119-2125.
18. DeLellis RA. World Health Organization classification of tumours. *Pathology & genetics: tumours of endocrine organs*. 2004; 110.
19. Fassnacht M, Allolio B. Clinical management of adrenocortical carcinoma. *Best practice & research Clinical endocrinology & metabolism*. 2009;23(2): 273-289.
20. Fassnacht M, Kroiss M, Allolio B. Update in adrenocortical carcinoma. *The Journal of Clinical Endocrinology & Metabolism*. 2013;98(12): 4551-4564.
21. Libé R. Adrenocortical carcinoma (ACC): diagnosis, prognosis, and treatment. *Frontiers in cell and developmental biology*. 2015;3: 45.
22. Postlewait LM, Ethun CG, Tran TB, et al. Outcomes of adjuvant mitotane after resection of adrenocortical carcinoma: a 13-institution study by the US Adrenocortical Carcinoma Group. *Journal of the American College of Surgeons*. 2016;222(4): 480-490.
23. Bonnet-Serrano F, Bertherat J. Genetics of tumors of the adrenal cortex. *Endocrine-related cancer*. 2018;25(3): R131-R152.
24. Lughezzani G, Sun M, Perrotte P, et al. The European Network for the Study of Adrenal Tumors staging system is prognostically superior to the international union against cancer-staging system: a North American validation. *European journal of cancer*. 2010;46(4): 713-719.

25. Kostiainen I, Hakaste L, Kejo P, et al. Adrenocortical carcinoma: presentation and outcome of a contemporary patient series. *Endocrine*. 2019;65(1): 166-174.
26. Amin MB, Greene FL, Edge SB, et al. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA: a cancer journal for clinicians*. 2017;67(2): 93-99.
27. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2014;99(6):1915-1942.
28. Plouin PF, Amar L, Dekkers OM, et al. European Society of Endocrinology Clinical Practice Guideline for long-term follow-up of patients operated on for a phaeochromocytoma or a paraganglioma. *European journal of endocrinology*. 2016;174(5): G1-G10.
29. Fassnacht M, Arlt W, Bancos I, et al. Management of adrenal incidentalomas: European society of endocrinology clinical practice guideline in collaboration with the European network for the study of adrenal tumors. *European journal of endocrinology*. 2016;175(2): G1-G34.
30. Lloyd RV, Osamura RY, Klöppel G, et al. WHO classification of tumours of endocrine organs. IARC: Lyon, France, 2017.
31. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2014;99(6):1915-1942.
32. Pacak K, Eisenhofer G, Ahlman H, et al. Pheochromocytoma: recommendations for clinical practice from the First International Symposium. *Nature clinical practice Endocrinology & metabolism*. 2007;3(2): 92-102.
33. Rao D, Van Berkel A, Piscaer I, et al. Impact of 123I-MIBG Scintigraphy on Clinical Decision-Making in Pheochromocytoma and Paraganglioma. *The Journal of Clinical Endocrinology & Metabolism*. 2019;104(9): 3812-3820.
34. Taïeb D, Hicks RJ, Hindié E, et al. European association of nuclear medicine practice guideline/society of nuclear medicine and molecular imaging procedure standard 2019 for radionuclide imaging of phaeochromocytoma and paraganglioma. *European journal of nuclear medicine and molecular imaging*. 2019;46(10): 2112-2137.
35. Castinetti F, Kroiss A, Kumar R, et al. 15 years of paraganglioma: imaging and imaging-based treatment of pheochromocytoma and paraganglioma. *Endocrine-related cancer*. 2015;22(4): T135-T145.
36. Han S, Suh CH, Woo S, et al. Performance of 68Ga-DOTA-conjugated somatostatin receptor-targeting peptide PET in detection of pheochromocytoma and paraganglioma: A systematic review and metaanalysis. *Journal of Nuclear Medicine*. 2019;60(3): 369-376.
37. Irwin MS, Park JR. Neuroblastoma: paradigm for precision medicine. *Pediatric Clinics*. 2015;62(1): 225-256.
38. Tas ML, Reedijk AMJ, Karim-Kos HE, et al. Neuroblastoma between 1990 and 2014 in the Netherlands: Increased incidence and improved survival of high-risk neuroblastoma. *European Journal of Cancer*. 2020;124: 47-55.
39. Morgenstern DA, London WB, Stephens D,et al. Prognostic significance of pattern and burden of metastatic disease in patients with stage 4 neuroblastoma: A study

- from the International Neuroblastoma Risk Group database. *European Journal of Cancer*. 2016; 65: 1-10.
40. Brodeur GM, Pritchard J, Berthold F, et al. Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment. *Journal of clinical oncology*. 1993;11(8): 1466-1477.
  41. Simon T, Hero B, Benz-Bohm Get al. Review of image defined risk factors in localized neuroblastoma patients: results of the GPOH NB97 trial. *Pediatric blood & cancer*. 2008;50(5): 965-969.
  42. Nour-Eldin NEA, Abdelmonem O, Tawfik AM, et al. Pediatric primary and metastatic neuroblastoma: MRI findings: pictorial review. *Magnetic resonance imaging*. 2012;30(7): 893-906.
  43. Brisse HJ, McCarville MB, Granata C, et al. Guidelines for imaging and staging of neuroblastic tumors: consensus report from the International Neuroblastoma Risk Group Project. *Radiology*. 2011;261(1): 243-257
  44. Cohn SL, Pearson AD, London WB, et al. The International Neuroblastoma Risk Group (INRG) classification system: an INRG task force report. *Journal of clinical oncology*. 2009;27(2): 289.
  45. Monclair T, Brodeur GM, Ambros PF, et al. The international neuroblastoma risk group (INRG) staging system: an INRG task force report. *Journal of clinical oncology*. 2009;27(2): 298.
  46. Yanik GA, Parisi MT, Shulkin BL, et al. Semiquantitative mIBG scoring as a prognostic indicator in patients with stage 4 neuroblastoma: a report from the Children's oncology group. *Journal of nuclear medicine*. 2013;54(4): 541-548.
  47. Matthay KK, Edeline V, Lumbroso J, et al. Correlation of Early Metastatic Response by 123I- Metaiodobenzylguanidine Scintigraphy With Overall Response and Event-Free Survival in Stage IV Neuroblastoma. *Journal of clinical oncology*. 2013;31(13): 2486-2491.
  48. Lewington V, Lambert B, Poetschger U, et al. 123I-mIBG scintigraphy in neuroblastoma: development of a SIOPEN semi-quantitative reporting, method by an international panel. *European Journal of Nuclear Medicine and Molecular Imaging*. 2017;44(2): 234-241.
  49. Siegel MJ, Jaju A. MR imaging of neuroblastic masses. *Magnetic Resonance Imaging Clinics of North America*. 2008;16(3): 499-513.
  50. Bar-Sever Z, Biassoni L, Shulkin B, et al. Guidelines on nuclear medicine imaging in neuroblastoma. *European journal of nuclear medicine and molecular imaging*. 2018;45(11): 2009-2024.
  51. Rozovsky K, Koplewitz BZ, Krausz Y, et al. Added value of SPECT/CT for correlation of MIBG scintigraphy and diagnostic CT in neuroblastoma and pheochromocytoma. *American Journal of Roentgenology*. 2008;190(4): 1085-1090.
  52. Fukuoka M, Taki J, Mochizuki T, et al. Comparison of diagnostic value of I-123 MIBG and high-dose I-131 MIBG scintigraphy including incremental value of SPECT/CT over planar image in patients with malignant pheochromocytoma/paraganglioma and neuroblastoma. *Clinical nuclear medicine*. 2011;36(1): 1-7.

53. Liu B, Servaes S, Zhuang H. SPECT/CT MIBG imaging is crucial in the follow-up of the patients with high-risk neuroblastoma. *Clinical nuclear medicine*. 2018;43(4): 232-238.
54. Biermann M, Schwarzmüller T, Fasmer KE, et al. Is there a role for PET-CT and SPECT-CT in pediatric oncology?. *Acta radiologica*. 2013;54(9): 1037-1045.
55. Sharp SE, Trout AT, Weiss BD, et al. MIBG in neuroblastoma diagnostic imaging and therapy. *Radiographics*. 2016;36(1): 258-278.
56. Vallabhajosula S, Nikolopoulou A. Radioiodinated metaiodobenzylguanidine (MIBG): radiochemistry, biology, and pharmacology. In. *Seminars in nuclear medicine*. WB Saunders; 2011. pp. 324-333.
57. Zhang H, Huang R, Cheung NKV, et al. Imaging the Norepinephrine Transporter in Neuroblastoma: A Comparison of [18F]-MFBG and 123I-MIBG [18F]-MFBG PET Imaging of Neuroblastoma. *Clinical Cancer Research*. 2014;20(8): 2182-2191.
58. Hofman MS, Lau WE, Hicks RJ. Somatostatin receptor imaging with 68Ga DOTATATE PET/CT: clinical utility, normal patterns, pearls, and pitfalls in interpretation. *Radiographics*. 2015;35(2): 500-516.