

BÖLÜM 27

TİROİD DİFERANSİYE TÜMÖRLERİ YAKLAŞIMI



Bilal SİZER ¹

GİRİŞ-SINIFLAMA

Tiroid bezinin benign tümörlerine nazaran hayatı tehdit edici malign tümörleri çok az görülmektedir. Tiroid ultrasonografisi ve ince igne aspirasyon biyopsinin daha sık yapılması ile tiroid tümörlerinin saptanması daha sık ve kolay hale gelse de halen tanı ve tedavi ile ilgili çeşitli belirsizlikler mevcuttur.

Endokrin ilişkili kanserler içerisinde tiroid bezi kanserleri en sık görülenlerdir. Bu kanserlerin büyük çoğunluğunu (%90) iyi прогноз gösteren diferansiyeli tiroid kanserleri oluşturmaktadır. Diferansiyeli tiroid karsinomları genellikle yavaş bir gelişim seyri göstermektedir. Bu tümörlerin %85 kadarı papiller karsinomdan oluşurken, %12 kadarı da foliküler karsinomdan olmaktadır (1, 2).

Papiller ve foliküler kanserler birçok farklılık barındırmalarına rağmen tedavileri benzerdir. (3).

EPİDEMİYOLOJİ

Son yıllarda tiroid kanseri insidansında, her iki cinsiyette ve tüm etnik kökenlerde görülen bir artış izlenmektedir (4, 5). Tiroid kanserindeki artış, temel olarak bo-

¹ Dr. Öğr. Üyesi, İstanbul Arel Üniversitesi, Tıp Fakültesi, Kulak Burun ve Boğaz Hastalıkları AD, bilalsizer@hotmail.com



KAYNAKLAR

1. Pacini F, Castagna MG, Brilli L, et al. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2010;21 (5):214-v219. doi:10.1093/annonc/mdq190
2. Links TP, Van Tol KM, Jager PL, et al. Life expectancy in differentiated thyroid cancer: a novel approach to survival analysis. *Endocr Relat Cancer.* 2005;12 (2):273-80. doi:10.1677/erc.1.00892
3. Uptodate (2021). *Differentiated thyroid cancer: Overview of management.* (20/12/2021 tarihinde <https://www.uptodate.com/contents/differentiated-thyroid-cancer-overview-of-management> adresinden ulaşılmıştır).
4. SEER (2018). *SEER Cancer Statistics Review 1975-2018.* (20/12/2021 tarihinde https://seer.cancer.gov/csr/1975_2018/ adresinden ulaşılmıştır).
5. Jemal A, Simard EP, Dorell C, et al. Annual Report to the Nation on the Status of Cancer, 1975-2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst.* 2013;105 (3):175-201. doi:10.1093/jnci/djs491
6. Davies L, Welch HG. Current thyroid cancer trends in the United States. *JAMA Otolaryngol Head Neck Surg.* 2014;140 (4):317-322. doi:10.1001/jamaoto.2014.1
7. Ahn HS, Kim HJ, Welch HG. Korea's thyroid-cancer "epidemic"--screening and overdiagnosis. *N Engl J Med.* 2014;371 (19):1765-1767. doi:10.1056/NEJMmp1409841
8. Vaccarella S, Franceschi S, Bray F, et al. Worldwide Thyroid-Cancer Epidemic? The Increasing Impact of Overdiagnosis. *N Engl J Med.* 2016;375 (7):614-617. doi:10.1056/NEJMmp1604412
9. Lim H, Devesa SS, Sosa JA, et al. Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013. *JAMA.* 2017;317 (13):1338-1348. doi:10.1001/jama.2017.2719
10. SEER (2017). Stat fact sheets: thyroid cancer 2016. (20/12/2021 tarihinde <http://seer.cancer.gov/statfacts/html/thyro.html> adresinden ulaşılmıştır).
11. Pettersson B, Adami HO, Wilander E, et al. Trends in thyroid cancer incidence in Sweden, 1958-1981, by histopathologic type. *Int. J. Cancer.* 1991;48 (1):28-33.
12. Harach HR, Escalante DA, Oñativia A, et al. Thyroid carcinoma and thyroiditis in an endemic goitre region before and after iodine prophylaxis. *Eur J Endocrinol.* 1985;108 (1):55-60.
13. Schneider AB, Sarne DH. Long-term risks for thyroid cancer and other neoplasms after exposure to radiation. *Nat Clin Pract Endocrinol Metab.* 2005;1 (2):82-91.
14. Williams D. Cancer after nuclear fallout: lessons from the Chernobyl accident. *Nat Rev Cancer.* 2002;2 (7):543-549. doi:10.1038/nrc845
15. Harach HR, Escalante DA, Day ES. Thyroid cancer and thyroiditis in Salta, Argentina: a 40-yr study in relation to iodine prophylaxis. *Endocr Pathol.* 2002;13 (3):175-81.
16. Takahashi MH, Thomas GA, Williams ED. Evidence for mutual interdependence of epithelium and stromal lymphoid cells in a subset of papillary carcinomas. *Br J Cancer.* 1995;72 (4):813-817. doi:10.1038/bjc.1995.418
17. Hemminki K, Li X. Familial risk of cancer by site and histopathology. *Int J Cancer.* 2003;103 (1):105-109. doi:10.1002/ijc.10764
18. Kimura ET, Nikiforova MN, Zhu Z, et al. High prevalence of BRAF mutations in thyroid cancer: genetic evidence for constitutive activation of the RET/PTC-RAS-BRAF signaling pathway in papillary thyroid carcinoma. *Cancer Res.* 2003;63 (7):1454-1457.
19. Nikiforova MN, Kimura ET, Gandhi M, et al. BRAF mutations in thyroid tumors are restricted to papillary carcinomas and anaplastic or poorly differentiated carcinomas arising from papillary carcinomas. *J Clin Endocrinol Metab.* 2003;88 (11):5399-5404. doi:10.1210/jc.2003-030838



20. Nikiforova MN, Lynch RA, Biddinger PW, et al. RAS point mutations and PAX8-PPAR gamma rearrangement in thyroid tumors: evidence for distinct molecular pathways in thyroid follicular carcinoma. *J Clin Endocrinol Metab.* 2003;88 (5):2318-2326. doi:10.1210/jc.2002-021907
21. Antonelli A, Ferri C, Fallahi P, et al. Thyroid cancer in HCV-related chronic hepatitis patients: a case-control study. *Thyroid.* 2007;17 (5):447-451. doi:10.1089/thy.2006.0194
22. Rossing MA, Voigt LF, Wicklund KG, et al. Reproductive factors and risk of papillary thyroid cancer in women. *Am J Epidemiol.* 2000 ;151 (8):765-772. doi: 10.1093/oxfordjournals.aje.a010276.
23. Kitahara CM, Pfeiffer RM, Sosa JA, et al. Impact of Overweight and Obesity on US Papillary Thyroid Cancer Incidence Trends (1995-2015). *J Natl Cancer Inst.* 2020;112 (8):810-817. doi:10.1093/jnci/djz202
24. McCarthy RP, Wang M, Jones TD, et al. Molecular evidence for the same clonal origin of multifocal papillary thyroid carcinomas. *Clin Cancer Res.* 2006;12 (8):2414-2418. doi:10.1158/1078-0432.CCR-05-2818
25. Tiemens ET, Sherman SI, Hruban RH, et al. Follicular variant of papillary thyroid carcinoma. A clinicopathologic study. *Cancer.* 1994;73 (2):424-431. doi:10.1002/1097-0142.
26. Johnson TL, Lloyd RV, Thompson NW, et al. Prognostic implications of the tall cell variant of papillary thyroid carcinoma. *Am J Surg Pathol.* 1988;12 (1):22-27. doi:10.1097/00000478-198801000-00003
27. Ghossein R, Livolsi VA. Papillary thyroid carcinoma tall cell variant. *Thyroid.* 2008;18 (11):1179-1181. doi:10.1089/thy.2008.0164
28. Hubert JP Jr, Kiernan PD, Beahrs OH, et al. Occult Papillary Carcinoma of the Thyroid. *Arch Surg.* 1980; 115 (4):394-398. DOI: 10.1001/archsurg.1980.01380040028004.
29. Ascoli S, Erickson LA, Sebo TJ, et al. Papillary thyroid carcinoma with prominent hobnail features: a new aggressive variant of moderately differentiated papillary carcinoma. A clinicopathologic, immunohistochemical, and molecular study of eight cases. *The Am J Surg Pathol.* 2010;34 (1):44-52.
30. Motosugi U, Murata S-I, Nagata K, et al. Thyroid papillary carcinoma with micropapillary and hobnail growth pattern: a histological variant with intermediate malignancy? *Thyroid.* 2009;19 (5):535-537. doi:10.1089/thy.2008.0271 .
31. Koç, C. (2013). *Kulak burun boğaz hastalıkları ve baş-boyun cerrahisi.* Ankara: Güneş Tip Kitabevleri.
32. Co Collini P, Sampietro G, Rosai J, et al. Minimally invasive (encapsulated) follicular carcinoma of the thyroid gland is the low-risk counterpart of widely invasive follicular carcinoma but not of insular carcinoma. *Virchows Arch.* 2003;442 (1):71-76. doi:10.1007/s00428-002-0701-2
33. D'Avanzo A, Treseler P, Ituarte PH, et al. Follicular thyroid carcinoma: histology and prognosis. *Cancer.* 2004;100 (6):1123-1129. doi:10.1002/cncr.20081
34. Baloch ZW, LiVolsi VA. Prognostic factors in well-differentiated follicular-derived carcinoma and medullary thyroid carcinoma. *Thyroid.* 2001;11 (7):637-645. doi:10.1089/105072501750362709
35. Baloch ZW, LiVolsi VA. Follicular-patterned afflictions of the thyroid gland: reappraisal of the most discussed entity in endocrine pathology. *Endocr Pathol.* 2014;25 (1):12-20. doi:10.1007/s12022-013-9293-4
36. Uptodate (2020). Diagnostic approach to and treatment of thyroid nodules. (20/12/2021 tarihinde https://www.uptodate.com/contents/diagnostic-approach-to-and-treatment-of-thyroid-nodules?sectionName=History%20and%20physical%20examination&topicRef=7860&anchor=H3&source=see_link#H3 adresinden ulaşılmıştır)



37. Shah JP. Thyroid carcinoma: epidemiology, histology, and diagnosis. *Clin Adv Hematol Oncol.* 2015;13 (4):3-6.
38. Uptodate (2021). *Follicular thyroid cancer (including Hurthle cell cancer)*. (20/12/2021 tarihinde <https://www.uptodate.com/contents/follicular-thyroid-cancer-including-hurthle-cell-cancer> adresinden ulaşılmıştır)
39. Tuttle M, Morris LF, Haugen B, et al. Chapter 73. Thyroid-differentiated and anaplastic carcinoma. In: MB Amin, SB Edge, FL Greene, et al, eds. *AJCC Cancer Staging Manual*. 8th ed. New York: Springer International Publishing; 2017: 873- 901.
40. Tuttle RM, Haugen B, Perrier ND. Updated American Joint Committee on Cancer/Tumor-Node-Metastasis Staging System for Differentiated and Anaplastic Thyroid Cancer (Eighth Edition): What Changed and Why? *Thyroid*. 2017;27 (6):751-756. doi:10.1089/thy.2017.0102
41. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19 (11):1167-214. doi:10.1089/thy.2009.0110
42. Vaisman F, Momesso D, Bulzico DA, et al. Spontaneous remission in thyroid cancer patients after biochemical incomplete response to initial therapy. *Clin Endocrinol (Oxf)*. 2012;77 (1):132-138. doi:10.1111/j.1365-2265.2012.04342.x
43. Vaisman F, Tala H, Grewal R, et al. In differentiated thyroid cancer, an incomplete structural response to therapy is associated with significantly worse clinical outcomes than only an incomplete thyroglobulin response. *Thyroid*. 2011;21 (12):1317-1322. doi:10.1089/thy.2011.0232
44. Vaisman F, Shaha A, Fish S, et al. Initial therapy with either thyroid lobectomy or total thyroidectomy without radioactive iodine remnant ablation is associated with very low rates of structural disease recurrence in properly selected patients with differentiated thyroid cancer. *Clin Endocrinol (Oxf)*. 2011;75 (1):112-119. doi:10.1111/j.1365-2265.2011.04002.x
45. Pitoia F, Bueno F, Urciuoli C, et al. Outcomes of patients with differentiated thyroid cancer risk-stratified according to the American thyroid association and Latin American thyroid society risk of recurrence classification systems. *Thyroid*. 2013;23 (11):1401-1407. doi:10.1089/thy.2013.0011
46. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;26 (1):1-133. doi:10.1089/thy.2015.0020
47. NCCN (2021). *Thyroid Carcinoma NCCN Guidelines*. (20/12/2021 tarihinde <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1470> adresinden ulaşılmıştır.)
48. Pacini F, Schlumberger M, Dralle H, et al. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. *Eur J Endocrinol*. 2006;154 (6):787-803. doi:10.1530/eje.1.02158
49. Solorzano CC, Lee TM, Ramirez MC, et al. Surgeon-performed ultrasound improves localization of abnormal parathyroid glands. *Am Surg*. 2005;71 (7):557-563.
50. Shimamoto K, Satake H, Sawaki A, et al. Preoperative staging of thyroid papillary carcinoma with ultrasonography. *Eur J Radiol*. 1998;29 (1):4-10.doi: 10.1016/S0720-048X(97)00184-8
51. Stulak JM, Grant CS, Farley DR, et al. Value of preoperative ultrasonography in the surgical management of initial and reoperative papillary thyroid cancer. *Arch Surg*. 2006;141 (5):489-96. doi:10.1001/archsurg.141.5.489
52. Kouvaraki MA, Shapiro SE, Fornage BD, et al. Role of preoperative ultrasonography in the surgical management of patients with thyroid cancer. *Surgery*. 2003;134 (6):946-955. doi:10.1016/s0039-6060 (03)00424-0



53. Leboulleux S, Girard E, Rose M, et al. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. *J Clin Endocrinol Metab.* 2007;92 (9):3590-3594. doi:10.1210/jc.2007-0444.
54. Uptodate (2021). *Differentiated thyroid cancer: Surgical treatment.* (20/12/2021 tarihinde <https://www.uptodate.com/contents/differentiated-thyroid-cancer-surgical-treatment/print> adresinden ulaşılmıştır.)
55. Sherman SI, Angelos P, Ball DW, et al. Thyroid carcinoma. *J Natl Compr Canc Netw.* 2007;5 (6):568-621. doi:10.6004/jnccn.2007.0052
56. Cobin RH, Gharib H, Bergman DA, et al. AACE/AAES medical/surgical guidelines for clinical practice: management of thyroid carcinoma. *Endocr Pract.* 2008;14 (6):802-803.
57. British Thyroid Association, Royal College of Physicians (2007). *Guidelines for the management of thyroid cancer* (2nd edition). London: Royal College of Physicians.
58. McLeod DS, Sawka AM, Cooper DS. Controversies in primary treatment of low-risk papillary thyroid cancer. *Lancet.* 2013;381 (9871):1046-1057. doi:10.1016/S0140-6736(12)62205-3
59. Uptodate (2021). Thyroidectomy. (20/12/2021 tarihinde <https://www.uptodate.com/contents/thyroidectomy/print#!> adresinden ulaşılmıştır.)
60. Pujol P, Daures JP, Nsakala N, et al. Degree of thyrotropin suppression as a prognostic determinant in differentiated thyroid cancer. *J Clin Endocrinol Metab.* 1996;81 (12):4318-4323. doi:10.1210/jcem.81.12.8954034
61. Uptodate (2021). *Differentiated thyroid cancer: External beam radiotherapy.* (20/12/2021 tarihinde <https://www.uptodate.com/contents/differentiated-thyroid-cancer-external-beam-radiotherapy#!> adresinden ulaşılmıştır.)
62. Uptodate (2021). *Differentiated thyroid cancer refractory to standard treatment: Systemic therapy.* (20/05/2021 tarihinde <https://www.uptodate.com/contents/differentiated-thyroid-cancer-refractory-to-standard-treatment-systemic-therapy#!> adresinden ulaşılmıştır.)
63. Tuttle RM, Haugen B, Perrier ND. Updated American Joint Committee on Cancer/Tumor-Node-Metastasis Staging System for Differentiated and Anaplastic Thyroid Cancer (Eighth Edition): What Changed and Why?. *Thyroid.* 2017;27 (6):751-756. doi:10.1089/thy.2017.0102
64. Momesso DP, Tuttle RM. Update on differentiated thyroid cancer staging. *Endocrinol Metab Clin North Am.* 2014;43 (2):401-421. doi:10.1016/j.ecl.2014.02.010
65. Ganly I, Nixon IJ, Wang LY, et al. Survival from Differentiated Thyroid Cancer: What Has Age Got to Do with It?. *Thyroid.* 2015;25 (10):1106-1114. doi:10.1089/thy.2015.0104
66. Hay ID, Bergstrahl EJ, Goellner JR, et al Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. *Surgery.* 1993;114 (6):1050-1058.
67. Machens A, Holzhausen HJ, Dralle H. The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma. *Cancer.* 2005;103 (11):2269-2273. doi:10.1002/cncr.21055
68. Uptodate (2021). *Papillary thyroid cancer: Clinical features and prognosis.* (20/12/2021 tarihinde <https://www.uptodate.com/contents/papillary-thyroid-cancer-clinical-features-and-prognosis#!> adresinden ulaşılmıştır.)
69. Casara D, Rubello D, Saladini G, et al. Different features of pulmonary metastases in differentiated thyroid cancer: natural history and multivariate statistical analysis of prognostic variables. *J Nucl Med.* 1993;34 (10):1626-1631.
70. Chiu AC, Delpassand ES, Sherman SI. Prognosis and treatment of brain metastases in thyroid carcinoma. *J Clin Endocrinol Metab.* 1997;82 (11):3637-3642. doi:10.1210/jcem.82.11.4386