

# Bölüm 1

# BAŞ BOYUN TÜMÖRLERİNDE EPİDEMİYOLOJİ VE ETYOPATOGENEZ

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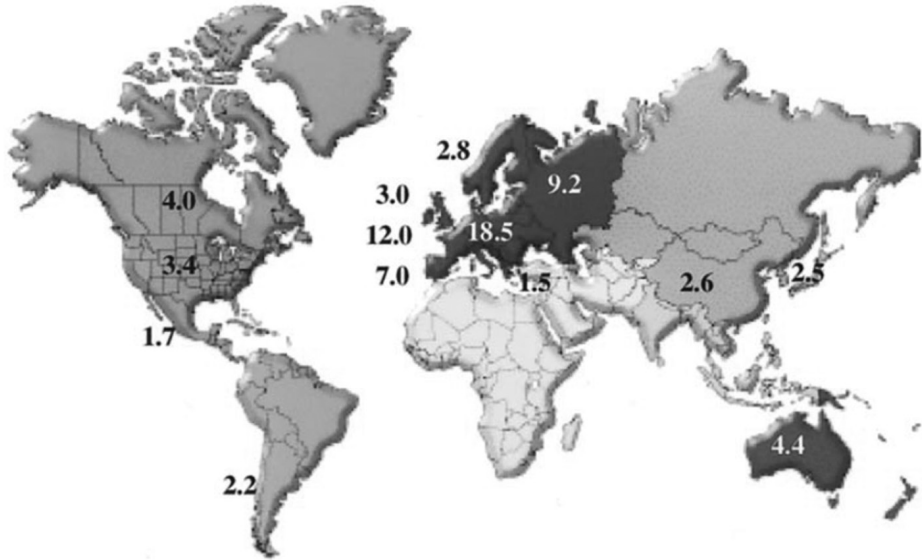
## GİRİŞ

Baş boyun kanserleri tüm maligniteler içerisinde 6. sıradışı yer almakta olup, kanser nedenli ölümlerin %5'ini oluşturmaktadır(1). Baş boyun kanserleri genelde 50-60 yaşlardaki hastalarda görülür. Bununla birlikte yaş ortalamaları artışına paralel olarak hastalığın daha ileri yaşlarda ortaya çıktığı olgular giderek artmaktadır. Kanser insidansı 65 yaş üstünde 2163.9/100.000'lere ulaşmaktadır(42). Yakın bir zamanda kanser, insan ölümlerinde birinci sıraya oturacak ve yeni solid kanserlerin yarısından fazlası 70 yaş üzerindeki kişilerde görülecektir. Gelişmiş ülkelerdeki madde bağımlılığının artması, açlığın tehdidindeki 3. dünya ülkelerinde tarımsal alanlarda temel gıda ana maddelerinin yerine alkol, tütün ve uyuşturucu hammaddelerinin üretilmesi, genetiği değiştirilmiş ürünlerin azalan tarım alanlarıyla giderek artan oranda yiyeceklerimize girmesi, modern hayatın getirdiği düzensiz ve dengesiz beslenme, önlenemeyen çevre kirliliği gelecek nesillerde kanser gibi ölümcül hastalıkların daha sık görüleceği beklentisine yol açmaktadır.

Baş boyun tümörleri larinks, oral kavite(alt ve üst dudak, gingiva, gingivo bukkal sulkus, bukkal mukoza, sert damak, retromolar trigon, ağız tabanı, dil), orofarinks( yumuşak damak, tonsiller, dil kökü, faringeal duvar), nazofarinks, nazal kavite ve paranasal sinüsler, göz, kulak, tükrük bezi, tiroid ve yumuşak dokuyu kapsamaktadır.

Dünya genelinde baş boyun kanserlerin %42'si oral kavite ve %25'i larinkste yerleşim gösterir. Bunu %15 orofarenks ve hipofarenks, %7 major tükrük bezleri, %4 nazofarinks, %4 burun ve paranasal sinüsler, %3 tiroid, deri ve konnektif doku takip eder (2). Dünyada her yıl oral kavite, larinks ve nazofarinks kanserli yaklaşık 500.000 hasta tanımlanmış olup bunların 270.000'i mortalite ile sonuçlanmakta-

sağlar. Günümüzde magnetik rezonans görüntüleme(MR), bilgisayarlı tomografi(BT) ve pozitron emisyon tomografi(PET) ile hastanın preoperatif değerlendirilmesi yapılmaktadır. Özellikle ileri evre tümörlerde metastaz öncelikle boyuna daha sonrada uzak organa metastaz olabilir. En sık metastaz akciğere, daha nadiren kemik,beyin ve karaciğere olabilir. Bu sebeple ileri evre tümörlerde toraks tomografisi çekilmesi hem ileri evre hemde ikinci primer odak açısından değerlendirilmesine yardımcı olur. Görüntülemeler kontrastlı yapılmalıdır. Oral kavite ve nazofarenks tümörlerinde MR yumuşak dokuyu değerlendirme açısından biraz daha tercih edilebilir.PET, erken evre tümörlerde rutin değerlendirme için tercih edilmez, ancak ileri evre tümörlerde giderek önem kazanmaktadır.



**Resim1.** Erkerlerde oral kavite ve farinks kanserli hastalardaki ölüm oranlarının ülkelerdeki dağılımı. Canada (4.0), United States (3.4), Chile (2.2), Norway (2.8), United Kingdom (3.0), France (12.0), Spain (7.0), Hungary (18.5), Russian Federation (9.2), Israel (1.5), China (2.6), Japan (2.5), andAustralia (4.4). Source document does not includedatafromseveralhigh-incidenceareassuch as Melanesia, IndiaandBrazil. (Data from: Landis SH, Murray T, Bolden S, Wingo PA. Cancerstatistics, 1998. CA Cancer J Clin 1998;48:6–29.)

## KAYNAKLAR

1. Shibuya K, Mathers CD, Boschi-Pinto C, et al. Global andregionalestimates of cancermortality andincidenceby site: II. Results for the global burden of disease 2000. BMC Cancer 2:37, 2002.
2. Coniglio JU, Nettekville JL: Guidelines for patient management. Bailey BJ (Ed),:HeadandNeck-Surgery-Otolaryngology. LippincottCompany, Philadelphia, 1993, s. 1021-1028.
3. Parkin DM, Pisani P, Ferlay J. Global cancerstatistics. CA Cancer J Clin 1999;49:33–64.
4. Siegel RL, Miller KD, Jemal A. Cancerstatistics, 2016. CA Cancer J Clin 2016;66(1):7-30.

5. Gatta G, Botta L, Sanchez MJ, Anderson LA, Pierannunzio D, Licitra L, et al. Prognoses and improvement for head and neck cancers diagnosed in Europe in early 2000s: The EUROCARE-5 population-based study. *Eur J Cancer* 2015.
6. Erkal HS, Mendenhall WM, Amdur RJ, Villaret DB, Stringer SP. Synchronous and metachronous squamous cell carcinomas of the head and neck mucosal sites. *J ClinOncol* 2001;19(5):1358-62.
7. Rogers SJ, Harrington KJ, Rhys-Evans P, et al. Biological significance of c-erbB family oncogenes in head and neck cancer. *Cancer Metastasis Rev* 24: 47-69, 2005.
8. Califano J, van der Riet P, Westra W, et al. Genetic progression model for head and neck cancer: implications for field cancerization. *Cancer Res* 56: 2488-2492, 1996.
9. Jeon GA, Lee JS, Patel V, et al. Global gene expression profiles of human head and neck squamous carcinoma cell lines. *Int J Cancer* 112:249-258, 2004.
10. Chen YJ, Lin SC, Kao T, et al. Genome-wide profiling of oral squamous cell carcinoma. *J Pathol* 204:326-332, 2004.
11. Grandis JR, Melhem MF, Barnes EL, Twardy DJ. Quantitative immunohistochemical analysis of transforming growth factor- $\alpha$  and epidermal growth factor receptor in patients with squamous cell carcinoma of the head and neck. *Cancer* 78: 1284-1292, 1996.
12. Santini J, Formento JL, Francoual M, et al. Characterization, quantification, and potential clinical value of the epidermal growth factor receptor in head and neck squamous cell carcinomas. *Head Neck* 13: 132-139, 1991.
13. Dassonville O, Formento JL, Francoual M, et al. Expression of epidermal growth factor receptor and survival in upper aerodigestive tract cancer. *J Clin Oncol* 11: 1873-1878, 1993.
14. Caponigro F, Formato R, Caraglia M, et al. Monoclonal antibodies targeting epidermal growth factor receptor and vascular endothelial growth factor with a focus on head and neck tumors. *Curr Opin Oncol* 17: 212-217, 2005.
15. Kyzas PA, Stefanou D, Batistatou A. Potential autocrine function of vascular endothelial growth factor in head and neck cancer via vascular endothelial growth factor receptor-2. *Mod Pathol* 18: 485-494, 2005.
16. Hatano, T. et al. Identification of human papilloma virus (HPV) 16 DNA integration and the ensuing patterns of methylation in HPV - associated head and neck squamous cell carcinoma cell lines. *Int J Cancer* .2017;140:1571-1580.
17. Lydiatt WM, Patel SG, O'Sullivan B, Brandwein MS, Ridge JA, Migliacci JC et al. Head and Neck cancers-major changes in the American Joint Committee on cancer eighth edition cancer staging manual. *CA Cancer J Clin*. 2017;67:122- 137.
18. Tinhofer, I. et al. Contribution of human papilloma virus to the incidence of squamous cell carcinoma of the head and neck in a European population with high smoking prevalence. *Eur J Cancer*. 2015;51, 514-521.
19. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papilloma virus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol*. 2011;29:4294-4301.
20. Kreimer A, Clifford G, Boyle P, et al. Human papillomavirus types in head and neck squamous cell carcinomas world wide: a systematic review. *Cancer Epidemiol Biomarkers Prev*. 2005;14:467-475.
21. Devesa SS, Silverman DT, Young JL Jr, et al. Cancer incidence and mortality trends among whites in the United States, 1947-84. *J Natl Cancer Inst* 1987;79:701-70.
22. Ries LAG. Rates. In: Hurray A, editor. *Cancer: Rates and risks*. Washington, DC, National Institutes of Health; 1996. p.9-55.
23. Wingo PA, Ries LA, Giovino GA, et al. Annual report to the nation on the status of cancer, 1973-1996, with a special section on lung cancer and tobacco smoking [see comments]. *J Natl Cancer Inst* 1999;91:675-90.
24. Schwartz LH, Ozahin M, Zhang GN, et al. Synchronous and metachronous head and neck carcinomas. *Cancer* 1994;74:1933-8.

25. Blot WJ, McLaughlin JK, Winn DM, et al. Smoking and drinking in relation to oral and pharyngeal cancer. *CancerRes* 1988;48:3282-7.
26. Agudelo D, Quer M, Leon X, et al. Laryngealcarcinoma in patients without a history of tobacco and alcohol use. *HeadNeck* 1997;19:200-4.
27. Harris JA, Meyers AD, Smith C. Laryngealcancer in Colorado. *HeadNeck* 1993;15:398-404.
28. Wynder EL, Covey LS, Mabuchi K, Mushinski M. Environmental factors in cancer of the larynx: a second look. *Cancer* 1976;38:1591-601.
29. Brugere J, Guenel P, Leclerc A, Rodriguez J. Differential effects of tobacco and alcohol in cancer of the larynx, pharynx, and mouth. *Cancer* 1986;57:391-5.
30. Maier H, Dietz A, Gewelke U, et al. [Tobacco- and alcohol associated cancer risk of the upper respiratory and digestive tract]. *Laryngorhinootologie* 1990;69:505-11.
31. Olsen J, Sabreo S, Fasting U. Interaction of alcohol and tobacco as risk factors in cancer of the laryngeal region. *JEpidemiolCommunityHealth* 1985;39:165-8.
32. Guenel P, Chastang JF, Luce D, et al. A study of the interaction of alcohol drinking and tobacco smoking among French cases of laryngeal cancer. *J Epidemiol Community Health* 1988;42:350-4.
33. Schildt EB, Eriksson M, Hardell L, Magnuson A. Oral infections and dental factors in relation to oral cancer: a Swedish case-control study. *Eur J CancerPrev* 1998;7:201-6.
34. Levi F, Pasche C, La Vecchia C, et al. Food groups and risk of oral and pharyngeal cancer. *Int J Cancer* 1998;77:705-9.
35. Velly AM, Franco EL, Schlecht N, et al. Relation ship between dental factors and risk of upper aerodigestive tract cancer. *Oral Oncol* 1998;34:284-91.
36. Schildt EB, Eriksson M, Hardell L, Magnuson A. Occupational exposures as risk factors for oral cancer evaluated in a Swedish case-control study. *OncolRep* 1999;6:317-20.
37. Maier H, Dietz A, Gewelke U, Heller WD. [Occupational exposure to hazardous substances and risk of cancer in the area of the mouth cavity, oropharynx, hypopharynx and larynx. A case-control study]. *Laryngorhinootologie* 1991;70:93-8.
38. Flanders WD, Rothman KJ. Occupational risk for laryngeal cancer. *Am J PublicHealth* 1982;72:369-72.
39. Zagraniski RT, Kelsey JL, Walter SD. Occupational risk factors for laryngeal carcinoma: Connecticut, 1975-1980. *Am J Epidemiol* 1986;124:67-76.
40. Tisch M, Enderle G, Zoller J, Maier H. [Cancer of the oral cavity in machineworkers]. *Laryngorhinootologie* 1996; 75:759-63.
41. Singh B, Balwally AN, Shaha AR, et al. Upper aerodigestive tract squamous cell carcinoma. The human immunodeficiency virus connection [publishederratum appears in *Arch Otolaryngol HeadNeckSurg* 1996; 122(9):944]. *Arch Otolaryngol Head Neck Surg* 1996;122:639-43.
42. Ramesh HS, Pope D, Gennari R, Audisio RA. Optimising surgical management of elderly cancer patients. *World J Surg Oncol* 2005;3:17
43. Gillison ML, D'Souza G, Westra W, et al. Distinct risk factor profiles for human papillomavirus type 16 positive and human papillomavirus type 16 negative head and neck cancers. *J Natl Cancer Inst* .2008;100:407-420.
44. Spitz MR, McPherson RS, Jiang H, et al. Correlates of mutagen sensitivity in patients with upper aerodigestive tract cancer. *Cancer Epidemiol Biomarkers Prev* 1997;6: 687-92.
45. Freije JE, Beatty TW, Campbell BH, et al. Carcinoma of the larynx in patients with gastroesophageal reflux. *Am J Otolaryngol* 1996;17:386-90.
46. Winn DM, Ziegler RG, Pickle LW, et al. Diet in the etiology of oral and pharyngeal cancer among women from the southern United States. *Cancer Res* 1984;44:1216-22.
47. Esteve J, Riboli E, Pequignot G, et al. Diet and cancers of the larynx and hypopharynx: the IARC multi-center study in southwestern Europe. *Cancer Causes Control* 1996;7: 240-52.