

BÖLÜM 17

İNCE BAĞIRSAK TÜMÖRLERİ

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GİRİŞ

Gastrointestinal sistemde en geniş yüzey alanına sahip olmasına rağmen, ince bağırsaklar nadiren neoplazmalar geliştirir. Aslında, ince bağırsak tümörleri tüm gastrointestinal neoplazmaların %1 ila %2'sini oluşturur (tüm neoplazmaların yalnızca %0.3'ü) (1). İnce bağırsak tümörleri nadir görülmeleri, özgün belirtiler göstermemeleri nedeniyle genellikle geç tanı alan tümörler olup öncelikle malign ve benign olarak iki ana başlıkta toplanabilir(2). Malign tümörler başlıca adenokarsinomlar, nöroendokrin tümörler, lenfomalar ve sarkomlar iken benign ince bağırsak neoplazmaları arasında adenomlar, hamartomlar, leiomyomlar, fibromlar ve lipomları sayabiliriz(2).

EPİDEMİYOLOJİ

Ulusal Kanser Enstitüsü'nün (NCI) 1987'de yayınlanan verilerinde en yaygın malign ince bağırsak tümörleri %45'le adenokarsinom iken ardından NET (%29), lenfoma (%16) ve sarkomlar (%10) onu takip etmekteydi (3). Zaman içerisinde bu oranlar değişmiş ve nöroendokrin tümörler ön plana çıkmıştır. Son 30 yılda ince bağırsak karsinoid tümörlerin insidansında gerçekleşen %400'lük artış ince bağırsak tümörlerinin genel insidansına da yansımıştır (4). 2000 yılında, NET'ler, Ulusal Kanser Veritabanına (NCDB) bildirilen en yaygın ince bağırsak tümörü olarak adenokarsinomları geride bırakmıştır (5). 1985-2005 yılları arasında, karsinoid tümörlerin tüm ince bağırsak kanserleri arasındaki oranı yüzde 28'den yüzde 44'e gelmiş, adenokarsinomların oranı yüzde 42'den yüzde 33'e düşmüşken sarkom ve lenfomalı hastaların oranı sabit kalmıştır (5).

İnce bağırsak tümörlerinden adenokarsinomlar duodenumda daha sık görülürken nöroendokrin tümörler ileumda daha sıktır. Bununla birlikte duodenumda da NET insidansı artmaktadır (1). Sarkom ve lenfomalar ise ince bağırsakta belli bir kısma lokalize değildir tamamında benzer şekilde görülürler (6).

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KAYNAKLAR

1. Hatzaras I, Palesty JA, Abir F, Sullivan P, Kozol RA, Dudrick SJ, et al. Small-bowel tumors: epidemiologic and clinical characteristics of 1260 cases from the connecticut tumor registry. *Archives of surgery*. 2007;142(3):229-35.
2. Overman MJ, Kunitake H: *Epidemiology, clinical features, and types of small bowel neoplasms*. www.uptodate.com. son erişim 20.09.2022
3. Weiss NS, Yang CP. Incidence of histologic types of cancer of the small intestine. *J Natl Cancer Inst*. 1987;78(4):653-6.
4. Maggard MA, O'Connell JB, Ko CY. Updated population-based review of carcinoid tumors. *Ann Surg*. 2004;240(1):117-22.
5. Bilimoria KY, Bentrem DJ, Wayne JD, Ko CY, Bennett CL, Talamonti MS. Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years. *Ann Surg*. 2009;249(1):63-71.
6. Gabos S, Berkel J, Band P, Robson D, Whittaker H. Small bowel cancer in western Canada. *Int J Epidemiol*. 1993;22(2):198-206.
7. Howlander N, Noone A, Krapcho M, Miller D, Bishop K, Altekruse S, et al. SEER *Cancer Statistics Review, 1975–2013*. 2016, from the National Cancer Institute, Bethesda, MD. MD http://seer.cancer.gov/csr/1975_2013/November. 2015.
8. Bilimoria KY, Bentrem DJ, Wayne JD, Ko CY, Bennett CL, Talamonti MS. Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years. *Annals of surgery*. 2009;249(1):63-71.
9. Lepage C, Bouvier A-M, Manfredi S, Dancourt V, Faivre J. Incidence and management of primary malignant small bowel cancers: a well-defined French population study. *Official journal of the American College of Gastroenterology* | ACG. 2006;101(12):2826-32.
10. Kummar S, Ciesielski TE, Fogarasi MC. Management of small bowel adenocarcinoma. *Onco-logy (Williston Park, NY)*. 2002;16(10):1364-9; discussion 70, 72.
11. Rodriguez-Bigas MA, Vasen HF, Lynch HT, Watson P, Myrholm T, Järvinen HJ, et al. Characteristics of small bowel carcinoma in hereditary nonpolyposis colorectal carcinoma. International Collaborative Group on HNPCC. *Cancer*. 1998;83(2):240-4.
12. Aparicio T, Zaanani A, Svrcek M, Laurent-Puig P, Carrere N, Manfredi S, et al. Small bowel adenocarcinoma: Epidemiology, risk factors, diagnosis and treatment. *Digestive and Liver Disease*. 2014;46(2):97-104.
13. Ross RK, Hartnett NM, Bernstein L, Henderson BE. Epidemiology of adenocarcinomas of the small intestine: is bile a small bowel carcinogen? *Br J Cancer*. 1991;63(1):143-5.
14. Kaerlev L, Teglbjærg PS, Sabroe S, Kolstad HA, Ahrens W, Eriksson M, et al. Is there an association between alcohol intake or smoking and small bowel adenocarcinoma? Results from a European multi-center case-control study. *Cancer Causes & Control*. 2000;11(9):791-7.
15. Chow W-H, Linet MS, McLaughlin JK, Hsing AW, Co Chien HT, Blot WJ. Risk factors for small intestine cancer. *Cancer Causes & Control*. 1993;4(2):163-9.
16. Schrock AB, Devoe CE, McWilliams R, Sun J, Aparicio T, Stephens PJ, et al. Genomic Profiling of Small-Bowel Adenocarcinoma. *JAMA Oncol*. 2017;3(11):1546-53.
17. Wheeler J, Warren B, Mortensen NM, Kim H, Biddolph S, Elia G, et al. An insight into the genetic pathway of adenocarcinoma of the small intestine. *Gut*. 2002;50(2):218-23.
18. Breuhahn K, Singh S, Schirmacher P, Bläker H. Large-scale N-terminal deletions but not point mutations stabilize β -catenin in small bowel carcinomas, suggesting divergent molecular pathways of small and large intestinal carcinogenesis. *The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland*. 2008;215(3):300-7.
19. Jagelman D, DeCosse J, Bussey H, GROUP TLCP. Upper gastrointestinal cancer in familial adenomatous polyposis. *The Lancet*. 1988;331(8595):1149-51.
20. Abrahams NA, Halverson A, Fazio VW, Rybicki LA, Goldblum JR. Adenocarcinoma of the small bowel: a study of 37 cases with emphasis on histologic prognostic factors. *Dis Colon Rec-*

- tum. 2002;45(11):1496-502.
21. Palascak-Juif V, Bouvier AM, Cosnes J, Flourié B, Bouché O, Cadiot G, et al. Small bowel adenocarcinoma in patients with Crohn's disease compared with small bowel adenocarcinoma de novo. *Inflammatory bowel diseases*. 2005;11(9):828-32.
 22. Halfdanarson TR, McWilliams RR, Donohue JH, Quevedo JF. A single-institution experience with 491 cases of small bowel adenocarcinoma. *Am J Surg*. 2010;199(6):797-803.
 23. Howe JR, Karnell LH, Menck HR, Scott-Conner C. The American College of Surgeons Commission on Cancer and the American Cancer Society. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985-1995. *Cancer*. 1999;86(12):2693-706.
 24. Boudiaf M, Jaff A, Soyer P, Bouhnik Y, Hamzi L, Rymer R. Small-bowel diseases: prospective evaluation of multi-detector row helical CT enteroclysis in 107 consecutive patients. *Radiology*. 2004;233(2):338-44.
 25. Tran TB, Qadan M, Dua MM, Norton JA, Poultides GA, Visser BC. Prognostic relevance of lymph node ratio and total lymph node count for small bowel adenocarcinoma. *Surgery*. 2015;158(2):486-93.
 26. Kaklamanos IG, Bathe OF, Franceschi D, Camarda C, Levi J, Livingstone AS. Extent of resection in the management of duodenal adenocarcinoma. *The American journal of surgery*. 2000;179(1):37-41.
 27. Tanrıverdi Ö. İnce Bağırsak Tümörleri. Türkiye Klinikleri. 2020.
 28. Ye X, Zhang G, Chen H, Li Y. Meta-analysis of postoperative adjuvant therapy for small bowel adenocarcinoma. *PLoS One*. 2018;13(8):e0200204.
 29. Czaykowski P, Hui D. Chemotherapy in small bowel adenocarcinoma: 10-year experience of the British Columbia Cancer Agency. *Clinical Oncology*. 2007;19(2):143-9.
 30. Fishman PN, Pond GR, Moore MJ, Oza A, Burkes RL, Siu LL, et al. Natural history and chemotherapy effectiveness for advanced adenocarcinoma of the small bowel: a retrospective review of 113 cases. *American journal of clinical oncology*. 2006;29(3):225-31.
 31. Zhang L, Wang LY, Deng YM, Wang FH, Feng F, Chen YC, et al. Efficacy of the FOLFOX/CAPOX regimen for advanced small bowel adenocarcinoma: a three-center study from China. *J buon*. 2011;16(4):689-96.
 32. Horimatsu T, Nakayama N, Moriwaki T, Hirashima Y, Fujita M, Asayama M, et al. A phase II study of 5-fluorouracil/L-leucovorin/oxaliplatin (mFOLFOX6) in Japanese patients with metastatic or unresectable small bowel adenocarcinoma. *International Journal of Clinical Oncology*. 2017;22(5):905-12.
 33. Gulhati P, Raghav K, Shroff RT, Varadhachary GR, Kopetz S, Javle M, et al. Bevacizumab combined with capecitabine and oxaliplatin in patients with advanced adenocarcinoma of the small bowel or ampulla of Vater: A single-center, open-label, phase 2 study. *Cancer*. 2017;123(6):1011-7.
 34. Thota R, Gonzalez RS, Berlin J, Cardin DB, Shi C. Could the PD-1 Pathway Be a Potential Target for Treating Small Intestinal Adenocarcinoma? *Am J Clin Pathol*. 2017;148(3):208-14.
 35. Larouche V, Akirov A, Alshehri S, Ezzat S. Management of Small Bowel Neuroendocrine Tumors. *Cancers*. 2019;11(9):1395.
 36. Barsouk A, Rawla P, Barsouk A, Thandra KC. Epidemiology of Cancers of the Small Intestine: Trends, Risk Factors, and Prevention. *Med Sci (Basel)*. 2019;7(3).
 37. Scott AT, Howe JR. Management of Small Bowel Neuroendocrine Tumors. *Journal of Oncology Practice*. 2018;14(8):471-82.
 38. Williams ED, Sandler M. The classification of carcinoid tumors. *Lancet*. 1963;1(7275):238-9.
 39. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020;76(2):182-8.
 40. Auernhammer CJ, Spitzweg C, Angele MK, Boeck S, Grossman A, Nölting S, et al. Advanced neuroendocrine tumours of the small intestine and pancreas: clinical developments, controversies, and future strategies. *Lancet Diabetes Endocrinol*. 2018;6(5):404-15.
 41. Howe JR, Cardona K, Fraker DL, Kebebew E, Untch BR, Wang Y-Z, et al. The surgical mana-

- gement of small bowel neuroendocrine tumors: consensus guidelines of the North American Neuroendocrine Tumor Society (NANETS). *Pancreas*. 2017;46(6):715.
42. Hellman P, Lundström T, Öhrvall U, Eriksson B, Skogseid B, Öberg K, et al. Effect of surgery on the outcome of midgut carcinoid disease with lymph node and liver metastases. *World journal of surgery*. 2002;26(8):991-7.
 43. Modlin IM, Kidd M, Latich I, Zikusoka MN, Shapiro MD. Current status of gastrointestinal carcinoids. *Gastroenterology*. 2005;128(6):1717-51.
 44. Strosberg JR, Halfdanarson TR, Bellizzi AM, Chan JA, Dillon J, Heaney AP, et al. The North American Neuroendocrine Society (NANETS) consensus guidelines for surveillance and medical management of midgut neuroendocrine tumors. *Pancreas*. 2017;46(6):707.
 45. Chambers AJ, Pasiaka JL, Dixon E, Rorstad O. Role of imaging in the preoperative staging of small bowel neuroendocrine tumors. *J Am Coll Surg*. 2010;211(5):620-7.
 46. Sundin A, Arnold R, Baudin E, Cwikla JB, Eriksson B, Fanti S, et al. ENETS consensus guidelines for the standards of care in neuroendocrine tumors: radiological, nuclear medicine and hybrid imaging. *Neuroendocrinology*. 2017;105(3):212-44.
 47. Kasai Y, Mahuron K, Hirose K, Corvera CU, Kim GE, Hope TA, et al. Prognostic impact of a large mesenteric mass >2 cm in ileal neuroendocrine tumors. *J Surg Oncol*. 2019;120(8):1311-7.
 48. Mayo SC, De Jong MC, Pulitano C, Clary BM, Reddy SK, Gamblin TC, et al. Surgical management of hepatic neuroendocrine tumor metastasis: results from an international multi-institutional analysis. *Annals of surgical oncology*. 2010;17(12):3129-36.
 49. Sbaraglia M, Businello G, Bellan E, Fassan M, Dei Tos AP. Mesenchymal tumours of the gastrointestinal tract. *Pathologica*. 2021;113(3):230-51.
 50. Michael J Overman KSP. *Diagnosis and staging of small bowel neoplasms*. www.uptodate.com. son erişim 20.09.2022
 51. Jeffrey Morgan MPR, MD, MSc, FACSAnette Duensing, MDVicki L Keedy, MD, MSCI. *Clinical presentation, diagnosis, and prognosis of gastrointestinal stromal tumors*. www.uptodate.com. son erişim 20.09.2022
 52. Vernuccio F, Taibbi A, Picone D, La Grutta L, Midiri M, Lagalla R, et al. Imaging of gastrointestinal stromal tumors: from diagnosis to evaluation of therapeutic response. *Anticancer research*. 2016;36(6):2639-48.
 53. Chacón M, Roca E, Huertas E, Loria FS, Domenechini E. CASE 3. Pathologic complete remission of metastatic gastrointestinal stromal tumor after imatinib mesylate. *J Clin Oncol*. 2005;23(7):1580-2.
 54. Chen Y-H, Liu K-H, Yeh C-N, Hsu J-T, Liu Y-Y, Tsai C-Y, et al. Laparoscopic resection of gastrointestinal stromal tumors: safe, efficient, and comparable oncologic outcomes. *Journal of Laparoendoscopic & Advanced Surgical Techniques*. 2012;22(8):758-63.
 55. Demetri GD, Benjamin RS, Blanke CD, Blay JY, Casali P, Choi H, et al. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)--update of the NCCN clinical practice guidelines. *J Natl Compr Canc Netw*. 2007;5 Suppl 2:S1-29; quiz S30.
 56. Eisenberg BL. The SSG XVIII/AIO trial: results change the current adjuvant treatment recommendations for gastrointestinal stromal tumors. *American journal of clinical oncology*. 2013;36(1):89-90.
 57. Parab TM, DeRogatis MJ, Boaz AM, Grasso SA, Issack PS, Duarte DA, et al. Gastrointestinal stromal tumors: a comprehensive review. *J Gastrointest Oncol*. 2019;10(1):144-54.
 58. Zhao Z, Zhang J, Zhang W, Tan S, Wei H-t, You J, et al. Efficacy evaluation of nilotinib treatment in different genomic subtypes of gastrointestinal stromal tumors: A meta-analysis and systematic review. *Current Problems in Cancer*. 2021;45(3):100705.
 59. Blay J-Y, Kang Y-K, Nishida T, von Mehren M. Gastrointestinal stromal tumours. *Nature Reviews Disease Primers*. 2021;7(1):1-22.
 60. Chi P, Qin LX, Nguyen B, Kelly CM, D'Angelo SP, Dickson MA, et al. Phase II Trial of Imatinib Plus Binimetinib in Patients With Treatment-Naive Advanced Gastrointestinal Stromal Tumor. *J Clin Oncol*. 2022;40(9):997-1008.

61. Schöffski P, Mir O, Kasper B, Papai Z, Blay JY, Italiano A, et al. Activity and safety of the multi-target tyrosine kinase inhibitor cabozantinib in patients with metastatic gastrointestinal stromal tumour after treatment with imatinib and sunitinib: European Organisation for Research and Treatment of Cancer phase II trial 1317 'CaboGIST'. *Eur J Cancer*. 2020;134:62-74.
62. Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. *World J Gastroenterol*. 2011;17(6):697-707.
63. Rizvi MA, Evens AM, Tallman MS, Nelson BP, Rosen ST. T-cell non-Hodgkin lymphoma. *Blood*. 2006;107(4):1255-64.
64. Dawson I. Primary malignant lymphoid tumours of the intestinal tract. *Br J surg*. 1961;49:80-9.
65. Schottenfeld D, Beebe-Dimmer JL, Vigneau FD. The epidemiology and pathogenesis of neoplasia in the small intestine. *Annals of epidemiology*. 2009;19(1):58-69.
66. Jaffe ES, Harris NL, Stein H, Isaacson PG. Classification of lymphoid neoplasms: the microscope as a tool for disease discovery. *Blood, The Journal of the American Society of Hematology*. 2008;112(12):4384-99.
67. Li B, Shi Y-k, He X-h, Zou S-m, Zhou S-y, Dong M, et al. Primary non-Hodgkin lymphomas in the small and large intestine: clinicopathological characteristics and management of 40 patients. *International journal of hematology*. 2008;87(4):375-81.
68. Pennazio M. Small-intestinal pathology on capsule endoscopy: spectrum of vascular lesions. *Endoscopy*. 2005;37(09):864-9.
69. Juweid ME, Stroobants S, Hoekstra OS, Mottaghy FM, Dietlein M, Guermazi A, et al. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. *J Clin Oncol*. 2007;25(5):571-8.
70. Kadakia SC, Parker A, Canales L. Metastatic tumors to the upper gastrointestinal tract: endoscopic experience. *Am J Gastroenterol*. 1992;87(10):1418-23.
71. Lens M, Bataille V, Krivokapic Z. Melanoma of the small intestine. *Lancet Oncol*. 2009;10(5):516-21.
72. Spigelman AD, Williams CB, Talbot IC, Domizio P, Phillips RK. Upper gastrointestinal cancer in patients with familial adenomatous polyposis. *Lancet*. 1989;2(8666):783-5.
73. Dudiak KM, Johnson CD, Stephens DH. Primary tumors of the small intestine: CT evaluation. *AJR Am J Roentgenol*. 1989;152(5):995-8.