

ÖZOFAGOGASTRİK BİLEŞKE TÜMÖRLERİ

30.
BÖLÜM

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ÖZET

Özofagus ve midenin birleşim noktasında yer alan adenokarsinomlara özofagogastrik bileşke (ÖGB) tümörleri denir. Özofagogastrik bileşkede oluşan skuamöz hücreli karsinomlar, özofagogastrik bileşkeyi geçseler bile distal özofagus karsinomları olarak kabul edilir.

En sık Barrett özofagusa bağlı olarak gelişen özofagogastrik bileşke kanserleri mide ve özofagus kanserlerine göre farklı patofizyolojik ve moleküler altyapı ve klinik seyre sahiptir. Özofagus ve distal mide tümörleri sıklığı azalırken, özofagogastrik bileşke tümörlerinin sıklığı artmaktadır.

ÖGB adenokarsinomlarının gelişiminden sorumlu intestinal yolak ve non-intestinal yolak olmak üzere 2 farklı patofizyoloji söz konusudur. Her iki yolakta ayrı moleküler ve genetik faktörler etkindir.

Özofagogastroduodenoskopisi (ÖGD), tercih edilen tanısal incelemedir. Malignite teşhisi konulduktan sonra, hastlığın durumunu tanımlamak için Bilgisayarlı tomografi, PET-CT taraması ve endoskopik ultrason yapılması gereklidir.

ÖGB kanserlerinde çoğu hasta ileri evre olana kadar asemptomatik kalır. Bundan dolayı kür şansı olan tedavi modalitesi cerrahi olsada preoperatif tedavi önemli yere sahiptir.

ÖGB kanserlerine cerrahi yaklaşımda fikir birliği yoktur. Cerrahi rezeksiyon makroskopik ve mikroskopik (R0) negatif sınır elde etmek olduğundan, özofagus ve mide tutulumunun derecesi ameliyat öncesi net değerlendirilmelidir.

Postop dönemde hasta aşamalarında kontrollü gidilmeli, oluşabilecek komplikasyonların gürültülü seyredebileceği akıldan çıkarılmamalıdır.

GİRİŞ

Özofagogastrik bileşke (ÖGB) kanserleri, farklı patofizyolojik ve moleküler altyapıları ve klinik seyirleri nedeniyle mide ve özofagus kanserlerinden ayrı incelenirler.

Özofagus ve distal mide tümörleri sıklığı azalırken, özofagogastrik bileşke kanserleri son 40

yılda yaklaşık % 10 artmıştır (1,2). Bu durum artan obezite, gastroözofagiyal reflü hastlığı ve azalan Helikobakter pilori infeksiyon oranı ile ilişkilendirilmektedir (3).

Bu bölümde özofagogastrik bileşke kanserlerine klinik bir bakışla, patofizyoloji, görülme sıklığı, risk faktörleri, tanı ve sınıflama, tedavi se-

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miktarda drenaj, şilotoraksın ilk belirtisi olabilir. Triglycerid seviyesinin 500 mg / dL'den yüksek olması tanışaldır. Tedavide diyet kesilerek parenteral beslenme başlanmalıdır. Önlemler işe yaramazsa, girişimsel radyoloji eşliğinde lenfositografi kullanarak perkütan torasik kanal embolizasyonu gerçekleştirilebilir yada torasik kanalı bağlamak için ameliyat gereklili olabilir (81).

Mortalite oranları % 1 ila% 10 arasında değişmektedir (83).

KAYNAKLAR

1. Buas M, Vaughan T. Epidemiology and risk factors for gastroesophageal junction tumors: understanding the rising incidence of this disease. *Semin Radiat Oncol* 2013;23:3–9.
2. Ashraf N, Hoffe S, Kim R. Locally Advanced Gastroesophageal Junction Tumor: A Treatment Dilemma. *TheOncologist* 2015;20:134-142
3. Kubo A, Corley DA. Body mass index and adenocarcinomas of the esophagus or gastric cardia: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2006;15:872–878.
4. Kahrilas PJ., Pandolfino J.E. Esophageal neuromuscular function and motility disorders. In : Feldman M., Friedman L.S., Brandt L.J. (eds). *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. Volume 1. 9th edition. Philadelphia : Saunders, Elsevier, 2010 : 677-704.
5. Chandrasoma P, Makarewicz K, Wickramasinghe K, Ma Y, Demeester T. A proposal for a new validated histological definition of the gastroesophageal junction. *Hum. Pathol.*, 2006, 37 : 40-7.
6. Spechler SJ., Dixon M.F, Genta R., Hainaut P., Lambert R., Siewert R. Tumours Of The Esophagogastric Junction. In : Hamilton S.R, Aaltonen L.A. (eds). *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System*. Lyon : IARC Press, 2000 : 31-6.
7. Mickael Chevallay, Elfriede Bollschweiler, Servarayan M. Chandramohan, Thomas Schmidt, Oliver Koch, Giovanni Demanzoni, Stefan Mönig, and William Allum : Cancer of the gastroesophageal junction: a diagnosis, classification, and management review : ANNALS OF THE NEW YORK ACADEMY OF SCIENCES (2018) 1-7
8. Siegel R. Miller K.D, Jemal A. Cancer statistics, 2015. *CA. Cancer J. Clin.*, 2015, 65 : 5-29.
9. Demeester S.R. Epidemiology and biology of esophageal cancer. *Gastrointest. Cancer Res.* 2009, 3 : S2-5.
10. Bollschweiler, E., E. Wolfgarten, C. Gutschow, et al. 2001. Demographic variations in the rising incidence of esophageal adenocarcinoma in white males. *Cancer*92: 549– 555.
11. Arnold,M.,M.Laversanne,L.M.Brown,etal.2017.Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. *Am. J. Gastroenterol.* 112: 1247–1255.
12. Souza R. From reflux esophagitis to esophageal adenocarcinoma. *Dig Dis* 2016; 34:483–90. 13. Chak A, Faulx A, Eng C, et al. Gastroesophageal reflux symptoms in patients with adenocarcinoma of the esophagus or cardia. *Cancer* 2006;107:2160–6.
14. Weston A, Krmpotich P, Makdisi W, et al. Short segment Barrett's esophagus: clinical and histological features, associated endoscopic findings, and association with gastric intestinal metaplasia. *Am J Gastroenterol* 1996;91:981–6.
15. Abnet C, Freedman N, Hollenbeck A. A prospective study of BMI and risk of oesophageal and gastric adenocarcinoma. *Eur J Cancer* 2008;44:465–7.
16. Jiang G, Li B, Liao X, et al. Poultry and fish intake and risk of esophageal cancer: a meta-analysis of observational studies. *Asia Pac J Clin Oncol* 2016;12:82–91.
17. Kabat G, Ng S, Wynder E. Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and gastric cardia. *Cancer Causes Control* 1993;4: 123–32.
18. Liakakos T, Katsios C., Roukos D.H. Gastroesophageal junction carcinoma multimodal treatment : standards, debate and new therapeutic options. *Expert Rev. Gastroenterol. Hepatol.*, 2011, 5 : 1-4.
19. Buas M.F, Vaughan T.L. Epidemiology and risk factors for gastroesophageal junction tumors : understanding the rising incidence of this disease. *Semin. Radiat. Oncol.*, 2013, 23 : 3-9.
20. Lutz M.P., Zalcberg J.R., Ducreux M., Ajani J.A., Allum W., Aust D. et al. First St Gallen EORTC Gastrointestinal Cancer Conference
21. Mccoll K.E., Going J.J. Aetiology and classification of adenocarcinoma of the gastro-oesophageal junction/ cardia. *Gut*, 2010, 59 : 282-4.
22. Liu W, Hahn H, Odze R.D., Goyal R.K. Metaplastic esophageal columnar epithelium without goblet cells shows DNA content abnormalities similar to goblet cell-containing epithelium. *Am. J. Gastroenterol.*, 2009, 104 : 816-24.
23. Demicco E.G., Farris A.B. 3rd, Baba Y, Agbor-Etang B, Bergethon K., Mandal R. et al. The dichotomy in carcinogenesis of the distal esophagus and esophago-gastric junction : intestinal-type vs cardiac-type mucosa-associated adenocarcinoma. *Mod. Pathol.*, 2011, 24 : 1177-90.
24. Duhaylongsod F.G., Wolfe W.G. Barrett's esophagus and adenocarcinoma of the esophagus and gastroesophageal junction. *J Thorac. Cardiovasc. Surg.*, 1991, 102 : 36-41, discussion 41-2.
25. Menke-Pluymers M.B., Schoutte N.W., Mulder A.H., Hop W.C., Van Blankenstein M., Tilanus Hw. Outcome of surgical treatment of adenocarcinoma in Barrett's oesophagus. *Gut*, 1992, 33 : 1454-8.
26. Hansen S., Vollset S.E., Derakhshan M.H., Fyfe V., Melby K.K., Aase S. et al. Two distinct aetiologies of cardia cancer ; evidence from premorbid serological markers of gastric atrophy and Helicobacter pylori status. *Gut*, 2007, 56 : 918-25.
27. Derakhshan M.H., Malekzadeh R., Watabe H., Yazdabod A., Fyfe V., Kazemi A. et al. Combination of gastric atrophy, reflux symptoms and histological subty-

- pe indicates two distinct aetiologies of gastric cardia cancer. *Gut*, 2008, 57 : 298-305.
28. K. A. Ekmekzoglou, P. Apostolopoulos, G. Samelis, G. Alexandrakis : Gastroesophageal junction and gastroesophageal junction carcinoma : a short update ; *Acta Gastro-Enterologica Belgica*, Vol. LXXIX, October-December 2016
 29. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of gastric adenocarcinoma. *Nature*, 2014, 513 : 202-9
 30. Dulak A.M., Stojanov P., Peng S., Lawrence M.S., Fox C., Stewart C., et al. Exome and whole-genome sequencing of esophageal adenocarcinoma identifies recurrent driver events and mutational complexity. *Nat. Genet.*, 2013, 45 : 478-86
 31. Villanacci V., Rossi E., Zambelli C., Galletti A., Cestari R., Missale G. Et Al. COX-2, CDX2, and CDC2 immunohistochemical assessment for dysplasia-carcinoma progression in Barrett's esophagus. *Dig. Liver Dis.*, 2007, 39 : 305-11.
 32. Stachler M.D., Taylor-Weiner A., Peng S., McKenna A., Agoston A.T., Odze R.D. et al. Paired exome analysis of Barrett's esophagus and adenocarcinoma. *Nat. Genet.*, 2015, 47 : 1047-55.
 33. Atherfold P.A., Jankowski J.A. Molecular biology of Barrett's cancer. *Best Pract. Res. Clin. Gastroenterol.*, 2006, 20 : 813-27
 34. Conio M., Lapertosa G., Blanchi S., Filiberti R. Barrett's esophagus : an update. *Crit. Rev. Oncol. Hematol.*, 2003, 46 : 187-206.
 35. Schmidt P.H., Lee J.R., Joshi V., Playford R.J., Poulsom R., Wright N.A. et al. Identification of a metaplastic cell lineage associated with human gastric adenocarcinoma. *Lab. Invest.*, 1999, 79 : 639-46.
 36. SAROSI G., BROWN G., JAISWAL K. Reflux-damaged esophageal epithelium is replaced by cells derived from the bone marrow in a rat model of Barrett's esophagus. *Gastroenterology*, 2004, 126 : A35.
 37. Goldman A., Shahidullah M., Goldman D., Khailova L., Watts G., Delamere N. Et Al. A novel mechanism of acid and bile acid-induced DNA damage involving Na+/H+ exchanger : implication for Barrett's oesophagus. *Gut*, 2010, 59 : 1606-16.
 38. Mcadam E., Haboubi H.N., Forrester G., Eltahir Z., Spencer-Harty S., Davies C. et al. Inducible nitric oxide synthase (iNOS) and nitric oxide (NO) are important mediators of reflux-induced cell signalling in esophageal cells. *Carcinogenesis*, 2012, 33 : 2035-43.
 39. Markar S., Karthikesalingam A., Low DE. Outcomes assessment of the surgical management of esophageal cancer in younger and older patients. *Ann Thorac Surg* 2012;94:1652-8.
 40. Wu, A.J. & K.A. Goodman. 2013. Positron emission tomography imaging for gastroesophageal junction tumors. *Semin. Radiat. Oncol.* 23: 10-15.
 41. Grotenhuis, B., B.P. Wijnhoven, J.W. Poley, et al. 2013. Preoperative assessment of tumor location and station-specific lymph node status in patients with adenocarcinoma of the gastroesophageal junction. *World J. Surg.* 37: 147-155.
 42. Pedrazzani,G.,M.Bernini,S.Giacopuzzi,etal.2005.Evaluation of Siewert classification in gastro-esophageal junction adenocarcinoma: what is the role of endoscopic ultrasonography? *J. Surg. Oncol.* 91: 226.
 43. Schröder W, Mönig SP, Baldus SE, et al: Frequency of nodal metastases to the upper mediastinum in Barrett's cancer. *Ann Surg Oncol* 2002;9:807-811.
 44. Kakeji Y, Yamamoto M, Ito S, et al. Lymph nodemetaстasis from cancer of the esophagogastric junction, and determination of the appropriate nodal dissection. *Surg Today* 2012;42:351-358
 45. Nunobe S, Ohyama S, Sonoo H, et al: Benefit of mediastinal and paraaortic lymphnode dissection for advanced gastric cancer with esophageal invasion. *J Surg Oncol* 2008;97:392-395.
 46. Amenabar A, Hoppo T, Jobe BA. Surgical Management of Gastroesophageal Junction Tumors. *Semin Radiat Oncol* 2013;23:16-23
 47. Gökhan Kocaman, Serkan Enön: Özofagogastrik Bileşke Kanserleri ve Cerrahi Tedavisi ; Ankara Üniversitesi Tip Fakültesi Mecmuası 2016, 69 (3)
 48. Pedrazzani C, de Manzoni G, Marrelli D, et al. Lymph node involvement in advanced gastroesophageal junction adenocarcinoma. *J Thorac Cardiovasc Surg* 2007;134:378-385.
 49. Zhang YF, Shi J, Yu HP, et al. Factors predicting survival in patients with proximal gastric carcinoma involving the esophagus. *World J Gastroenterol* 2012;18:3602-3609
 50. Lerut T, Nafteux P, Moons J, et al. Three-field lymphadenectomy for carcinoma of the esophagus and gastroesophageal junction in 174 R0 resections: Impact on staging, disease-free survival, and outcome: A plea for adaptation of TNM classification in upper-half esophageal carcinoma. *Ann Surg* 2004;240:962-972.
 51. Cunningham, D., W.H. Allum, S.P. Stenning, et al. for the MAGIC Trial Participants. 2006. Perioperative chemotherapy versus surgery alone for resectable gasto-oesophageal cancer. *N. Engl. J. Med.* 355: 11–20.
 52. Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *Br J Surg* 1998;85:1457-1459
 53. Ajani JA, D'Amico TA, Almhanna K, et al. Esophageal and Esophagogastric Junction Cancers, Version 1.2015. JNCCN-Journal of the National Comprehensive Cancer Network, Volume 13 Number 2, February 2015.
 54. Davies AR, Gossage JA, Zylstra J, et al. Tumor Stage After Neoadjuvant Chemotherapy Determines Survival After Surgery for Adenocarcinoma of the Esophagus and Esophagogastric Junction. *J Clin Oncol* 2014;32:2983-2990
 55. Van Hagen P, Hulshof J, Van Lanschot E, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med* 2012;366:2074-84.
 56. Niu J, Weber J, Gelbspan D. Change of HER2 status in metastatic esophageal adenocarcinoma: heterogeneity of the disease? Case report and review of literature. *J Gastrointest Oncol* 2012;3:358-6
 57. Safran H, DiPetrillo T, Akerman P, et al. Phase I/II study of trastuzumab, paclitaxel, cisplatin and radiation for locally advanced, HER2 overexpressing, esophageal adenocarcinoma. *Int J Rad Oncol* 2007;67:405-9.

58. Mariette, C., M.L. De Botton & G. Piessen. 2012. Surgery in esophageal and gastric cancer patients: what is the role for nutrition support in your daily practice? *Ann. Surg. Oncol.* 19: 2128–2134
59. Imai K, Kakushima N, Tanaka M, et al. Validation of the application of the Japanese curative criteria for superficial adenocarcinoma at the esophagogastric junction treated by endoscopic submucosal dissection: a long-term analysis. *SurgEndosc* 2013;27:2436-2445.
60. Pech O, Behrens A, May A, et al: Longterm results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. *Gut* 2008;57:1200-1206
61. Casson A, Darnton S, Subramanian S. What is the optimal distal resection margin for esophageal carcinoma? *Ann Thorac Surg* 2000;69:205–9
62. Hölscher, A.H., M. Stahl, H. Messmann, et al. 2016. Die neue S3-Leitlinie zum "Oosphaguskarzinom. *Chirurg* 87: 865.
63. Siewert JR, Stein HJ, Feith M. Adenocarcinoma of the esophago-gastricjunction. *Scand J Surg* 2006;95:260-269.
64. Siewert JR, Feith M, Werner M, et al. Adenocarcinoma of the esophagogastric junction: Results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. *Ann Surg* 2000;232:353-361.
65. Gertler R, Stein HJ, Langer R, et al. Longterm outcome of 2920 patients with cancers of the esophagus and esophagogastric junction: Evaluation of the New Union Internationale Contre le Cancer/American Joint Cancer Committee staging system. *Ann Surg* 2011;253:689-698.
66. Von Rahden BH, Stein HJ, Siewert JR: Surgical management of esophagogastric junction tumors. *World J Gastroenterol* 2006;12:6608-6613.
67. Haverkamp, L., J.P. Ruurda, M.S. van Leeuwen, et al. 2014. Systematic review of the surgical strategies of adenocarcinomas of the gastroesophageal junction. *Surg. Oncol.* 23: 222–228.
68. Blank, S., T. Schmidt, P. Heger, et al. 2018. Surgical strategies in true adenocarcinoma of the esophagogastricjunction (AEG II): thoracoabdominal or abdominal approach? *Gastric Cancer* 21: 303–314.
69. Siewert JR, Feith M, Stein H. Surgical approach to gastroesophageal junction cancers. In Sugerbaker D, Bueno R, Krasna MJ, ed. *Adult Chest Surgery*, 1st ed. New York City: McGraw-Hill 2009;109-116
70. Hulscher JBF, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med* 2002;347:1662-1669.
71. Feith M, Stein HJ, Siewert JR. Adenocarcinoma of the esophagogastric junction: Surgical therapy based on 1602 consecutive resected patients. *Surg Oncol Clin N Am* 2006;15:751-764.
72. Omloo JM, Lagarde SM, Hulscher JB, et al: Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: Five-year survival of a randomized clinical trial. *Ann Surg* 2007;246:992-1000.
73. Stein HJ, Feith M, Siewert JR: Individualized surgical strategies for cancer of the esophagogastric junction. *Ann Chir Gynaecol* 2000;89:191-198
74. Fuchs H, Hölscher AH, Leers J, et al. Long-term quality of life after surgery for adenocarcinoma of the esophagogastric junction: extended gastrectomy or transthoracic esophagectomy? *Gastric Cancer* 2016;19:312–317.
75. Sasako M, Sano T, Yamamoto S, et al. Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomized controlled trial. *Lancet Oncol* 2006;7:644-651.
76. Kocaman G, Enön S. Ivor-Lewis Özofajektomi. Erişim tarihi: 26.05.2016, <http://www.toraks.org.tr/Download.aspx?book=1474>
77. Mine S, Sano T, Hiki N, et al. Proximal margin length with transhiatal gastrectomy for Siewert type II and III adenocarcinomas of the oesophagogastric junction. *British Journal of Surgery* 2013;100:1050-1054.
78. Xiao JW, Liu ZL, Ye PC, et al. Clinical comparison of antrum- preserving double tract reconstruction vs roux-en-Y reconstruction after gastrectomy for Siewert types II and III adenocarcinoma of the esophagogastric junction. *World J Gastroenterol* 2015;21:9999-10007.
79. Haverkamp, L., M.F.J. Seesing, J.P. Ruurda, et al. 2017. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. *Dis. Esophagus* 30: 1–7.
80. Briez, N., G. Piessen, F. Bonnetaïn, et al. 2011. Open versus laparoscopically-assisted oesophagectomy for cancer: a multicentre randomised controlled phase III trial—the MIRO trial. *BMC Cancer* 11: 310.
81. O. Van Daele E, Van de Putte D, Ceelen W. Risk factors and consequences of anastomotic leakage after Ivor Lewis oesophagectomy. *Interact Cardiovasc Thorac Surg* 2016;22:32-7.
82. Ikenna C. Okereke : Management of Gastroesophageal Junction Tumors : *Surg Clin N Am* 97 (2017) 265-275
83. E, Ward R, Pearson S. Oesophagectomy rates and post-resection outcomes in patients with cancer of the oesophagus and gastro-oesophageal junction: a population-based study using linked health administrative linked data. *BMC Health Serv Res* 2012;12:384.