

## SAFRA KESESİ TÜMÖRLERİ

*Yusuf TANRIKULU<sup>1</sup>*

### SAFRA KESESİNİN BENIGN TÜMÖRLERİ

Safra kesesi, tüm dünyada patoloji laboratuvarlarında karşılaşılan en yaygın örneklerden biridir. Bunların büyük çoğunluğu sadece kolelitiazis ve kronik kolesistiti gösterir, ancak safra kesesinde çeşitli iyi huylu tümörler ve tümör benzeri lezyonlar ortaya çıkabilir ve büyük ölçüde tesadüfen keşfedilir. Epitelyal tümörler arasında adenomlar ve kist adenomlar bulunur. Tümör benzeri lezyonlar, çeşitli metaplazi, hiperplazi, heterotopi ve kronik kolesistit ile ilişkili lezyonları içerir. Bu çeşitli iyi huylu ve tümör benzeri lezyonlar klinik, radyolojik ve hatta bazen mikroskopik olarak maligniteyi taklit edebilir. Hastaların büyük bir kısmı karın ağrısı ve kusma ile ortaya çıkan dispeptik şikayetlerle polikliniğe başvururken, yaklaşık %30'u asemptomatik olabilir. Tanıda ultrasonografi, bilgisayarlı tomografi ve endoskopik ultrasonografi kullanılabilir. Özellikle polipler olmak üzere tüm benign tümörler malignite riski açısından öncelikli değerlendirilmeli ve malignite açısından risk artışı teşkil eden lezyonlar için kolesistektomi yapılmalıdır.

### ANATOMİ

Safra kesesi, karaciğerin alt yüzeyinde IV. ve V. karaciğer segmentlerinin hemen altında yer alan armut biçimli kese şeklinde bir yapıdır. Altta peritoneal yüzeye ve karaciğerdeki safra kesesi yatağına yakından ilişkili üst hepatik yüzeye sahiptir. Safra kesesi yaklaşık 7-10 cm uzunluğunda ve yaklaşık 2,5-3,5 cm genişliğindedir. Normalde yaklaşık 30-50 mL sıvı içerir, ancak 300 mL'ye kadar sıvayı depolayabilir (1).

Fundus, korpus, infundibulum ve boyun olmak üzere 4 kısma ayrılır. Safra kesesini drenajını sistik kanalla ana safra kanalına boşaltır. Sistik kanal, Heister'in "valfleri" olarak adlandırılan spiral mukoza kıvrımlarına sahiptir. Bazen safra kesesi infundibulumunun veya boynunun daha düşük bir keseleşmesi görülebilir ve buna Hartmann kesesi denir. Calot üçgeni, sağdaki kistik kanal, soldaki ortak hepatik kanal ve yukarıda karaciğerin alt yüzeyi ile sınırlıdır; sistik arter ve sistik lenf nodu Calot üçgeninde bulunur (2).

Safra kesesini karaciğer parankiminden ayıran fibro-areolar dokunun yoğunlaşması olarak adlandırılan kistik plaka, karaciğer ve safra kesesi arasındaki visseral peritonun yansımasıdır. Kistik plaka, safra kesesi gövdesinde iyi oluşur, ancak safra kesesi fundusuna doğru incelir. Kolesistektomi sırasında safra kesesi ve karaciğer arasında

<sup>1</sup> Doç Dr. Yusuf TANRIKULU, KTO Karatay Üniversitesi Tıp Fakültesi, Genel Cerrahi AD. drtanrikulu@hotmail.com

## Sonuç

Safra kesesi benign tümörlerinde kanserleşme ihtimali oldukça az olduğundan kesin tanı netleştilirmeden rutin profilaktik kolesistektomi önerilmemektedir. Ancak belrgin malignite ihtimalinin arttığı safra kesesi polipleri, büyük safra taşları ve porselen kese gibi benign durumlarda kolesistektomi bir tedavi seçeneği olarak hala önemini korumaktadır.

Safra kesesi kanserleri, ortalama yaşam süresi oldukça az olan agresif tümörlerdir. Ancak son zamanlarda yapılan çalışmalar, optimal bir evrelem sonucunda seçilmiş vakalarda uygulanacak radikal cerrahilerin uzun süreli sağkalım sağlayabileceğini ortaya koymaktadır. Yine benign tümörlerde olduğu gibi safra kesesi taşı ile safra kesesi taşları arasındaki ilişkiye rağmen asemptomatik vakalarda rutin profilaktik kolesistektomi önerilmemektedir.

Aynı seansta yapılan radikal genişletilmiş kolesistektomiler, sekonder kolesistektomilerden daha iyi sonuç verdiği için, safra kesesi kanseri düşünen ve bu amaçla kolesistektomi planlanan hastalarda preoperatif ve intraoperatif değerlendirme büyük bir titizlilikle yapılmalıdır.

Kolesistektomi sonrası ortaya konulan patoloji raporlarına göre, T1 tümörlerde cerrahi sınırlar temiz ise başka bir işleme gerek duyulmamaktadır. Ancak diğer tümörlerde kolesistektominin yanısıra karaciğer rezeksiyonları ve bölgesel lenf nodu diseksiyonu yapılması gerekmektedir. Rezeke edilemeyen olgularda ise adjuvan kemoterapinin yanısıra sarılık, bası bulguları ve intestinal obstruksyonlar için cerrahi girişimler yapılabilmektedir.

## KAYNAKLAR

- Shirai Y, Yoshida K, Tsukada K, et al. Identification of the regional lymphatic system of the gallbladder by vital staining. *Br J Surg.* 1992;79(7):659-62.
- Pilgrim CH, Usatoff V, Evans P. Consideration of anatomical structures relevant to the surgical strategy for managing gallbladder carcinoma. *Eur J Surg Oncol.* 2009;35(11):1131-6. Doi: 10.1016/j.ejso.2009.02.006. Epub 2009 Mar 18. Review.
- Cancer Facts and Figures 2019. American Cancer Society. Available at <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf>. 2019; Accessed: June 28, 2019.
- Salmenkivi K. Cholesterosis of the gall-bladder. A clinical study based on 269 cholecystectomies. *Acta Chir Scand Suppl* 1964;105:Suppl 324:1.
- Feldman M, Feldman M Jr. Cholesterosis of the gall-bladder; an autopsy study of 165 cases. *Gastroenterology* 1954; 27:641.
- Jørgensen T, Jensen KH. Polyps in the gallbladder. A prevalence study. *Scand J Gastroenterol* 1990; 25:281.
- Farinon AM, Pacella A, Cetta F, et al. "Adenomatous polyps of the gallbladder" adenomas of the gallbladder. *HPB Surg* 1991;3:251.
- Golse N, Lewin M, Rode A, et al. Gallbladder adenomyomatosis: Diagnosis and management. *J Visc Surg.* 2017;154(5):345-353.
- Van Patten K, Jain D. Benign tumors and tumor-like lesions of the gallbladder and extrahepatic biliary tract. *Diagnostic Histopathology* 2010;16(8):371-379.
- Albores-Saavedra J, Henson DE. Pyloric gland metaplasia with perineural invasion of the gallbladder: a lesion that can be confused with adenocarcinoma. *Cancer* 1999;86:2625e31.
- Mukhopadhyay S, Landas SK. Putative precursors of gallbladder dysplasia: a review of 400 routinely resected specimens. *Arch Pathol Lab Med* 2005;129:386e90.
- Fernandes JE, Franco MI, Suzuki RK, et al. Intestinal metaplasia in gallbladders: prevalence study. *Sao Paulo Med J* 2008; 126: 220e2.
- Albores-Saavedra J, Vardaman CJ, Vuitch F. Non-neoplastic polypoid lesions and adenomas of the gallbladder. *Pathol Annu* 1993;28(Pt1):145e77.
- Roa JC, Roa I, Correa P, et al. Microsatellite instability in preneoplastic and neoplastic lesions of the gallbladder. *J Gastroenterol* 2005; 40: 79e86.
- Albores-Saavedra J, Henson DE. Tumors of the gallbladder and extrahepatic bile ducts. Washington, D.C.: Armed Forces Institute of Pathology under the auspices of Universities Associated for Research and Education in Pathology, 1986. p. 208. (For sale by the Armed Forces Institute of Pathology).
- Maccarty WC. The Pathology of the Gall-bladder and some Associated Lesions: A Study of Specimens from 365 Cholecystectomies. *Ann Surg* 1910;51:651.
- Jutras JA, Levesque HP. Adenomyoma and adenomyomatosis of the gallbladder, radiologic and pathologic correlations. *Rad Clin N Amer* 1966;4:483.
- King ES, McCallum P. Cholecystitis glandularis Proliferans. *Br J Surg* 1931;19:310.
- Hide GDS, Bloxham CA. Malakoplakia of the gall-bladder: imaging and histological features. *Clin Radiol* 2001;56:326e37.
- Albores-Saavedra J, Gould E, Manivel-Rodriguez C, et al. Chronic cholecystitis with lymphoid hyperplasia. *Rev Invest Clin* 1989;41:159e64.
- Dilek ON, Karasu S, Dilek FH. Diagnosis and Treatment of Gallbladder Polyps: Current Perspectives. *Euroasian J Hepatogastroenterol.* 2019;9(1):40-48. doi: 10.5005/jp-journals-10018-1294. Review.
- Albores-Saavedra J, Henson DE. Tumors of the gallbladder, extrahepatic bile ducts, and ampulla of vater. Washington, DC: Armed Forces Institute of Pathology under the auspices of Universities Associated for Research and Education in Pathology, 2000. p. 365.
- Christensen AH, Ishak KG. Benign tumors and pseu-

- dotumors of the gallbladder. Report of 180 cases. Arch Pathol 1970;90:423.
24. Coffin CM, Patel A, Perkins S, et al. ALK1 and p80 expression and chromosomal rearrangements involving 2p23 in inflammatory myofibroblastic tumor. Mod Pathol 2001;14:569e76.
  25. Weedon D (1984). Benign mucosal polyps. In: Pathology of the gallbladder. p. 195. Mason, New York.
  26. Laitio M. Histogenesis of epithelial neoplasms of human gallbladder II. Classification of carcinoma on the basis of morphological features. Pathol Res Pract 1983;178:57.
  27. Yang HL, Sun YG, Wang Z. Polypoid lesions of the gallbladder: diagnosis and indications for surgery. Br J Surg 1992; 79:227.
  28. Jutras JA. Hyperplastic cholecystoses; Hickey lecture. Am J Roentgenol Radium Ther Nucl Med 1960;83:795.
  29. UpToDate. Gallbladder polyps and cholesterolosis, 4 May 2020, [https://www.uptodate.com/ contents/gallbladder-polyps-and-cholesterolosis?search=Gallbladder%20polyps%20and%20 cholesterolosis &source=search\\_result&selectedTitle=1~14&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/gallbladder-polyps-and-cholesterolosis?search=Gallbladder%20polyps%20and%20 cholesterolosis &source=search_result&selectedTitle=1~14&usage_type=default&display_rank=1).
  30. McGregor JC, Cordiner JW. Papilloma of the gallbladder. Br J Surg 1974; 61:356.
  31. Kane Cf, Brown Ch, Hoerr So. Papilloma of the gallbladder; report of eight cases. Am J Surg 1952;83:161.
  32. Takii Y, Shirai Y, Kanemura H, H et al. Obstructive jaundice caused by a cholesterol polyp of the gallbladder: report of a case. Surg Today 1994;24:1104.
  33. Parrilla Paricio P, García Olmo D, Pellicer Franco E, et al. Gallbladder cholesterolosis: an aetiological factor in acute pancreatitis of uncertain origin. Br J Surg 1990;77:735.
  34. McCain RS, Diamond A, Jones C, Coleman HG. Current practices and future prospects for the management of gallbladder polyps: A topical review. World J Gastroenterol. 2018;24(26):2844-2852. doi: 10.3748/wjg.v24.i26.2844. Review.
  35. Berk RN, van der Vegt JH, Lichtenstein JE. The hyperplastic cholecystoses: cholesterolosis and adenomyomatosis. Radiology 1983;146:593.
  36. Meacock LM, Sellars ME, Sidhu PS. Evaluation of gallbladder and biliary duct disease using microbubble contrast-enhanced ultrasound. Br J Radiol 2010;83:615.
  37. Tsuji S, Sofuni A, Moriyasu F, et al. Contrast-enhanced ultrasonography in the diagnosis of gallbladder disease. Hepatogastroenterology 2012;59:336.
  38. Li D, Dong BW, Wu YL, et al. Image-directed and color Doppler studies of gallbladder tumors. J Clin Ultrasound 1994;22:551.
  39. Hayakawa S, Goto H, Hirooka Y, et al. Colour Doppler-guided spectral analysis of gall-bladder wall flow. J Gastroenterol Hepatol 1998;13:181.
  40. Jang JY, Kim SW, Lee SE, et al. Differential diagnostic and staging accuracies of high resolution ultrasonography, endoscopic ultrasonography, and multidetector computed tomography for gallbladder polypoid lesions and gallbladder cancer. Ann Surg 2009;250:943.
  41. Andrén-Sandberg A. Diagnosis and management of gallbladder polyps. N Am J Med Sci 2012;4:203-211. Doi:10.4103/1947-2714.95897.
  42. Furukawa H, Kosuge T, Shimada K, et al. Small polypoid lesions of the gallbladder: differential diagnosis and surgical indications by helical computed tomography. Arch Surg 1998;133:735-739 Doi:10.1001/archsurg.133.7.735.
  43. Lou MW, Hu WD, Fan Y, et al. CT biliary cystoscopy of gallbladder polyps. World J Gastroenterol 2004;10:1204-1207. Doi:10.3748/wjg.v10.i8.1204.
  44. Sugiyama M, Xie XY, Atomi Y, et al. Differential diagnosis of small polypoid lesions of the gallbladder: the value of endoscopic ultrasonography. Ann Surg 1999;229:498.
  45. Sugiyama M, Atomi Y, Yamato T. Endoscopic ultrasonography for differential diagnosis of polypoid gall bladder lesions: analysis in surgical and follow up series. Gut 2000;46:250.
  46. Kimura K. Diagnosis for pedunculated polypoid lesions of the gallbladder by endoscopic ultrasonography. Nihon Shokakibyo Gakkai Zasshi 1997; 94:249.
  47. Matsumoto J. Endoscopic ultrasonography diagnosis of gallbladder lesions. Endoscopy 1998;30:A124.
  48. Azuma T, Yoshikawa T, Araida T, et al. Differential diagnosis of polypoid lesions of the gallbladder by endoscopic ultrasonography. Am J Surg 2001;181:65.
  49. Muguruma N, Okamura S, Ichikawa S, et al. Endoscopic sonography in the diagnosis of gallbladder wall lesions in patients with gallstones. J Clin Ultrasound 2001;29:395.
  50. Irie H, Kamochi N, Nojiri J, et al. High b-value diffusion-weighted MRI in differentiation between benign and malignant polypoid gallbladder lesions. Acta Radiol 2011;52:236-240. Doi:10.1258/ar.2010.100234.
  51. Rodríguez-Fernández A, Gómez-Río M, Medina-Benítez A, et al. Application of modern imaging methods in diagnosis of gallbladder cancer. J Surg Oncol 2006;93:650.
  52. Csendes A, Becerra M, Rojas J, et al. Number and size of stones in patients with asymptomatic and symptomatic gallstones and gallbladder carcinoma: A prospective study of 592 cases. J Gastrointest Surg 2000;4:481-5.
  53. Miyazaki M, Takada T, Miyakawa S, et al. Risk factors for biliary tract and ampullary carcinomas and prophylactic surgery for these factors. J Hepatobiliary Pancreat Surg 2008;15:15-24.
  54. Gurusamy KS, Abu-Amara M, Farouk M, et al. Cholecystectomy for gallbladder polyp. Cochrane Database Syst Rev 2009;21(1):CD007052.
  55. Sun Y, Yang Z, Lan X, et al. Neoplastic polyps in gallbladder: a retrospective study to determine risk factors and treatment strategy for gallbladder polyps. Hepatobiliary Surg Nutr 2019;8:219.
  56. Patiño JF, Quintero GA. Asymptomatic cholelithiasis revisited. World J Surg 1998;22:1119.
  57. Buckles DC, Lindor KD, Larusso NF, et al. In primary sclerosing cholangitis, gallbladder polyps are frequently malignant. Am J Gastroenterol 2002;97:1138-42.
  58. Kmiot WA, Perry EP, Donovan IA, et al. Cholesterolosis in patients with chronic acalculous biliary pain. Br J Surg 1994; 81:112.
  59. American Society for Gastrointestinal Endoscopy (ASGE) Standards of Practice Committee, Anderson MA, Appalaneni V, et al. The role of endoscopy in the evaluation and treatment of patients with biliary neoplasia. Gastrointest Endosc 2013;77:167.
  60. Kubota K, Bandai Y, Noie T, et al. How should polypoid

- lesions of the gallbladder be treated in the era of laparoscopic cholecystectomy? *Surgery* 1995;117:481.
61. Koga A, Watanabe K, Fukuyama T, et al. Diagnosis and operative indications for polypoid lesions of the gallbladder. *Arch Surg* 1988;123:26.
  62. Koga A, Yamauchi S, Nakayama F. Primary carcinoma of the gallbladder. *Am Surg* 1985;51:529.
  63. Yamamoto T. A study of cholesterol gallstone formation in cases of cholesterosis of the gallbladder (author's transl). *Nihon Shokakibyo Gakkai Zasshi* 1979;76:91.
  64. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. *Int J Cancer*. 2006;118(7):1591-602. Review.
  65. Lazcano-Ponce EC, Miquel JF, Muñoz N, et al. Epidemiology and molecular pathology of gallbladder cancer. *CA Cancer J Clin*. 2001;51(6):349-64. Review.
  66. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol*. 2014;6:99-109. doi: 10.2147/CLEP.S37357. eCollection 2014. Review.
  67. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin*. 2014;64(2):104-17. doi: 10.3322/caac.21220.
  68. Diehl AK. Epidemiology of gallbladder cancer: a synthesis of recent data. *J Natl Cancer Inst*. 1980;65(6):1209-14.
  69. Zatonský W, La Vecchia C, Levi F, et al. Descriptive epidemiology of gall-bladder cancer in Europe. *J Cancer Res Clin Oncol*. 1993;119(3):165-71.
  70. Serra I, Calvo A, Báez S, et al. Risk factors for gallbladder cancer. An international collaborative case-control study. *Cancer*. 1996;78(7):1515-7.
  71. Levy AD, Murakata LA, Rohrmann CA Jr. Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics*. 2001;21(2):295-314; questionnaire, 549-555.
  72. Myers R, Shaffer E, Beck P. Gallbladder polyps: Epidemiology, natural history and management. *Can J Gastroenterol* 2002;16:187-94.
  73. Funabiki T, Matsubara T, Miyakawa S, et al. Pancreaticobiliary maljunction and carcinogenesis to biliary and pancreatic malignancy. *Langenbecks Arch Surg* 2009;394:159-69.
  74. Lewis J, Talwalkar J, Rosen C, et al. Prevalence and risk factors for gallbladder neoplasia in patients with primary sclerosing cholangitis: Evidence for a metaplasia-dysplasia-carcinoma sequence. *Am J Surg Pathol* 2007;31:907-13.
  75. Shukla V, Singh H, Pandey M, et al. Carcinoma of the gallbladder—Is it a sequel of typhoid? *Dig Dis Sci* 2000;45:900-3.
  76. Fernandez E, La Vecchia C, D'Avanzo B, et al. Family history and the risk of liver, gallbladder, and pancreatic cancer. *Cancer Epidemiol Biomarkers Prev* 1994;3:209-12.
  77. Misra S, Chaturvedi A, Misra N, et al. Carcinoma of the gallbladder. *Lancet Oncol* 2003;4:167-76.
  78. Albores-Saavedra J, Nadji M, Henson DE. Intestinal-type adenocarcinoma of the gallbladder. A clinicopathologic study of seven cases. *Am J Surg Pathol*. 1986;10(1):19-25.
  79. Kozuka S, Tsubone N, Yasui A, Hachisuka K. Relation of adenoma to carcinoma in the gallbladder. *Cancer*. 1982;50(10):2226-34.
  80. Choi JH, Yun JW, Kim YS, et al. Pre-operative predicti- ve factors for gallbladder cholesterol polyps using conventional diagnostic imaging. *World J Gastroenterol*. 2008;14(44):6831-4.
  81. Zieliński MD, Atwell TD, Davis PW, et al. Comparison of surgically resected polypoid lesions of the gallbladder to their pre-operative ultrasound characteristics. *J Gastrointest Surg*. 2009;13(1):19-25. doi:10.1007/s11605-008-0725-2.
  82. Cantürk Z, Sentürk O, Cantürk NZ, et al. Prevalence and risk factors for gall bladder polyps. *East Afr Med J*. 2007;84(7):336-41.
  83. Ito H, Hann LE, D'Angelica M, et al. Polypoid lesions of the gallbladder: diagnosis and follow-up. *Journal of the American College of Surgeons*, 2009, 208(4): 570-575.
  84. Bazoua G, Hamza N, Lazim T. Do we need histology for a normal-looking gallbladder? *J Hepatobiliary Pancreat Surg*. 2007;14(6):564-8.
  85. Pitt SC, Jin LX, Hall BL, et al. Incidental gallbladder cancer at cholecystectomy: when should the surgeon be suspicious? *Ann Surg*. 2014;260(1):128-33. doi: 10.1097/SLA.0000000000000485.
  86. Daines WP, Rajagopalan V, Grossbard ML, et al. Gallbladder and biliary tract carcinoma: A comprehensive update, Part 2. *Oncology (Williston Park)*. 2004;18(8):1049-59; discussion 1060, 1065-6, 1068. Review.
  87. Rajagopalan V, Daines WP, Grossbard ML, et al. Gallbladder and biliary tract carcinoma: A comprehensive update, Part 1. *Oncology (Williston Park)*. 2004 Jun;18(7):889-96. Review.
  88. Albores-Saavedra J, Tuck M, McLaren BK, et al. Papillary carcinomas of the gallbladder: analysis of noninvasive and invasive types. *Arch Pathol Lab Med*. 2005;129(7):905-9.
  89. Sumiyoshi K, Nagai E, Chijiwa K, et al. Pathology of carcinoma of the gallbladder. *World J Surg*. 1991;15(3):315-21.
  90. Adsay V, Jang KT, Roa JC, et al. Intracholecystic papillary-tubular neoplasms (ICPN) of the gallbladder (neoplastic polyps, adenomas, and papillary neoplasms that are  $\geq 1.0$  cm): clinicopathologic and immunohistochemical analysis of 123 cases. *Am J Surg Pathol*. 2012;36(9):1279-301.
  91. Reid K, Ramos-De la Medina A, Donohue J. Diagnosis and surgical management of gallbladder cancer: A review. *J Gastrointest Surg* 2007;11:671-81.
  92. Blechacz B, Gores GJ, (2016). Tumors of the bile ducts, gallbladder, and ampulla. Mark Feldman (Ed.) In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease, Tenth Edition, p. 1184-1200. Saunders, an imprint of Elsevier Inc.
  93. Roa I, de Aretxabaleta X, Araya J, et al. Preneoplastic lesions in gallbladder cancer. *J Surg Oncol* 2006; 93:615-23.
  94. Jarnagin WR, Klimstra DS, Hezel M, et al. Differential cell cycle-regulatory protein expression in biliary tract adenocarcinoma: Correlation with anatomic site, pathologic variables, and clinical outcome. *J Clin Oncol* 2006;24:1152-60.
  95. Hui AM, Li X, Shi YZ, et al. p27(Kip1) expression in normal epithelia, precancerous lesions, and carcinomas of the gallbladder: Association with cancer progression and prognosis. *Hepatology* 2000;31:1068-72.

96. Sasatomi E, Tokunaga O, Miyazaki K. Precancerous conditions of gallbladder carcinoma: Overview of histopathologic characteristics and molecular genetic findings. *J Hepatobiliary Pancreat Surg* 2000;7:556-67.
97. Miller G, Jarnagin WR. Gallbladder carcinoma. *Eur J Surg Oncol*. 2008;34(3):306-12. Epub 2007 Oct 26. Review.
98. Duffy A, Capanu M, Abou-Alfa GK, et al. Gallbladder cancer (GBC): 10-year experience at Memorial Sloan-Kettering Cancer Centre (MSKCC). *J Surg Oncol*. 2008;98(7):485-9. doi: 10.1002/jso.21141.
99. Thorbjarnarson B, Glenn F. Carcinoma of the gallbladder. *Cancer*. 1959;12:1009-15. doi: 10.1002/1097-0142(195909/10)12:5<1009::aid-cncr2820120522>3.0.co;2-y
100. Grobmyer SR, Lieberman MD, Daly JM. Gallbladder cancer in the twentieth century: single institution's experience. *World J Surg*. 2004;28(1):47-9.
101. Strom BL, Maislin G, West SL, et al. Serum CEA and CA 19-9: potential future diagnostic or screening tests for gallbladder cancer? *Int J Cancer*. 1990;45(5):821-4.
102. Ritts RE Jr, Nagorney DM, Jacobsen DJ, et al. Comparison of preoperative serum CA19-9 levels with results of diagnostic imaging modalities in patients undergoing laparotomy for suspected pancreatic or gallbladder disease. *Pancreas*. 1994;9(6):707-16.
103. Choi JH, Seo DW, Choi JH, et al. Utility of contrast-enhanced harmonic EUS in the diagnosis of malignant gallbladder polyps (with videos). *Gastrointest Endosc*. 2013;78(3):484-93. doi:10.1016/j.gie.2013.03.1328.
104. Imazu H, Mori N, Kanazawa K, et al. Contrast-enhanced harmonic endoscopic ultrasonography in the differential diagnosis of gallbladder wall thickening. *Dig Dis Sci*. 2014;59(8):1909-16. doi: 10.1007/s10620-014-3115-5. Epub 2014 Mar 25.
105. Sato M, Ishida H, Konno K, et al, Hirata M. Localized gallbladder carcinoma: sonographic findings. *Abdom Imaging*. 2001;26(6):619-22.
106. Kalra N, Suri S, Gupta R, et al. MDCT in the staging of gallbladder carcinoma. *AJR Am J Roentgenol*. 2006;186(3):758-62.
107. Schwartz LH, Black J, Fong Y, et al. Gallbladder carcinoma: findings at MR imaging with MR cholangiopancreatography. *J Comput Assist Tomogr*. 2002;26(3):405-10.
108. Kim JH, Kim TK, Eun HW, et al. Preoperative evaluation of gallbladder carcinoma: efficacy of combined use of MR imaging, MR cholangiography, and contrast-enhanced dual-phase three-dimensional MR angiography. *J Magn Reson Imaging*. 2002;16(6):676-84.
109. Petrowsky H, Wildbrett P, Husarik DB, et al. Impact of integrated positron emission tomography and computed tomography on staging and management of gallbladder cancer and cholangiocarcinoma. *J Hepatol*. 2006;45(1):43-50. Epub 2006 Apr 19.
110. Corvera CU, Blumgart LH, Akhurst T, et al. 18F-fluoro-deoxyglucose positron emission tomography influences management decisions in patients with biliary cancer. *J Am Coll Surg*. 2008;206(1):57-65.
111. Fong Y, Wagman L, Gonan M, et al. Evidence-based gallbladder cancer staging: changing cancer staging by analysis of data from the National Cancer Database. *Ann Surg*. 2006;243(6):767-71; discussion 771-4.
112. Hu JB, Sun XN, Xu J, et al. Port site and distant metastases of gallbladder cancer after laparoscopic cholecystectomy diagnosed by positron emission tomography. *World J Gastroenterol*. 2008;14(41):6428-31.
113. Merz BJ, Dodge GG, Abellera RM, et al. Implant metastasis of gallbladder carcinoma in situ in a cholecystectomy scar: a case report. *Surgery*. 1993;114(1):120-4.
114. Amin MB, (2017). Ed AJCC Cancer Staging Manual. In: Cancer AJCo, ed (ed 8<sup>th</sup>). Chicago, IL: Springer.
115. Ito H, Matros E, Brooks D, et al. Treatment outcomes associated with surgery for gallbladder cancer: A 20-year experience. *J Gastrointest Surg* 2004;8:183-90.
116. Paolucci V, Schaeff B, Schneider M, et al. Tumor seeding following laparoscopy: International survey. *World J Surg* 1999;23:989-95.
117. Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Engl J Med* 2010;362:1273-81.