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Gallbladder cancer- causes, symptoms and chirurgical treatment: systematic review

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Abstract

Gallbladder cancer (GBC) is the most common cancer of bile ducts. This is one of the worst prognostic tumors of the digestive tract. The disease is a symptomatic for a long time, which is why it is detected in a high stage, which shortens the chances of healing. Surgery has a fundamental role in the treatment of gallbladder cancer. The patient survival prognosis depends mainly on the local severity of the disease, distant metastases and the radicality of surgical resection (R0).

Key words: Gallbladder cancer; risk factors; cholecystectomy; hepatic resection; chirurgical treatment

Introduction- statistic data

Gallbladder cancer (GBC) is a potentially fatal, most common malignant biliary tract tumor. and the fifth most common malignancy of the gastrointestinal tract. [1, 2]

According to the statistics of the National Cancer Registry in Poland in 2015, 81649 men and 81632 women were diagnosed with malignant cancer. The incidence of gallbladder cancer in the sex area is <1% of all cancers (in women 0.81%, in men 0.27%). In men, it is ranked 38 in the orderly registered morbidity (221 cases), in women in 22nd place (663 cases). In both men and women, gall bladder cancer was diagnosed most often at the age of 65-69 years, 39 and 137 cases, respectively. [3]

There are significant geographical differences in the prevalence of the disease. The highest rate of gallbladder is in Asia and South America, and the lowest rate is in Africa. The highest incidence of gallbladder cancer has Chile, Bolivia and the Republic of Korea. Poland ranks 17th in the world (2.9 / 100,000). [4]

Risk factors

1. Cholelithiasis and gallstones - the most important risk factor, 7-fold increases the risk of cancer. 70-88% of cases of gallbladder cancer coexist with stones, while the incidence of cancer in patients with cholelithiasis is 0.3-3% according to various sources. Stones over 3 cm correlate with a ten-fold increase in the risk of developing the disease.
2. Porcelain gallbladder
3. Adenoma, most often in the form of a polyp, especially those above 10 mm.
4. Female gender - twice as much in women.
5. Age > 65 years.
6. Obesity.
7. Chronic cholecystitis caused by irritation of the mucosa with stones or bacteria (*Salmonella typhi* and *paratyphi*).
8. Smoking cigarettes, PSC (Primary sclerosing cholangitis), Crohn's disease, Ulcerative colitis. [5, 6]

Symptoms

The disease is asymptomatic for a long time, which is an important clinical problem because it delays the diagnosis. Diagnosis of gall bladder cancer is most often at a high stage of the disease. The cancer is most often diagnosed during cholecystectomy performed due to cholelithiasis. According to various sources, gallbladder cancer is found in 0.5-1.5% of

cholecystectomy performed due to cholelithiasis. [7] The main symptom of biliary tract cancer is a non-painful mechanical jaundice, which is pain free during the first stage of the disease. In addition to jaundice, signs that the tumor is very advanced and correlate with a poor prognosis are: weight loss, loss of appetite, stool discoloration, dark urine, pruritus (especially if the bilirubin concentration in blood exceeds 15-20 mg), palpable tumor in right hypochondrium region and pain, hepatosplenomegaly, ascites. The symptomatic phase of the disease usually indicates a high degree of progress and unresection of the tumor, about 40% there are metastases to the lymph nodes or distant metastases.

The AJCC/ TNM Staging system

The AJCC staging system differentiates gallbladder cancer based on tumor invasion depth (T-stage), lymph node metastases (N-stage) and distant metastases (M-stage). The depth of carcinoma invasion and nodal metastasis are well-proven prognostic factors for gallbladder cancer. [8]

T describes how deeply the tumour has grown into the gallbladder

N describes whether there is cancer in the lymph nodes

M describes whether the cancer has spread to any other part of the body

T0 – there is no primary tumor

Tis – carcinoma in situ

T1 – the tumor infiltrating the lamina propria of the mucous membrane or the muscle layer

T1a - the tumor infiltrating the lamina propria of the mucous membrane

T1b - the tumor infiltrating the muscle layer

T2 - the tumor infiltrates the peri-muscular connective tissue; it does not go beyond the serous layer or infiltrate the liver.

T3 - the tumor passes beyond the serous layer (visceral peritoneum) and / or directly infiltrates the liver and / or one adjacent organ or structure such as the stomach, duodenum, colon, pancreas or extrahepatic bile ducts.

T4 - The tumor infiltrates the portal vein or hepatic artery or infiltrates two or more organs or extrahepatic structures.

N0 – no lymph node involvement

N1 – lymph node involvement within hepatoduodenal ligament

N2 – lymph node involvement beyond hepatoduodenal ligament

M0 – no distant metastasis

M1 – distant metastasis

Staging	T-stage	N-stage	M-stage
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IIIB	T1-3	N1	M0
IVA	T4	N0-1	M0
IVB	Any T	Any N	M1
		N2	M0

Treatment

Surgery is the main treatment for the gallbladder cancer. Chemotherapy and radiotherapy are ineffective as primary treatment, they are only complementary treatment. The basic surgical procedure for the treatment of gallbladder cancer is resection R0, which gives the potential for cure. [9] The extent of resection has a wide range, depending on the local severity of the disease (T-stage on the TNM scale), the extent of liver resection and the extent of local lymphadenectomy should be considered. [10]. Simple cholecystectomy is performed in patients with T1a stage, with T1b-T3 advanced, extent cholecystectomy is performed, the resection range includes cholecystectomy, limited liver resection (wedge resection, anatomic resection of segments 4b and 5 and extended right hepatectomy), regional lymphadenectomy and resection of adjacent organs / anatomical structures. There is no consensus on the appropriate extent of resection and aggressiveness of surgical treatment. Patients with T4 stage an individual approach, usually unresectable cases due to the local severity of the cancer and the presence of distant metastases. [11, 12, 13, 14] The prognosis for survival depends in the main extent of the local severity of the disease and the presence of distant metastases. The prognosis is generally poor, according to the literature the 5-year survival for gallbladder cancer is about 5% - 12%. [15, 16]

Conclusions

Gallbladder cancer is a highly lethal and aggressive disease with dismal prognosis in advanced stages. Prognosis of GBC has been poor due to aggressive nature of the disease and late presentation. R0 resection is the most important prognostic factor.

Bibliography

1. Stojcev Z., Maliszewski D., Pytka M., Bobowicz M.: Chirurgiczne leczenie chorych na raka pęcherzyka żółciowego: doświadczenia własne na podstawie 16 przypadków, *Journal of Oncology*, 2013; 63 (4): 295-298.
2. Shukla SK., Singh G., Shahi KS., Bhuvan, Pant P., Staging, treatment and future approaches of gallbladder carcinoma, *Journal of gastrointestinal Cancer*, 2018; 49 (1): 9-15.
3. Didkowska J., Wojciechowska U., Olasek P.: Nowotwory złośliwe w Polsce w 2015 roku. *Cancer In Poland In 2015*, Warszawa: Centrum Onkologii- Instytut im. M.Skłodowskiej- Curie, 2017 r.
4. World Cancer Research: Gallbladder cancer statistic. Dostęp: <https://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/gallbladder-cancer-statistics> [31.08.2018]
5. Gallbladder cancer: Epidemiology, risk factors, clinical features, clinical features, and diagnosis. Dostęp: <https://www.uptodate.com/contents/gallbladder-cancer-epidemiology-risk-factors-clinical-features-and-diagnosis>
6. Rustagi T., Dasanu C.A.: Risk Factors for Gallbladder Cancer and Cholangiocarcinoma: Similarities, Differences and Updates, *Journal of Gastrointestinal Cancer*, 2012; 43: 137-147.
7. Dorobisz T., Dorobisz K., Chabowski M., Pawłowski W., Janczak D., Patrzalek D. et in, Incidental gallbladder cancer after cholecystectomy: 1990 to 2014, *OncoTargets and Therapy*, 2016; 9: 4913-4916.
8. AJCC Cancer Staging Handbook From the AJCC Cancer Staging Manual, 7th ed., Edge S.B., Byrd D.R., Compton C.C., Fritz A.G., Greene F.L., Trotti A. (eds.), Springer New York Dordrecht Heidelberg London, 2010
9. Shih SP., Schulick RD., Cameron JL. Et in., Gallbladder cancer: the role of laparoscopy and radical resection, *Annals Surgery*, 2007; 245: 893-901.
10. Oh TG., Chung MJ., Bang S., Park SW., Chung JB., Song SY., Choi GH., Kim KS., Lee WJ., Park JY., Comparison of the sixth and seventh editions of the AJCC TNM classification for gallbladder cancer, *Journal of gastrointestinal Surgery*, 2013; 17 (5): 925-930.
11. D'Angelica M., Dalal KM., DeMatteo RP., Fong Y., Blumgart LH., Jarnagin WR., Analysis of the extent of resection for adenocarcinoma of the gallbladder, *Annals of Surgical Oncology*, 2009; 16 (4): 806-816.

12. Yokomizo H., Yamane T., Hirata T., Hifumi M, Kawaguchi T., Fukuda S., Surgical treatment of pT2 gallbladder carcinoma: a reevaluation of the therapeutic effect of hepatectomy and extrahepatic bile duct resection base on the long-term outcome, *Annals of Surgical Oncology*, 2007; 14 (4): 1366-1373.
13. Mengoa QC., De la Cruz RG., Puma CS., Durand MC., Right hepatectomy in block with hilar extra hepatic bile duct for gallbladder cancer: clinical case, *Revista de Gastroenterologia del Peru*, 2016; 36 (4): 369-372.
14. Birnbaum DJ., Vigano L., Ferrero A., Langella S., Russolillo N., Capussotti L., Locally advanced gallbladder cancer: which patients benefit from resection?, *European Journal of Surgical Oncology*, 2014; 40(8): 1008-1015.
15. Chan CP., Chang HC., Chen YL, et al., A 10-year experience of unsuspected gallbladder cancer after laparoscopic cholecystectomy, *International Surgery*, 2003; 88: 175-179.
16. Muller BG., DeAretxabala X., Gonzales DM., A review of recent data in the treatment of gallbladder cancer: what we know, what we do, and what should be done, *American Society of Clinical Oncology educational book*, 2014; 165-170.