



## Case report

## Gallbladder adenocarcinoma with upper abdominal pain: A case report

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## ARTICLE INFO

## Keywords:

Adenocarcinoma  
Gallbladder  
Cholecystectomy  
Carcinoma  
Case report

## ABSTRACT

**Introduction:** The most prevalent malignancy of the biliary system and the fifth most common cancer of the gastrointestinal tract is gallbladder cancer. This cancer is extremely aggressive with a 19 % 5-year survival rate. Herein, we report a case of gallbladder cancer with an ambiguous symptom of upper abdominal pain.

**Presentation of case:** A 51-year-old woman presented with abdominal pain persisting for 3 months. On examination, a lump on the right abdomen measuring 7 × 5 cm was found. Ultrasound showed a gallbladder mass measuring 8 cm, and magnetic resonance imaging showed an infiltrating gallbladder mass suggestive of segment VI liver malignancy. The patient underwent radical cholecystectomy with en bloc hepatectomy and lymph node dissection. Histopathology revealed poorly differentiated gallbladder adenocarcinoma that metastasized to the liver. The postoperative course was uneventful, and the patient was discharged on postoperative day 5.

**Discussion:** In our case, we performed radical (extended or margin-clearing) cholecystectomy to remove the gallbladder with a margin of normal liver tissue along with regional lymphadenectomy. This procedure is used to improve staging and decrease the risk of recurrence.

**Conclusion:** Although gallbladder cancer is rare in Indonesian populations, it has a high mortality rate because of the frequently advanced stage of the disease at the time of diagnosis. Radiography may determine its degree and malignancy features. Regardless of the tumor size, the prognosis of gallbladder cancer depends on its stage and removability.

## 1. Introduction

Gallbladder cancer is the most prevalent malignancy of the biliary tree and the sixth most common malignancy of the gastrointestinal tract worldwide, accounting for 80–95 % of all malignancies [1,2]. In Japan, Korea, Pakistan, South America, and Northern India, this cancer has a high incidence rate [3,4]. According to the Surveillance, Epidemiology, and End Results Program, gallbladder cancer is extremely aggressive with a 5-year survival rate of 19 %; a successful outcome then hinges on early disease detection and aggressive surgical resection [1].

Herein, we report the case of a patient with gallbladder adenocarcinoma who underwent laparotomy, cholecystectomy, liver resection, and transverse anastomosis at our institution. This work has been reported in line with the updated SCARE guidelines [5].

## 2. Presentation of case

A 51-year-old woman was admitted to our hospital with right upper abdominal pain persisting for 3 months. The patient described the pain as intermittently occurring: It usually appeared when she consumed fatty foods and disappeared after taking pain relievers. The pain was felt on the back and radiated to the right breast. The patient lost 5 kg in 1 month. She had no history of smoking, diabetes, dyslipidemia, hypertension, or gallstone disease.

On physical examination, she was anicteric, with a Karnofsky Performance Scale score of 90. Her vital signs were stable, and her body mass index was 20.2 kg/m<sup>2</sup> (within the normal limit). However, tenderness in the right upper quadrant, a palpable mass in the right hypochondrium measuring 7 × 5 cm, and a positive Murphy sign were noted. The laboratory findings were as follows: hemoglobin level of 9.6 g/dL, leukocyte count of 21.500/μL, direct bilirubin level of 0.43 g/dL,

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<https://doi.org/10.1016/j.ijscr.2022.107734>

Received 9 August 2022; Received in revised form 25 September 2022; Accepted 4 October 2022

Available online 11 October 2022

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and total bilirubin level of 0.86 g/dL. Meanwhile, the tumor biomarker levels were as follows: carbohydrate antigen (CA) 19-9 level of >500 U/mL and carcinoembryonic antigen (CEA) level of 71.23 ng/mL. Ultrasound (US) revealed a gallbladder mass measuring 8 cm (Fig. 1). Abdominal magnetic resonance imaging (MRI) showed a gallbladder mass infiltrating segment VI of the liver, suggestive of malignancy (Fig. 2A). Magnetic resonance cholangiopancreatography revealed a cystic duct stenosis (Fig. 2B).

The clinical diagnosis of the patient was a gallbladder tumor suspected as cT3N0M1 stage IVb malignancy. The cT3N0M1 stage was established, since no enlarged lymph nodes were found on physical examination and computed tomography (CT). Nevertheless, lymph node resection was performed during surgery. The patient underwent radical cholecystectomy with en bloc hepatectomy and lymph node dissection (Fig. 3). Histopathological examination revealed poorly differentiated adenocarcinoma that metastasized to the liver (Fig. 4). In accordance with the American Joint Committee on Cancer (AJCC) guidelines, the staging was pT3N1M1 (stage IVb; infiltration to liver segments IVb and V, the gastric wall, and the proximal transverse colon).

The postoperative course was uneventful, and the patient was discharged on postoperative day 5. The patient was alive up to 6 months postoperatively and until this case report was made.

### 3. Discussion

Gallbladder cancer is an aggressive malignancy that frequently invades the local environment and spreads to distant sites. Each year, there are >1000 new cases of gallbladder cancer in the United States [6]. Approximately 70 % of gallbladder cancer cases are identified in women, while 64 % of Caucasians, 17 % of Hispanics, 9 % of African Americans, and 2 % of Pacific Islanders/Asians have gallbladder cancer [7,8]. Despite being a rare cancer in western nations, gallbladder cancer continues to be a major cause of death in several countries, including Chile, India, and Japan [9]. The prevalence of laparoscopic cholecystectomies, where approximately 0.7 % of cases are discovered to have gallbladder cancer, may in part be attributed to the increasing incidence of gallbladder cancer [6,7].

Gallbladder cancer is most commonly associated with advanced age, female sex, obesity, cholelithiasis or other benign gallbladder pathology [3,7], porcelain gallbladder, chronic infection with *Helicobacter pylori* or *Salmonella* species, aberrant pancreatobiliary duct junction, and gallbladder polyps [3,6].

The clinical manifestation of gallbladder cancer is frequently ambiguous or delayed in comparison with the pathologic progression, which leads to advanced staging and a poor prognosis at the time of

diagnosis [1,10,11]. The majority of patients present to the hospital with a vague upper abdominal pain or a palpable tumor on physical examination; this may be an accidental discovery on imaging or a histological finding [12,13]. Jaundice, abdominal lump, anorexia, and weight loss are frequent signs of advanced stages. In the absence of any stones, a gallbladder mucocele may serve as an early indicator of cancer that would develop in the neck or cystic duct [13]. Gallbladder cancer is rarely detected before it has progressed or spread [14]. Its development may be a nidus in a background of chronic cholecystitis, delaying the identification of cancer [15]. This was demonstrated in our case, in which the 51-year-old female patient had been experiencing non-specific abdominal pain for 3 months.

It is critical to distinguish gallbladder cancer early, which will likely have a better prognosis. The ability to distinguish between conditions and select the best course of treatment has improved with the use of US, CT, and MRI. At the time of initial discovery, 40–65 % of patients with gallbladder cancer may have a mass-occupying lesion. Imaging methods, including contrast-enhanced CT and MRI, can identify gallbladder cancer as focal or diffuse asymmetric wall thickening [10]. The characteristics suggestive of gallbladder cancer on CT include an irregular focal wall thickening, a discrete focal gallbladder mass, an infiltration of the surrounding structures, a “two-layer pattern” of enhancement in a thickened gallbladder wall, a locoregional lymphadenopathy, and a metastatic deposit in the liver, peritoneum, and omentum [16]. While marked, asymmetric, or irregular wall thickening with an apparent enhancement should raise the suspicion for gallbladder cancer, diffuse symmetric wall thickening may suggest a benign disease [10]. CT angiography can be used to visualize the blood vessels near the gallbladder and show marked vascular abnormalities. This can help determine whether surgery can be performed; however, CT angiography is not available in our research center and was thus not performed.

The majority of the currently available laboratory examinations for gallbladder cancer remain non-sensitive and non-specific. Although they are not specific to the gallbladder, the levels of tumor markers, including CEA and CA 19-9, may be raised in some cases. Similarly, the serum levels of bilirubin and alkaline phosphatase may be elevated, although usually only when the disease has advanced to the point where bile duct obstruction is possible [17].

The high mortality rate of gallbladder cancer is linked to the vague symptoms, frequently advanced stage upon diagnosis, and importance of organs situated close to the gallbladder. Currently, surgery is the primary method for treating gallbladder cancer, mainly consisting of radical cholecystectomy with removal of 3 cm of segments IVb and V of the liver parenchyma and local lymphadenectomy. A minimum of six recovered lymph nodes are required to stage the tumor properly; this shows whether complete lymphadenectomy has been performed.

In our case, we performed radical (extended or margin-clearing) cholecystectomy to remove the gallbladder with a margin of normal liver tissue along with regional lymphadenectomy. This procedure is used to improve staging and decrease the risk of recurrence. In addition to liver resection, adequate lymphadenectomy of the porta hepatis should be performed to assess six or more regional nodes. Advanced (T3) tumors involve the proximal transverse colon and liver. En bloc resection of involved organs with colon resection is required to achieve clear margins. In our patient, surgery was conducted although the tumor was unresectable, since this treatment option was considered to yield a good prognosis. The patient was young and had a Karnofsky Performance Scale score of 90, which indicated that her performance and functional statuses were good. She also showed clear tumor boundaries and no blood vessel involvement. Generally, regional lymphadenectomy increases the survival rates of patients with T1b to T3 gallbladder cancer [18]. Lymph node dissection for patients with resectable gallbladder cancer that has invaded the muscular layer (T1b) is widely endorsed by the AJCC, Americas Hepato-Pancreato-Biliary Association, and National Comprehensive Cancer Network. A positive lymph node is associated

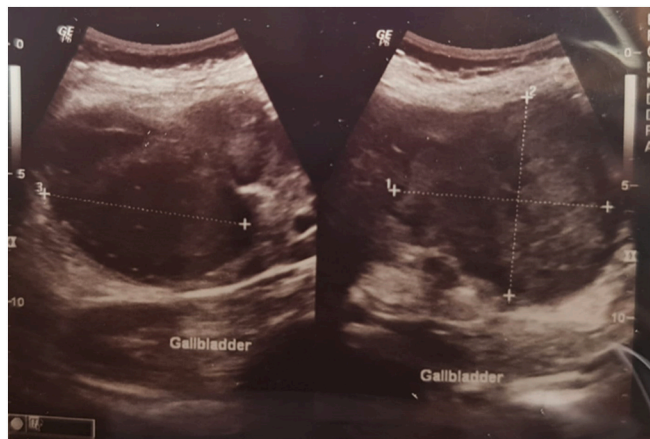
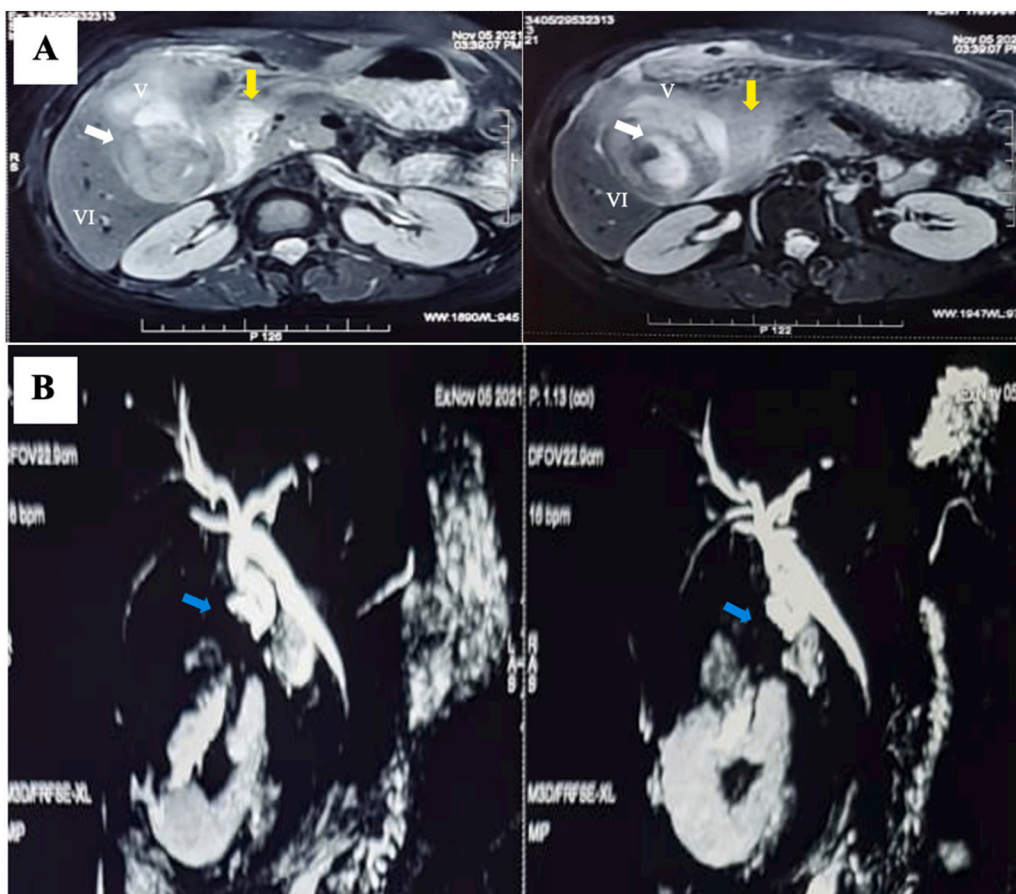
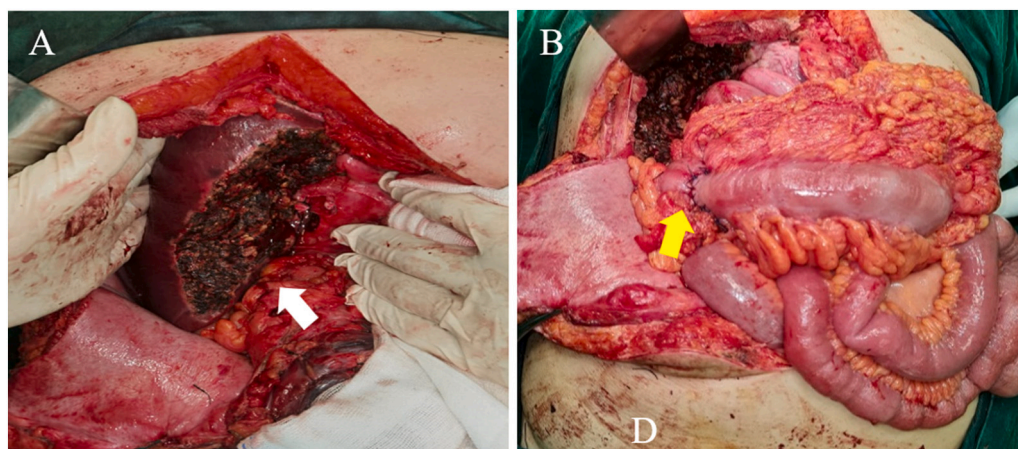


Fig. 1. Abdominal ultrasound showing a gallbladder mass measuring 8 × 7.4 × 7.8 cm and multiple hyperechoic lesions on the gallbladder wall, with the largest size being 0.9 cm.



**Fig. 2.** (A) Abdominal magnetic resonance imaging revealing a heterogeneous, slight hypotensive mass (white arrow) with fat and solid components originating from the gallbladder. The mass has a strong post-contrast at the edges, relatively firm borders, irregular edges, and a size of 9.88 × 8.70 × 6.95 cm, with lesion infiltration to segment VI of the liver covering an area of 6.7 × 4.39 × 3.21 cm (yellow arrow: portal vein). (B) Magnetic resonance cholangiopancreatography showing a cystic duct stenosis (blue arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



**Fig. 3.** (A) Resection of liver segments IVb and V (white arrow); (B) transverse colon anastomosis (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

with worse long-term survival and is a main indication for adjuvant systemic therapy [18]. Although no intraoperative freezing was conducted in our case, the digestive surgeons classified the resection as R0. Histological examination showed free margins without damaged lymph nodes among the 10 resected lymph nodes.

**4. Conclusion**

Although gallbladder cancer is rare in Indonesian populations, it has a high mortality rate because of the frequently advanced stage of the

disease at the time of diagnosis. Radiography may determine its degree and malignancy features. Regardless of the tumor size, the prognosis of gallbladder cancer depends on its stage and removability.

**Funding**

No funding or sponsorship.

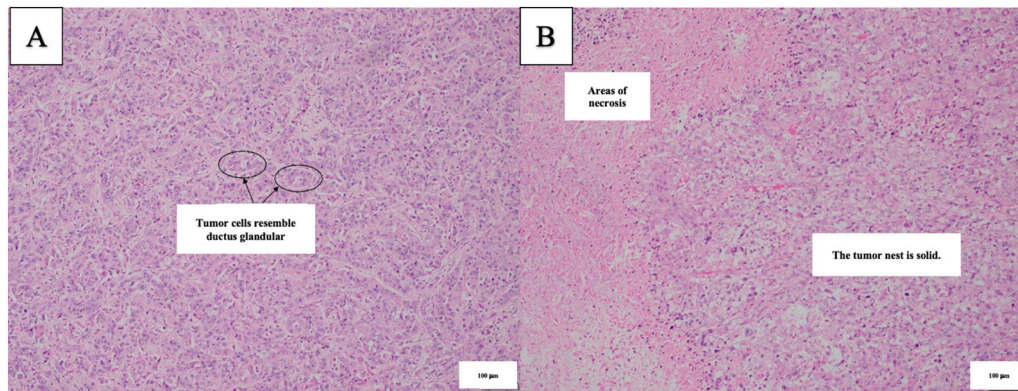


Fig. 4. Histological examination (hematoxylin and eosin staining, 4 $\times$ ).

### Ethical approval

The study is exempt from ethical approval in our institution.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Author contribution

Samuel Sampetoding and Muhammad Ihwan Kusuma: study concept and surgical therapy for this patient. Yulianti Pratiwi: Data collection and Writing-Original draft preparation. Samuel Sampetoding and Muhammad Ihwan Kusuma: Senior author and the manuscript reviewer. Devby Ulfandi and Muhammad Faruk: Editing and Writing. All authors read and approved the final manuscript.

### Registration of research studies

Not applicable – single case report.

### Guarantor

Samuel Sampetoding.

### Declaration of competing interest

Nothing to declare.

### Acknowledgment

None.

### Provenance and peer review

Not commissioned, externally peer-reviewed.

### References

- [1] L. Bains, H. Maranna, P. Lal, R. Kori, D. Kaur, V. Mallya, V. Singh, The giant resectable carcinoma of gall bladder—a case report, *BMC Surg.* 21 (2021) 133, <https://doi.org/10.1186/s12893-021-01117-2>.
- [2] L. Guo, J. Zhang, X. Liu, H. Liu, Y. Zhang, J. Liu, Successful treatment of metastatic gallbladder carcinoma with PD-L1 expression by the combination of PD-1 inhibitor plus bevacizumab with chemotherapy: a case report, *OncoTargets Ther.* 15 (2022) 629–636, <https://doi.org/10.2147/OTT.S346635>.
- [3] R. Hundal, E.A. Shaffer, Gallbladder cancer: epidemiology and outcome, *Clin. Epidemiol.* 6 (2014) 99–109, <https://doi.org/10.2147/CLEP.S37357>.
- [4] R. Maharaj, C. Cave, K. Sarran, N. Bascombe, D. Dan, W. Greaves, W.A. Warner, A case report of the clear cell variant of gallbladder carcinoma, *Int. J. Surg. Case Rep.* 32 (2017) 36–39, <https://doi.org/10.1016/j.ijscr.2017.01.020>.
- [5] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, A.J. Beamish, A. Noureldin, A. Rao, B. Vasudevan, B. Challacombe, B. Perakath, B. Kirshtein, B. Ekser, C.S. Pramesh, D.M. Laskin, D. Machado-Aranda, D. Miguel, D. Pagano, F. H. Millham, G. Roy, H. Kadioglu, I.J. Nixon, I. Mukhejee, J.A. McCaul, J. Chi-Yong Ngu, J. Albrecht, J.G. Rivas, K. Raveendran, L. Derbyshire, M.H. Ather, M. A. Thorat, M. Valmasoni, M. Bashashati, M. Chalkoo, N.Z. Teo, N. Raison, O. J. Muensterer, P.J. Bradley, P. Goel, P.S. Pai, R.Y. Afifi, R.D. Rosin, R. Coppola, R. Klappenbach, R. Wynn, R.L. De Wilde, S. Surani, S. Giordano, S. Massarut, S. G. Raja, S. Basu, S.A. Enam, T.G. Manning, T. Cross, V.K. Karanth, V. Kasivisvanathan, Z. Mei, The SCARE 2020 guideline: updating consensus Surgical CAsE RReport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230, <https://doi.org/10.1016/j.ijssu.2020.10.034>.
- [6] Y. Jia, S. Samadzadeh, M. Cornford, P. Ji, S.W. French, Educational case: incidental gallbladder adenocarcinoma, *Acad. Pathol.* 7 (2020), 2374289520909504, <https://doi.org/10.1177/2374289520909504>.
- [7] L. Hickman, C. Contreras, Gallbladder cancer: diagnosis, surgical management, and adjuvant therapies, *Surg. Clin.* 99 (2019) 337–355.
- [8] A. Sharma, K.L. Sharma, A. Gupta, A. Yadav, A. Kumar, Gallbladder cancer epidemiology, pathogenesis and molecular genetics: recent update, *World J. Gastroenterol.* 23 (2017) 3978.
- [9] T.A. Aloia, N. Járufe, M. Javle, S.K. Maithel, J.C. Roa, V. Adsay, F.J.F. Coimbra, W. R. Jarnagin, Gallbladder cancer: expert consensus statement, *HPB* 17 (2015) 681–690.
- [10] Å. Andrén-Sandberg, Diagnosis and management of gallbladder cancer, *N. Am. J. Med. Sci.* 4 (2012) 293.
- [11] T. Adachi, M. Haraguchi, J. Irie, T. Yoshimoto, R. Uehara, S. Ito, H. Tokai, K. Noda, N. Tada, M. Hirabaru, K. Inoue, S. Minami, S. Eguchi, Gallbladder small cell carcinoma: a case report and literature review, *Surg. Case Rep.* 2 (2016) 71, <https://doi.org/10.1186/s40792-016-0200-3>.
- [12] M.A.R. Junior, M. de L. Favaro, S. Santin, C.M. Silva, A.P.M. Iamarino, Giant squamous cell carcinoma of the gallbladder: a case report, *World J. Clin. Cases* 7 (2019) 2787–2793, <https://doi.org/10.12998/wjcc.v7.i18.2787>.
- [13] L. Bains, D. Kaur, A.K. Kakar, A. Batish, S. Rao, Primary carcinoma of the cystic duct: a case report and review of classifications, *World J. Surg. Oncol.* 15 (2017) 1–5.
- [14] A.N.D. Dwivedi, S. Jain, R. Dixit, Gall bladder carcinoma: aggressive malignancy with protean loco-regional and distant spread, *World J. Clin. Cases* 3 (2015) 231.
- [15] A. Furlan, J.V. Ferris, K. Hosseinzadeh, A.A. Borhani, Gallbladder carcinoma update: multimodality imaging evaluation, staging, and treatment options, *Am. J. Roentgenol.* 191 (2008) 1440–1447.
- [16] C.H. Mitchell, P.T. Johnson, E.K. Fishman, R.H. Hruban, S.P. Raman, Features suggestive of gallbladder malignancy: analysis of T1, T2, and T3 tumors on cross-sectional imaging, *J. Comput. Assist. Tomogr.* 38 (2014) 235.
- [17] D. Jefferys, S. Roy, A. Majid, Incidental adenocarcinoma of the gallbladder in a patient with Y insertion gallbladder duplication in the context of recurrent biliary colic, *Medicine* 101 (2022), e28829, <https://doi.org/10.1097/MD.00000000000028829> (Baltimore).
- [18] B. Widmann, R. Warschkow, U. Beutner, M. Weitzendorfer, K. Ukegjini, B. M. Schmied, I. Tarantino, T. Steffen, Effect of lymphadenectomy in curative gallbladder cancer treatment: a systematic review and meta-analysis, *Langenbeck's Arch. Surg.* 405 (2020) 573–584.