**Name of Journal:** *World Journal of Clinical Oncology*

**Manuscript NO:** 65716

**Manuscript Type:** SYSTEMATIC REVIEWS

**Carcinosarcoma of gallbladder: A world review**

Teng TZJ *et al*. Carcinosarcoma of gallbladder

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**Received:** March 14, 2021

**Revised:** May 14, 2021

**Accepted: November 24, 2021**

**Published online:**

**Abstract**

BACKGROUND

Gallbladder carcinosarcoma is a rare hepatobiliary tumor comprising of both carcinomatous and sarcomatous components. Due to its rarity, the literature with regards to the topic is scarce and currently lacking, spanning less than 100 cases.

AIM

to summarize the current literature on gallbladder carcinosarcoma.

METHODS

A literature review was performed on the PubMed database using the keywords “Gallbladder” AND “Carcinosarcoma” from 1970 to 2021. Additionally, similar searches were performed on Medline and Web of Science.

RESULTS

Risk factors noted include female gender, gallstones and chronic cholecystitis. In the absence of any diagnostic biochemical testing or tumor markers, imaging modality serves as the key initial impression tool, which can be histologically confirmed only post-resection. While surgery is the only curative option, the use of adjunctive chemotherapy has been considered on top of excision in recent years, with some success.

CONCLUSION

While this study has taken steps to bridge the gap in the literature, more cases should be reported to further ascertain the current associations and management potential for gallbladder carcinosarcoma.

**Key Words:** Carcinosarcoma; Gallbladder; Gallstone; Malignancy; Carcinoma; Sarcoma

Teng TZJ, Chua BQY, Shelat VG. Carcinosarcoma of gallbladder: A world review. *World J Clin Oncol* 2021; 0(0): 0000-0000 URL: https://www.wjgnet.com/2218-4333/full/v0/i0/0000.htm

DOI: https://dx.doi.org/10.5306/wjco.v0.i0.0000

**Core Tip:** Gallbladder carcinosarcoma (GBCS) while rare, is an important histological subtype of gallbladder malignancy as it is associated with poor prognosis. Most GBCS patients tend to present late. As of now, the primary method of diagnosis is that of a pathological analysis with the main stay of treatment being surgical excision. Furthermore, the clinical diagnosis of GBCS remains extremely challenging given its seemingly nonspecific clinical features. We aim to provide an in-depth world review of the known cases of GBCS in order to identify unifying features of the disease and to assess effective management strategies that have been employed by clinicians.

**INTRODUCTION**

Gallbladder carcinosarcoma (GBCS) is defined by the presence of both carcinomatous and sarcomatous components in the tumor, making it a rarity even amongst the uncommon gallbladder cancer family[1]. While its history is deep-rooted, with the first case being reported by Karl[2] in 1907, less than 100 cases have been reported since. In 2008, Zhang *et al*[3] sought to collectively analyze the 70 cases in the literature at that time. However, Zhang *et al*[3] noted the need for a larger scale case series to provide more information on the neoplasm for better accuracy and reliability. Since then, there has been a gap in the literature for such an analysis (Figure 1). This study aims to fill this gap by providing a comprehensive overview of GBCS.

**MATERIALS AND METHODS**

A literature review was performed on the PubMed database using the keywords “Gallbladder” AND “Carcinosarcoma” from 1970 to 2021. Additionally, similar searches were performed on Medline and Web of Science. The last search was performed on January 31, 2021. After removing duplicate results from similar databases, the search yielded 105 articles: 16 non-English and non-Japanese studies and 12 unrelated topics (animal studies, gallbladder carcinoma and non-gallbladder pathology) were excluded. Out of the remaining 77 articles, seven were not case reports or case series on GBCS and thus excluded. The remaining 70 articles including 76 patients were included in the final analysis (Table 1)[1,4-72]. Article filtering and exclusion was done according to PRISMA guidelines (Figure 2). Data extracted included study year, age and gender of the patient, clinical presentation, risk factors, laboratory investigations, tumor markers, the ultrasound imaging findings, location of the lesion within the gallbladder, size of the lesion, initial diagnosis, method of confirming the diagnosis, immunohistochemical results (vimentin, cytokeratin, Ki-67), management and prognosis of the patient. Kaplan-Meier survival curves were compared between lesions larger than 5 cm and those smaller than 5 cm as data by Zhang *et al*[3] suggested that tumors smaller than 5 cm had better survival. For all statistical tests, a *p* value of 0.05 was used to determine statistical significance.

**RESULTS**

seventy-eight patients with a mean age of 66.4 years (range: 40-91 years) were reported during the study period. The patients were predominantly female (*n* = 55, 72.4%) with a gender ratio of 2.62. Nine patients (11.8%) had chronic cholecystitis, and 1 patient each had hepatitis C and abnormal pancreaticobiliary maljunction (APBJ). Of those who reported the presence of gallstones, a majority noted the presence of gallstones (*n* = 35/42, 83.3%). The majority of patients complained of abdominal pain (*n* = 58, 76.3%), most of which was localized to the right upper quadrant. Twenty-two patients (28.9%) presented with constitutional symptoms (either unexplained loss of weight, anorexia or lethargy). Nineteen patients (25.0%) had nausea and vomiting, and 13 patients (17.1%) were febrile. Two patients (2.6%) were asymptomatic when diagnosed.

Liver function test was the common serum biochemical test reported (*n* = 57). Deranged liver function tests were reported in 25 (43.9%) patients. Tumor markers were variably reported. The following tumor markers were elevated: carbohydrate antigen 19-9 (CA19-9) (*n* = 9/27, 33.3%), carcinoembryonic antigen (*n* = 5/27, 18.5%) and alpha-fetoprotein (*n* = 2/12, 16.6%) in some patients. Also, CA-125 was elevated in 2 patients.

Forty-three patients had the location of the gallbladder tumor reported. Fundus was the most common location (*n* = 15, 34.9%), followed by body (*n* = 10, 23.3%) and neck (*n* = 5, 11.6%). In 14 patients (32.5%), the tumor filled the entire gallbladder lumen, and thus exact position could not be determined. Fifty-nine patients had initial diagnosis reported. Out of these 59 patients, gallbladder malignancy was the primary diagnosis in the majority of patients (*n* = 49, 83.1%). Ten patients (16.9%) were initially diagnosed with other pathologies: cholelithiasis (*n* = 1), cholecystitis (*n* = 3), gallbladder empyema (*n* = 2), diffuse peritonitis (*n* = 1), pancreatic cancer (*n* = 1), biliary neoplasm (*n* = 1) and pyogenic liver abscess (*n* = 1).

Confirmation of diagnosis was reported in all but 1 patient (*n* = 75). It was mostly done *via* surgical resection, either diagnostic cholecystectomy or laparotomy (*n* = 70, 93.3%). In the remaining 5 patients, diagnosis was made by fluid analysis from percutaneous cholecystostomy (*n* = 1, 1.3%), computerized tomography (CT) scan guided needle biopsy (*n* = 1, 1.3%) and autopsy (*n* = 3, 4.0%). Staging of the cancer was reported infrequently, with TNM system being the most common (*n* = 15, 19.7%). The majority of patients had stage II (*n* = 6, 40.0%) and stage III disease (*n* = 5, 33.3%). Three patients had stage IV disease (20.0%), and 1 patient had stage I disease (6.67%). Immunohistochemical stains (vimentin for mesenchymal components and cytokeratin for epithelial components) were reported in 50 patients (68.5%). Vimentin (*n* = 42, 84.0%), cytokeratin (*n* = 39, 78.0%) and Ki-67 staining (*n* = 7, 14.0%) were variably positive.

Fourteen patients (18.4%) received adjuvant chemotherapy. Various chemotherapy combinations included: gemcitabine and cisplatin, leucovorin and 5-fluorouracil (5-FU), cisplatin and doxorubicin, cisplatin and 5-FU, tegafur-uracil and gemcitabine and oxaliplatin and 5-FU. Palliative treatment was chosen in 4 patients (5.26%). Amongst all those reported, 32 patients contained both survival and tumor size data. Kaplan-Meier survival analysis was performed (Figure 3), and there was no significant difference in survival times (*P* = 0.301) for patients with tumors less than 5 cm in diameter compared to those with larger tumors.

**DISCUSSION**

Gallbladder cancer is a rare neoplasm, accounting for about 0.5% of all gastrointestinal malignancies[73]. Most common gallbladder cancer is adenocarcinoma. GBCS is a rare form of gallbladder cancer, with only 78 cases reported. GBCS is characterized by carcinomatous and sarcomatous components and is made up of both epithelial and mesenchymal components. Commonly, the epithelial component consists of adenocarcinoma followed by the less common squamous cell carcinoma[74]. While there are multiple theories to justify the mixture of the epithelial and mesenchymal components, there is no consensus on the pathophysiology of the neoplasm. GBCS is considered the most aggressive biliary tract malignancy, usually discovered at late stages, and has poor prognosis[3].

***Incidence***

In terms of patient demographics, our results are consistent with the report of Zhang *et al*[3]. In a report including 68 GBCS patients, those authors reported a median age of 68 years (range: 45 to 91 years) with female predominance (female:male = 2.7:1), consistent with our results with a gender ratio of 2.32 and a mean age of 66.0 years (range: 40-91 years). Female preponderance is likely due to increased prevalence of gallstones in females. Zhang *et al*[3] noted gallstones in 66.7% of their patients. In our study, the incidence of gallstones was high (83%). However, gallstone presence was not specific nor sensitive in the diagnosis of GBCS, as not only are they a common finding in cancers of the gallbladder, only 1%-5% of patients with gallstones develop gallbladder malignancies. In our analysis of the literature, gallstone presence was only noted in 83.3% of patients where the presence of gallstones was assessed.

APBJ is also another risk factor of gallbladder malignancy[12]. Matsubayashi *et al*[12] reported a 72-year-old female patient with symptoms of abdominal pain. Laboratory investigations revealed raised alkaline phosphatase and gamma-glutamyl transpeptidase. CT scan confirmed a polypoid gallbladder mass. Magnetic resonance cholangiopancreatography scan showed ABPJ, and this was confirmed at subsequent endoscopic retrograde cholangiopancreatography. While APBJ is a well-known risk factor for gallbladder cancers[75], this was the first case of APBJ in GBCS noted in the literature.

Other risk factors mentioned include chronic cholecystitis, which could be both a risk factor and the manifestation of gallbladder malignancy. Unique to the gallbladder is a cycle of gallbladder epithelium damage and repair, enabling a chronic inflammatory environment from chronic cholecystitis[76]. This cycle of inflammation, injury, repair and regeneration increases cell turnover and oxidative stress. Yildiz *et al*[77] stated biliary tract to be the “consummate example of inflammation-associated carcinoma.” Chronic inflammation from gallstone disease can lead to protein damage, genetic mutations, inhibition of apoptosis, promotion of angiogenesis, modulation of cell adhesion and motility as well as immunosuppression. Chronic cholecystitis leads to gallbladder wall thickening, and CT or magnetic resonance imaging (MRI) scans are sensitive to detect wall thickness. However, it is not possible to distinguish if thickening of the gallbladder wall is due to inflammation or malignancy[78]. Thus, multidisciplinary discussion involving experienced radiologists and hepatobiliary surgical team is essential to make management plans for patients with suspicious gallbladder lesions.

***Signs and symptoms***

Clinical manifestations of GBCS are nonspecific, with symptoms such as abdominal pain localized to the right upper quadrant, constitutional symptoms, nausea, vomiting and fever. The mechanism resulting in constitutional symptoms in patients with cancer is multifactorial and not yet fully understood. It is thought that multiple pathways involving pro-cachectic and pro-inflammatory signals from tumor cells along with systemic inflammation of the host combine with widespread metabolic changes contribute to the manifestations of symptoms like anorexia and cachexia[79]. In particular, cholecystokinin is an integral peptide involved in satiety and regulating diet intake[80]. Given its role in gallbladder contraction, dysregulation of cholecystokinin could be involved in the manifestation of constitutional symptoms of anorexia in patients with GBCS.

Similarly, the pathophysiology of febrile response in malignancies is complex. Released pyrogenic cytokines from tumor cells and tissue macrophages induces a chain of events that result in reset of hypothalamic thermostat due to prostaglandin E2 and related pathways[81]. On physical examination, the presence of a right hypochondria tenderness or mass is not specific, and it does not rule out malignancy. Thus, if a patient is managed for suspected acute or chronic cholecystitis, a follow-up physical examination and imaging needs to be arranged to document resolution of inflammatory process. In this review, 2 asymptomatic patients were diagnosed with GBCS. From our analysis, Ishida *et al*[36] and Akatsu *et al*[46] reported incidental findings of GBCS on imaging findings for unrelated issues. Ishida *et al*[36] reported a 62-year-old female with unexpected calcification in the right upper abdomen in a CT meant for follow-up of percutaneous pinning of a left calcaneal fracture. Akatsu *et al*[46] reported a 76-year-old female who was on regular follow-up for cholelithiasis. Abdominal ultrasound revealed a heterogeneously hypoechoic mass around the gallbladder bed. In both patients, a preoperative diagnosis of possible gallbladder malignancy was made, and surgical exploration with subsequent cholecystectomy was performed.

***Biochemical investigations***

Biochemical abnormalities in GBCS are also mostly nonspecific. The most common derangements were transaminitis, hyperbilirubinemia and anemia. This was consistent with Ayoub *et al*[5] who reported that hepatic and inflammatory markers were often normal.

Presurgical diagnosis of gallbladder malignancies is difficult due to its varying presentations. Differentials to consider for such lesions when calcification is present include calcified gallstones, porcelain gallbladder and GBCS[78]. Our analysis noted cases where GBCS was initially diagnosed with cholelithiasis, acute cholecystitis, gallbladder empyema, diffuse peritonitis, pancreatic cancer and pyogenic liver abscess.

***Imaging***

As there are no radiological signs identified in the current literature that distinguishes GBCS from other gallbladder malignancies[50,51], the diagnosis is difficult even with imaging. For instance, Appelman *et al*[72] described a 91-year-old male presenting with yellow sclera, pale stools, dark urine and pruritus. His liver function tests were deranged with obstructive pattern, and a diagnosis of pancreatic cancer with biliary tract obstruction was made. The patient refused surgical intervention and died within 2 wk. Autopsy confirmed the diagnosis of metastatic disease with GBCS primary.

Khurram *et al*[4] reported a 64-year-old lady presented with right upper quadrant mass, intermittent fever and abdominal distension following a recent travel history to Ghana. CT scan revealed a hepatic lesion with coexisting gallbladder distension consistent with pyogenic liver abscess. Due to failure to respond to intravenous antibiotics, MRI scan was done. MRI scan showed a gallbladder fundus soft tissue lesion with local invasion into the liver[22]. Histopathological diagnosis of GBCS was made after surgical excision. Hence, in the absence of a confirmatory preoperative diagnosis, all suspicious gallbladder lesions must be reviewed at multidisciplinary meetings.

Porcelain gallbladder, gallbladder tuberculosis and xanthogranulomatous cholecystitis are common benign conditions that can be confused with malignancy. Porcelain gallbladder is described as a hyperechoic focus with posterior acoustic shadowing on an ultrasound scan[82]. Ultrasound scan is not sensitive for regional and distant spread of malignancy. CT and MRI scans are more sensitive to detect contiguous spread to liver, regional lymph node involvement and distant metastases. Diffuse nodular thickening without layering, early enhancement, low apparent diffusion coefficient and high lesion to spinal cord ratio are MRI features suggestive of gallbladder cancer[83]. In addition, CT and MRI scans provide details that assist in surgical planning. 18-fluorodeoxyglucose-positron emission tomography-CT can aid in distinguishing between benign and malignant gallbladder lesions. Malignant lesions have high standardized uptake value. In a study reporting 30 patients with a mean age of 48.22 ± 31.33 years and gallbladder wall thickening (focal > 4 mm and diffuse > 7 mm), Gupta *et al*[84] reported that 18-fluorodeoxyglucose-positron emission tomography had high overall sensitivity (91%), specificity (79%), positive predictive value (77%), negative predictive value (92%) and diagnostic accuracy (84%).

***Histological diagnosis***

Diagnosis of GBCS is usually made after pathological analysis of a surgical specimen. In patients with unresectable neoplasms, tissue diagnosis can be achieved by percutaneous biopsy. This is essential to plan definitive chemotherapy[85]. In clearly resectable lesions, the role of percutaneous biopsy is debated due to risk of needle-tract seeding[86]. Furthermore, as the gallbladder is a hollow organ, bile spill and peritonitis remain a risk too[87]. As GBCS are rare tumors with poor prognostic outcomes, treatment options are not well defined, with little evidence supporting or refuting any postoperative adjuvant therapy. Okabayashi *et al*[88] and Mochizuki *et al*[8] both corroborate that surgical treatment remains the only cure for GBCS. While the histopathological features between GBCS and adenocarcinoma of the gallbladder are different, management is similar.

***Surgical management***

Currently, the consensus for treatment involves surgical excision of the gallbladder and extrahepatic bile duct, regional lymphadenectomy and even a pancreaticoduodenectomy depending on the extent of the growth[88]. Completion liver resection with or without lymphadenectomy and/or bile duct resection is an accepted standard for post simple cholecystectomy discovered gallbladder cancer with T1b and higher stage. This approach not only involves two surgeries but also increases the risk of cutting through the tumor with potential for tumor seeding and dissemination. Yip *et al*[89] in a series of 40 patients with incidental gallbladder cancer reported that the majority of patients were not amenable for further curative resection. A report from Memorial Sloan-Kettering Cancer Centre involving 116 patients showed that survival of patients with residual disease was not different than survival of patients with stage IV disease, and neither group of patients benefit from reoperation[90]. Thus, single surgery may be better.

Radical cholecystectomy has higher morbidity as compared to simple cholecystectomy. Thus, the concept of something intermediate, *i.e.*, extended cholecystectomy, is attractive. Fujisaki *et al*[91] reported a case describing the concept of laparoscopic extended cholecystectomy with 1 cm liver margin; however, they proposed open conversion when intraoperative histology showed gallbladder cancer invading the subserosal layer. With current advancements, laparoscopic extended cholecystectomy was noted to have lesser intraoperative and postoperative complications than open extended cholecystectomy[92].

The key differences between a ‘radical’ and ‘extended’ cholecystectomy are restricting the liver parenchyma transection to the 2 cm wedge of liver tissue and performing regional lymphadenectomy and choledochectomy only in selected patients. Radical cholecystectomy can be done by open, laparoscopic or robot assisted approach, with comparable short-term outcomes[93]. Overall, more data is required to determine the safety and feasibility of minimal access techniques in gallbladder malignancies. Due to the absence of histological diagnosis, management of suspicious gallbladder lesions must be determined by local resources, surgeon experience and access to technology.

In a recent systematic review, Frountzas *et al*[94] reported that many patients with xanthogranulomatous cholecystitis were managed with complex procedures like wedge hepatic resection and bile duct excision with high open conversion rate (35.0%) at planned cholecystectomy. Intraoperative frozen section analysis is a useful adjunct in surgical planning. While intraoperative frozen tissue diagnosis is relatively reliable to determine whether lesions are benign or malignant, it does not reliably detail the depth of invasion of gallbladder malignancies[95]. Furthermore, the accuracy of intraoperative frozen tissue diagnosis for GBCS has yet to be determined due to paucity of scientific data.

***Adjuvant treatment***

The adjuvant treatment reduces recurrence risk and improves survival outcomes by eliminating or controlling the micrometastatic disease. A meta-analysis of retrospective studies including 6712 gallbladder cancer patients reported that lymph node positive patients enjoyed the survival benefit[96]. Few reported patients consider the use of UFT: tegafur/uracil, gemcitabine or a combination of tegafur/gimeracil/oteracil. The median survival of GBCS is 7.8 mo[10], and the addition of such regimes has not shown to improve survival[38]. There is a report by Pu *et al*[38] of using a combination of 5-FU (commonly used in gallbladder cancer) and oxaliplatin (commonly used in sarcomas). They reported a 59-year-old female coming in with right upper quadrant pain, fever and a raised CA19-9 level of 12000 U/mL, which was confirmed to be GBCS. The patient received oxaliplatin 150 mg and 5-FU 500 mg intravenously every 30 d for 6 cycles. At 6-mo follow-up, she did not reveal any signs of recurrence.

Adjuvant radiotherapy is shown to be of value in reducing local recurrence in selected patients with gallbladder cancer. In a study including 4180 patients with resected gallbladder cancer diagnosed from 1988 to 2003 from the Surveillance, Epidemiology, and End results database, Wang *et al*[97] reported that adjuvant radiotherapy provides survival benefit in node positive or T2 and higher stage disease. A single arm phase II study conducted by South West Oncology Group reported that gemcitabine plus capecitabine, followed by radiation (45 Gy to regional lymphatics, 54-59.4 Gy to tumor bed) and capecitabine resulted in 56% 2-year survival rate for patients with gallbladder cancer. Based on these results, the American Society of Clinical Oncology guidelines recommend chemotherapy plus radiation in gallbladder cancer patients with R1 resection[98]. There is no data to support neoadjuvant chemotherapy. Due to aggressive biological behavior, rapid progression or recurrence is common, and this is associated with a myriad of constitutional symptoms. For holistic care, management of the patients’ subjective symptoms of anorexia and lethargy needs to be considered. Testosterone replacement therapy helps alleviate such symptoms in male patients with advanced cancer[99].

***Prognosis***

Generally, the prognosis of GBCS is poor. The majority of patients presenting to the hospital are locally advanced, with liver metastasis and peritoneal dissemination. Other metastasis sites reported include adrenal glands, pancreas, diaphragm and the lower thoracic vertebrae. Zhang *et al*[3] reported a mean survival time of 17.5 mo, with 1-year and 5-year survival rates at (19 ± 5)% and (16 ± 5)%, respectively. While it was previously noted the longest survival time to be reported as 54 mo by Uzun *et al*[44], our review noted 86 mo to be the longest survival time[10]. Aldossary *et al*[10] reported a 62-year-old female patient who complained of severe intermittent right upper quadrant pain of 2 mo duration. Laboratory investigations were normal, and ultrasound suggested a gallbladder with large stones and a non-mobile echogenic mass. A stage II (pT2, pN0, M0) moderately differentiated GBCS was noted on histology after laparoscopic cholecystectomy. The patient underwent 14 cycles of adjuvant chemotherapy. She had local recurrence at 2 years. Wide local excision of the mass with wedge resection of the liver, lymphadenectomy and partial gastrectomy was done. The patient remained disease free for 86 mo. Zhang *et al*[3] also claim that tumors smaller than 5 cm had a more prolonged survival, however we did not observe this. More data is required to confirm this, as only 28 patients detailing both the survival data and size of tumor have been reported.

***Role of tumor markers***

GBCS is not noted to have association with any tumor markers. Consistent with the current literature, most of the patients did not note any raised tumor markers[5]. However, it is still common practice for physicians to perform tumor marker levels such as CA19-9, carcinoembryonic antigen and alpha-fetoprotein when considering possible differentials for masses in the gallbladder as well as for prognostication. For instance, Hayashi *et al*[100] propose that alpha-fetoprotein-producing carcinomas of the gallbladder are more likely to metastasize to the liver and have poor prognosis. CA19-9 is typically associated with pancreatobiliary malignancies but has a limited role in clinical practice[101]. Thus, prognostication is relied typically on histological features, pathologic stage as well as immunohistochemistry. Immunohistochemistry for the mesenchymal and epithelial components yield positive staining for vimentin and cytokeratin[45]. Our review shows that the majority of the patients had positive staining for vimentin (81.2%) and cytokeratin (79.2%). Additionally, Ki-67 was suggested by Kubota *et al*[45] to have prognostic value, whereby its presence signifies a possibly higher malignant proliferative potential for GBCS. However, this claim needs to be further investigated as Kubota *et al*[45] examined this immunohistochemical marker in only 1 patient with CSGB.

***Comparison to gallbladder adenocarcinoma***

There is substantial overlap of risk factors, diagnosis and treatment of GBCS with gallbladder adenocarcinoma. Thus, the majority of authors extrapolate the clinical characteristics of gallbladder adenocarcinoma to determine the best approach to diagnosis and management of GBCS. From this review, we can determine three key differences between GBCS and gallbladder adenocarcinoma. First, tumor markers have limited utility in patients with GBCS. In a study of 55 cases by Shukla *et al*[102], it is noted that the combination of CA-125 and CA19-9 helped detect gallbladder malignancy in patients with gallstones (80.7%). Second, the prognosis of GBCS may be marginally better compared to carcinoma of the gallbladder. In the meta-analysis by Zhang *et al*[3], it was noted that the survival rate was slightly better (16% ± 5% 5-year survival) compared to carcinoma of the gallbladder (0-10% 5-year survival). Thus, the identification of GBCS will be useful to determine the prognosis for patients albeit with only a small variation between the two. Third, immunohistochemistry markers like vimentin and cytokeratin are associated with diagnosis of GBCS.

**CONCLUSION**

In conclusion, GBCS is more common in females. Gallstones and chronic cholecystitis are risk factors for GBCS. Serum biochemistry and tumor markers have a limited role in diagnosis. Typical imaging modalities can assist to establish a diagnosis in patients with suspicious gallbladder lesions. Multiple imaging modalities are complementary. Multidisciplinary oncology board discussions are essential to guide management plans. Surgery is currently the only curative option for GBCS, and size of the tumor does not impact prognosis. While most features of GBCS parallel that of carcinomas of the gallbladder clinically, identification of GBCS specifically allows clinicians to determine overall prognosis. Due to paucity of reported cases, more evidence is required before meaningful and valid evidence-based patient-centric recommendations can be made. This review serves to educate and raise awareness among the clinicians dealing with gallbladder malignancies. It is likely that there are more clinical differences between GBCS and common forms of gallbladder cancer; active reporting of cases will help enhance understanding of this rare cancer.

**ARTICLE HIGHLIGHTS**

***Research background***

Literature on gallbladder carcinosarcoma (GBCS) is currently scarce, with less than 100 cases reported since the first case by Karl Lansteiner.

***Research motivation***

While there has been efforts by Zhang *et al* in 2008 to consolidate the literature, there has not been a review of the current literature since.

***Research objectives***

This study aims to fill this gap by providing a comprehensive overview of GBCS.

***Research methods***

A literature review was performed on the PubMed database using the keywords “Gallbladder” AND “Carcinosarcoma” from 1970 to 2021, where relevant articles were included. Animal studies, gallbladder carcinoma and non-gallbladder pathology as well as articles that were not in English or Japanese were excluded.

***Research results***

GBCS is more common in females. Gallstones and chronic cholecystitis are risk factors for GBCS. Serum biochemistry and tumor markers a have limited role in diagnosis. Typical imaging modalities can assist to establish a diagnosis in patients with suspicious gallbladder lesions. Multiple imaging modalities are complementary. Multidisciplinary oncology board discussions are essential to guide management plans. Surgery is currently the only curative option for GBCS, and size of the tumor does not impact prognosis.

***Research conclusions***

While most features of GBCS parallel that of carcinomas of the gallbladder clinically, identification of GBCS specifically allows clinicians to determine overall prognosis. Due to paucity of reported cases, more evidence is required before meaningful and valid evidence-based patient-centric recommendations can be made.

***Research perspectives***

Due to the paucity of the number of reported cases, more active reporting of such should be encouraged to further understand this malignancy.

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**Footnotes**

**Conflict-of-interest statement:** There is no conflict of interest to declare.

**PRISMA 2009 Checklist statement:** The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** March 14, 2021

**First decision:** May 4, 2021

**Article in press:**

**Specialty type:** Surgery

**Country/Territory of origin:** Singapore

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Ruess DA **S-Editor:** Gong ZM **L-Editor:** Filipodia **P-Editor:** Gong ZM

**Figure Legends**

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**Figure 1 Paucity of gallbladder carcinosarcoma reports and trends by decade.**



**Figure 2 PRISMA diagram of articles searched on gallbladder carcinosarcoma.** GB: Gallbladder.

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**Figure 3 Kaplan-Meier survival curve measuring the difference in survival between patients with gallbladder carcinosarcoma of less than 5 cm diameter and more than 5 cm diameter (*P* = 0.301).**

**Table 1 Summary of 76 reported cases of gallbladder carcinosarcoma from 1970 to 2021**

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| **No.**  | **Year**  | **Ref.** | **Age/sex** | **Risk factors for GB CA (stones)** | **Clinical presentation** | **Liver function tests** | **Position of CA** | **Tumor markers (CEA, AFP, CA 19-9)** | **Size (mm)** | **Initial diagnosis** | **Confirmatory diagnosis (mode)** | **Stage (UICC)** | **Survival (mo)**  | **IHC positives** | **Further management** |
| 1 | 2020 | Khurram *et al*[4] | 64/F | No stones  | RUQ pain, intermittent fever, abdominal distension | AST, GGT elevated | Fundus | Normal | 132 × 97 × 110  | Hepatic abscess | Cholecystectomy  | NA | NIL mentioned | CK  | NA |
| 2 | 2020 | Ayoub *et al*[5] | 66/M | NA | RUQ pain | Normal | Body  | Normal | 150 × 80 × 60 | Gallbladder malignancy | Cholecystectomy and lymphadenectomy  | IVA | 12+ | Vimentin, CK | NA |
| 3 | 2020 | Kaneko *et al*[6] | 70/F | NA | Obstructive jaundice | NA | NA | Normal | 110 × 70 × 34 | Gallbladder malignancy | Cholecystectomy  | NA | 44+ | CK, Ki-67 | NA |
| 4 | 2020 | Siddiqui *et al*[7] | 57/M | NA | Abdominal pain, nausea, LOW, LOA | ALP, total bilirubin elevated | Fundus | NA | 620 | Gallbladder malignancy | ERCP (unsuccessful), PTC with internal-external biliary drainage catheter | NA | NA | Vimentin | NA |
| 5 | 2020 | Mochizuki *et al*[8] | 88/F | Gallstones | Chills, tremors, vomiting | NA | Body | NA | 60 × 25  | Acute cholecystitis | Cholecystectomy  | NA | 10 +  | Ki-67 | NA |
| 6 | 2019 | Varshney *et al*[9] | 50/M | Gallstones | RUQ pain, obstructive jaundice | AST, ALT, bilirubin elevated | Fundus | Normal | 65 × 55  | Gallbladder malignancy | radical cholecystectomy with standard lymphadenectomy | NA | 6+  | Vimentin, CK | Adjuvant chemotherapy |
| 7 | 2019 | Aldossary *et al*[10] | 40/M | Gallstones | RUQ pain | Normal | Entire gallbladder | Normal | 115 × 92 × 50 | Gallbladder malignancy | Open lap, radical cholecystectomy, extended R hemi w IC anastomosis, liver resection | IVB | 6 | Vimentin | Adjuvant chemotherapy |
| 8 | 2019 | Aldossary *et al*[10] | 52/F | No stones | RUQ pain | ALT, AST elevated | Fundus | CA19-9 level of 154.3 IU/mL, with normal levels of AFP and CEA | 136 × 120 × 95 | Gallbladder Malignancy | Open lap, radical CCY, transverse chole, Roux en Y + distal gastrectomy | IVB | 3 | Vimentin, CK | NA |
| 9 | 2019 | Aldossary *et al*[10] | 62/F | Gallstones | RUQ pain, nausea, anorexia | Normal | Body  | Normal | 27 × 9 | Gallbladder malignancy | Lap CCY | II | 86+ | Vimentin, CK | Adjuvant chemotherapy |
| 10 | 2019 | Alratroot *et al*[11] | 52/F | Xanthogranulomatous cholecystitis | RUQ pain | GGT elevated | Fundus | CA 19-9 154.33 IU/mL | 110 × 60 | Gallbladder malignancy | Laparotomy with radical cholecystectomy, transverse colectomy, distal gastrectomy, omentectomy and liver bed resection | III | 1.5+ | Vimentin, CK | Adjuvant chemotherapy |
| 11 | 2019 | Matsubayashi *et al*[12] | 72/F | Pancreaticobiliary maljunction | RUQ pain | ALP, GGT elevated | Entire gallbladder | Normal | 90 × 85  | Gallbladder malignancy | Laparotomy and extended cholecystectomy  | IIIA | 73+ | Vimentin, CK | NA |
| 12 | 2018 | Doniparthi *et al*[13] | 49/M | NA | Epigastric pain | AST, ALT, lipase elevated | NA | Normal | 32 | Acute cholecystitis | Lap cholecystectomy, followed up by robotic liver resection and lymphadenectomy | NA | NA | NA | NA |
| 13 | 2018 | Koustav *et al*[14] | 40/F | NA | RUQ pain |  | NA | CA19-9 elevated | 43 × 51 | Gallbladder malignancy | Staging laparoscopy + extended cholecystectomy | NA | NA | NA | NA |
| 14 | 2018 | Trautman *et al*[15] | 73/F | Chronic cholecystitis | Abdominal distension, constipation, vomiting, LOW | AST, ALT, ALP elevated | NA | Beta-HCG elevated |  | Gallbladder malignancy | Diagnostic laparoscopy  | NA | 0.5 | Vimentin | Palliative (NM) |
| 15 | 2017 | Furuya *et al*[16] | 61/F | NA | RUQ pain | Normal | NA | Normal | 15 × 15 | Chronic cholecystitis with stone | Cholecystectomy  | NA | NA | NA | NA |
| 16 | 2016 | Hu *et al*[17] | 68/F | Cholelithiasis  | RUQ pain, fever | Normal | Body | CA19-9 elevated | 16 × 15 × 13  | Gallbladder malignancy | Cholecystectomy  | NA | 1 | NA | NA |
| 17 | 2016 | Cruz *et al*[18] | 52/F | Gallstones | RUQ pain | ALT AST elevated | Entire gallbladder | Normal | 170 × 125 | Gallbladder malignancy | Cholecystectomy  | NA | 1 | Vimentin, CK | Palliative (NM) |
| 18 | 2016 | Dong *et al*[19] | 61/M | NA | Abdominal distension | NA | NA | Normal | 180 | Gallbladder malignancy | Resection (not specified)  | NA | NIL mentioned | Ki-67 | NA |
| 19 | 2016 | Gupta *et al*[20] | 46/F | NA | RUQ pain | NA | Fundus | All normal | 350 × 250 × 200 | Gallbladder malignancy | Radical cholecystectomy with hepato-duodenal ligament lymph node clearance and segment 4b/5 liver resection | NA | 15 (still alive) | Vimentin, CK | Adjuvant chemotherapy |
| 20 | 2016 | Wong *et al*[21] | 52/F | NA | Abdominal pain | NA | Entire gallbladder | CA19-9 elevated | 75 | NA | Autopsy | III | 6 | Vimentin, CK | Adjuvant chemotherapy |
| 21 | 2016 | Ansari *et al*[22] | 50/F | NA | RUQ pain | Normal | Entire gallbladder | Normal |  50 × 40 | NA | Radical cholecystectomy | II | 13 mo (still alive) | Vimentin, CK, Ki-67 | Adjuvant chemotherapy |
| 22 | 2015 | Gao *et al*[23] | 62/M | Chronic cholecystitis | RUQ pain | Normal | Entire gallbladder | Normal |  50 × 40 | Gallbladder malignancy | Simple cholecystectomy  | II | 0 | Vimentin, CK | NA |
| 23 | 2015 | Tonouchi *et al*[24] | 87/M | No stones | Abdominal pain | NA | NA | NA | 60 × 55  | Diffuse peritonitis  | Cholecystectomy with partial transverse colectomy around the fistula | NA | Lost to follow-up | Vimentin, CK | NA |
| 24 | 2015 | Faujdar *et al*[25] | 60/F | NA | RUQ pain, fever | Normal | Entire gallbladder |  | 120 ×70 × 60 | Gallbladder malignancy | Cholecystectomy | NA | 60+ | Vimentin, CK | NA |
| 25 | 2014 | Wada *et al*[26] | 68/M | NA | Right flank pain | GGT elevated | NA | Normal | 85 × 70 | Gallbladder malignancy | Extended right hepatectomy with portal thrombectomy with hepatoduodenal ligament lymphadenectomy | NA | 51+ | Vimentin, CK, Ki-67 | Adjuvant chemotherapy |
| 26 | 2014 | Kishino *et al*[27] | 70s/F | NA | Referred for suspected GB cancer (presenting complaint not mentioned) | NA | Fundus | NA | 68 | Gallbladder malignancy | Cholecystectomy  | NA | 1.5+ | Vimentin, CK | NA |
| 27 | 2013 | Wang *et al*[28] | 68/F | Chronic cholecystitis, cholecystolithiasis | RUQ pain, jaundice, fever  | ALT, ALP elevated | NA | CEA, CA19-9, AFP elevated | 100 × 70 × 50  | Gallbladder malignancy | Cholecystectomy with liver segmentectomy (S4a+S5) and a lymph node dissection, followed by resection of the extrahepatic bile duct and a Roux-en-Y type hepatic cholangiojejunostomy  | NA | 6+ | Vimentin, CK | NA |
| 28 | 2013 | Khanna[29]  | 45/F | NA | RUQ pain | Normal | Body |  | 60 × 40 | Gallbladder malignancy | Laparotomy and simple cholecystectomy with wedge resection  | NA | 3 | Vimentin, CK, Ki-67 | NA |
| 29 | 2013 | Li *et al*[30] | 64/M | Chronic cholecystitis  | RUQ pain | NA | NA | CEA, CA19-9 elevated | 40 × 30 × 30  | NA | Cholecystectomy, R hemicolectomy, resection of multiple hepatic metastases | NA | 3+ | Vimentin, CK, Ki-67 | NA |
| 30 | 2012 | Kim *et al*[31] | 72/F | Gallstones | Abdominal pain | Normal | Fundus | Normal | 65 × 45 × 45 | Gallbladder malignancy | Radical cholecystectomy with wedge resection of liver combined with hepatoduodenal ligament lymphadenectomy | NA | 4 | NA | Adjuvant chemotherapy |
| 31 | 2012 | Kim *et al*[31] | 81/M | NA | Epigastric pain | Normal | Fundus | Normal |  | Gallbladder malignancy | Cholecystectomy with liver segmentectomy (S4a,5) and lymph node dissection | NA | 13 | Vimentin, CK | NA |
| 32 | 2012 | Sadamori *et al*[32] | 80/M | NA | RUQ pain, fever |  | Entire gallbladder |  | 76 × 27 | Gallbladder malignancy | Cholecystectomy with liver segmentectomy (S4a and S5) and lymph node dissection | NA | 2+ |  | Adjuvant chemotherapy |
| 33 | 2012 | Kataria *et al*[33] | 55/F | NA | RUQ pain | Normal | Fundus | Normal | 70 × 50 × 30 | NA | Cholecystectomy, wedge resection of liver with resection of transverse colon and paraduodenal lymph node | NA | 6 | Vimentin, CK | NA |
| 34 | 2012 | Parreira *et al*[34] | 59/F | NA | RUQ pain | Normal | NA | NA | NA | NA | Conventional cholecystectomy  | NA | 2 | NA | NA |
| 35 | 2012 | Park *et al*[35] | 77/F | NA | RUQ pain | AST, ALT elevated | NA | CA19-9, CA-125 elevated | 78 × 55 × 12 | Gallbladder malignancy | Laparotomy, followed by cholecystectomy and lymph node dissection | IIIB | 10+ | NA | NA |
| 36 | 2012 | Ishida *et al*[36] | 62/F | NA | Incidental finding on radiograph for left calcaneal fracture  | Normal | Entire gallbladder | Normal | 52 × 38 | Gallbladder malignancy | Open cholecystectomy  | NA | 8 | NA | NA |
| 37 | 2011 | Lee *et al*[37] | 77/F | No stones | RUQ pain | Not mentioned | Body | CA19-9, CA-125 elevated | 80 × 70 × 30 | Gallbladder malignancy | Cholecystectomy  | NA | 1.5+ | Vimentin, CK | NA |
| 38 | 2011 | Pu *et al*[38] | 59/F | Cholecystolithiasis  | RUQ pain, fever | Normal | Body | CA19-9 elevated | 120 × 25 × 60 | Gallbladder malignancy | Exploratory laparotomy, followed by radical LN resection and hepatocholangojejunostomy Roux-En-Y  | II | 0 | CK | Adjuvant chemotherapy |
| 39 | 2011 | Krishnamurthy *et al*[39] | 83/M | No stones | Abdominal pain | NA | NA | NA | NA | NA | Laparoscopic cholecystectomy  | NA | 48+ | Vimentin, CK | NA |
| 40 | 2009 | Kohtani *et al*[40] | 84/M | Chronic cholecystitis | RUQ pain | Serum glutamic oxaloacetic transaminase, GGT elevated  | Neck | NA |  | Gallbladder malignancy | Open cholecystectomy  | II | 3+ | Vimentin, CK, Ki-67 | Adjuvant chemotherapy |
| 41 | 2009 | Agarwal *et al*[41] | 60/F | NA | RUQ pain, fever | Normal | Neck | NA | 70 × 50 × 40 | Gallbladder malignancy | Staging laparoscopy, laparotomy, simplex cholecystectomy | NA | 24+ | Vimentin, CK | NA |
| 42 | 2009 | Magata *et al*[42] | 78/F | NA | RUQ pain | NA | Body | CEA elevated | 115 x 40 x 35 | Gallbladder malignancy | Whole-layer cholecystectomy with regional lymph node dissection | NA | 6+ | Vimentin, CK | NA |
| 43 | 2009 | Shimada *et al*[43] | 69/M | Choledocholithiasis | Fever | Normal | Entire gallbladder | AFP elevated | 90 × 50 | Gallbladder malignancy | Laparotomy, cholecystectomy, lymph node dissection | NA | 54+ | Vimentin, CK, Ki-67 | NA |
| 44 | 2009 | Uzun *et al*[44] | 70/M | NA | RUQ pain | Normal | Fundus  | Normal | 100 × 60 × 30 | Gallbladder malignancy | Radical cholecystectomy, wedge resection of liver-gallbladder bed with hepatoduodenal ligament lymphadenectomy | NA | 8 | CK, Ki-67 | NA |
| 45 | 2006 | Kubota *et al*[45] | 72/M | NA | RUQ pain, fever | AST, ALT, ALP elevated | NA | Normal | 70 × 55 × 40 | Gallbladder malignancy | En bloc resection of the gallbladder and segments 4a and 5 of the liver, partial colectomy, and lymph node dissection | NA | 6 | NA | NA |
| 46 | 2005 | Akatsu *et al*[46] | 76/F | Gallstones | Incidental finding on follow-up for cholelithiasis | Normal | NA | Normal |  | Gallbladder malignancy | Extended cholecystectomy, liver 4b and 5 resection | NA | 2 | Vimentin, CK | NA |
| 47 | 2005 | Huguet *et al*[47] | 64/F | Cholecystitis  | RUQ pain, fever | Normal | Entire gallbladder | Normal | 120 × 100 × 70 | Gallbladder malignancy | A cholecystectomy with wedge resection of the gallbladder fossa (involving liver segments 4 and 5), extrahepatic bile duct excision, non–pylorus-preserving pancreaticoduodenectomy with excision of 15 cm of proximal jejunum, and right hemicolectomy | NA | 60 | Vimentin, CK | NA |
| 48 | 2005 | Sodergren *et al*[48] | 64/F | NA | Malaise and LOA | ALP Elevated | NA | NA | 20 × 12 × 12 | NA | Extrahepatic radical bile duct resection with hepatic and coeliac lymph node clearance followed by right hepaticodochojejunostomy to a jejunal Roux loop | NA | 5 | Vimentin, CK | NA |
| 49 | 2005 | Sodergren *et al*[48] | 60/F | NA | Painless jaundice | NA | NA | NA | 90 | Gallbladder malignancy | Cholecystectomy and extrahepatic bile duct resection with lymph node clearance | NA | 2 | Vimentin, CK | Palliative (NM) |
| 50 | 2004 | Takahashi *et al*[49] | 84/F | NA | RUQ pain | NA | Body | CEA, CA19-9 elevated | 84 × 40 × 30 | Gallbladder malignancy | Cholecystectomy and transverse colon partial colectomy  | NA | 2 | Vimentin, CK |  |
| 51 | 2003 | Kim *et al*[50] | 61/F | No stones | RUQ pain | Normal | Neck | Normal | 45 × 40 × 40 | Gallbladder malignancy | Cholecystectomy with common bile duct resection | NA | 2 | Vimentin | Palliative (NM) |
| 52 | 2002 | Al-Sheneber *et al*[1] | 68/F | Acute cholecystitis, gallstones | RUQ pain | Normal | NA | CEA elevated | 148 × 80  | Gallbladder malignancy | CT guided needle biopsy of the upper abdominal mass | NA | 7 | Vimentin, CK | NA |
| 53 | 2002 | Hotta *et al*[51] | 53/M | Chronic cholecystitis, gallstones | RUQ Pain | Normal | NA | Normal | 1100 | Gallbladder malignancy | Cholecystectomy with resection of subsegmentectomy of liver S5 and a resection of transverse colon at the second operation | II  | 2 | NA | Adjuvant chemotherapy |
| 54 | 2002 | Ajiki *et al*[52] | 69/F | Gallstones, left renal tumor | Epigastric pain | Normal | NA | CA19-9 elevated | NA | Double cancers of the left kidney and gallbladder | left renal excision, cholecystectomy with liver segmentectomy (S4a, S5), and lymph node dissection | NA | NA | NA | Adjuvant chemotherapy |
| 55 | 2000 | Yavuz *et al*[53] | 50/F | NA | RUQ pain | NA | Body | NA | 80 × 60 × 60 |  | Exploratory laparotomy -> cholecystectomy, liver wedge biopsy | NA | NA | NA | NA |
| 56 | 1999 | Eriguchi *et al*[54] | 65/F | Gallstones | RUQ pain | Normal | Entire gallbladder | NA |  | Gallbladder malignancy | Cholecystectomy | I | 16+ | NA | NA |
| 57 | 1997 | Ryś *et al*[55] | 67/F | Gallstones | Abdominal pain, LOW | NA | Fundus | NA | 10 × 15 | Gallbladder malignancy | Hemicolectomy and cholecystectomy  | NA | 2 | Vimentin | NA |
| 58 | 1996 | Nakagawa *et al*[56] | 60/F | NA | Abdominal pain, fever | Normal | Body | NA | 70 × 40 | Gallbladder malignancy | Mass reduction surgery  | NA | NA | NA | NA |
| 59 | 1994 | Fagot *et al*[57] | 83/F | Gallstones | Vomiting, fever, right RHC pain | Total bilirubin elevated | Fundus | NA | 45 | NA | Surgery (not defined) | NA | 12+ | NA | NA |
| 60 | 1992 | Nakazawa *et al*[58] | 63/F | NA | Nausea | Normal | Body | Normal | 30 × 30 | Gallbladder malignancy | Pancreaticoduodenectomy  | NA | NA | NA | NA |
| 61 | 1990 | Ishihara *et al*[59] | 58/F | NA | Abdominal pain | NA | Fundus | NA | 50 × 80 | Gallbladder malignancy | Cholecystectomy | NA | 11+ | Vimentin | NA |
| 62 | 1988 | Lumsden *et al*[60] | 81/F | Gallstones | RUQ pain, LOW, LOA | Total bilirubin, ALP, GOT elevated | NA | NA | 50 × 20 × 20 | Biliary neoplasm  | Cholecystectomy | NA | 12+ | NA | NA |
| 63 | 1987 | Hasegawa *et al*[61] | 61/M | NA | RUQ pain | Normal | Entire gallbladder | NA | 150 | Gallbladder malignancy | Resection (not specified)  | NA | 6 | NA | NA |
| 64 | 1987 | Herrera-Goepfert *et al*[62] | 60/F | Gallstones | Abdominal pain, jaundice, LOW |  | Entire gallbladder | NA | 70 × 40 | Gallbladder malignancy | Autopsy | NA | NA | NA | NA |
| 65 | 1986 | inoshita *et al*[63] | 53/M | Gallstones | RUQ pain, jaundice | Total bilirubin, ALP, GOT, GPT elevated | Neck | NA | NA | Choledocholithiasis | Open laparotomy | NA | 17 | NA | NA |
| 66 | 1985 | Lopez *et al*[64] | 78/F | No stones | Anorexia, LOW | Normal | NA | NA | NA | Gallbladder empyema | Open laparotomy | NA | NA | NA | NA |
| 67 | 1984 | Born *et al*[65] | 90/F | Gallstones | Anorexia, nausea, vomiting | Amylase elevated | NA | NA | 150 × 150 × 10 | NA | Exploratory laparotomy | NA | 3 | NA | NA |
| 68 | 1982 | von Kuster *et al*[66] | 91/F | Gallstones | RUQ pain, fever | GOT, ALP elevated | NA | NA | 20 | Gallbladder empyema | Exploratory laparotomy | NA | 0 | NA | NA |
| 69 |  |  | 77/F | NA | Bleeding in GI tract (lower) | Normal | NA | NA | 30 | NA | Exploratory laparotomy | III | 31+ | NA | NA |
| 70 | 1982 | Aldovini *et al*[67] | 75/F | Gallstones | Abdominal pain | ALP, SGT elevated | NA | NA | 90 | NA | Cholecystectomy | NA | 8+ | NA | NA |
| 71 | 1982 | Yamagiwa *et al*[68] | 78/F | NA | RUQ pain | NA | NA | NA | NA | NA | NA | NA |  | NA | NA |
| 72 | 1980 | Mansori *et al*[69] | 81/M | Gallstones | Abdominal pain | GOT, ALP elevated | NA | NA | NA | NA | Exploratory laparotomy | NA | 0.5 | NA | NA |
| 73 | 1973 | Higgs *et al*[70] | 77/M | Gallstones | Jaundice | ALP, GOT elevated | NA | NA | NA | NA | Cholecystectomy and CBDE | NA | 1 | NA | NA |
| 74 | 1971 | Mehrotra *et al*[71] | 45/F | Gallstones | RUQ pain | Normal | Neck | NA | 50 × 40 × 30 | NA | Open laparotomy | NA | 4 | NA | NA |
| 75 | 1970 | Appelman *et al*[72] | 91/M | Gallstones, chronic cholecystitis | Obstructive jaundice | AST, ALT, ALP elevated | Fundus | NA | NA | Pancreatic cancer | Autopsy | NA | 0.5 | NA | NA |
| 76 | 1970 | Appelman *et al*[72] | 75/F | Gallstones, chronic cholecystitis | RUQ pain | ALP elevated | Fundus | NA | 50 × 50 × 20 | NA | Cholecystectomy | NA | 1 | NA | NA |

GBCA: Gallbladder cancer; CEA: Carcinoembryonic antigen; AFP: Alpha-fetoprotein; CA 19-9: Carbohydrate antigen 19-9; UICC: Union for International Cancer Control; IHC: Immunohistochemistry; RUQ: Right upper quadrant; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; ERCP: Endoscopic retrograde cholangiopancreatography; PTC: Percutaneous transhepatic cholangiogram; CCY: Cholecystectomy; NA: Not available; NM: Not mentioned; NIL: None; CR: Complete response; LOA: Loss of appetite; LOW: Loss of weight; R hemi w C: Right hemihepatectomy with cholecystectomy; M: Male; F: Female; Lap: Laparoscopic; Chole: Cholecystectomy; LN: Lymph node; CT: Computerized tomography; RH: Right hepatectomy; GI: Gastrointestinal; CBDE: Common bile duct exploration; HCG: Human chorionic gonadotropin; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase.