

Treatment outcomes for gallbladder carcinoma at Viet Duc University Hospital from 2015 to 2022

Tran Dinh Tho, Nguyen Hai Nam, Nguyen Thi Lan, Nguyen Thu Ha, Chu Minh Phuc

Viet Duc University Hospital

Corresponding author:

Chu Minh Phuc
Viet Duc University Hospital
40 Trang Thi, Hoan Kiem, Hanoi,
Vietnam
Mobile: +84 338 151 294
Email: phucchuminh@gmail.com

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Abstract

Introduction: Gallbladder carcinoma (GBC) is a rare but aggressive tumor. Operability is crucial for survival, yet late-stage diagnosis is common due to its asymptomatic nature. This study evaluates the clinical features and surgical outcomes of GBC treatment.

Patients and Methods: A retrospective study was conducted on GBC patients who underwent surgery at Viet Duc University Hospital (2015–2022). Inoperable cases and those with incomplete records were excluded. Clinical characteristics, surgical details, and outcomes were analyzed.

Results: Among 41 patients, most were diagnosed at advanced stages, with T3 being the most common stage (51.2%). Open surgery (51.2%) was slightly more frequent than laparoscopic procedures. Cholecystectomy alone was performed in 31.7%, while others required hepatectomy or lymphadenectomy. The average hospital stay was 8 ± 3.5 days, with complications occurring in 3 cases and one postoperative death. Mid-term survival was poor, with 31.7% surviving less than six months and 29.3% living for 1–3 years.

Conclusions: GBC is often diagnosed late, limiting surgical success and survival. Despite surgical resection, prognosis remains poor, highlighting the need for earlier detection and improved treatment strategies.

Abbreviations: GBC: Gallbladder carcinoma, CT: Computed tomography, MRI: Magnetic resonance imaging, CA 19-9: Carbohydrate antigen 19-9, CEA: Carcinoembryonic antigen

Keywords: Gallbladder cancer, surgical treatment, mid-term survival

Introduction

Gallbladder carcinoma (GBC) is a rare cancer of the biliary system, with an incidence of 0.33/100000 men and 0.43/100000 women in Vietnam [1]. However, it is an aggressive malignancy, with a poor prognosis due to late diagnosis and limited treatment options. Despite its low prevalence, GBC is highly lethal, as early-stage disease is often asymptomatic [2], [3]. Surgery remains the only curative option, but recurrence rates are high. GBC incidence varies globally, with the highest rates in South America, Japan, and Northern India. In Vietnam, precise epidemiological data are limited, but hospital-based registries suggest an increasing trend [1], [3–5]. Risk factors include gallstone disease (70–90% of cases), chronic inflammation, obesity, and infections like *Salmonella typhi*. Genetic predisposition and environmental factors may also contribute [4].

Early-stage GBC is often asymptomatic or presents with mild abdominal discomfort. Advanced disease manifests with jaundice, weight loss, and a palpable mass. Diagnosis relies on imaging and biomarkers. Ultrasonography, CT and MRI assess tumor invasion and metastasis, while CA 19-9 and CEA serve as tumor markers. Histopathological examination following cholecystectomy remains the gold standard [3], [6], [7].

Treatment depends on the disease stage. For early-stage tumors, radical cholecystectomy with lymphadenectomy and possible liver resection is the preferred approach [8]. Many patients present with advanced disease, requiring palliative chemotherapy, with gemcitabine-cisplatin regimens offering modest survival benefits. Radiation therapy is selectively used in certain patients [3]. Targeted therapies and immunotherapy are emerging treatment options [9].

GBC management in Vietnam faces challenges such as late-stage presentation, limited access to advanced diagnostics, and a lack of standardized treatment protocols. Radical surgery has significant risks, including bile leaks and liver failure. Recurrence rates remain high, necessitating

effective adjuvant strategies. Multimodal approaches combining surgery, chemotherapy, and radiotherapy are under investigation as potential strategies to improve the outcomes [4], [5].

Given GBC's aggressive nature, evaluating treatment outcomes at high-volume centers is crucial. Viet Duc University Hospital offers comprehensive care for hepatobiliary cancer. This study analyzes treatment outcomes from 2015 to 2022, focusing on patient demographics, clinical characteristics, diagnostic approaches, staging, surgical outcomes, complications, and survival rates. Identifying prognostic factors that influence patient outcomes will help improve treatment strategies and optimize patient care.

Patients and Method

Objects

Our research included patients diagnosed with gallbladder carcinoma who underwent surgery at the Department of Hepato-biliary and Pancreatic Surgery, Viet Duc University Hospital from January 2015 to December 2022.

All patients who were surgically treated for gallbladder carcinoma, with a definitive diagnosis confirmed through post-operative pathological examination were included.

Exclusion criteria included patients who met the selection criteria but were not included in the study due to confounding factors that distorted the results, as well as patients who refused to participate and those without sufficient information in their clinical record.

Method

This is a descriptive, retrospective study, with patients being selected by convenience sampling. All medical records of patients meeting the inclusion criteria, within the research period are collected. Data analyses were conducted in R (R version 4.4.2, <https://www.r-project.org>).

Research variables

Research variables include:

Clinical and paraclinical characteristics of patients, including age, gender, medical history,

clinical symptoms, laboratory tests, imaging manifestation, and pre-operative diagnosis.

Operative treatment (open or laparoscopic surgery, operative method, intra-operative events and complications) and post-operative diagnosis of stage.

Short-term post-operative result (duration of hospital stay, early result and complications) and mid-term post-operative survival.

Results

Clinical, imaging and laboratory characteristics

Table 1: Clinical, imaging and laboratory characteristics (N = 41)

Characteristics	Number (N)	Percentage (%)
Gender		
Male	15	36.6
Female	26	63.4
Age	63.5 ± 12.7 (34 – 87 years old)	
Medical history		
Gallbladder abnormalities	6	14.6
Biliary diseases	3	7.3
Other unrelated diseases / no significant medical history	32	78.1
Clinical symptoms		
Abdominal pain	32	78.1
Jaundice	3	7.3
Other (fever, weight loss, palpable mass...)	8	19.5
Asymptomatic	5	12.2
Laboratory tests		
Total bilirubin > 19 µmol/L	11	26.8
CA 19-9 > 37 U/L	25	61.0
CEA > 5 ng/mL	20	48.7

Imaging		
Computed tomography		
Gallstone(s)	8	19.5
Cholecystitis	16	39.0
Tumor(s)	25	61.0
Liver invasion	11	26.8
Enlarged lymph node(s)	16	39.0
Invasion to other organ(s)	3	7.3
Magnetic resonance imaging		
Gallstone(s)	5	12.2
Cholecystitis	3	7.3
Tumor(s)	7	17.1
Liver invasion	3	7.3
Enlarged lymph node(s)	4	9.8
Invasion to other organ(s)	2	4.9
Pre-operative diagnosis		
Gallbladder cancer	21	51.3
Other gallbladder diseases	20	48.7

From January 2015 to December 2022, we were able to collect information on 41 patients who met the inclusion criteria. The average age of the patients was 63.5, with the majority falling within the 50 to 70 age group (58.2%). There were 15 males (36.6%) and 26 females (63.4%). Most patients did not have any prior biliary disease, and only 9 (22.0%) patients had a history of biliary system related-condition.

Regarding pre-operative symptoms, right-upper quadrant abdominal pain was the most common symptom, with 30 patients (73.2%), followed by fever (12.2%) and jaundice (7.3%). 5 patients (12.2%) were asymptomatic.

Among 41 patients, 26.8% showed increased total bilirubin levels. Tumor markers,

including carbohydrate antigen (CA 19-9) and carcinoembryonic antigen (CEA) were also significant, with CA 19-9 being elevated in 61.0% of patients and CEA in 48.8%. Imaging findings revealed that gallstones were present in 31.7% of patients based on ultrasound, 19.5% on computed tomography (CT) scan, and 12.2% on magnetic resonance imaging (MRI). Cholecystitis was detected in 39.0% by CT, and 7.3% by MRI. Tumors were identified in 61.0% by CT, and 17.1% by MRI. Liver invasion was noted in 24.4% by ultrasound, 26.8% by CT, and only 7.3% by MRI. Dilated common bile ducts (defined as common bile duct diameter of more than 7mm in patients with gallbladder [10]) were found in 29.3% on CT, and 9.8% on MRI. Enlarged lymph nodes (defined as length of the short axis diameter of more than 10mm [11]) were present 39.0% on CT, and 9.8% on MRI. More advanced disease findings included invasion into other organs, observed in 7.3% of patients through CT and 4.9% through MRI. These results highlight the role of imaging in diagnosing gallbladder carcinoma and assessing tumor spread, with CT scans detecting a higher percentage of malignancies compared to MRI.

Operative treatment

Table 2: Operative treatment of the studied group (N = 41)

Characteristics	Number (N)	Percentage (%)
Surgical modalities		
Laparoscopic	20	48.7
Open	21	51.3
Intra-operative findings		
Dilated common bile duct	10	24.3
Liver invasion	14	34.1
Enlarged lymph nodes	13	31.7
Another organ invasion	5	12.2

Surgical method		
Cholecystectomy only	13	31.7
Cholecystectomy + common bile duct exploration	3	7.3
Cholecystectomy + hepatectomy	9	21.9
Cholecystectomy + hepatectomy + lymphadenectomy	5	12.2
Cholecystectomy + lymphadenectomy	4	9.8
Cholecystectomy + another organ resection	5	12.2
Cholecystectomy + gastrojejunostomy	2	4.9
Intraoperative complications		
Perforated duodenum	2	4.9
Perforated hepatic flexure	1	2.4
Common bile duct injury	1	2.4
Operative time		
Laparoscopic	81 ± 25 (40 – 140) minutes	
Open	149 ± 21 (80 – 300) minutes	

Among the 41 cases analyzed, 20 patients (48.8%) underwent laparoscopic surgery, while 21 patients (51.2%) had open surgery, indicating a slight preference for open procedures, likely due to the complexity of the disease. The most common surgical approach was simple cholecystectomy, performed in 13 cases (31.7%). More advanced procedures included cholecystectomy with common bile duct exploration in 3 cases (7.3%) and cholecystectomy with hepatectomy in 9 cases (22.0%). Additionally, 5 patients (12.2%) underwent cholecystectomy with both hepatectomy and lymphadenectomy, while 4 cases (9.8%) involved cholecystectomy with only lymphadenectomy. In some cases, more extensive resections were required, with 5 patients (12.2%) undergoing cholecystectomy combined with another organ resection and 2 patients (4.9%) requiring gastrojejunostomy.

Intraoperative incidents occurred in a small number of cases, with duodenal perforation observed in 2 patients (4.9%) and perforation of the hepatic flexure in 1 patient (2.4%). Additionally, 1 patient (2.4%) suffered a common bile duct injury, emphasizing the risks associated with these procedures. Operative time varied significantly between surgical approaches, with laparoscopic procedures averaging 81 ± 25 minutes (40 – 140 minutes), while open surgeries took considerably longer, with an average duration of 149 ± 21 minutes. This difference suggests that open surgeries were more complex and likely involved more extensive tissue resection. Overall, the data highlight that while laparoscopic surgery was performed in nearly half of the cases, open surgery remained the more frequent choice, likely due to the need for more aggressive tumor removal in advanced stages.

Anatomo-pathologic results and post-operative results

Table 3: Post-operative result (N = 41)

Characteristics	Number (N)	Percentage (%)
Staging		
T1	9	21.9
T2	7	17.1
T3	21	51.3
T4	4	9.8
Nx	13	31.7
N0	13	31.7
N1	15	36.6
Stage I	9	21
Stage II	6	14.6
Stage III	22	53.7
Stage IV	4	9.8

Short-term results		
Complications	3	7.3
Death	1	2.4
Duration of hospital stay	8 ± 3.5 (2 – 17 days)	
Mid-term survival		
Less than 6 months	13	31.7
6 months – 1 year	9	21.9
1 year – 3 years	12	29.3
Loss in follow-up	7	17.1

Among the 41 cases, 9 patients were classified as T1, 7 as T2, 21 as T3, and 4 as T4, indicating that most cases (51.2%) were diagnosed at an advanced T3 stage. Regarding lymph node involvement, 13 patients had no nodal metastasis (N0), while 15 had N1 involvement, suggesting that a significant number of cases had regional lymph node metastasis. We were unable to obtain data on nodal metastasis of 13 patients, probably due to variations in surgical protocols among different surgeons. We were unable to obtain reliable information on post-operative chemotherapy because some of the patients were operated on a long time ago, and their family members were unable to provide the necessary information.

Short-term outcomes show that the average hospital stay was 8 ± 3.5 days. Postoperative complications were recorded in 3 cases, and there was one death following surgery. In terms of mid-term survival, 13 patients (31.7%) survived less than six months, 9 patients (22.0%) lived between six months and one year, and 12 patients (29.3%) survived between one and three years. Additionally, 7 patients (17.1%) were lost to follow-up, limiting the analysis of long-term survival. These results highlight the aggressive nature of gallbladder carcinoma, with a high percentage of cases presenting at advanced stages and a relatively short survival duration post-surgery.

Discussion

Gallbladder carcinoma (GBC), which only accounts for 1.4% of newly diagnosed cancer in women, and 0.8% in men, is a highly aggressive malignancy [2]. It is often diagnosed at advanced stages due to its asymptomatic nature in early stage of development. This study provides a comprehensive analysis of the clinical and paraclinical characteristics of GBC, as well as surgical outcomes, based on data from 41 patients who underwent surgery at Viet Duc University Hospital between 2015 and 2022.

Demographics and clinical presentation

The average age of patients in this study was 63.5 years, with a higher prevalence among females (63.4%). This aligns with global epidemiological data indicating a higher incidence of GBC in women, potentially due to hormonal influences and a higher prevalence of gallstone disease in females [1], [2], [4], [5]. The most common presenting symptom was abdominal pain (73.2%), followed by jaundice and fever. Notably, 12.2% of patients were asymptomatic, underscoring the challenge of early detection. This is consistent with other studies in Vietnam, with the incidence of asymptomatic gallbladder cancer being 10 – 10.5% [12], [13]. Incidental asymptomatic gallbladder cancer can occur in up to 27 – 41% of all cases [14] – thus surgeons should always be vigilant when operating on high-risk patients. Chronic inflammation of the gallbladder is a well-established risk factor for GBC. Gallstones (cholelithiasis) are the most important risk factor for GBC, with gallstones larger than 3cm being a strong predictor of cancer. Porcelain gallbladder, or gallbladder calcification, is also associated with malignancy. Another risk factor is gallbladder polyps, especially adenomatous gallbladder polyps, with growing polyps and polyps larger than 1cm being at increased risk for cancer. Other risk factors include sclerosing cholangitis, congenital biliary cysts and exposure to external carcinogens. In this cohort, 31.7% of patients had gallstones, confirming a possible association with GBC development. Elevated levels of tumor markers were observed, with CA 19-9 elevated in 61.0% and CEA in 48.8% of cases. While these

markers are not specific, their elevation in a significant proportion of patients suggests their potential utility in supporting the diagnosis and monitoring of GBC. Furthermore, CA 19-9 and CEA levels are important prognostic factors, as they are predictors of metastatic disease and later stages, with CA 19-9 being a better predictor of tumor burden than CEA [6], [15].

Surgical approaches and outcomes

Surgical resection remains the primary curative approach for GBC. In this study, 51.2% of patients underwent open surgery, while 48.8% had laparoscopic procedures. The choice of surgical method was influenced by the stage of the disease and anatomical considerations. The most frequently performed procedure was cholecystectomy alone (31.7%), which was mostly indicated for patients with T1 and T2 tumors. 39.1% of the patients received cholecystectomy with or without common bile duct exploration, while only 21.9% of patients had T1 tumors. This suggests that some patients did not achieve R0 resection, thus affecting the overall outcome. A second-look strategy is recommended in the literature for patients with T2 tumors, however, at the time of surgery, due to a lack of a national-wide guideline, this was not done for the researched patients [16–18]. More extensive resections, including hepatectomy and lymphadenectomy, were performed in advanced cases. The average hospital stay was 8.0 ± 3.5 days, with postoperative complications occurring in 7.3% of patients, and one postoperative death was recorded. Cholecystectomy, with or without other concurrent procedure, performed by experienced hepato-biliary surgeons is a generally safe operation, with favorable early results [18–21]. The extent of surgical resection has been shown to impact survival outcomes. A study analyzing the impact of surgical strategies on GBC survival found that patients undergoing extended resections for T2 tumors had improved overall survival compared to those with simple cholecystectomy [8], [18]. However, the decision to pursue more extensive surgery must be balanced against the potential for increased morbidity and mortality.

In this study, laparoscopic surgery was indicated for T1 and T2 tumors, as well as some T3 tumors, if invasion to the hepatic side can be safely resected with wedge hepatectomy. The decision to perform a laparoscopic or open procedure remains controversial in the literature. In a meta-analysis in 2018, laparoscopic surgery and open surgery are comparable in terms of long-term results (44.8% vs 42.2% recurrence rate), but the laparoscopic procedure increased the risk of scar recurrence (7.1% vs 4.0%), while the open procedure has worse short-term results (longer hospital stay, more complications) [22].

Despite surgical intervention, the prognosis for GBC remains poor. In this cohort, 31.7% of patients survived less than six months postoperatively, while 29.3% survived between one and three years. These findings are consistent with existing literature, which reports a 5-year survival rate of approximately 60% for localized GBC, decreasing significantly with regional spread and distant metastasis. The late-stage presentation in many patients contributes to these poor outcomes [18], [19], [21].

The asymptomatic nature of early-stage GBC contributes to delayed diagnoses. Imaging modalities such as ultrasound, CT, and MRI are commonly used for evaluation, but their sensitivity in detecting early-stage GBC is limited. The incidental discovery of GBC during cholecystectomy for presumed benign conditions highlights the need for heightened vigilance and possibly more aggressive investigation in patients with risk factors.

The findings of this study underscore the importance of considering GBC in the differential diagnosis when evaluating patients, especially older females presenting with nonspecific abdominal symptoms and a history of gallstones. Given the association between gallstones and GBC, prophylactic cholecystectomy for patients with gallstones has been proposed by some authors in areas with a high incidence of GBC. This is because laparoscopic cholecystectomy is a generally safe and minimally invasive procedure, with a very low

complication rate, and the outcome of GBC remains poor in later stages [23], [24].

Limitation of the study

This study reviewed medical records over a long period, thus there may be discrepancies and loss of data. We were unable to collect reliable data on post-operative treatment, including further adjuvant or palliative therapy, which might improve survival and quality-of-life greatly. Some of the recommended chemotherapy regimens are mitomycin C and 5-fluorouracil, with modest but significant survival benefits after 5 years (26% survived after 5 years with adjuvant therapy vs 14.4% survived without any other treatment) [25]. Further studies that consider these factors may generate better results. Finally, as of the time of writing, there has been no standard, nationwide surgical protocol for gallbladder carcinoma, thus surgical approaches may differ greatly between different surgeons. This may affect treatment outcomes between different periods and studies.

Conclusion

Gallbladder carcinoma presents significant diagnostic and therapeutic challenges due to its aggressive nature and tendency for late presentation, with more than 10% of patients remaining asymptomatic. While surgical resection offers the best chance for cure, outcomes remain suboptimal, particularly in advanced stages. A standardized surgical protocol should be established to improve survival in GBC patients. Early detection through vigilant clinical assessment and consideration of prophylactic measures in high-risk populations, combined with research into adjuvant therapies, are critical steps toward improving patient outcomes.

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