Original Article

Gallbladder Cancer in Rajavithi Hospital: Five-year Experience

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Background: Gallbladder cancer remains a relatively rare malignancy with a highly variable presentation in the initial stage, leading to difficulties in treatment. It has the worst overall prognosis with the only chance of cure being through surgery. No database of gallbladder cancer has been published in Thailand so far.

Objective: The present study aimed to identify the initial presentation and evaluate survival rates by stage in a tertiary centre.

Materials and Methods: After the study had been approved by the ethics committee, Rajavithi Hospital, the records were retrospectively reviewed of 523 patients diagnosed with suspected gallbladder cancer during the period January 2007 to December 2015. Clinical information, biochemical tests and radiologic findings were recorded, and descriptive data were presented as number, percent, and median. Survival rates were estimated using the Kaplan-Meier method.

Results: The data of the 31 patients who satisfied the inclusion criteria were analysed. The presentation symptoms of the patients were abdominal mass, jaundice, gallstone-like symptoms, acute cholecystitis and gallbladder thickening. The median survival rates of the patients in Stage 0, II, III, and IV were 33, 106, 41 and 7 months respectively.

Conclusion: Gallbladder cancer can present with a variety of symptoms, and survival rates depend on staging at presentation.

Keywords: Gallbladder cancer, Incidence, Survival rate

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Gallbladder cancer is rare in Thailand and worldwide. The majority of patients with gallbladder cancer who present for therapy show signs of stage IV, resulting in meagre 5-year survival rates of just 4 to 5%[1,2]. Their symptoms are highly variable, and the cancer is often found accidentally during open or laparoscopic cholecystectomy in patients who undergo emergency surgery. The only curative treatment for gallbladder cancer is surgery, with chemotherapy and radiation used only for palliative purposes. The main factor related to survival rates is the stage of cancer. A recent study[3] revealed that jaundice and extrahepatic bile duct involvement are factors that lead to poorer disease progression. Jaundice in patients with gallbladder cancer is usually the result of tumor infiltration or invasion of adjacent organs, indicating an advanced stage of the disease.

As analysis of laboratory parameters for diagnosis of the disease and classification of its severity is decidedly difficult, standard diagnosis is made with CT scan, which can be used to classify the stages of the cancer and to assess whether treatment should be in the form of surgery or palliative care. The appropriate operation is usually extended cholecystectomy, but tumors confined at T1a can be treated by cholecystectomy alone.

This study was designed to review the presentation of patients with gallbladder cancer and assess their survival rates.

Materials and Methods

After the research proposal had been approved by the Institution Review Board (No. 027/2559), medical records were reviewed from January 2007 to December 2015. CA gallbladder and gallbladder cancer were the searched terms, and 523 patients with suspected gallbladder cancer were identified from both OPD and IPD records. The number of patients selected by pathology was 31. PIH was used to collect data including demographic information, lab investigation data, treatment options, date of diagnosis and date of death. Inclusion criteria were patients diagnosed with gallbladder cancer in Rajavithi Hospital who underwent operative or non-operative treatment. Tumor stage was determined in accordance with the seventh edition of the American Joint Committee on Cancer (AJCC) staging system[4].

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Operative procedures were defined as follows: simple cholecystectomy (SCx) referred to cholecystectomy alone; and extended cholecystectomy (ECx) consisted of cholecystectomy, liver wedge resection or segment 4b and 5 segmentectomy and regional lymph node (LN) dissection.

Statistical analysis

Non-parametric data were presented as median and range while categorical data were presented as frequency and proportion (%). Overall survival rates were measured from the date of diagnosis to the date of death, including death due to cancer or other causes. The survival rates were estimated using the Kaplan-Meier method, and the difference between survival curves was tested using the log-rank test. A *p*-value <0.05 was considered significant. Data manipulation and statistical analyses were performed using the IBM SPSS statistic version 22.0.

Results

A total of 31 patients who were diagnosed with gallbladder cancer between January 2007 and December 2015 underwent surgery and had diagnosis confirmed by pathology. The demographic data and clinical features are presented in Table 1. There were twenty-one female patients and ten males, with a median age of 62 years (range 40 to 82 years). The most common presentations in this study were abdominal mass (25.8%), symptomatic gallstone and jaundice (22.6%), acute cholecystitis (19.3%), gallbladder wall thickening 9.7%, and concomitant gallstones (38.7%). We found incidental gallbladder cancer in 29.0% of cases.

The stages of gallbladder cancer of the patients are displayed in Table 2 which shows that stage IV (41.9%) was the most common.

From the 31 patients who met the inclusion criteria, 17 (54.8%) underwent extended cholecystectomy, 9 (29.0%) had simple cholecystectomy alone, and 5 (16.1%) underwent biopsy (Figure 1). We did not perform any major hepatectomy during this period.

The overall median survival rate of the entire group was 33 months (Figure 2). The median survival rates of the patients in Stage 0, II, III, and IV were 33, 106, 41 and 7 months respectively (log-rank test = 0.017).

Table 1. Demographic data of patients diagnosed with gallbladder cancer in Rajavithi Hospital (n = 31)

Demographic factors	n (%)
Age (years), median (min-max)	62 (40.0 to 82.0)
Sex	
Male	10 (32.3)
Female	21 (67.7)
Initial presentation	
Abdominal mass	8 (25.8)
Jaundice	7 (22.6)
Symptomatic gallstones	7 (22.6)
Acute cholecystitis	6 (19.3)
Gallbladder wall thickening	3 (9.7)
Gallbladder polyp	0 (0.0)
Underlying disease	
DM	4 (12.9)
HT	8 (25.8)
Dyslipidemia	5 (16.1)
Concomitant gallstones	12 (38.7)
Pre-operative suspected gallbladder cancer	22 (71.0)
Incidental gallbladder cancer	9 (29.0)

Data presented as median (min-max), n (%)

Table 2. Stages of gallbladder cancer of patients who underwent operation

Stages of gallbladder cancer	n (%)
Tissue biopsy	2 (6.5)
I	0 (0.0)
II	11 (35.5)
III	5 (16.1)
IV	13 (41.9)
Total	31 (100.0)

Discussion

Gallbladder cancer (GBC) has variable presentations at initial treatment. Some symptoms mimic those of gallstones, cholecystitis or gallbladder polyp. Incidental GBC has been found to vary from 0.25% to 50% of patients discovered during or after cholecystectomy[5]. Presentation with abdominal mass or jaundice indicates aggressive disease and probable poor outcomes. The depth of penetration is a critical prognostic factor in patients with GB cancer, and it is one of the most important factors to consider when deciding on the most appropriate operative procedure.

Oertli D. et al[6] reported a 16-year experience between 1975 to 1990 with 55 consecutive patients with GBC whose overall median survival rate was 8.6 months. D'Hondt M et al[7] reported an evaluation at their tertiary academic hospital over a period of 11 years of 102 gallbladder cancer patients whose overall median survival was 7.2 months; however, it was also found that patients who presented with incidental gallbladder cancer had a longer median survival rate compared with that of patients with non-incidental cancer (median: 25.8 vs. 4.4 months, $p<0.0001$). A recent study[2] found that stage 0, 1, 2 had 5-year survival rates of 80%, 50%, and 28% respectively while stage 3 and 4 had just 7 to 8% and 2 to 4% respectively.

The highest proportion of patients in this study referred to our hospital were in stage 4 (41.93%), and the outcomes from treatment were, predictably, extremely poor. We performed radical resection on only 16% of patients in stages 3 and 4 and on 29% in stage 2. Our series did not include anyone in stage 1, but we performed simple cholecystectomy in stage 0 which is sufficient for patients in this stage. Some patients diagnosed with gallbladder carcinoma after the first operation did not undergo curative resection

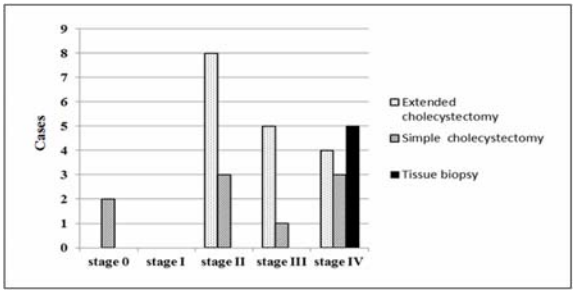

Figure 1. Operation by stage.

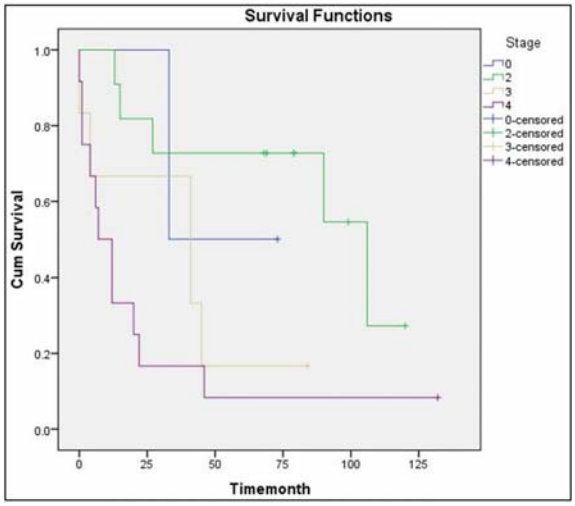

Figure 2. Median survival in each stage.

for a number of reasons, such as refusing or being unfit for surgery. Overall median survival rates in Stage 0, II, III, and IV were 33, 106, 41 and 7 months. While stage 3 and 4 survival rates were similar to those of other studies, we found that stage 2 had prolonged survival, while our stage 0 patients had median survival of only 33 months, which was lower than that found in other studies[8]; this was probably because there were only two such patients in our study, and this is too low a number to interpret.

Limitations of this study included its retrospective data and the fact that at that time, our institute did not classify disease subdivisions. Another limiting factor was that some operations and decision making were done by general surgeons.

Conclusion

The only way of curing gallbladder cancer is by performing surgery. The chance of survival depends on tumor staging, with patients in the early stages usually having a good prognosis. All other stages, starting from T1b should be treated with lymphadenectomy and resection of at least 2 to 3 cm of liver parenchyma around the gallbladder bed, provided that no residual microscopic cancer remains. Careful preoperative evaluation imaging and surveillance in high-risk patients, such as those who have anomalous pancreatico-biliary junction, is the most crucial step in early detection.

What is already known on this topic?

Gallbladder carcinoma is rare, has a low resectability rate, and generally has very poor outcomes. Prevention or early detection is difficult, and the prevalence of incidental gallbladder cancer has increased dramatically in recent times. Patients should be encouraged to undergo radical surgery after the operation, and the higher index of suspicion in high-risk patients is warranted.

What this study adds?

This study gives background data of the patients, as well as their resection and survival rates after radical resection in a tertiary care center.

Potential conflicts of interest

The authors declare no conflicts of interest.

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