Long-term prognosis of gallbladder cancer diagnosed after laparoscopic cholecystectomy

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Abstract

Background: Several clinical and laboratory studies concerning port-site recurrence have raised the concern that laparoscopic procedures might worsen the prognosis of malignant disease. However, the long-term prognosis of patients with malignancy who undergo laparoscopic surgery is still unknown. The purpose of this study was to examine the long-term prognosis of patients with unexpected gallbladder cancer diagnosed after laparoscopic cholecystectomy (LC).

Methods: A clinicopathologic study was performed on 41 patients with postoperatively diagnosed gallbladder cancer from among 5,027 patients undergoing LC at 24 institutions. The cumulative survival rate was compared with that reported for gallbladder cancer diagnosed after open cholecystectomy (OC).

Results: Of 26 patients with early gallbladder cancer (pTis or pT1), 23 were simply followed up, and 9 of 15 patients with advanced cancer (pT2 or pT3) had additional resection after the diagnosis of gallbladder cancer. Port-site recurrence occurred in four patients, and two of them died of the cancer. However, at this writing, the other two are still alive after abdominal wall resection or radiation therapy, having survived for 31 and 71 months, respectively. The 5-year survival rate was 92% for early cancer and 59% for advanced cancer. These results were comparable with 5-year survival rates for gallbladder cancer diagnosed after OC.

Conclusions: Although port-site recurrence occurred in four patients with advanced gallbladder cancer, the long-term prognosis of patients with undiagnosed gallbladder cancer who underwent LC was not worsened by the laparoscopic procedure. We conclude that surgeons can perform LC with reasonable confidence, even if the lesion is possibly malignant.

Key words: Laparoscopic cholecystectomy — Long-term prognosis — Multicenter study — Undiagnosed gallbladder cancer

Many kinds of laparoscopic surgery including laparoscopic cholecystectomy (LC), laparoscopic fundoplication, laparoscopic repair of perforated duodenal ulcer, and laparoscopic splenectomy have been accepted widely for the treatment of benign abdominal diseases [3]. However, it is thought that patients with malignancy are not good candidates for laparoscopic surgery for two reasons: One is the difficulty of removing the affected organ with an adequate tumor-free margin and resecting the regional lymph nodes, and the other is possible port-site recurrence [13, 17].

We previously reported that the 3-year survival rate of patients with gallbladder cancer diagnosed after LC was comparable with that of patients diagnosed after open cholecystectomy (OC) [16]. The objective of the current study was to examine the long-term prognosis of gallbladder cancer diagnosed after LC.

Methods

Among 5,027 patients undergoing LC at 24 institutions in Shizuoka prefecture between February 1992 and April 1998, 41 patients (0.84%) were histologically diagnosed to have unexpected gallbladder cancer. Their medical records, imaging data, surgery records, and pathologic findings were reviewed. These patients comprised 9 men and 32 women, ages 39 to 86 years (mean, 65.9 years). Follow-up data were obtained on April 30, 1998 for all patients by contact with the treating physicians.

In 16 patients, 5-mm serial sections of the whole gallbladder were prepared, whereas sections of the main tumor were obtained in the others. One pathologist reexamined the hematoxylin and eosin–stained specimens, and the tumors were staged according to the pathologic tumor (pT) system [15] (Table 1). Statistical analysis was performed using the chi-square test (or Fisher's exact test) for categorical information. The cumulative survival rate was calculated by the Kaplan-Meier method, using the Stat View 4.5 program (Abacus Concepts, Inc., Berkeley CA, USA) and a Macintosh...
Table 1. Pathologic TNM classification of gallbladder tumors

<table>
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<tr>
<th>Pathologic primary tumor (pT) classification</th>
<th>pTis</th>
<th>pT1a</th>
<th>pT1b</th>
<th>pT2</th>
<th>pT3</th>
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<tr>
<td>Carcinoma in situ</td>
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<td>Tumor invades lamina propria or muscle layer</td>
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<tr>
<td>Tumor invades lamina propria</td>
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<tr>
<td>Tumor invades muscle layer</td>
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<td>Tumor invades perimuscular connective tissue; no extension beyond serosa or into liver</td>
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<td>Tumor perforates serosa (visceral peritoneum) or directly invades into one adjacent organ or both (extension 2 cm or less into liver)</td>
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<tr>
<td>Tumor extends more than 2 cm into liver and/or into two or more adjacent organs (stomach, duodenum, colon, pancreas, omentum, extrahepatic bile ducts; any involvement of liver)</td>
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computer (Apple Computer Inc., Cupertino CA, USA). Statistical significance was defined as p less than 0.05.

Results

Preoperative diagnosis

The preoperative diagnosis was cholecystitis in 13 patients, cholecystitis in 14 patients, gallbladder polyp in 11 patients, and a combination of cholecystitis and gallbladder polyp in 3 patients. In 4 of the 14 patients with polypoid lesions, the possibility of early gallbladder cancer was raised based on the size of their polyps (13, 15, 16, and 17 mm, respectively). However, there was no clear evidence of cancer, so these four patients underwent LC.

Intraoperative findings

Bile spillage occurred in 18 of 41 patients (44%). The cause was gallbladder perforation during dissection of the gallbladder bed or perforation by the grasping forceps in 13 patients, injury during removal of the gallbladder from the abdomen in 3 patients, slippage of clips in 1 patient, and laparoscopic cholecystectomy [5] in 1 patient. An isolation sac was used in only five patients to extract the resected gallbladder. In six patients, LC was converted to OC, including three in whom laparoscopic procedures proved difficult, two who had a diagnosis of cancer on frozen section, and one who had a diagnosis of cancer on laparoscopic cholecystectomy. In one patient, malignancy was confirmed directly during surgery by LC. However, no evidence of malignancy or metastasis was noted during the laparoscopic procedure in the others.

Pathologic characteristics

Histologic examination revealed a carcinoid tumor in one patient and adenocarcinoma in all the other patients. The lesion was well-differentiated adenocarcinoma in 35 patients, moderately differentiated adenocarcinoma in three patients, and poorly differentiated adenocarcinoma in two patients. The tumor stage was pTis in 1 patient, pT1a in 19 patients, pT1b in 6, pT2 in 14 patients, and pT3 in 1 patient. No patient had pT4 disease. Lymphatic invasion was found in 8 patients, venous invasion in 10 patients, and perineural infiltration in 3 patients. All of these patients had pT2 or pT3 tumors, whereas the pTis and pT1 patients were all negative for such invasion. A significant correlation was found between disease stage (pT) and lymphatic invasion (p < 0.01), venous invasion (p < 0.01), or perineural infiltration (p < 0.01). Invasion of the cut end of the cystic duct was found in two pT2 patients, and metastasis to the cystic lymph nodes was observed in another pT2 patient.

Additional management

After a diagnosis of gallbladder cancer was made, 12 patients underwent second operations. Only 2 of these patients underwent immediate additional resection, and the other 10 patients underwent additional resection 14 to 38 days after LC. Eleven pT2 or pT3 patients in fair or good condition were recommended for further surgery, and nine of them agreed. One patient underwent regional lymphadenectomy and liver bed excision, whereas one had regional lymphadenectomy and extrahepatic bile duct resection. Six patients underwent regional lymphadenectomy, liver bed excision and/or partial liver resection (S4a, S5), and extrahepatic bile duct resection. The umbilical and midabdominal ports also were excised widely in three patients. In one patient with pT3 disease, only exploratory laparotomy was performed because peritoneal dissemination was detected. Among the patients with early cancer, two with pT1a tumors were subjected to liver bed excision because invasion of the muscle layer near the liver bed was diagnosed by the initial pathologic examination. The umbilical and midabdominal ports also were excised widely in one patient. One of the patients with pT1b disease had a carcinoid tumor, so the regional lymph nodes also were dissected.

Malignant cells were found in the additionally resected specimens of four patients with pT2 disease: near the cut end of the cystic duct (lymphatic involvement) in one patient, around the common bile duct (perineural infiltration) in one patient, at the cut end of the cystic duct in one patient, and in the pericholedochal and paraaortic lymph nodes in one patient.

Outcome

The follow-up time ranged from 1 to 74 months (mean, 38 months). There were no operative deaths, and all but one patient could be followed up. Recurrence was found in 7 (18%) of the 41 patients, including 6 with pT2 disease and 1 with pT3 disease. The site of recurrence was the abdominal wall including the ports in four patients, whereas there was local recurrence in one patient, liver metastasis in one patient, and lung metastasis in one patient. Among four patients with abdominal wall recurrence, three had pT2 disease and one had pT3 disease. Bile spillage occurred during the procedure in all four patients, and an isolation sac was used in only one patient. There was a relationship between abdominal wall recurrence and bile spillage (p = 0.03). However, there was no significant relationship between abdominal wall recurrence and the use of an isolation sac (p = 0.41).