

Incidental Gallbladder Cancer Diagnosed during and after Laparoscopic Cholecystectomy

Tetsuya Shimizu, Yasuo Arima, Shigeki Yokomuro, Hiroshi Yoshida, Yasuhiro Mamada,
Tsutomu Nomura, Nobuhiko Taniai, Takayuki Aimoto, Yoshiharu Nakamura,
Yoshiaki Mizuguchi, Yutaka Kawahigashi, Eiji Uchida,
Koho Akimaru and Takashi Tajiri

Surgery for Organ Function and Biology Regulation, Nippon Medical School Graduate School of Medicine

Abstract

With the increasingly widespread acceptance of laparoscopic cholecystectomy (LC), the number of cases of incidental gallbladder carcinoma (GBC) has increased; however, management of incidental GBC is a difficult issue in the absence of established guidelines. The present study aims to evaluate the treatment of patients with incidental GBC diagnosed with LC. We performed a 14-year review of 10 patients with GBC discovered with LC. From April 1991 through March 2004, we performed LC for 1,195 patients at Nippon Medical School Main Hospital. Of these patients, 10 (0.83%) were found to have GBC. Seven patients were women and 3 were men, with a mean age of 61.4 years. Four patients had mucosal tumors (pT1a), 5 had subserosal tumors (pT2), and 1 had a serosal lesion (pT3). Eight of the 10 patients underwent radical surgery. Two patients with pT1a tumors underwent no additional surgery. All 4 patients with pT1a tumors are alive without recurrence. One patient with a pT2 tumor with metastases to the liver and pericholedochal lymph nodes found with additional resection died of recurrence of metastasis to the liver and lung 70 months after LC. One patient with a pT2 tumor died of primary lung cancer 35 months after LC. The remaining 3 patients with pT2 tumors are alive without recurrence 51 to 128 months after surgery. One patient with a pT3 tumor is alive with no recurrence for 9 months. For stage Tis or T1a tumors, LC is sufficient. Patients with T1b tumors should undergo liver-bed resection and lymphadenectomy, and patients with >pT2 tumors should undergo systematic liver resection with lymphadenectomy. Even when incidental GBC diagnosed with LC is advanced, adequate additional surgery may improve the prognosis.

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Key words: laparoscopic cholecystectomy, incidental gallbladder cancer, additional surgery

Introduction

Laparoscopic procedures have been reported to be

less invasive than conventional open procedures¹,
and recent developments in laparoscopic
instrumentation and improvements in surgical skill
have enabled laparoscopic surgery for various

Correspondence to Tetsuya Shimizu, MD, Surgery for Organ Function and Biology Regulation, Nippon Medical School Graduate School of Medicine, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

E-mail: tetsuya@nms.ac.jp

Journal Website (<http://www.nms.ac.jp/jnms/>)

Table 1 Clinical findings in the 10 cases of gallbladder carcinoma diagnosed by laparoscopic cholecystectomy

Case	Age	Sex	Preoperative diagnosis
1	49	F	GB stone
2	78	F	GB stone
3	65	F	GB polyp (12 mm), GB stone
4	47	F	GB polyp (20 mm), GB stone
5	50	M	GB stone
6	37	M	adenomyomatosis
7	71	F	GB stone
8	76	F	GB stone
9	68	M	GB polyp (20 mm), GB stone
10	73	F	adenomyomatosis, GB stone

F, female; M, male; GB, gall bladder

malignant diseases²⁻⁵. Laparoscopic cholecystectomy (LC) has become a standard procedure for the treatment of gallstones. Because of the increased use of LC and difficulties in diagnosing gallbladder cancer (GBC) preoperatively, incidental GBC discovered during and after LC has become more frequent. Incidental GBC after LC has been reported to be detected in 0.5% to 1.0% of cases⁶⁻¹⁰. A problem associated with incidental GBC related to LC is the decision whether to perform additional surgery. Controversy remains regarding the effectiveness of additional resection in incidental GBC. We reviewed the medical records of patients with incidental GBC detected during and after LC to determine the adequacy of additional resection.

Patients and Methods

We performed a 14-year review of patients with GBC discovered with LC. From April 1991 through March 2004, 1,195 patients underwent LC at Nippon Medical School Main Hospital. The patients were 641 females and 554 males, aged 5 to 88 years. The preoperative diagnosis was made with ultrasonography and computed tomography. When necessary, drip infusion cholangiography, endoscopic retrograde cholangiopancreatography, or magnetic resonance cholangiopancreatography was also performed. All histological examinations were performed at the Department of Pathology, Nippon Medical School. TNM staging was determined

according to the International Union Against Cancer criteria.

If the gallbladder wall was suspected to contain a malignant lesion during or before LC, intraoperative histopathologic exam was done during LC. If malignancy was recognized with intraoperative pathological examination, LC was converted to open surgery intraoperatively. Patients underwent a routine follow-up examination every 3 months. The patient's condition was verified by the patient, the patient's family, or the attending physician.

Results

In 10 of 1,195 cases (0.83%), incidental GBC was detected during or after LC. There were 7 women and 3 men, with a mean age of 61.4 years (women, 65.6 years; men, 51.7 years; range, 37 to 78 years). The preoperative diagnoses are shown in **Table 1**. There were gallbladder polyp (n=3, all with gallstone) and adenomyomatosis (n=2, 1 of 2 cases with gallstone), and 9 of the 10 patients had gallstones. One patient with a gallbladder stone had a history of severe acute cholecystitis (case 10). Six of the 10 patients complained of right upper quadrant pain and tenderness, 2 patients had more than 2 colicky events in the past few months, and 3 patients had asymptomatic gallstones. No patient had jaundice before surgery. Although tumor markers were preoperatively evaluated in only 6 of the 10 patients, no patients showed elevation of carcinoembryonic antigen or CA19-9. In the three cases of polyp, we could not rule out malignancy preoperatively because of signs of intraluminal irregularity or enlargement of the polyp. The sizes of gallbladder polyps in the three patients were 12, 20, and 20 mm, respectively. All 3 patients with polyps who underwent intraoperative pathological examination were diagnosed with GBC, and LC was converted to open surgery intraoperatively. In the remaining cases, there was no preoperative suspicion of malignancy, and GBC was recognized with postoperative histologic examination. Four patients had mucosal tumors (pT1a), 5 had subserosal tumors (pT2), and 1 had a serosal lesion (pT3). The location of cancer was the fundus (2

Table 2 Histological findings and Outcome of the 10 cases with incidental gallbladder carcinoma diagnosed after laparoscopic cholecystectomy

Case	Differentiation	Depth	location	bm	hinf	binf	n	m	Intraoperative Conversion to open surgery	Additional Operation	Comprehensive stage	Outcome
1	Well	T1a	Gb	0	—	0	0	0		—	I	6y 4m, alive
2	Well	T1a	Gn	0	—	0	0	0		—	I	2y 7m, alive
3	Pap	T1a	Gn	0	0	0	0	0	+	LN	I	4y 7m, alive
4	Pap	T1a	Gb	0	0	0	0	0	+	LBE, LN	I	8y, alive
5	Poor	T2	Gb	0	0	0	0	0		LBE, CBD, LN	II	4y 3m, no follow
6	Pap	T2	Gfbn	0	0	0	0	0		LBE, LN	II	10y 8m, alive
7	Mod	T2	Gf	0	0	0	2	1		S4a + S5, CBD, LN	IVb	5y 10m, dead for rec
8	Well	T2	Gf	0	0	0	0	0		LBE, LN	II	8y 5m, alive
9	Mod	T2	Gb	0	1a	0	0	0	+	LBE, CBD, LN	II	2y 11m, dead for PLC
10	Well	T3	Gn	0	0	0	0	0		S4a + S5, CBD, LN	III	9m, alive

Well, well-differentiated adenocarcinoma; Mod, moderately-differentiated adenocarcinoma; poorly-differentiated adenocarcinoma; Pap, papillary adenocarcinoma; T1a, mucosa; T2, subserosa; T3, serosa; Gn, neck; Gb, body; Gf, fundus; bm, biliary margin; hinf, hepatic infiltration; binf, biliary infiltration; n, node; m, metastasis; LN, lymphadenectomy; LBE, liver bed excision; S4a + S5, liver resection of S4a + S5; CBD, extra hepatic bile duct resection; rec, recurrence; PLC, primary lung ca

cases), the body (4 cases), the neck (3 cases), and the entire gallbladder (1 case). In all 10 cases, surgical margins were negative. LC was performed with CO₂ pneumoperitoneum, and there was no biliary spillage in any of the 10 cases.

Histological findings and outcomes with GBC diagnosed during and after LC are shown in **Table 2**. Eight of the 10 patients with GBC underwent surgery: 3 with intraoperative conversion to open surgery and 5 with a second operation. Second operations were performed 12 to 21 days after LC.

Two of the 4 patients with pT1a tumors underwent only LC. The other 2 patients with pT1a tumors underwent additional surgery after conversion to open surgery: 1 with regional lymphadenectomy (porta hepatis and hepatoduodenal ligament) and 1 with liver-bed excision and regional lymphadenectomy. One of the 5 patients with pT2 tumors underwent additional operation with intraoperative conversion to open surgery: liver-bed excision, extrahepatic bile duct resection, and regional lymphadenectomy. The remaining 4 patients with pT2 tumors underwent second operations: 2 with liver-bed excision and regional lymphadenectomy; 1 with liver-bed excision,

extrahepatic bile duct resection, and regional lymphadenectomy; and 1 with systematic liver resection (S4a, S5), extrahepatic bile duct resection, and regional lymphadenectomy. In 1 patient with a pT3 tumor, systematic liver resection (S4a, S5), extrahepatic bile duct resection, and regional lymphadenectomy were also performed postoperatively. Malignant cells were found in the additionally resected specimen of only 1 patient with a pT2 tumor (case 7): liver metastasis and pericholedochal lymph node metastasis.

The follow-up time ranged from 9 to 128 months (mean, 66.8 months). There were no operative deaths, and we were able to follow up all patients except 1 (case 5). All 4 patients with pT1a tumors are alive with no evidence of recurrence at 31 to 96 months, whether or not additional surgery was performed. One patient with a pT2 tumor (case 7) with liver and pericholedochal lymph node metastasis in the additionally resected specimen died of recurrence of liver and lung metastases 70 months after LC. One patient with a pT2 tumor died of primary lung cancer 35 months after LC. The remaining 3 patients with pT2 tumors are alive without recurrence 51 to 128 months after surgery.

One patient with pT3 is alive with no recurrence for 9 months. In all cases, no abdominal wall metastasis, including port-site recurrence, was seen.

Discussion

Additional surgery related to the depth of cancer invasion is recommended for the treatment of incidental GBC after LC. Our study demonstrates that patients with <pT1a GBC diagnosed during or after LC might enjoy long-term survival regardless of the addition of liver resection or lymphadenectomy. This finding suggests that in patients with pTis or pT1a GBC, no additional surgery is necessary and follow-up alone is sufficient. Controversy surrounds additional surgery for pT1b tumors. Some authors suggest pT1b GBC does not require any operation after simple cholecystectomy¹⁰⁻¹², and good results have been reported after simple cholecystectomy in patients with pT1b GBC^{13,14}. In contrast, some authors have advocated resection more extensive than simple cholecystectomy because of the problem of locological recurrence or lymph node metastasis following simple cholecystectomy^{9,15-18}. Ouchi and colleagues¹⁹ have reported that 2 of 7 patients with pT1b had venous invasion or lymphatic invasion, findings that support additional resection for pT1b GBC.

Patients with pT1b tumors undergo liver-bed resection and regional lymphadenectomy, and patients with >pT2 tumors undergo systematic liver resection (segment IVa + V or right hepatectomy) with regional lymphadenectomy if they can tolerate invasive hepatectomy. If malignant cells are found at the edge of the cystic duct in a resected specimen, extrahepatic bile duct resection should also be performed. It is also important to exclude advanced cases of gallbladder cancer from treatment with LC cases preoperatively, although preoperative diagnosis of GBC is generally difficult, particularly in patients with inflammation and cholelithiasis. Cases of obvious advanced gallbladder cancer diagnosed before surgery should not be treated with LC.

Many reports have indicated the risk of peritoneal dissemination, including trocar site metastasis, with

laparoscopic surgery for malignancy^{20,21}. Peritoneal dissemination has been induced by the spread of tumor cells through gallbladder perforation²² or CO₂ pneumoperitoneum²³. We did not observe any gallbladder perforation in our cases of incidental GBC. We used an isolation bag to remove the resected gallbladder from the abdominal cavity, and this method caused no peritoneal dissemination in our study. We believe that the prevention of intraperitoneal bile spillage during LC is extremely important for preventing peritoneal recurrence and for improving the prognosis.

In summary, even when the incidental GBC diagnosed after LC is advanced, adequate additional surgery improves the prognosis. Unless a gallbladder lesion is diagnosed as being clearly advanced GBC preoperatively, we consider LC the treatment of first choice.

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