# Occult Gallbladder Carcinoma after Laparoscopic Cholecystectomy: A Report of Four Cases

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### Abstract

Eighty-four patients underwent laparoscopic cholecystectomy (LC) from January through August 2006. Of these patients, 4 (4.7%) were found to have occult gallbladder carcinoma (GC) either during or after the procedure. Two of the patients were women and 2 were men. The mean age was 75.0 years. One patient had mucosal tumors, 2 had subserosal tumors, and 1 had a serosal lesion. One of the 2 patients with subserosal tumors underwent radical surgery. In a previous study, 0.83% (10 of 1,195) of patients who had undergone LC were found to have occult GC, either during of after the procedure. The prevalence of gallbladder carcinoma has recently been increasing. GC has been reported in 0.3% to 1.5% of patients who have undergone cholecystectomy. Since the introduction of laparoscopic surgery, the number of cholecystectomies being performed has increased, which may explain why occult GC seems to be occurring more frequently. The prognosis for GC is poor, and surgical resection is the only potentially curative treatment. However, GC is difficult to diagnose at an early stage and difficult to recognize even in the advanced stages. Fifteen percent to 30% of patients show no preoperative or intraoperative evidence of malignancy. Occult GC is also increasing. Because flat infiltrating GC and GC with cholecystitis and numerous stones are difficult to diagnose preoperatively, we recommend taking frozen sections from patients who are of advanced age (older than 70 years), have a long history of stones, or have a thickened gallbladder wall. (J Nippon Med Sch 2007; 74: 300-305)

Key words: occult gallbladder carcinoma, laparoscopic surgery, cholecystectomy

## Introduction

Gallbladder cancer (GC) has recently been increasing in Japan. GC is an aggressive disease with an extremely poor outcome after surgical treatment and a poor prognosis. Since the introduction of laparoscopic cholecystectomy (LC), more patients are undergoing gallbladder removal, so an increase in the number of cases of occult GC might be expected<sup>1</sup>. Generally, LC should not be performed when there is a high index of suspicion of malignancy due to the frequent association with factors (such as gallbladder perforation and bile spill), which may lead to implantation of cancer cells and dissemination.

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Case	Age	Sex	Preoperative diagnosis	Differentiation	Dept h	Intraoperative Conversion to open surgery	Additional Operation	Outcome
1	70	F	GB stone	well	pT2	_	S4a + S5,	8m, alive
2	77	F	adenomyomatosis	well	pT3	-	_	6m, alive
3	80	F	adenomyomatosis	poor	pT2	+	S4a + S5	2m, alive
4	74	М	GB stone	well	pT1	_	-	19m, alive

Table 1 Clinical and histological findings of the 4 cases of incidental GC carcinoma diagnosed with LC



Fig. 1 Magnetic resonance cholangiopancreatography showed gallstones and a slightly thickened gallbladder wall. The resected specimen showed chronic cholecystitis and gallstones, and well-differentiated adenocarcinoma and pT2 were diagnosed during the pathologic examination.

In a previous study, we reported that 0.83% (10 of 1,195) of patients who were undergoing or had undergone LC were found to have occult  $GC^2$ . We also reported that additional surgery may improve the prognosis even in cases of advanced incidental GC with  $LC^2$ .

Recently, we examined 4 cases of occult gallbladder carcinoma and concluded that flat infiltrating GC and GC with cholecystitis and numerous stones are extremely difficult to diagnose.

## **Patients and Methods**

From January through August 2006, 84 patients underwent LC at the Nippon Medical School Main Hospital. The preoperative diagnosis was made with ultrasonography and computed tomography (CT). When necessary, drip infusion cholangiography, endoscopic retrograde cholangiopancreatography, or magnetic resonance cholangiopancreatography was also performed. All histological examinations were

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A: CT showed increased thickness in part of the gallbladder wall.B: Abdominal ultrasonography showed elevated lesions without blood flow.C: The resected specimen showed chronic cholecystitis without tumor.D: Well-differentiated adenocarcinoma and pT3 were diagnosed during the pathologic examination.

performed at the Department of Pathology, Nippon Medical School. TNM staging was determined according to the International Union Against Cancer criteria<sup>3</sup>.

#### Results

Incidental GC was detected during or after LC in 4 of 84 patients (4.7%). The patients were 2 women and 2 men. The mean age was 75.0 years. The preoperative diagnoses, histological findings, and outcome of the 4 cases of incidental GC diagnosed with LC are shown in **Table 1**.

Case 1: A 70-year-old woman was admitted with a chief complaint of right hypochondriac pain. Magnetic resonance cholangiopancreatography revealed gallstones and a slightly thickened gallbladder wall (**Fig. 1**). The patient underwent LC for gallstones and cholecystitis. The resected specimen showed chronic cholecystitis and

gallstones (**Fig. 1**), and well-differentiated adenocarcinoma and pT2 were diagnosed during the pathologic examination (**Fig. 1**).

Case 2: A 77-year-old woman was admitted with a diagnosis of adenomyomatosis or GC. CT revealed increased thickness in part of the gallbladder wall (**Fig. 2**). Abdominal ultrasonography showed elevation lesions without blood flow (**Fig. 2**). No malignant cells were found during a bile cytological examination. The patient underwent LC for adenomyomatosis. The resected specimen showed chronic cholecystitis (**Fig. 2**), and well-differentiated adenocarcinoma and pT3 were diagnosed during the pathologic examination (**Fig. 2**). Additional surgery was not performed because of the patient's poor general condition.

Case 3: An 80-year-old woman was admitted with a chief complaint of right hypochondrium pain. CT revealed a thickened gallbladder wall (Fig. 3). The patient underwent a laparoscopic cholecystectomy

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Fig. 3

A: CT showed a thickened gallbladder wall.

B: The resected specimen showed chronic cholecystitis with adenomyomatosis; carcinoma was not ruled out.

C: Poorly differentiated adenocarcinoma and pT2 were diagnosed during the pathologic examination.

for adenomyomatosis. The resection specimen showed chronic cholecystitis with adenomyomatosis; carcinoma was not ruled out (**Fig. 3**) Poorly differentiated adenocarcinoma and pT2 were diagnosed during the pathologic examination (**Fig. 3**).

Case 4: A 74-year-old man was admitted with a chief complaint of right hypochondriac pain. Abdominal ultrasonography revealed a  $3 \times 2$ -cm gallstone and a slightly thickened gallbladder wall (**Fig. 4**). The patient underwent LC for the gallstone and cholecystitis. The resection specimen showed mild chronic cholecystitis and the gallstone (**Fig. 4**), and well-differentiated adenocarcinoma and pT1 were diagnosed during the pathologic examination (**Fig. 4**).

# Discussion

In a previous study, 0.83% (10 of 1,195) of patients who had undergone or were undergoing LC from April 1991 through March 2004 were found to have occult GC<sup>3</sup>. From January through August 2006, we performed LC for 84 patients at Nippon Medical School Main Hospital, of whom 4 (4.7%) were found to have occult GC. Cases of occult GC have been diagnosed more frequently since the introduction of LC. Of patients undergoing cholecystectomy, 0.3% to 1.5% are found to have GC<sup>4</sup>. The increased incidence of occult GC parallels the striking three-fold increase in cholecystectomies since the introduction of laparoscopic surgery. The increase in occult GC can be attributed to the increase prophylactic resection by LC for adenomyomatosis.

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Fig. 4

A: Abdominal ultrasonography revealed a 3×2-cm gallstone and a slightly thickened gallbladder wall.

B: The resected specimen showed mild chronic cholecystitis and a gallstone.

C: Well-differentiated adenocarcinoma and pT1 were diagnosed during the pathologic examination.

It may be possible to obtain a more precise diagnosis preoperatively. One of our patients with occult GC underwent endoscopic gallbladder bile cytology, endoscopic ultrasonography, and CT before LC, but a precise diagnosis could not be obtained preoperatively. Flat infiltrating GC, GC with cholecystitis, and multiple GB stones are extremely difficult to diagnose. A frozen section is recommended for patients who are older than 70 years, have a long history of stones, or have a thickened gallbladder wall. These conditions were present in most of the patients in previous studies<sup>5-18</sup>.

Recent reports indicate that LC may increase the risks of tumor implantation and dissemination in patients with gallbladder cancer<sup>19</sup>, despite the reported lower depressive effect on cell-mediated immunity after laparoscopy. Metastasis after laparoscopy may occur at all trocar sites and is often evident 1 to 6 months after surgery. In addition to this "early-type" metastasis, a "late-type," trocar

metastasis<sup>20</sup>, has been observed as late as 2 years after a laparoscopic procedure. Gallbladder perforation occurred during laparoscopic procedures in case 4, but trocar site metastasis was not seen 19 months after LC.

Additional surgery to determine the depth of cancer invasion is the recommended treatment for occult GC after LC. Our study demonstrates that patients with <pT1a GC, diagnosed during or after LC, might enjoy long-term survival regardless of the addition of liver resection or lymphadenectomy<sup>3</sup>. 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<sup>3</sup>. In conclusion, occult GC is increasing. Because flat infiltrating GC and GC with cholecystitis and numerous stones are difficult to diagnose preoperatively, we recommend taking frozen sections from patients who are of advanced age (older than 70 years), have a long history of stones, or have a thickened gallbladder wall.

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