

## Incidental Finding of Gallbladder Carcinoma

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### Abstract

**Background:** Carcinoma of the gallbladder is diagnosed in 0.3–1.5% of all cholecystectomy specimens.

**Objectives:** To establish the overall rate of gallbladder carcinoma and unexpected gallbladder carcinoma based on our experience.

**Methods:** We retrospectively evaluated all consecutive cholecystectomies performed in our ward during a 6 year period in order to determine the incidence of gallbladder carcinoma and to identify common characteristics of this particular group of patients.

**Results:** Of the 1,697 cholecystectomies performed in our ward during the 6 years, gallbladder carcinoma was diagnosed in six patients (0.35%) but was not suspected prior to surgery in any of them. In accordance with the literature, the occurrence in women (5/6) was higher than in men (1/6). The mean age was 70 years (range 55–90). The most common symptom was abdominal pain; the majority (5/6) had cholelithiasis, and the pathologic report confirmed the diagnosis of adenocarcinoma in all six patients.

**Conclusions:** The overall incidence of unsuspected gallbladder carcinoma in our series was 0.35%. We could not find any common characteristics for this particular group of patients when compared to patients with non-malignant pathology.

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Gallbladder carcinoma is a rare entity, diagnosed in 0.3–1.5% of all cholecystectomies [1]. In this study we aimed to establish the overall rate of gallbladder carcinoma and unsuspected gallbladder carcinoma based on our experience. We evaluated all consecutive cholecystectomies performed in our ward during a 6 year period and compared our data to those reported in the literature. We also tried to detect common characteristics among this particular group of patients.

### Patients and Methods

We retrospectively reviewed the clinical records of 1,697 patients who underwent cholecystectomy during a 6 year period. Both open and laparoscopic procedures were included. From the collected data we retrieved six patients with unsuspected gallbladder carcinoma. Their relevant medical data are presented in Table 1. Special attention was paid to the presence of preoperative or intraoperative findings, which raise the suspicion of gallbladder carcinoma.

### Results

During this period 1,697 cholecystectomies were performed in our ward; 690 were “open” procedures and 1,007 were laparoscopic. These operations included elective operations due to symptomatic

gallstones and urgent operations for acute cholecystitis. We wish to emphasize that during this period it was our custom to perform the “open” method in emergency cases of suspected cholecystitis, and a laparoscopic trial in elective cholecystectomies. Evaluation of all the pathologic specimens revealed six cases of gallbladder carcinoma, which comprised 0.35% of all cholecystectomies performed (0% of the laparoscopic group of operations and 0.9% of the “open” group operations). All identified cases were unsuspected preoperatively, however intraoperative findings in two patients gave rise to the suspicion of gallbladder carcinoma [Table 1]. Five of the six patients diagnosed as having the condition were female. The mean age of these patients was 70 years (range 55–90). The clinical data and follow-up are reported in Table 1.

### Discussion

De Stoll in 1771 was the first to report on gallbladder carcinoma [2]. Although the entity is quite rare, it is the fifth most common gastrointestinal malignancy (and the most common of the biliary tract) and is usually discovered accidentally [3]. Gallbladder carcinoma is diagnosed pathologically in 0.3–1.5% of cholecystectomy specimens. The prognosis of patients in whom it is diagnosed preoperatively is very poor. In 15–30% of the cases there is no evidence of malignancy before or during the operation, and the disease is diagnosed microscopically postoperatively. Theoretically, this group carries the best prognosis [4].

Demographically, gallbladder carcinoma is more common in women and its frequency increases with age [5]. The etiology is unknown, but risk factors include cholelithiasis (found in 70–90% of cases), various carcinogens, ethnic background, benign tumors and abnormalities in the union of the pancreatobiliary ducts. Arnaud et al. [6] found that when symptoms did appear they included abdominal pain in 72%, jaundice in 58%, weight loss in 47.5%, fever in 30.8% and ascites in 14%. Relevant laboratory data showed obstructive jaundice in 51.7%, abnormal liver function tests in 37%, leukocytosis in 34.4% and anemia in 22.4% [6]. The majority (90%) of the malignant gallbladder lesions are adenocarcinoma and less than 2% are adenosquamous carcinoma. The most important prognostic factor is the pathologic staging. The only hope for survival is the operative option [5].

It is important to know preoperatively whether the surgeon is dealing with gallbladder carcinoma, as this will lead to a more radical preoperative evaluation and operation. Endoscopic ultrasound might be of help [7]. The suspicion of malignancy increases

Table 1. Clinical data

Age/ Gender	Clinical presentation	Laboratory data	Sonography	Operation: open/lap emerg/elec	Operative findings	Pathology	Treatment/ follow-up	Suspicious operative findings
59/F	Abdominal pain, fever	Normal	Cholelithiasis, thickened wall	Open, emergency	Cholelithiasis, thickened wall, diffuse abdominal lymphaden- opathy, enlarged ovary, adhesions	Mod. diff. adenocarcinoma, metastases to ovary & mesentery	Chemotherapy/ died after 4 months	Yes
90/F	Abdominal pain, nausea	Normal, except for Bil-t 4.9 mg/dl, Bil-c 3.6 mg/dl	Cholelithiasis, mild widening of intra & extra hepatic bile ducts, CBD 0.9 cm	Open, emergency	Dilated gallbladder, thickened wall, large stone, CBD 1.5 cm	Acute & chronic cholecystitis with focal carcinoma <i>in situ</i>	Alive after 8 months NED	No
70/F	Abdominal pain, fever	Normal except for Hb 9.1 g/dl	Cholelithiasis, thickened wall, air in wall, fluid surrounding gallbladder	Open, emergency	Dilated gallbladder, edematous, pus in gallbladder, air in wall	Mod. diff. adenocarcinoma extending through serosa, blood vessels & surgical margins, no stones found	Died after 7 months	No
72/F	Abdominal pain	Normal	Cholelithiasis, thickened wall, dilated gallbladder	Open, emergency	Cholelithiasis, inflamed gallbladder filled with tumorous tissue, cholelithiasis, lymphadenopathy in hepatoduodenal ligament. After positive frozen section resection of omentum & gallbladder bed	Well-mod. diff. adenocarcinoma extending to surgical margins	Died after 25 months	Yes
73/M	Abdominal pain	Normal	Cholelithiasis	Lap-> open, elective	Pus in gallbladder, adhesions	Poorly diff. adenocarcinoma extending to surrounding fatty tissue, cholelithiasis, extensive squamous metaplasia, acute & chronic cholecystitis	Died after 4 months	No
55/F	Abdominal pain, loss of appetite	Normal	cholelithiasis, CBD 1.1 cm	Open, emergency	Dilated gallbladder, thickened wall, liver abscess, edema & necrosis in head of pancreas, free intraabdominal turbid fluid	Cholelithiasis, mod. diff. adenocarcinoma extending to subserosa, liver metastases	Died after 1 day	No

NED = no evidence of disease, CBD = common bile duct

when sonography displays large polyps (45% risk of cancer for a polyp >15 mm) [8], or a porcelain gallbladder.

In five of six patients in our series, the operation was performed on an emergency basis and an open approach was adopted. In the sixth patient, whose surgery was elective, the laparoscopic

approach was converted to an open procedure due to technical difficulties. Hence, in our series all patients with unsuspected gallbladder carcinoma were operated upon with the open technique. However, a major question has yet to be resolved. Is laparoscopic cholecystectomy the best approach for unsuspected

gallbladder carcinoma, given that numerous reports deal with malignant cell implantation in trocar sites following laparoscopic cholecystectomy performed in cases of unsuspected malignancy? Trocar site metastases are more common when the tumor invades the whole depth of the gallbladder wall and when spillage has occurred during surgery. Therefore, when gallbladder carcinoma is suspected, extraction of the gallbladder in an endo-bag is recommended. One should consider treating the port site, through which the gallbladder is removed, by radiotherapy or local excision when the diagnosis of unsuspected gallbladder carcinoma is made postoperatively. If carcinoma is suspected prior to the operation, an open approach is recommended [9–14].

The overall prognosis of patients diagnosed with gallbladder carcinoma is poor, and fatal when it is unresectable. Is there any advantage in performing a second more radical operation after laparoscopic cholecystectomy in the case of an incidental finding of gallbladder carcinoma? The answer depends on the stage of the disease [13,15]. For T1 disease, no further surgery is needed since the prognosis is good and there is no justification for the morbidity of a second more radical operation. For a T2-T4 disease, a complementary operation should be considered after performing imaging studies to rule out dissemination of the disease [13,16]. Chemotherapy and radiotherapy have not been used routinely for patients with a resectable or a non-resectable tumor, so no definitive conclusion can be reached on this question. In a group of 149 patients with gallbladder carcinoma [16], a 5 year survival rate of 51% was reported, following a complementary operation for unsuspected gallbladder carcinoma post-cholecystectomy [17,18].

Of the 1,697 cholecystectomies that we performed, 6 cases of unsuspected gallbladder carcinoma were diagnosed, equivalent to 0.35% of all cholecystectomies performed. In accordance with the literature we found the occurrence in women to be higher than in men (five females compared to one male) and characteristic of old age (mean 70 years, range 55–90). The most common symptom was abdominal pain (in all our patients), 5/6 had cholelithiasis in the specimen and all the pathologic results revealed adenocarcinoma with none of them being diagnosed before the operation. There were no unusual laboratory or sonographic findings. In only two patients with a relatively progressive disease were there suspicious findings of carcinoma during the operation, which included lymphadenopathy and distant metastases. Only one patient received chemotherapy.

Five of the six patients died from the disease at an average time of 8 months (range 0–25); the sixth patient, in whom the diagnosis was that of carcinoma *in situ*, is alive with no evidence of disease during a follow-up of 8 months.

It is not possible to discuss the issue of trocar site metastases in our series since in only one case was a laparoscopic operation attempted. In fact, we did not diagnose any unsuspected malignancy preoperatively throughout our experience with laparoscopic cholecystectomy.

To conclude, the overall incidence of gallbladder carcinoma in

our series was 6/1,697, or 0.35%. All were unexpected findings and all patients were operated upon by the open technique. The overall prognosis of a patient diagnosed with malignancy is poor, except for the small group of patients with carcinoma *in situ*.

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