DOI:10.1111/hpb.12189 HPB

ORIGINAL ARTICLE

# Management of incidental and suspicious gallbladder cancer: focus on early referral to a tertiary centre

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## Abstract

**Objectives:** This study was conducted to assess the management of incidental gallbladder cancer and indeterminate gallbladder lesions. Its secondary aim referred to the devising of a management pathway for these patients.

**Methods:** Patients referred with incidental gallbladder cancer and indeterminate gallbladder lesions during 2002–2011 were identified from a prospectively maintained database. Collated data included operative findings, histopathological data and survival outcomes.

**Results:** The study included a total of 104 patients, 40 of whom had incidental gallbladder cancer following cholecystectomy. In this group, the index cholecystectomy was considered curative (T-*is*/T1a stage) in three patients; 11 patients underwent further resection, and 26 patients were inoperable. One-, 3- and 5-year overall survival rates were 91.1%, 91.0% and 60.7%, respectively, in patients who underwent re-resection. Of the 64 patients with indeterminate gallbladder lesions, 54 patients underwent modified radical cholecystectomy. Seven patients were found to have gallbladder cancer. One-, 3- and 5-year overall survival rates were 85.9%, 43.1% and 42.8%, respectively. Five-year overall survival in patients treated with surgery for gallbladder cancer was 59.9%.

**Conclusions:** The majority of patients with incidental gallbladder cancer were not amenable to further potentially curative resection. The radiological suspicion of gallbladder cancer should lead to prompt referral to a tertiary hepatobiliary unit for further management.

Received 20 May 2013; accepted 3 September 2013

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## Introduction

Gallbladder cancer is a rare malignancy in Western populations and is associated with a poor prognosis,[1] mainly as a result of rapid tumour progression. Patients usually present with metastatic disease. In patients who are suitable for surgery, extensive liver resection, with or without portal lymphadenectomy and bile duct resection, is frequently required for disease eradication, but is associated with high morbidity and occasional mortality.[2] However, the definitive surgical treatment for gallbladder cancer remains controversial, especially with respect to the extent of resection in different stages and modes of presentation. Some centres would consider radical surgery for advanced T3 gallbladder cancer.[2,3]

In the majority of cases, gallbladder cancers are discovered incidentally following cholecystectomy.[4,5] Using the American Joint Committee on Cancer (AJCC) staging system, simple cholecystectomy alone is considered definitive treatment if the histological T-stage is T *in situ* or T1a, and provided there is no biliary spillage during surgery.[6] Some centres have reported reduced disease recurrence rates and better survival outcomes with resection of the liver bed following the incidental diagnosis of gallbladder cancer post-cholecystectomy.[2,7,8] The recommended treatment for suspected but resectable gallbladder cancer on imaging is hepatic resection with or without lymphadenectomy and bile duct resection.[2,9] However, the management strategy is unclear when cross-sectional imaging is indeterminate. There is a risk that either a patient with gallbladder cancer will be undertreated with simple

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cholecystectomy, which may potentially affect his or her longterm survival, or that a patient with a benign inflammatory process may be overtreated by liver resection with portal lymphadenectomy, in which there is significant increase in risk for postoperative complications.

The aim of this study was to assess the management of incidental gallbladder cancer found following simple cholecystectomy and of gallbladder lesions that are indeterminate on imaging. The secondary aim referred to the devising of a management pathway for patients in whom possible gallbladder cancer is suspected on initial diagnostic imaging.

## Materials and methods

Patients in whom an initial diagnostic scan raised radiological suspicion and patients with histologically proven gallbladder cancer following cholecystectomy were identified from a prospectively maintained hepatobiliary database. All patients had been referred to the study centre during the 9.5-year period from January 2002 to August 2011. Ethics approval for this study was obtained from the University Hospital Aintree.

There were two patterns of referral to this tertiary centre: (i) patients with incidental gallbladder cancer after cholecystectomy carried out at a non-tertiary centre were referred for further management, and (ii) patients with radiologically indeterminate gallbladder lesions were referred for modified radical cholecystectomy. A radiologically indeterminate gallbladder lesion was defined as focal or diffuse thickening of the gallbladder wall, a mass in the gallbladder fossa or an intraluminal mass, with or without associated findings of cholelithiasis, biliary duct dilatation, invasion of the adjacent structures, distant metastases other than those of the liver, and porcelain gallbladder.[10,11] Patients were excluded if preoperative imaging clearly suggested gallbladder cancer, N2 stage or M1 stage disease, and if their follow-up after surgery amounted to <12 months.

Collated data included patient demographics, laboratory analyses, type of surgical resection, histopathology analysis and clinical outcome. Preoperative radiological assessment included abdominal ultrasonography (US), computed tomography (CT) scans of the thorax, abdomen and pelvis, and magnetic resonance imaging (MRI) of the liver (from 2008).

All patients were discussed in a specialist multidisciplinary team (MDT) meeting that included hepatobiliary surgeons, and a hepatologist, medical oncologist, radiologist and pathologist prior to surgery or systemic or palliative management.

Revision radical cholecystectomy was offered to patients with incidental gallbladder cancer after cholecystectomy, and without distant metastases on staging CT. T-stages of T-*is* or T1a disease were considered as curative following the initial cholecystectomy and no further radical intervention was provided.[6] In patients with indeterminate gallbladder lesions on imaging, modified radical cholecystectomy was offered. No preoperative histological diagnosis is obtained in this group of patients.

### Surgical data

The operative data from the initial cholecystectomy in the incidental gallbladder cancer group were obtained from referral centres and surgical procedures were graded as simple or difficult. A procedure was defined as 'difficult' either according to clear documentation in the operation notes and/or because a laparoscopic procedure had required to be converted to an open approach. Other data collated included: bile spillage during cholecystectomy; surgical incision (laparoscopic versus open); type of surgery (simple versus resection of the gallbladder bed); other organ involvement, and intraoperative tumour status.

Modified radical cholecystectomy was performed using either a laparoscopic or an open approach. The laparoscopic approach involved the placement of four ports as per standard laparoscopic cholecystectomy. Following initial assessment, a decision was made to proceed either laparoscopically or to convert to an open procedure based on whether the critical view of safety could be dissected.[12] Following dissection, the proximal cystic duct was sent for frozen section examination. The gallbladder was removed en bloc with a 1–2-cm cuff of segment IVb/V of the liver using a Harmonic scalpel (Ethicon Endo-Surgery, Inc, Cincinnati, OH, USA). If the frozen sections were suspicious or positive for gallbladder cancer, the operation was converted to open in order to facilitate a more extensive lymphadenectomy and bile duct excision with biliary reconstruction using Roux-en-Y hepaticojejunostomy.[13] All gallbladders harvested using the laparoscopic approach were routinely retrieved using a specimen retrieval bag. Trocar sites were not routinely excised in this cohort. Open procedures were performed in exactly the same manner.

The length of hospital stay, postoperative complications and 30-day mortality were recorded.

### Histopathology analysis

Histological tumour–node–metastasis (TNM) staging, tumour status at the cystic duct and resection margins were recorded. Microvascular involvement was also noted. As the majority of patients in the incidental gallbladder cancer group were referred from other hospitals, highly accurate histological T-staging was not always available for all patients for data analysis. However, provided that there was an indication for re-resection after the confirmation of incidental gallbladder cancer, all histological sections of the gallbladder were reviewed at the study centre.

### Follow-up protocol

Patients were followed up in a specialist hepatobiliary clinic. Following initial postoperative review at 1 month, all patients were examined in the outpatient clinic at 3, 6, 12, 18 and 24 months and annually thereafter. All patients in this study had a minimum follow-up of 1 year following surgery. Surveillance imaging included CT scans of the thorax, abdomen and pelvis. Patients underwent 6-monthly CT during the first 2 years postoperatively and annual CT scans thereafter.


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