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# Incidental gallbladder carcinoma diagnosed after laparoscopic cholecystectomy

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## ABSTRACT

**Introduction:** Laparoscopic cholecystectomy (LC) is one of the most performed general surgeries. Incidental gallbladder carcinoma (IGBC) is diagnosed in 0.3–2.9% of all cholecystectomies and accounts for most detected gallbladder cancers (GBCs). This study aims to evaluate the incidence, clinical, and prognostic features of IGBC diagnosed after LC for benign gallbladder disease.

**Materials and Methods:** We performed a retrospective analysis of patients who underwent cholecystectomy between January 2016 and October 2021 at the Istanbul Sultanbeyli State Hospital General Surgery Clinic. Data regarding the demographics, pathological features of the tumors, and survival times of patients were examined.

**Results:** A total of 745 patients were analyzed. The patients' median age was 43 (18–78), and the male-to-female ratio was 137:608. Four patients were diagnosed with gallbladder carcinoma after LC; however, one patient had pre-operative suspicious GBC. Three patients were diagnosed with IGBC. The cancer stages and survival times of the IGBC patients were pT2, pT2, and pT1a and 8, 34, and 40 months, respectively.

**Conclusion:** Most GBCs are detected incidentally. The most significant factor determining the prognosis is an early stage detection. To detect IGBC, cholecystectomy specimens must be carefully examined histopathologically.

**Keywords:** Cancer of gallbladder, Cholelithiasis, Gallbladder neoplasm, Laparoscopic cholecystectomy, Incidental gallbladder carcinoma

## Introduction

According to Global Cancer Statistics, more than 115,000 new gallbladder cancer (GBC) cases and 85,000 deaths were estimated to have occurred in 2020. The most common bile duct carcinoma is GBC, which is one of the cancers with a poor prognosis. Early GBCs have more favorable outcomes, but they do not have specific symptoms, so they are mostly discovered incidentally, usually on histopathological examination of the gallbladder specimen after cholecystectomy is performed for a benign diagnosis.[1-4]

Laparoscopic cholecystectomy (LC) is one of the most often performed general surgeries. Incidental gallbladder carcinoma (IGBC) is diagnosed in 0.3–2.9% of all cholecystectomies and accounts for the majority of detected GBCs. Risk factors for IGBC include cholelithiasis, old

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age, female sex, and obesity. For pre-operative diagnosis, suspicious clinical and radiologic findings of IGBC are not specific. Pathological examinations after cholecystectomy are essential in the diagnosis of GBC.[2-4]

This study aims to evaluate the incidence, clinical characteristics, and prognostic features of IGBC diagnosed after LC for benign gallbladder disease in rural areas.

## Materials and Methods

### Study Design

We performed a retrospective evaluation of patients who underwent cholecystectomy between January 2016 and October 2021 at the Istanbul Sultanbeyli State Hospital General Surgery Clinic. This study was approved by the Clinical Research Ethics Committee of Istanbul Kartal Dr. Lutfi Kirdar City Hospital (Number: 2021.514.212.12).

### Inclusion and Exclusion Criteria

Patients diagnosed with GBC through histopathological examination after LC were included in the study.

Exclusion criteria were as follows: Patients under 18 years of age, preoperatively suspected GBC cases, patients who underwent open cholecystectomy, conversion to open surgery during operation, and patients with missing data.

### Data Collection

We used patients' files and hospital records for data acquisition. Data regarding the demographics, pathological features of the tumors, and survival times of patients were examined. The tumor stages were classified according to the American Joint Committee on Cancer 7$^{th}$ edition.[5]

### Statistical Analysis

We performed a statistical analysis using the Statistical Package for the Social Sciences (Version 24 for Mac, IBM Corporation). Descriptive data for continuous variables are shown as the mean and standard deviation. The frequency procedure was applied to the categorical variables. Overall survival is the time from the surgery to the date of death or, if the patient is still alive (months), to the last visit. The confidence interval is set at 95% for statistical significance, and the two-sided $p<0.05$ was considered.

The primary outcome of this study was to determine the incidence and clinicopathological features of IGBC diagnosed after LC in a secondary care hospital.

## Results

All cholecystectomy procedures were evaluated, and after applying the exclusion criteria, 745 patients were analyzed (Fig. 1). The patients' median age was 43 (18–78) years, and the male-to-female ratio was 137:608 (Table 1).

Four patients were diagnosed with gallbladder carcinoma after LC; however, one patient had a pre-operative suspicious GBC. A 41-year-old female patient had an approximately 20 mm polypoid lesion on the gallbladder wall, and after surgery, she was diagnosed with GBC (Stage pT1; overall survival: 25 months; still alive). Three patients had no pre-operative suspicious signs of malignancy, and after a pathological examination of their gallbladder specimens, they were diagnosed with GBC. Detailed information on the patients diagnosed with IGBC is given in Table 2. The incidence of IGBC in our patient cohort was 0.4%.

Patients with IGBC were referred to the tertiary center after diagnosis because the secondary care hospital had no on-

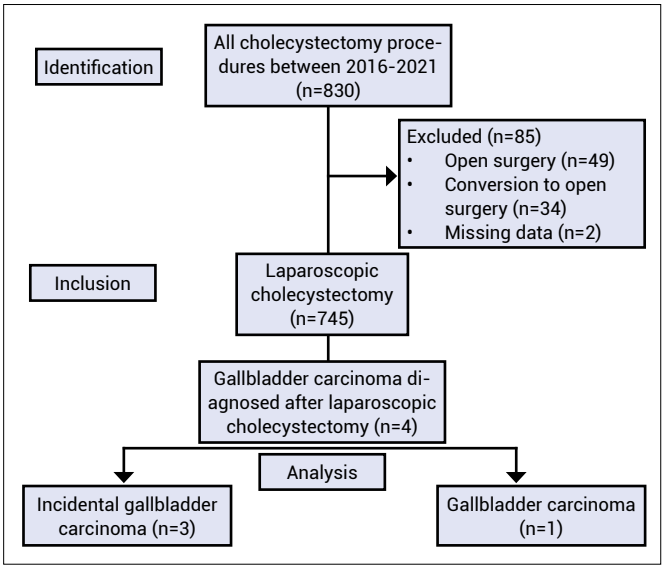


**Figure 1.** Flowchart of patient selection.

**Table 1. Demographics of laparoscopic cholecystectomy patients**

| Parameters | Laparoscopic Cholecystectomy n=745 (%) |
|---|---|
| Age (years, median-range) | 43 (18-78) |
| Sex | |
| Female | 608 (81,6) |
| Male | 137 (18,4) |

**Table 2. Characteristics of patients diagnosed with incidental gallbladder carcinoma**

| Patients | Preoperative Diagnosis | Depth of invasion (T) Status | Overall survival |
|---|---|---|---|
| 39 years old, Female | Chronic cholecystitis + Cholelithiasis | pT2 | Dead, 34 months |
| 46 years old, Male | Cholelithiasis | pT1a | Alive, 40 months |
| 68 years old, Female | Chronic cholecystitis + Cholelithiasis | pT2 | Alive, 8 months |

cology department. Two patients at Stage pT2 of the disease underwent complementary surgery. All three IGBC patients received adjuvant chemotherapy. The survival times of the IGBC patients were 8, 34, and 40 months. One patient died 34 months after being diagnosed, and two patients with IGBC were still alive (Table 2).

## Discussion

GBC is usually asymptomatic at an early stage and has a poor prognosis. While <10% of patients have resectable tumors during surgery, approximately 50% have lymph node metastases.[6] IGBC is defined as GBC found histopathologically after gallbladder removal for symptomatic benign gallbladder disease. GBC is suspected preoperatively in only 30% of patients; the remaining 70% of patients with GBC are discovered incidentally by the pathologist.[7] The incidence of IGBC is reported to be between 0.11% and 3%.[6,8-13] We found the incidence of IGBC in our study to be 0.4%. In recent years, the incidence of IGBC has increased because of an increase in the number of patients undergoing LC.[4]

Gallstones, especially those larger than 3 cm, chronic inflammation, chronic cholecystitis, primary sclerosing cholangitis, and gallbladder polyps larger than 1 cm, have been defined as risk factors for GBC.[14,15] The incidence of GBC in the female-to-male ratio is approximately 2:1.[16] Our patients also had histories of gallstones and chronic cholecystitis. Obesity is another risk factor for GBC, but unfortunately, we could not access records on the body mass indexes of our patients.[17]

The depth of tumor invasion (T stage) is considered the most important prognostic factor.[6,15] Therefore, pathologic examination of all gallbladder specimens removed for benign disease is necessary to detect GBC at an early stage.[10,18,19] Survival critically depends on early detection.[6] The 5-year survival rate is 41% in patients who undergo reresection and only 15% in those who do not.[18]

Surgical resection is the only curative treatment for GBC.[9] A second radical operation is recommended for IGBC. Simple cholecystectomy is sufficient for pT1a tumors.[15] In tumor Stage pT1b and above, and for reexploration, or detected resectable tumors, en bloc hepatic resection plus lymphadenectomy is recommended.[8,14] Adjuvant chemotherapy seems to be associated with better survival rates for IGBC.[4] Our patients received adjuvant chemotherapy.

Our study is a single-center, low-volume study with a limited number of patients and retrospectively collected data resulted in a lack of some information.

## Conclusion

Most GBCs are detected incidentally. The most significant factor determining the prognosis is detecting GBC in the early stage. To detect IGBC, cholecystectomy specimens must be carefully examined histopathologically.

### Disclosures

**Ethichs Committee Approval:** This study was approved by the Clinical Research Ethics Committee of Istanbul Kartal Dr. Lutfi Kirdar City Hospital (Number: 2021.514.212.12).

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

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