



Case series

Surgical strategy for suspected early gallbladder carcinoma including incidental gallbladder carcinoma diagnosed during or after cholecystectomy

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ARTICLE INFO

Keywords:

Suspected early gallbladder carcinoma
Gallbladder carcinoma
GBC
Laparoscopic cholecystectomy
Surgical strategy

ABSTRACT

Purpose: This paper presents an overview of the surgical strategy for patients with suspected gallbladder carcinoma (GBC), including incidental GBC cases, preoperatively or intraoperatively, as well as their outcomes.

Methods: Between April 2009 and December 2017, 529 patients underwent cholecystectomy for gallbladder disease at our hospital. Both intraoperative and postoperative histological examinations of the excised gallbladder facilitated the diagnosis of GBC. Surgery-related variables and surgical approaches were evaluated according to the extent of tumor invasion.

Results: Of 529 patients, eight were diagnosed with GBC during/after cholecystectomy, including four women and four men. Mean age was 75.4 (range, 59–89) years. Five patients had gallbladder stones and three had cholecystitis. Three patients with stages T1b and T2 underwent additional liver bed wedge resections with or without prophylactic common bile duct excision. Five of the eight patients are still alive and two of the remaining three died from other diseases; one patient with pT3 died of recurrent GBC (peritonitis carcinomatosa).

Conclusion: Because of the ability to obtain full-thickness frozen biopsies during laparoscopic cholecystectomy, we could diagnose GBC intraoperatively, allowing for rapid diagnosis and tumor resection. We recommend developing a surgical treatment strategy for suspected early GBC in advance of cholecystectomy.

1. Introduction

Laparoscopic cholecystectomy has become the standard approach for managing benign biliary diseases such as stones, polyps, and cholecystitis. Since the widespread adoption of the laparoscopic approach, the number of patients diagnosed with incidental gallbladder carcinoma (IGBC) has increased. IGBC is defined as carcinoma of the gallbladder identified for the first time during cholecystectomy or unintentionally discovered during histological examination of the gallbladder after cholecystectomy. Some authors have reported the occurrence rate of IGBC to be approximately 0.19%–2.8% [1–3]. We evaluated the surgical strategy for patients with suspected GBC, including incidental GBC cases, preoperatively or intraoperatively, as well as their outcomes.

2. Material and methods

Between April 2009 and December 2017, a total of 529 (273 men and 256 women) patients underwent cholecystectomy for gallbladder

disease at our hospital. Of these patients, 447 underwent a laparoscopic approach (84.5%) and 82 an open approach (15.5%). Eight patients (1.5%) were diagnosed with GBC. All patients underwent a postoperative histopathological examination of the gallbladder, which had been removed. The clinical data reviewed included patient demographics, clinical presentation, histopathological data, TNM stage, operative procedures, and patient outcomes (Table 1). We evaluated the surgery-related variables and surgical approaches according to the extent of tumor invasion.

This study was approved by our ethics committee (SHIROYAMA OP03 2017).

2.1. Surgical strategy for suspected early gallbladder carcinoma at our hospital

A flow chart of the surgical strategy for suspected gallbladder carcinoma cases is shown in Fig. 1. Suspected gallbladder cancer is diagnosed preoperatively based on the following characteristics: elevated lesion with a 10-mm diameter, increasing tumor size, sessile lesion,

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<https://doi.org/10.1016/j.amsu.2018.07.009>

Received 3 April 2018; Received in revised form 7 July 2018; Accepted 25 July 2018

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Table 1
Suspected early gallbladder carcinoma in our hospital.

Case	Age	Sex	Preoperative diagnosis	Diagnosis time	TNM Stage	Histology subtype	Operation	Common bile duct resection	Lymph node dissection	Time (minutes)	Bleeding (ml)	Outcome (recurrence)
1	89	female	Acute cholecystitis Cholecystolithiasis	Postoperative	T3a (liver)N0M0 stage IIIA	Por G3	Open cholecystectomy	no	no	250	400	dead 5 months (peritonitis carcinomatous)
2	79	male	Acute cholecystitis Cholecystolithiasis	Postoperative	T1bN0M0 stage I	tub2 G2	① Open cholecystectomy ② Segmental resection of IVb + V	no	yes	①120 ②340	③320 ④710	alive 6 years 2 months
3	87	female	Acute cholecystitis Cholecystolithiasis	Intraoperative	T2N0M0 stage II	tub2 G2	Open cholecystectomy	no	no	90	100	alive 9 months
4	75	male	Adenomyomatosis or Suspected gallbladder carcinoma	Intraoperative	T3a (liver)N0M0 stage IIIA	tub1 G1	Laparoscopic cholecystectomy ⇨ Wedge resection of the gallbladder bed (1cm)	no	yes	295	300	dead 6 months (brain hemorrhage)
5	63	female	Cholecystolithiasis	Postoperative	TisN0M0 stage 0	tub1 G1	Laparoscopic cholecystectomy	no	no	140	50	dead 2 years 6 months (aortic dissection)
6	67	female	Gallbladder polyp	Intraoperative	T2N1M0 stage IIIB	tub1 G1	Laparoscopic cholecystectomy ⇨ Wedge resection of the gallbladder bed (1cm)	yes	yes	305	460	alive 1 year 6 months
7	59	male	Gallbladder polyp	Postoperative	TisN0M0 stage 0	tub1 G1	Laparoscopic cholecystectomy	no	no	75	5	alive 6 months
8	84	male	Cholecystolithiasis	Postoperative	T2N0M0 stage II	tub1 G1	Laparoscopic cholecystectomy	no	no	95	5	alive 5 months

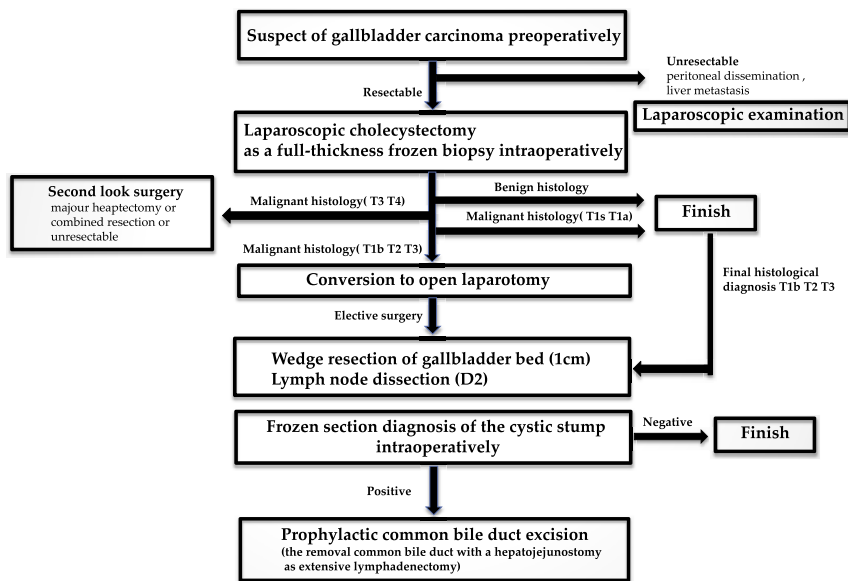


Fig. 1. Surgical strategy for suspected early gallbladder carcinoma in our hospital. This flow chart describes the surgical strategy for the intraoperative diagnosis and treatment of gallbladder carcinoma. It is important to have a surgical plan in place, so that gallbladder carcinoma can be diagnosed and treated during a single procedure.

irregular wall-thickness lesion mimicking cancer, elevated lesion with dense enhancement, FDG PET-positive based on intraoperative macroscopic findings of the resected specimen. We performed intraoperative, histological examinations in patients of suspected gallbladder cancer (GBC) to determine the extent of the surgery and the need for radical resection. Otherwise, full-thickness frozen biopsies were obtained by laparoscopic cholecystectomy, to the extent possible. In case of GBC with pT1b or pT2 or pT3 tumors, we converted to an open radical procedure, such as gallbladder bed resection, or hepatectomy of segments 4a and 5 with lymphadenectomy for pT2 and pT3 GBC cases. Prophylactic common bile duct excision was performed in cases with invasion of the cystic duct stump. For patients with GBC with pT1b or pT2 or pT3 tumors, additional radical surgeries were performed at 4–8 weeks after the original cholecystectomy.

3. Results

Of the 529 patients, eight were diagnosed with GBC during or after cholecystectomy at our hospital, with equal number of both sexes (four women and four men). The mean age was 75.4 (range, 59–89) years. All patients with GBC were Japanese. Five had gallbladder stones and three had cholecystitis. Other preoperative diagnoses included adenomyomatosis of the gallbladder and gallbladder polyps. Only one patient was suspected of gallbladder carcinoma preoperatively. Histological diagnosis of GBC (final diagnosis) was made in three intraoperative and five postoperative cases.

The depth of tumor invasion according to the pathological TNM classification system was confined to the mucosa (pT1s) in two patients, proper muscle layer (pT1b) in one, subserosa (pT2) in three, and beyond the serosa (pT3) in two. The histological subtypes of GBC were as follows: well-differentiated adenocarcinoma (tub1) in five cases, moderately differentiated adenocarcinoma (tub2) in two, and poorly differentiated adenocarcinoma (por) in one. Three patients with stage T1b and T2 tumors underwent additional liver bed wedge resections with or without prophylactic common bile duct excision (Table 1).

The median follow-up time was 17.9 (range, 12–74) months after surgery. Five of the eight patients are still alive, and two patients with stage IIIA and stage 0 died from other diseases (brain hemorrhage or

aortic dissection), and one patient with stage IIIA died of recurrent GBC (peritonitis carcinomatosa).

4. Discussion

Gallbladder cancer is the most common cancer of the biliary tract and is recognized to have both a poor prognosis and poor survival rate. The overall 5-year survival rate is currently reported to be 5%–13% [4–6], with a mean overall survival of three to eleven months [7]. The etiology of GBC is not yet fully understood, because of the significant difficulties associated with its diagnosis. In general, GBC incidence has a geographical distribution; it is common in Chile, Japan and North India [8]. The known risk factors are as follows: gallstones, advanced age, sclerosing cholangitis, and a porcelain gallbladder. The depth of tumor invasion (T) and the presence of lymph node metastasis (N) have also been identified as prognostic factors [9].

We concur with other authors that surgical resection for GBC is the only curative therapy [10,11,12]. However, more than 75% of GBC is not resectable [11]. In addition, one study found that only 30% of patients were suspected to have GBC preoperatively, whereas the remaining 70% were diagnosed during intra-postoperative pathological examination [8]. Therefore, it is difficult to select the appropriate radical surgery for GBC resection.

IGBC is extremely rare, with an occurrence rate of approximately 0.19%–2.8% [1–3]. In our study, only eight patients (1.5%) were diagnosed with GBC. Most patients with GBC tend to be at an early stage of tumor development and, therefore, can undergo surgical resection. Some reports have indicated that the risk factors for IGBC are female sex, age over 65 years, presence of gallstones or polypoid lesions, and Asian or African American descent [13,14,15]. In this study, the mean age of IGBC patients was 75.4 years, and half of the patients were women, five had gallbladder stones, and all were Japanese. All GBC cases in our study tended to be at an early stage, and there were no advanced stage IV cases.

The rationale for our strategy was to perform intraoperative histological examination before proceeding to open surgery, since there is no defined surgical approach for suspected GBC. With this, it is difficult to differentiate GBC from cholecystitis. Three of our eight patients with

IGBC had cholecystitis. Therefore, intraoperative histological examination is useful for suspected GBC. Intraoperative diagnosis by histological examination facilitates proper management in case of doubt and allows for the opportunity to perform radical surgery [16,17]. In our study, we were able to achieve intraoperative diagnosis and convert from cholecystectomy to radical surgery for two cases.

According to Cecilia et al. [18], once IGBC is discovered, re-resection is the recommended treatment strategy for patients with pT1b, pT2, and pT3 tumors, and the optimal time interval for re-resection for incidentally discovered GBC appears to be between four and eight weeks after the initial cholecystectomy. Therefore, we would be able to perform the radical surgery even if the diagnosis of GBC was made postoperatively.

We recommend developing a surgical treatment strategy for IGBC cases (Fig. 1) in advance, since it might be impossible to diagnose the GBC preoperatively, and the surgical resection of GBC contributes to improvements in prognosis. The ability to obtain full-thickness frozen biopsies from laparoscopic cholecystectomy allows for the diagnosis of GBC intraoperatively, including obtaining information on tumor depth. Therefore, surgeons have the ability to convert the procedure to an open radical surgery for GBC (except for pT1s and pT1a cases). The cystic plate is left after a simple cholecystectomy; therefore, additional resection may be required, depending on the depth of the tumor. Additionally, lymph node dissection has been shown to improve survival rates for patients with lymph node metastasis [6]; therefore, D2 lymph node dissection is effective for both accurate staging and survival benefit [19]. In cases with cystic duct involvement, we recommend the removal of the common bile duct with a hepatojejunostomy as an extensive lymphadenectomy [20]. The purpose of this liver resection is the removal of the invaded liver from gallbladder bed directly to prevent micrometastasis. According to Shirobe and Maruyama, wedge resection of the gallbladder bed (1 cm) is efficient than wedge resection of segments IVb and V [21].

5. Conclusion

The surgical strategy we have presented is currently indicated in our hospital, although the surgical treatment of GBC varies depending on the depth of tumor invasion (T), the presence of lymph node metastasis (N), and staging remains controversial. However, we emphasize the importance of constructing a pre-defined strategy for suspected early gallbladder carcinoma, including incidental gallbladder carcinoma, diagnosed during or after cholecystectomy.

Ethical approval

None of the authors has nothing to declare.

Sources of funding

None of the authors has any sources to declare.

Author contribution

Toshikatsu Nitta is first Author. Takashi Ishibashi is my supervisor and he checked my paper. Jun Kataoka, Masato Ohta, Kesuke Fujii, Yuko Takahashi, and Yoshihiro Inoue They work under my department of SHIROYAMA HOSPITAL. And they engaged in each operations together.

Conflicts of interest

The authors declare that there is no conflict of interests.

Research registration number

We registered the Research Registry.
researchregistry3914.

Guarantor

Takashi Ishibashi MEd PhD my supervisor Author Toshikatsu Nitta.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.amsu.2018.07.009>.

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