

Incidental Gallbladder Cancer with the Laparoscopic Treatment in the MRI Era: An Experience at a Single Institution

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Research

Keywords: Incidental gallbladder cancer, Magnetic resonance imaging, Laparoscopic treatment, Intraoperative histological examination, Ultrasonography, Gallbladder diseases

Posted Date: March 18th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-324781/v1>

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Abstract

Background: Magnetic resonance imaging (MRI) has been widely applied to the preoperative diagnosis of gallbladder diseases, among which laparoscopic cholecystectomy plays a critical role. Incidental gallbladder cancer (IGBC) is an unexpected guest of the patients who underwent cholecystectomy, forcing them to receive reoperation for complete resection. This study aimed to share our experience in pre-operative MRI evaluation and laparoscopic management of the IGBCs.

Methods: Between January 2011 and January 2020, 7917 patients with gallbladder diseases and treated by laparoscopy were enrolled in this study.

Results: A total of 49 patients were diagnosed as IGBCs. The incidence of IGBCs in polypoid lesions, biliary pancreatitis, cholecystitis, cholecystocholedocholithiasis and gallbladder stones was 0.42%, 1.19%, 0.62%, 1.20% and 0.49%, respectively. Moreover, 73.5% and 59.2% of the IGBCs had unremarkable preoperative imaging during the ultrasonographic and MRI evaluation respectively. Also, 14 of the patients were diagnosed as gallbladder cancer (GBC) via intraoperative histological examination, and 11 received laparoscopic extensive resection after cholecystectomy.

Conclusion: The patients with biliary pancreatitis and cholecystocholedocholithiasis have a higher incidence of incidental gallbladder cancer. Preoperative MRI evaluation and intraoperative histological examination may help some incidental gallbladder cancers to achieve one-stage laparoscopic extensive resection.

Background

Gallbladder cancer (GBC), an aggressive and highly lethal disease, is the most frequent malignancy of the biliary tract. Laparoscopic cholecystectomy (LC) is considered as the gold-standard management for benign gallbladder disease. It is recommended for the tumors limited to the lamina propria (T1a) in the case of gallbladder cancer. Furthermore, open extended surgery should be performed for T1b, T2, and T3 lesions¹⁻³. Only a third of gallbladder cancers are suspected preoperatively, while most of them are diagnosed incidentally by a pathological examination after surgery⁴. Therefore, to achieve complete resection, patients usually have to accept reoperation according to the cancer stage; while patients with T1a tumors are exceptions, who can be treated by simple cholecystectomy⁵.

With the development of laparoscopic skills, most of the gallbladder diseases have been treated by laparoscopic cholecystectomy; in the meantime, the incidence of IGBC has also risen, even up to 3% according to some reports⁶. Detecting incidental GBC preoperatively in clinical practice is hard since no mass can be observed on stone diseases; while cholecystectomy is generally performed to presumed benign polypoid lesions. Abdominal ultrasound (US) and computed tomography (CT) are commonly used in the pre-operational assessment of gallbladder diseases. Such imaging signs as suspicious lesions and irregularity of the gallbladder wall may provide useful information for preoperative diagnosis of incidental

GBC. Nonetheless, none of them has been widely accepted clinically due to their unsatisfactory sensitivity and specificity ⁷. In our hospital, applying US and MRI to gallbladder diseases for pre-operational evaluation is a common practice. This study aimed to share our experience in pre-MRI evaluation and laparoscopic management of the IGBCs.

Methods

Patients

This study was reviewed and approved by our institutional review board.

A retrospective study was performed on 7917 patients, who were referred to our institution from January 2011 to January 2020 for the management of gallbladder diseases. The preoperative diagnosis of these patients was as follows: cholecystitis (325 cases), gallbladder polyps (721 cases), biliary pancreatitis (252 cases) and gallbladder stones with (1164 cases) or without choledocholithiasis (5455 cases). This study was reviewed and approved by our institutional review board.

Treatment And Data Collection

Preoperative ultrasonography and magnetic resonance imaging/ magnetic resonance cholangiopancreatography (MRI/MRCP) were performed to determine the concomitant choledocholithiasis and to exclude gallbladder cancer in the patients. In addition, enhanced computer tomography was performed on preoperative suspicious cases to exclude the malignancy (Table 1).

Table 1
Baseline characteristics of the patients

Parameter	Number (%)
SEX	
Female	4354 (55)
Male	3563 (45)
Preoperative diagnosis	
Cholecystitis	325 (4.1)
Gallbladder polyps	721 (9.1)
Gallbladder stones	5455(68.9)
Cholecystocholedocholithiasis	1164 (14.7)
Biliary pancreatitis	252 (3.2)

The patients with acute pancreatitis, cholangitis, and jaundice were treated before the operation. Those with concomitant choledocholithiasis received intraoperative bile duct exploration after the laparoscopic cholecystectomy or ERCP/EST before the laparoscopic cholecystectomy. All postoperative histological reports were reviewed and 49 patients were diagnosed with IGBCs. Eventually, their preoperative radiology findings and clinicopathological characteristics were recorded and analyzed. The patient enrollment and treatment algorithm are present in Fig. 1.

Results

General information about the IGBC patients

Of the 7917 patients, 3 patients with polypoid lesions, 3 with biliary pancreatitis, 2 with cholecystitis, 14 with cholecystocholedocholithiasis and 27 with gallbladder stone diseases were diagnosed with IGBCs intraoperatively and(or) postoperatively. Among them, 13 were males and 36 were females, with the age range from 48 to 89 (Table 2).

Table 2
Baseline characteristics of the IGBCs

Parameter	Number (%)
Sex	
Female	36(73.5)
male	13(26.5)
Age	
≤60	16(32.7)
>60	33(67.3)
Presenting complaints	
Abdominal pain	39(79.9)
Jaundice	3(6.1)
NONE	7(14.0)
Preoperative diagnosis	
Cholecystitis	2(4.1)
Gallbladder polyps	3(6.1)
Gallbladder stones	27(55.1)
Biliary pancreatitis	3(6.1)
Cholecystocholedocholithiasis	14(28.6)

Incidence Of Igbc's In Different Gallbladder Diseases

The incidence of IGBCs in polypoid lesions, biliary pancreatitis, cholecystitis, cholecystocholedocholithiasis and gallbladder stones was calculated as 0.42% (3 to 721), 1.19% (3 to 252), 0.62% (2 to 325), 1.20% (14 to 1164) and 0.49% (27 to 5455), respectively (Table 3).

Table 3
Incidence of IGBCs in different gallbladder diseases

Gallbladder diseases	Number (%)
Cholecystitis	2 (0.62)
Gallbladder polyps	3 (0.42)
Gallbladder stones	27 (0.49)
Cholecystocholedocholithiasis	14 (1.20)
Biliary pancreatitis	3 (1.19)

Preoperative Radiology Of The Igbc's

All the IGBCs received ultrasonographic and MRI evaluation preoperatively. Diffuse thickening of the gallbladder with or without suspicion of malignancy and focal thickening of the gallbladder was observed in 2, 5 and 4 patients respectively through ultrasound examination. Furthermore, the suspicious lesion was observed in 2 patients. And 73.5% of the patients had unremarkable preoperative imaging during the ultrasonographic evaluation (Table 4). However, during the MRI examination, diffuse thickening of the gallbladder with or without suspicion of malignancy and focal thickening of the gallbladder were observed in 6, 3 and 8 patients respectively. Furthermore, 3 patients displayed the suspicious lesion. Overall, 59.2% of the patients had unremarkable preoperative MRI imaging (Table 4).

Table 4
Preoperative radiology of the IGBCs

Radiology Findings	Ultrasonography (Number,%)	MRI (Number,%)
Diffuse suspicious thickening	2(4.1)	6(12.2)
Diffuse thickening not suspicious of malignancy	5(10.2)	3(6.1)
Focal Thickening	4(8.2)	8(16.3)
Suspicious lesion	2(4.1)	3(6.1)
Non specific	36(73.5)	29(59.2)

Surgical Information And Postoperative Pathology Of The Igbcs

Additionally, 47 patients underwent laparoscopic cholecystectomy or the following common bile duct exploration; 2 received only laparoscopic exploration due to peritoneal dissemination; 15 received intraoperative histological examination, among whom 14 were diagnosed with GBC intraoperatively and 11 received laparoscopic extensive resection after the cholecystectomy. Of the 33 cases diagnosed after LC, 12 received laparoscopic extensive resection and the rest received open extensive resection four weeks later. According to the pathological TNM classification system, the tumor stages of the IGBCs were pT1a (10 cases), pT1b (14 cases), pT2 (16 cases), pT3 (7 cases) and pT4 (2 cases). Regarding the pathological characteristics of tumors, one case was squamous cell carcinomas, two were papillary carcinoma, one was adenosquamous carcinoma and 45 were adenocarcinomas. Further, among the 45 adenocarcinomas patients, 13 were poorly differentiated, 13 were moderately differentiated, and 19 were well differentiated. The tumor stages and histopathological characteristics of IGBCs are listed in Table 5.

Table 5
Tumor stage and histopathological type of incidental gallbladder cancer

	Intra-operative diagnosis	Post-operative diagnosis	Total
Tumor stage			
T1a	3	7	10
T1b	2	12	14
T2	6	10	16
T3	3	4	7
T4	2	0	2
Histopathological type			
Squamous cell carcinomas	0	1	1
Papillary carcinoma	0	2	2
Adenosquamous carcinoma	0	1	1
Adenocarcinomas	16	29	45

Discussion

Incidental cancer of gall bladder refers to malignancy that is diagnosed through intra-operative or post-operative histological examination for presumed benign gallbladder disease. Traditionally, IGBCs have been considered to be an early-stage tumors with more favorable pathologic characteristics compared to non-incidentally diagnosed GBCs⁸. However, recent studies revealed that stage-matched outcomes for

IGBCs were significantly worse than those operated with initially diagnosed GBCs. Thus, accurate preoperative diagnosis becomes imperative, which may reduce long-term morbidity and mortality of IGBCs⁹⁻¹¹.

Ultrasonography, CT and MRI are widely performed for the preoperative evaluation of the gallbladder diseases. Ultrasonography as a common tool for gallbladder diseases depends largely on the operator's skills¹², which is characterized with low accuracy. CT and MRI are able to capture more accurate and objective features, which help distinguish the benign from the malignant¹³. MRI shares the same sensitivity and specificity of detection with CT¹⁴. As shown in our study, 40.8% of the IGBCs had preoperative imaging findings during the MRI evaluation, such as diffuse thickening of the gallbladder with or without suspicion of malignancy, focal thickening of the gallbladder and suspicious lesions. Furthermore, after the macroscopic examination of the specimens, 15 of them (75%) received intraoperative histological examination. Therefore, it was speculated that macroscopic re-evaluation could improve the specificity of the MRI examination.

Laparoscopic cholecystectomy is the first choice for benign gallbladder diseases and even suspicious gallbladder cancers in some institutes. IGBCs are diagnosed more commonly among patients with laparoscopy cholecystectomy than those with open cholecystectomy. A recent study exposed that the laparoscopic and open cholecystectomy had little influence on the prognosis of incidental gallbladder cancer¹⁵. Even for the IGBCs' re-operation, laparoscopic management could be considered as a valid alternative in the extensive resection of IGBCs¹⁶. As shown in our study, 47 IGBC patients experienced laparoscopic cholecystectomy and 11 patients received laparoscopic extensive resection following the cholecystectomy after intra-operative diagnosis. Furthermore, 12 with T1b stage tumors received laparoscopic extensive resection 4 weeks later after the first LC. Compared to laparoscopic reoperation, one-stage laparoscopic extensive resection can be more easily handled. Therefore, accurate pre- or intra-operative diagnosis plays an important role in the management of IGBCs.

Nomograms have been increasingly used as diagnostic tools to distinguish GBC from gallbladder diseases¹⁷⁻¹⁸. Nevertheless, these tools may be not valuable in IGBCs, since many of them have no remarkable preoperative signs. Radiological findings such as thickening of the gallbladder wall and/or polyps can be the subtle signs of malignancy for gallbladder diseases¹⁹⁻²⁰. In our study, 26.5% and 40.8% of the patients had subtle preoperative imaging during the ultrasonographic and MRI evaluation, respectively. Although preoperative contrast-enhanced CT excluded the malignancy from these suspicious cases, macroscopic re-evaluation was still performed during the operation. Notably, 15 cases received frozen section examination, among whom, 14 were diagnosed with GBCs intra-operatively. Therefore, we conclude that the subtle MRI findings can provide useful information for the diagnosis of IGBC. The combination between macroscopic re-evaluation and intraoperative frozen pathological examination will increase the accuracy and allow some incidental gallbladder cancers to achieve one-stage laparoscopic extensive resection, especially for the cases confined to the gallbladder wall.

Conclusions

In conclusion, we found that the patients with biliary pancreatitis and cholecystocholedocholithiasis were associated with a higher incidence of incidental gallbladder cancer. Laparoscopic management could play an important role in the re-operation of IGBCs. Preoperative MRI evaluation and intraoperative histological examination may help some incidental gallbladder cancers to achieve one-stage laparoscopic extensive resection.

Abbreviations

MRI Magnetic resonance imaging

IGBC Incidental gallbladder cancer

US Abdominal ultrasound

CT Computed tomography

GBC Gallbladder cancer

LC Laparoscopic cholecystectomy

TNM Tumor-Node-Metastasis

Declarations

Authors' contributions

Yong Zhou, Wen-zhang Zha and Xu-dong Wu provided oversight for the project. Wen-zhang Zha, Yong Zhou, and Ren-gen Fan performed the operations. Yong Zhou and Ren-Gen Fan contributed to data collections, data analysis and writing.

Acknowledgements

None.

Funding

The study was supported by the Jiangsu Provincial Young Talents Program of Medicine (Grant No. QNRC2016471), Scientific Research Project of Jiangsu Provincial Health Commission (Grant No. M2020100) and Yancheng Medical Science Development Foundation (Grant No. YK2017006).

Conflict of interest

The authors declare no conflicts of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author on reasonable request.

Ethics approval and consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study is approved by Ethics Committee of Yancheng City NO.1 People's Hospital.

Consent for publication

It is unavailable.

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Figures

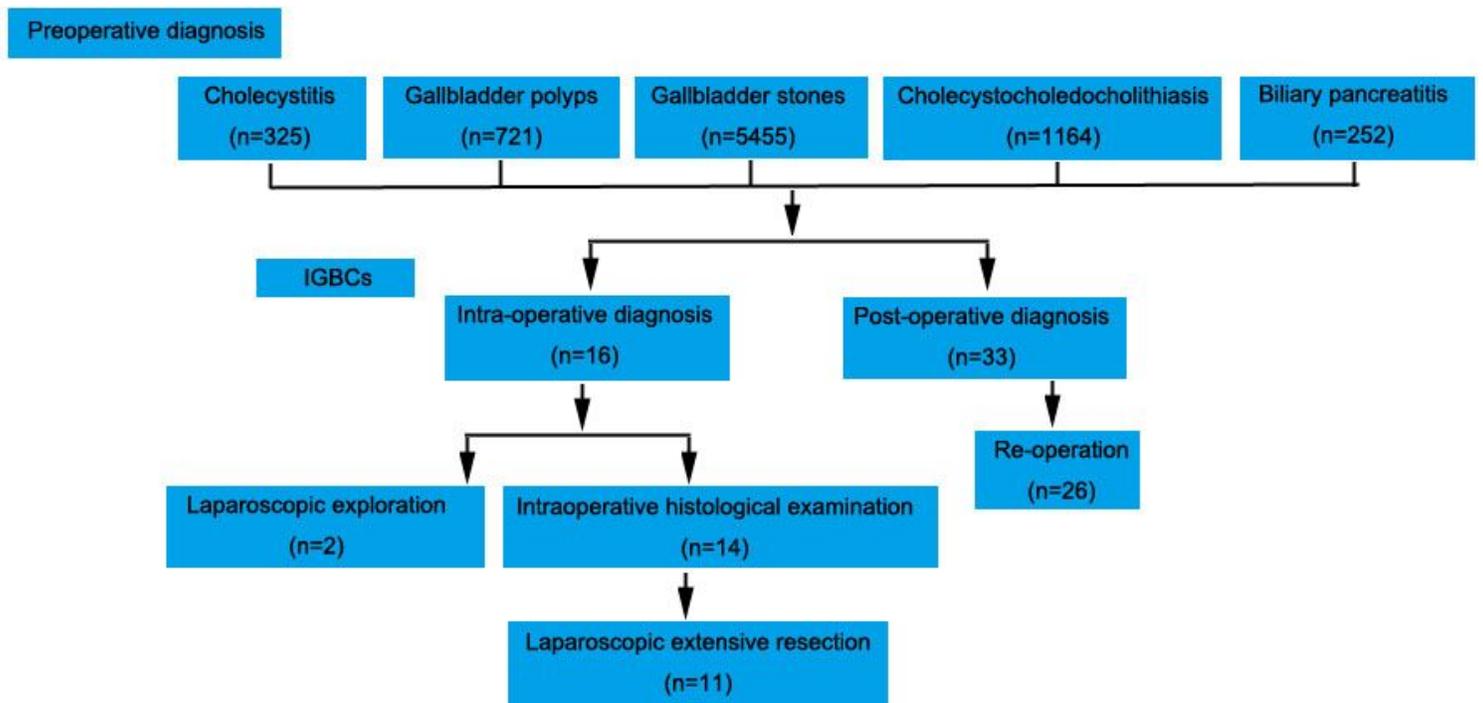


Figure 1

Flow chart of patient enrollment and treatment algorithm.