

Unexpected pathological findings after laparoscopic cholecystectomy – analysis of 1131 cases

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Videosurgery Miniinv 2018; 13 (1): 62–66

DOI: <https://doi.org/10.5114/wiitm.2017.69594>

Abstract

Introduction: Gallbladder specimens are routinely sent for histopathological examination after cholecystectomy in order to rule out the presence of unexpected pathological findings.

Aim: To establish the overall incidence of unexpected pathological findings in patients who underwent laparoscopic cholecystectomy for symptomatic gallbladder disease and determine whether the macroscopic appearance of the gallbladder in ultrasound examination could be a valid method for identifying patients with gallbladder malignancy.

Material and methods: A retrospective study was conducted between 2013 and 2015. All histological reports ($n = 1131$) after cholecystectomy were searched for unexpected pathological findings. In cases where unexpected pathological findings were identified the additional analysis of preoperative abdominal ultrasound examination (USG) was done to determine the usefulness of USG in diagnosis of gallbladder malignancy.

Results: Of the 1131 patients included in the study, 356 (31.47%) were male and 774 (68.43%) were female. Unexpected pathological findings were present in 21 cases. The overall incidence of unexpected pathological findings was 1.86%. Only in 5 patients were suspicious appearances of gallbladder observed in preoperative ultrasound examination. In 16 patients there was no suspicion of malignancy. The positive predictive value of USG was 0.238.

Conclusions: The incidence of unexpected pathological findings after laparoscopic cholecystectomy was 1.86%. Ultrasonography has low positive predictive value for identifying patients with malignant findings in a gallbladder specimen.

Key words: cholecystectomy, gallbladder, gallbladder malignancy, histopathological examination, ultrasound examination.

Introduction

Cholecystectomy is one of the most commonly performed surgical procedures. The laparoscopic approach is safe and feasible [1]. However, other minimal accesses have been described and may be more popular in the near future [2, 3]. The main indications are gallstone-related diseases and, therefore, changes related to gallstone pathology are commonly observed during routine histological examination (i.e. chronic or acute cholecystitis, empyema, mucocele,

cholesterol deposits) [4]. Pathology guidelines still advise routine histological examination of gallbladder specimens due to the possibility of unexpected pathological findings, including gallbladder carcinoma (CaGB), biliary intraepithelial neoplasia (BillIN), epithelial dysplasia or metastasis from other organs [5]. This is supported by data showing that incidental findings in cases of CaGB during routine histopathology vary from 0.17% to 3.3%, with a range of 0.4–0.7% in Western countries [6]. On the other hand, a selective approach for histological examina-

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tion of gallbladder specimens has been proposed by various authors, when considering the overall large scale economic implications and the low prevalence of the disease [7–9].

Aim

The aim of this study was to: (1) establish the overall incidence of unexpected pathological findings in patients who underwent laparoscopic cholecystectomy for symptomatic gallbladder disease and (2) determine whether the macroscopic appearance of the gallbladder in ultrasonography could be a valid method for identifying patients with gallbladder malignancy.

Material and methods

Between January 2013 and December 2015, a total of 1131 laparoscopic and open cholecystectomies were performed in a single institution. Clinical data were retrospectively collected and included age, sex, body mass index (BMI), indications for surgery, preoperative ultrasonography, methods of operation, intraoperative findings, histopathological reports and postoperative complications. Each cholecystectomy case was assessed for unexpected pathological findings detected in the histopathological examination. Unexpected pathological findings were defined as the presence of one of the following: adenocarcinoma, epithelial dysplasia, biliary intraepithelial neoplasia (BillIN), primary and secondary (metastatic) tumors of the gallbladder. In cases where unexpected pathological findings were identified, an additional preoperative abdominal ultrasound examination (USG) was performed to determine the usefulness of USG in the diagnosis of gallbladder malignancy.

Statistical analysis

Data were analyzed using SAS University Edition software (SAS Institute Inc., Cary, NC, USA). Logistic regression was performed to identify risk factors for unexpected pathological findings. Demographic variables were included in the analysis (age, gender and BMI).

Results

Of the 1131 patients included in the study, 356 (31.47%) were male and 774 (68.43%) were female. The youngest patient who underwent a cholecystec-

tomy was 19 years old and the oldest was 92 years old. The mean age was 55 ± 15 years. Descriptive characteristics are shown in Table I. The majority of patients underwent laparoscopy ($n = 1064$, 94%), while open surgery was performed in 16 (1.4%) cases. Forty-three (3.8%) procedures were started in laparoscopy, but had to be converted to the open technique due to operative findings/complications. One thousand and four (75.4%) operations were per-

Table I. Overview of 1131 patients in the study ($N = 1131$)

Parameter	Value
Sex, n (%):	
Male	356 (32.27)
Female	774 (68.43)
Age [years]:	
Mean	55 ± 15
Range	19–92
Method of operation, n (%):	
Laparoscopy	1064 (94)
Laparotomy	16 (1.4)
Conversion	43 (3.8)
Histopathological findings, n (%):	
Chronic inflammation	382 (33.76)
Cholelithiasis	273 (24.14)
Purulent cholecystitis	312 (27.59)
Polyps	17 (1.5)
Pathological findings	21 (1.86)
Body mass index [kg/m^2]:	
Range	15.2–58.4
Mean	28.6 ± 5.6
Operation priority, n (%):	
Emergency procedure	92 (6.91)
Postponed procedure	35 (2.62)
Planned procedure	1004 (75.4)
Hospitalization [days]:	
Mean	3.74
Duration	1–31

formed as planned. Emergency surgery was necessary in 92 (6.91%) cases. Thirty-five (2.62%) patients were treated with interval cholecystectomy between 4–8 weeks after the initial episode of acute cholecystitis. The mean length of hospitalization was 3.7 ±2.3 days. The mean BMI was 28.6 ±5.6 kg/m².

Unexpected pathological findings were present in 21 cases. The overall incidence of unexpected pathological findings was 1.86%. All findings are listed in Table II. Out of 21 cases with unexpected pathological findings, the most common histopathological diagnoses were partially tubular, partially papillary adenocarcinoma (*n* = 7, 0.61%), pseudopyloric metaplasia (*n* = 4, 0.35%), and minor grade epithelial dysplasia (*n* = 3, 0.27%). The majority of the rest of the 1131 gallbladder specimens' histological findings were chronic inflammation (*n* = 382, 33.8%), purulent cholecystitis (*n* = 312, 27.6%), cholelithiasis (*n* = 273, 21.5%) and gallbladder polyps (*n* = 17, 1.5%).

The patients with unexpected findings had a mean age of 65 ±13 years. The mean BMI was 27.5 ±5 kg/m². Fifteen (71%) were female and 6 (29%) were male. The majority of patients (*n* = 18, 85%) underwent a laparoscopic operation, 1 (5%) patient had open surgery and in 2 (1%) cases there was conversion to the open technique. Nineteen (90%) operations were performed as planned. Emergency surgery was necessary in 2 (10%) cases. The mean length of hospitalization was 4.48 ±2.82 days. Logistic regression analysis revealed a correlation be-

tween the presence of unexpected findings and age (OR = 1.047, 95% CI: 1.010–1.085, *p* = 0.0125). Body mass index and gender were not risk factors for unexpected findings in histological examination, and were: OR = 0.957, 95% CI: 0.861–1.064, *p* = 0.417 and OR = 0.939, 95% CI: 0.32–2.758, *p* = 0.908, respectively.

The ultrasonography results were analyzed in all 21 cases of unexpected pathological findings confirmed by histopathological examinations. Only 5 patients had a suspicious appearance of the gallbladder observed in preoperative ultrasonography. In the remaining 16 patients, there was no suspicion of

Table III. Analysis of 21 cases of malignancy confirmed by histopathological examination (*N* = 21)

Parameter	Value
Sex, <i>n</i> (%):	
Male	6 (29)
Female	15 (71)
Age [years]:	
Mean	65 ±13
Range	34–83
Method of operation, <i>n</i> (%):	
Laparoscopy	18 (85)
Laparotomy	1 (5)
Conversion	2 (10)
Body mass index [kg/m ²]:	
Range	19.5–39.0
Mean	27.43 ±5.01
Pre-operative suspicion, <i>n</i> (%):	
USG positive	5 (24)
USG negative	16 (76)
Operation priority, <i>n</i> (%):	
Emergency procedure	2 (10)
Postponed procedure	0
Planned procedure	19 (90)
Hospitalization [days]:	
Mean	4.48 ±2.82
Duration	3–15

Table II. Analysis of unexpected histopathological findings (*N* = 1131)

Pathological findings	<i>N</i> (%)
Partially tubular, partially papillary adenocarcinoma	7 (0.61)
Biliary adenocarcinoma	1 (0.09)
Well-differentiated adenocarcinoma	1 (0.09)
Adenocarcinoma with medium grade dysplasia of glandular epithelium	1 (0.09)
High grade intraepithelial neoplasia BILLIN-3	1 (0.09)
Low grade biliary intraepithelial neoplasia BILLIN-1	2 (0.18)
Pseudopyloric metaplasia	4 (0.35)
Minor grade epithelial dysplasia	3 (0.27)
Metastatic breast cancer	1 (0.09)

malignancy. The positive predictive value (PPV) of ultrasonography in detecting unexpected pathological findings is 0.238 (Table III).

Discussion

In our study, the incidence of unexpected pathological findings was 1.86%. Comparable data have been published by other authors [5, 7, 10]. For example, Samad reported an incidence of 1.1% of malignancy in patients who underwent cholecystectomy for presumed chronic cholecystitis with cholelithiasis [11]. Gallbladder malignancy usually does not have any characteristic clinical features in over 90% of patients presenting symptoms of acute or chronic cholecystitis [5]. Most of the patients in our study presented with prior history of chronic cholecystitis, and there were no symptoms or signs suggesting an underlying malignancy in any of the patients. Many authors suggest that ultrasonography has low diagnostic accuracy for both advanced and early gallbladder cancer [5, 12]. Only 5 of the unexpected pathological findings in this study were suspected on preoperative ultrasound. In a similar study by Siddiqui *et al.*, none of the six carcinomas were suspected on ultrasound [5]. This contrasts with a study by De Zoysa *et al.* [13] in which all four cancers were suspected either on preoperative ultrasonography or during surgery. The authors suggest a more selective approach to gallbladder histology. Similar observations and recommendations were also made in a study by Darmas *et al.* [7]. Recently, reports have also questioned the role of routine histopathological examination in all cholecystectomy specimens [8]. They state that the incidence of incidental gallbladder carcinoma is too low to justify routine histopathological examination and that the routine histopathological examination of all cholecystectomy specimens overburdens pathology departments and hospital resources. A selective approach for histological examination of gallbladders was suggested [5, 7–9, 14]. The proposed selective criteria were based on the intraoperative macroscopic appearance of the gallbladder. However, there are still reports in which unexpected findings were diagnosed only with the final histological examination. Byars *et al.* [15] suggested that advanced age and female sex combined with the data from radiological investigations, intra-operative macroscopic findings and the clinical picture

of the patient could further increase the accuracy of the selective criteria. Our analysis confirmed the association between age and the risk of unexpected findings. However, the association was not present regarding gender and BMI.

Moreover, there is a discussion regarding the cost of histopathological examination. Mohamed and colleagues postulate the importance of estimating the economic implications of a routine histological approach and the advantages of a selective approach [16]. Byars *et al.* also suggest that there is a feasible and effective approach to reducing the number of gallbladders sent for histology, which increases cost-effectiveness and saves time [15].

Therefore, we recommend routine histopathological examination of all gallbladders removed at surgery, as the preoperative USG examination has low positive predictive value. Despite the low incidence of unexpected pathological findings, some of them require further treatment and a selective approach may overlook serious disease.

There are some limitations to our study. Firstly, our study is retrospective. Prospective studies are necessary to further assess and test our findings. Secondly, the number of included patients is limited. In view of the low incidence of unexpected findings, a high number of patients is required to provide sufficient power. In order to safely modify the current guidelines, a prospective, multicenter study must be performed.

Conclusions

The incidence of gallbladder carcinoma and other pathological findings in patients who underwent laparoscopic cholecystectomy for symptomatic gallbladder disease was 1.86%. Advanced age was associated with higher risk of unexpected findings. Ultrasonography has low positive predictive value in detecting unexpected pathological findings. Therefore, we strongly advocate conducting routine histopathology of all cholecystectomy specimens.

Conflict of interest

The authors declare no conflict of interest.

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Received: 21.04.2017, **accepted:** 3.07.2017.