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Is Histopathological Examination After Cholecystectomy Necessary or Redundant?

Kolesistektomi Sonrası Histopatolojik İnceleme Gereklilik mi Yoksa Fazlalık mı?

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Abstract

Background: Although cholecystectomy is one of the most frequently performed surgeries in general surgical practice, the incidence of gallbladder cancer is very low. The aim of this study is to investigate whether selective histopathological examination, based on preoperative and perioperative suspicion, can replace routine examination of all specimens removed after cholecystectomy.

Materials and Methods: This study was conducted retrospectively with 2,355 patients who underwent cholecystectomy and were examined histopathologically between January 1, 2015 and December 31, 2024 at Amasya Sabuncuoğlu Şerefeddin Training and Research Hospital. Pathology results were divided into 3 groups as benign, premalignant and malignant.

Results: Of the 2,355 patients included in the study, 569 (24.2%) were male and 1,786 (75.8%) were female. The average age was found to be 56.45 (minimum: 18 maximum: 98). Benign lesions were detected in 99.2% of specimens. Premalignant lesions were found in 0.6% of the remaining specimens, including 6 (0.3%) cases of low-grade dysplasia and 7 (0.3%) cases of biliary intraepithelial neoplasia (low grade). Only five (0.2%) o f the patients had gallbladder cancer.

Conclusions: In the pathology of 2,355 patients included in this study, premalignant lesions were detected in 0.6% and malignancy in 0.2%. In all specimens that were malignant, either preoperative imaging or operative findings predicted malignancy. In this context, we believe routine histopathological examination is unnecessary when preoperative and intraoperative imaging does not reveal any suspicious findings and when there are no special risk factors. This suggests that, as it is a common surgery, there will be a reduction in labor loss and a potential decrease in costs

Keywords: Cancer, Cholecystectomy, Dsplasia, Gallbladder, Histopathological examination

Öz

Amaç: Kolesistektomi, genel cerrahi pratiğinde çok sık olarak yapılan ameliyatlardan biri olmakla beraber safra kesesi kanseri insidansı çok düşüktür. Bu çalışmanın amacı kolesistektomi sonrası çıkarılan tüm spesmenler yerine preoperatif ve peroperatif şüphe halinde seçici bir histopatolojik inceleme yapılıp yapılmayacağının sonucunu araştırmaktır.

Materyal ve metod: Bu çalışma, Amasya Sabuncuoğlu Şerefeddin Eğitim ve Araştırma Hastanesi'nde 1 Ocak 2015-31 Aralık 2024 tarihleri arasında kolesistektomi yapılan ve histopatolojik olarak incelenen 2.355 hasta ile retrospektif olarak gerçekleştirildi. Patoloji sonuçları benign, premalign ve malign olarak 3 grubaayrıldı.

Bulgular: Çalışmaya dahil edilen 2.355 hastanın 569'u (%24,2) erkek, 1.786'sı (%75,8) kadındı. Yaş ortalaması 56,45 minimum: 18 maximum: 98 olarak bulundu. Patoloji incelemesinin %99,2 sinde benign lezyonlar tespit edildi. Geriye kalan patolojik spesmenlerin 6 tanesi (%0,3) low grade displazi, 7 tanesi (%0,3) biliyer intraepitelyal neoplazi (low grade) olmak üzere %0,6'sında premalign lezyonlar bulundu. Hastaların sadece 5 tanesinde (%0,2) sinde safra kesesi kanseri tespit edildi.

Sonuç: Bu çalışmaya dahil edilen 2.355 hastanın patolojisinde %0,6'sında premalign lezyonlar, %0,2'sinde malignite tespit edilmiştir. Malignite tespit edilen tüm spesimenlerde ya preoperatif görüntülemelerde ya da intraoperatif bulgularda maligniteyi öngörebilecek durumlar mevcuttu. Bu bağlamda preoperatif görüntülemelerde ve intraoperatif olarak şüpheli bir durum olmaması halinde ya da özellikli risk faktörü taşımayan gruplarda rutin histopatolojik inceleme gerekmeyebileceğini düşünmekteyiz. Bu durum çok sık gerçekleştirilen bir ameliyat olması sebebiyle iş gücü kaybının azalacağını ve maliyetlerin düşebileceğini göstermektedir.

Anahtar Kelimeler: Displazi, Histopatolojik inceleme, Kanser, Kolesistektomi, Safra kesesi

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Introduction

Cholecystectomy is one of the most common operations performed by general surgeons worldwide (1). Cholecystectomy is performed for cholecystitis, symptomatic cholelithiasis, biliary dysfunction, biliary pancreatitis, gallbladder polyps and gallbladder cancer. Specimen pathologies are mostly benign. Gallbladder cancers are the most common type of cancer among biliary tract malignancies, though they are relatively rare (2). The most common types of gallbladder cancer (GBC) occur in various regions, including North India, Pakistan, South Asia, South America, and Eastern Europe (1).

GBC is 3 times more common in women than in men. After the age of 60, the incidence increases, but the average age of diagnosis is around 70. Additionally, risk factors include primary sclerosing cholangitis, certain medications such as methyldopa and isoniazid, obesity, and Western-style eating habits. A diet high in fat, calories, and processed foods can contribute to gallstones, and over time, this can lead to type 2 diabetes, obesity and a higher chance of gallbladder cancer. Incidental malignancy is observed in 0.2-2.9% of cholecystectomy pathologies (3,4). For the diagnosis of malignancy, preoperative imaging and intraoperative macroscopic findings may raise suspicion (5).

The surgical treatment for GBC varies depending on the tumor's stage. While a simple cholecystectomy is sufficient for treating patients with Tis and T1a tumors, more advanced surgery is required for T1b and above tumors (4,6). The guidelines suggest that the whole excised specimen be examined histopathologically. Recently, the necessity of examining all specimens, given the increased workload and higher costs, has been questioned (7-10). This study aimed to investigate the necessity of routine histopathological examination (HPE) of every specimen after cholecystectomy.

Materials and Methods

This study was conducted with 2,355 patients who underwent cholecystectomy and HPE at Amasya Sabuncuoğlu Şerefeddin Training and Research Hospital between January 1, 2015, and December 31, 2024. Patients under the age of 18 and pregnant women were excluded from the study. Only patients whose primary surgical indication was cholecystectomy were included. Patients with known malignancy or those who underwent cholecystectomy as a secondary procedure were excluded. The study was conducted retrospectively by reviewing age, sex, preoperative imaging results, perioperative surgical notes, and postoperative pathology results from the hospital's data system. The study was carried out in accordance with the Declaration of Helsinki and was approved by the ethics committee (Amasya University Non-Interventional Ethics Committee date: 10.04.2025, number: 2025/49)

Statistical Analysis

IBM Statistical Package for the Social Sciences (SPSS) version 21 software (SPSS Inc., Chicago, IL, USA) was used in the study. Frequency (n) and percentage values were used in the evaluation of categorical variables, and mean, standard deviation and minimum-maximum values were used in the evaluation of numerical variables. Chi-square test was used for categorical variables. The entire study was evaluated with 95% confidence interval. P value <0.01 was considered significant.

Results

Of the 2,355 patients included in the study, 569 (24.2%) were male and 1,786 (75.8%) were female. The mean age was 56.45 years (minimum: 18, maximum: 98). Benign lesions were detected in 99.2% of the pathology examinations. Pathological examination revealed that 2,158 patients (91.6%) had chronic cholecystitis and cholesterolosis, 37 patients (1.6%) had chronic cholecystitis with cholesterol polyps, 37 patients (1.6%) had xanthogranulomatous cholecystitis, 1 patient had biliary cystadenoma, 38 patients (1.6%) had pyloric metaplasia, and 66 patients (2.8%) had intestinal metaplasia; in the remaining specimens, premalignant lesions were found in 13 cases (0.6%), including 6 cases (0.3%) of low-grade dysplasia, and 7 cases (0.3%) of biliary intraepithelial neoplasia [(BilIN), low grade] (Figure 1). GBC was identified in only 5 patients (0.2%) (Table 1). In two of these cases, increased gallbladder wall thickness and significant adhesions to the liver bed were observed perioperatively, raising suspicion of malignancy. In two other patients, preoperative imaging revealed polypoid lesions measuring 2 cm in the gallbladder. In the remaining patient, a 23 mm gallstone was identified on preoperative imaging. Among the five patients with malignant pathology, four were female and one was male. All were older than the mean age of the overall study population (56.45 years). No statistically significant gender differences were found among benign, premalignant, and malignant pathologies. Although the frequency of malignant pathologies increased with age, this increase was not statistically significant (p=0.06).

Discussion

In our study, patients with malignant pathology showed preoperative or perioperative suspicion of malignancy. Conversely, there were no patients with malignant pathology who had no suspicion either preoperatively or perioperatively. Considering the current increase in population, obesity incidence, and Western-style dietary habits, it is expected that the number of cholecystectomy operations will continue to rise. Since examining every specimen causes increased workload and costs, we believe that HPE in selected cases, rather than routine examination of all specimens, would be more cost-effective.

In this study, GBC was detected in 5 patients (0.2%) out of 2,355 cholecystectomy specimens. Additionally, premalignant lesions were found in 13 patients (0.6%), including 6 cases (0.3%) of low-grade dysplasia and 7 cases (0.3%) of BilIN. None of the 13 premalignant cases in our series exhibited a gallbladder wall thickness exceeding 4 mm or a polyp size greater than 1 cm-features that would typically raise suspicion for malignancy on preoperative imaging or intraoperative macroscopic assessment. Furthermore, no radiological features predictive of premalignant lesions have been described in the literature. In a single-center study by Özel and Dinç (11), which evaluated 8,148 cholecystectomies, 173 patients were found to have premalignant pathology. That study reported no statistically significant difference in premalignant lesion frequency between men and women. All malignant cases occurred in patients over 50 years of age, and the frequency of premalignant lesions increased after the age of 50 years (11). Detection of premalignant lesions prior to histopathological evaluation remains unfeasible. Nevertheless, patients diagnosed with premalignant lesions on pathology do not require additional surgical intervention or follow-up beyond cholecystectomy. In a single-center study conducted by Olthof et al. (12) in the Netherlands, 2,763 cholecystectomy specimens were examined, with macroscopic anomalies observed in 199 cases, among which 4 cases of GBC were identified. Similarly, in another study by van Vliet et al. (13) in the Netherlands, 1,375 cholecystectomy specimens were examined, with macroscopic anomalies in 185 cases, among which 6 cases of GBC found. A study by Mittal et al. (14) examined 1,312 patients who underwent cholecystectomy due to gallstone disease; carcinoma was detected in 13 patients, and abnormalities were present in all of these samples. No cancer was diagnosed in gallbladders with a normal macroscopic appearance. In a study by Kalita et al. (15) including 4,115 patients, 18 cases of incidental GBC were identified. However, macroscopic evaluation of these 18 cases revealed localized growth in 10 patients and diffuse thickening of the gallbladder wall in 8 patients (15). In a study conducted by Hamdani et al. (16), 7 cases of incidental GBC were observed. Macroscopic evaluation of these incidental GBCs revealed polypoid mass lesions in 3 cases, wall thickening in 2 cases, and mucosal irregularity in 2 cases (16). The study by Benkhadoura et al. (10) demonstrated that all patients with GBC were diagnosed either preoperatively or intraoperatively, and none of the patients with GBC were diagnosed through HPE alone.

Table 1. Demographic distribution of pathological specimens

Pathology	**-**	**Female, n (%)**	**Male, n (%)**	**Total, n (%)**
Benign pathologies	-	1,771	566	2,337 (99.2%)
	Chronic cholecystitis and cholesterolosis	1,645	513	2,158
	Chronic cholecystitis and cholesterol polyps	22	15	37
	Xanthogranulomatous cholecystitis	16	21	37
	Biliary cystadenoma	1	0	1
	Pyloric metaplasia	33	5	38
	Intestinal metaplasia	54	12	66
Premalign pathologies	-	11	2	13 (0,6%)
	Low grade dysplasia	5	1	6
	Biliary intraepithelial neoplasia (BilIN) (Low Grade)	6	1	7
Malignant pathologies	-	4	1	5 (0.2%)
	Adenocancer	4	1	5 (0.2%)
Total	-	1,786 (75.8%)	569 (24.2%)	2,355

Findings in the literature that may suggest malignancy include gallbladder wall thickness of 12 mm or more, irregular and asymmetrical wall formation, and loss of the interface with the liver (17). Terzioglu et al. (18), in a single-center study of 278 patients, found neoplastic polyps to be present in 5% of cases and reported that sessile morphology ($p<0.001$) was an independent precursor to neoplastic polyps. They continued to suggest that sessile polyps, including focal gallbladder wall thickness >4 mm, are considered a risk factor (18). An important point in this regard is the need to distinguish true wall thickening from adenomyomatosis (19). Consistent with previous studies, in our study, there was an increase in gallbladder wall thickness in 2 of 5 patients with gallbladder cancer, with the wall thickness measured as 5 mm in one case and 4 mm

in the other case, and significant adhesion to the liver bed was seen perioperatively, raising the suspicion of malignancy. In 2 other patients, preoperative imaging revealed polypoid lesions measuring 2 cm in the gallbladder. Adenomatous polyps of the gallbladder occur in approximately 4-7% of the population and are considered neoplastic. The malignancy potential increases in polyps larger than 1 cm, and malignant polyps tend to be solitary and larger than 2 cm in diameter (20,21). In a study by Wennmacker et al. (22), polyps were found in 2,085 of 220,612 cholecystectomies performed between 2003 and 2013. Of these, 56.4% were neoplastic (40.1% premalignant, 59.9% malignant) and 43.6% were non-neoplastic (41.5% cholesterol polyp, 37.0% adenomyomatosis, 21.5% other). Pathologic polyp size was reported in 1,059 patients. There was a significant difference in size between neoplastic and non-neoplastic polyps (18.1 mm vs. 7.5 mm, p<0.001) (22). In 1 patient, a 23 mm gallstone was detected preoperatively. Gallstones increase the prevalence of cancer by approximately 4 to 5 times. The risk of cancer rises with the size of the gallstone and chronic inflammation. Compared to stones smaller than 1 cm, gallstones measuring 2-3 cm increase the cancer risk by 2.4 times, while stones 3 cm or larger increase the risk tenfold (23,24). Deng et al. (6) identified GBC in 46 (0.32%) of 14,369 cholecystectomy specimens, and only two patients with Tis and T1a stages showed no suspicious lesions during preoperative and intraoperative findings. There are concerns about the presence of early-stage GBC in a normal gallbladder specimen. However, in this case, simple cholecystectomy is considered sufficient, and no further treatment is required (12,13,25,26).

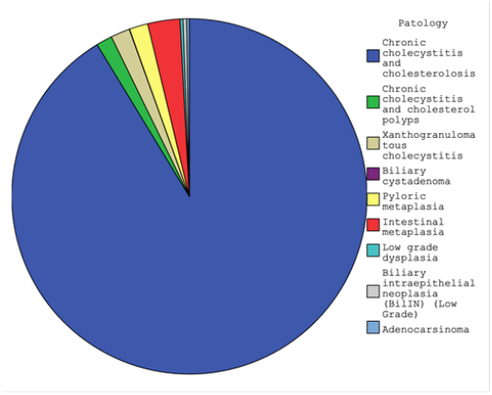

Figure 1. Gallbladder histopathological examination results

In the literature it is reported that gallbladder malignancy increases with age. Elshaer and colleagues suggested that age should also be used to select gallbladder specimens for HPE, as all patients with cancer in their study were over 51 years of age (26). Wrenn and colleagues concluded that selective screening based on risk factors (including elderly patients), intraoperative findings, and table examination of the specimen may be a feasible and more cost-effective alternative to universal screening (27). In our study, although the frequency of malignant pathologies increased with age, this increase was not statistically significant (p=0.06).

Conclusion

Current knowledge suggests that the risk of GBC increases in patients over 50 years of age, those with cholelithiasis, those with gallstones larger than 1 cm, those with primary sclerosing cholangitis, those with obesity, and those who are female. Furthermore, in perioperatively suspected cases, macroscopic examination of the specimen reveals findings such as polypoid masses, wall thickening, and mucosal irregularities, which can be interpreted as malignancy.

The strongest argument for routine HPE is the possibility of detecting incidental malignancy. However, in our study, only 5 malignancies and 13 premalignant lesions were identified among

2,355 cases. All malignancies had suspicious findings either on preoperative imaging or during intraoperative macroscopic assessment; therefore, these patients would have been sent for histopathological evaluation under the selective policy. None of the premalignant lesions were suspected preoperatively or intraoperatively, but in all such cases, cholecystectomy was curative and no additional surgical or oncological intervention was required.

From an ethical perspective, the balance between the risk of missing a diagnosis and the cost savings achieved through a selective histopathology policy is crucial. Our findings indicate that clinically significant malignancies can be safely identified without routine examination. While missing premalignant lesions is theoretically possible, the absence of any change in disease course or need for further treatment means this does not translate into clinically meaningful harm. Therefore, directing limited healthcare resources toward areas with greater potential health benefits appears ethically defensible without compromising patient safety.

However, we believe that this conclusion requires further studies and meta-analyses to support it.

Ethical Approval: *This study was approved by the Amasya University Non-Interventional Ethics Committee (approval no: 2025/49, date: April 10, 2025).*

Author Contributions:

Concept: F.C, B.B.S.

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Design: H.T, F.C.

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Analysis and interpretation: F.C, H.T.

Writing manuscript: F.C, H.T.

Critical revision of manuscript: B.B.S, S.N.Ö.

Conflict of Interest: *The authors have no conflicts of interest to declare.*

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