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Research

Gallbladder Cancer Incidentally Detected in the Histopathological Analysis of Patients Undergoing Cholecystectomy: The Case of Turkey

Kolesistektomi Yapılan Hastaların Histopatolojik İncelemesinde İnsidental Saptanan Safra Kesesi Kanseri: Türkiye Örneği

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ABSTRACT

Objective: Gallbladder cancer is a type of cancer that is difficult to diagnose. Although its prevalence is low, it may differ from one society to another. The current study evaluates whether the histopathological evaluation of specimen should be performed after cholecystectomy.

Methods: This research was designed as a retrospective, cross-sectional registry study. The diagnosis-related group data of 112,884 patients who underwent cholecystectomy in 2016 in hospitals affiliated with the Turkish Ministry of Health were used in the study. Descriptive statistics were used in the analysis of demographic data, diagnosis and types of procedures, and the chi-square analysis was used to compare the distribution of gallbladder cancer.

Results: Approximately 19% of the patients who underwent cholecystectomy were in the age group of 65 years and over. Approximately 75% were women. The rate of laparoscopic cholecystectomy was found to be higher in female patients. Because of the histopathological examination of the cholecystectomy specimen, 0.10% of the patients were diagnosed with gallbladder cancer. The incidence of benign neoplasms of the gallbladder was equal in men and women. Gallbladder cancer was seen at a higher rate in men than in women and in the ≥65-year group compared to the <65-year group. The incidence of gallbladder cancer according to the type of procedure was determined to be 16 times higher in patients who underwent open cholecystectomy and 17 times higher in cases converted to open cholecystectomy compared to laparoscopic cholecystectomy.

Conclusion: During the detection of gallbladder cancer, a thorough evaluation of the risk factors of patients involving detailed and careful macroscopic examinations can prevent unnecessary histological examinations. Thus, resources allocated to health services can be used more efficiently by reducing unnecessary health expenditures.

Keywords: Gallbladder cancer, cholecystectomy, histopathology

ÖZ

Amaç: Safra kesesi kanserleri tanı konulması zor olan kanser türlerinden biridir. Prevelansı düşük olduğu bilinmekle birlikte, prevelansı topluma göre farklılık gösterebilmektedir. Bu araştırmanın amacı kolesistektomi sonrası spesmenin histopatolojik değerlendirme yapılmasının gerekip gerekmediğini değerlendirmekti.

Gereç ve Yöntem: Araştırma geriye dönük, kesitsel bir kayıt araştırmasıdır. Araştırmada Türkiye Sağlık Bakanlığı hastanelerinde, 2016 yılında kolesistektomi işlemi yapılan 112.884 hastanın tanı ilişkili gruplar verileri kullanıldı. Demografik verilerin, tanı ve işlem türlerinin analizinde tanımlayıcı istatistikler; safra kesesi kanserlerinin dağılımının karşılaştırmasında ki-kare analizi kullanıldı.

Bulgular: Kolesistektomi yapılan hastaların yaklaşık %19'u 65 ve üzeri yaş grubundaydı. Yaklaşık %75'i kadınlardan oluşmaktaydı. Kadın hastalarda laparoskopik kolesistektomi yapılma oranı daha yüksek bulundu. Kolesistektomi spesmenin histopatolojik incelmeleri sonucunda hastaların toplam %0,10'unda safra kesesi kanseri teşhis edildi. Safra kesesinin selim neoplazm görülme oranı kadınlar ve erkeklerde eşit bulundu. Safra kesesi kanseri ≥65 yaş ve erkeklerde karşıt gruplarına göre daha yüksekti. İşlem türüne göre safra kesesi kanseri görülme oranı; laparoskopik

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kolesistektomi hastalarına göre açık kolesistektomi işlemi yapılan hastalarda 16 kat, açığa dönen kolesistektomi işlemi yapılan hastalarda 17 kat daha yüksek bulundu.

Sonuç: Safra kesesi kanserlerini tespit etmek için risk faktörlerinin iyi değerlendirilmesi, ayrıntılı ve dikkatli makroskobik incelemelerle gereksiz histopatolojik incelemelerin önüne geçilebilir. Böylece gereksiz sağlık harcamaları azaltılarak sağlık hizmetlerine ayrılan kaynakların daha etkin kullanılabileceğini söyleyebiliriz.

Anahtar Kelimeler: Safra kesesi kanseri, kolesistektomi, histopatoloji

INTRODUCTION

Gallbladder cancer is a type of cancer that is difficult to manage (1). It is a very aggressive malignancy with rapid progression and high mortality rate, and usually detected in advanced ages when it spreads to other organs (2,3). The prevalence of gallbladder cancer is low, but it occurs in approximately 1%-2% of all cholecystectomy patients (4). Although it is less common in developed countries, ethnicity is also known to be one of the risk factors, and its prevalence varies considerably (5). Age, gender, ethnicity, gallstones, chronic infection, obesity, environmental exposures, gallbladder polyps, and genetic predisposition increase the risk of gallbladder cancer (5). It is also more common in women than in men (6).

The treatment of the disease is surgery, and a pathological analysis is not performed in every patient (5,7). However, a histological examination has become routine practice in some countries (8,9). The diagnosis of gallbladder cancer can be made based on a macroscopic pathological examination (9). Some studies claim that a histopathological examination does not change the results obtained from macroscopic examinations during and after surgery (1,10). Therefore, significant savings in health expenditures can be achieved by eliminating unnecessary histopathological examinations (8,11,12).

Early-stage gallbladder cancer generally shows the same characteristics as cholecystitis (5,6,13), and among the patients who underwent laparoscopic cholecystectomy, the rate gallbladder cancer was reported to be 0.3% based on a histopathological examination (5). Studies indicate that it is more effective to decide whether to send gallbladder material for a histological examination according to the evaluations made at the end of the macroscopic examination since the rate of gallbladder cancer detected because of a histological examination is low (1,8). This will ensure the more efficient use of resources, such as time, space, human power, and health technologies.

This study examined the necessity of a histopathological evaluation of the specimen after cholecystectomy.

METHODS

Data

In this study, a total of 112,884 patients who underwent cholecystectomy in 2016 in public hospitals affiliated with the Turkish Ministry of Health were screened. The data of the study were obtained from the General Directorate of Health Services of the Turkish Ministry of Health with permission (dated 06.07.2018 and numbered 23642684-010.99). The research protocol was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University with the decision dated 24.08.2017 and numbered GO 17/709-32.

Patient data were obtained from the clinical coding data of diagnosis-related groups (DRG). The demographic data and pathology results of the patients were obtained retrospectively from the electronic records. Gender, age (<65 and ≥65 years) were used as demographic data. All patients diagnosed with gallbladder cancer were included in the study. Patients diagnosed with any other cancer were excluded from the sample. The diagnosis of gallbladder cancer was based on the pathology laboratory examinations of the patients' cholecystectomy procedure materials. In public hospitals in Turkey, cholecystectomy materials are routinely subjected to a histological examination, and gallbladder cancer is diagnosed on the basis of the results of this examination.

Statistical Analysis

Microsoft Office Excel 2016 was used to organize the data of the patients, and the analysis of the data was performed using IBM SPSS Statistics v. 23 software package (IBM Corp., Armonk, NY, 2016). Descriptive statistics were given for data on gender, age, gallbladder malignant neoplasms, benign gallbladder neoplasms, and cholecystectomy procedure type. The chi-square analysis was used to examine the distribution of gallbladder cancer by gender, age, and cholecystectomy procedure type and compare them variable groups. The confidence interval was set as 95% and the significance value as $p<0.05$.

RESULTS

According to the results of the study, approximately 19% of the patients who underwent cholecystectomy were in the age group of ≥65 years. It was observed that approximately 68% of this age group consisted of women. The incidence of malignant neoplasms of the gallbladder was approximately two times higher in male patients than in females. The incidence of benign neoplasms of the gallbladder was similar between the genders. In the female patients, the rate of laparoscopic cholecystectomy was higher but the rate of conversion from laparoscopic to open cholecystectomy was lower compared to the male patients (Table 1).

Although the number of female patients who underwent cholecystectomy was three times higher than that of male patients, the rate of gallbladder cancer detection in the male patients was approximately two times greater compared to the female patients. The detection rate of gallbladder cancer in patients aged 65 years and over was approximately five times higher than the group under 65 years, and this difference was found to be statistically significant ($p<0.001$). While gallbladder cancer was detected to be very low at 0.04% in laparoscopic cholecystectomy, this rate was approximately 19 times higher in patients undergoing open cholecystectomy and 16 times higher in cases converted from laparoscopic to open cholecystectomy ($p<0.001$ for both) (Table 2).

DISCUSSION

This study is critical since, among the studies conducted to date, it included the highest number of patients undergoing cholecystectomy and diagnosed with gallbladder cancer in Turkey.

In this study, we determined that the number of women who underwent cholecystectomy was approximately three times higher than that of men. Women having a cholecystectomy indication rate is similar to literature studies (5,8,9,11-15). However, contrary to the literature, we found the incidence of gallbladder cancer to be approximately twice greater than in men than in women. In other studies, the gallbladder cancer detection rate has been reported to be higher in female patients (8,14). In this study, the rate of benign gallbladder neoplasm detection was found to be equal between the male and female patients.

According to our results, the rate of gallbladder cancer detection in the ≥65-year group was approximately five times higher than the <65-year group. Similarly, other studies have also shown that the rate of gallbladder cancer detection is higher in elderly patients (9,11,12).

In our study, the rate of gallbladder cancer was found to be 0.10% according to the histopathological examination results of 112,884 patients. In a study by Bazoua et al. (12) with 2,890 patients who underwent cholecystectomy, the gallbladder cancer detection rate was reported to be 0.17%. In another study, van Vliet et al. (11) suspected gallbladder cancer in the macroscopic examinations of approximately 14% of patients who underwent cholecystectomy and detected gallbladder cancer in 6% of these patients after a histopathological examination. In the same study, according to the results of the histopathological examination, gallbladder cancer was not present in any patient without an abnormal finding in the macroscopic examination. Siddiqui et al. (13), evaluating 220 patients who underwent cholecystectomy, found the gallbladder cancer detection rate as 2.8%. In a study by Lundgren et al. (7), the rate of gallbladder cancer detection

Table 1. Distribution of age, neoplasm and cholecystectomy procedure type by gender in cholecystectomy patients

		Gender (n/%)		Total
		Male	Female	
Age	<65	21.611/76.2	69.918/82.7	91.529/81.1
	≥65	6.768/23.8	14.587/17.3	21.355/18.9
Malignant neoplasm of the gallbladder	No	28.334/99.8	84,434/99.9	112.768/99.9
	Yes	45/0.2	71/0.1	116/0.1
Benign neoplasm of the gallbladder	No	28.340/99.9	84.411/99.9	112.751/99.9
	Yes	39/0.1	94/0.1	133/0.1
Cholecystectomy type	Laparoscopy	24.403/86.0	77.958/92.3	102.361/90.7
	Laparoscopy converted to open	517/1.8	573/0.7	1.090/1.0
	Open	3.459/12.2	5.974/7.1	9.433/8.4
Total		28.379/25.1	84.505/74.9	112.884/100.0

Table 2. Gender and age group comparison of gallbladder cancer diagnosis

		Malignant neoplasm of the gallbladder (n/%)		p
		No	Yes	
Gender	Male	28.334/99.84	45/0.16	0.001*
	Female	84.434/99.92	71/0.08	
Age	<65	91.476/99.94	53/0.06	<0.001*
	≥65	21.292/99.70	63/0.30	
Cholecystectomy type	Laparoscopy	102.325/99.96	36/0.04	<0.001*
	Laparoscopy converted to open	1.083/99.36	7/0.64	
	Open	9.360/99.23	73/0.77	
Total		112.775/99.90	109/0.10	

*p<0.05, Pearson's chi-square test results

among cholecystectomy patients was 0.26%. Emmett et al. (8) reported that gallbladder cancer could be successfully diagnosed through a careful macroscopic evaluation and the incidence of undetectable gallbladder cancer during the macroscopic examination was very low. Therefore, the authors suggested that it was not necessary to send the gallbladder material of every patient for a histopathological examination (1,8,10). For patients with no clinical or imaging suspicion of gallbladder carcinoma (GBC) and no evident abnormalities on gross examination, there is no consensus on a uniform pathological examination protocol. It has been reported that in areas with high GBC prevalence, microscopic evaluation can be performed for at least three random areas and cystic duct margins in the gallbladder, which appears normal on examination (16). Evidence of dysplasia or neoplasia on the initial random sampling ensures complete sampling of the gallbladders in many countries, microscopic examination is not recommended or performed in these situations (17).

GBC has been associated with choledochal cysts, abnormal union of the pancreatobiliary ducts, and primary sclerosing cholangitis, particularly the presence of polyps larger than 1 cm detected preoperatively (16,18). A more comprehensive examination of the gallbladder is required in such circumstances. Additionally, cases of hyalinized cholecystitis with minimal or no calcification (incomplete porcelain gallbladder) tend to have a high prevalence of mild invasive cancer and should be thoroughly explored (19).

In our study, according to the results of the histological examination, the rate of gallbladder cancer was 0.04% for the patients who underwent laparoscopic cholecystectomy, 0.64% for the cases in which laparoscopic surgery was converted to open surgery, and 0.77% for those that underwent open cholecystectomy. In a study by Yamamoto et al. (20) with 1,829 patients who underwent cholecystectomy, gallbladder cancer was reported because of a histological examination in 0.54% of those who underwent laparoscopic cholecystectomy. In another study, the rate of gallbladder cancer detection was reported to be 0.5% among patients who underwent laparoscopic cholecystectomy (4). Kalita et al. (15), who performed laparoscopic cholecystectomy, determined this as 0.44%. In the same study, the authors stated that gallbladder cancer was detected at a rate of 0.1% in the histopathological examination of 9,991 patients without suspicious findings in the macroscopic examination.

This study has several limitations. First, this research is a retrospective cross-sectional study. Second, only public hospital patient data were used in the study. Research data were obtained from the Turkish DRG system. Therefore, the accuracy of the data is limited by the accuracy of the data in the DRG system.

CONCLUSION

During the detection of gallbladder cancer, a thorough evaluation of the risk factors of patients involving detailed and careful macroscopic examinations can prevent unnecessary histological examinations. Thus, resources allocated to health services can be used more efficiently by reducing unnecessary health expenditures.

ETHICS

Ethics Committee Approval: The research protocol was approved by the Non-Interventional Clinical Research Ethics Committee of Hacettepe University with the decision dated 24.08.2017 and numbered GO 17/709-32.

Informed Consent: Retrospective study.

Authorship Contributions

Concept: H.A., S.E., Design: H.A., S.E., Data Collection or Processing: H.A., Analysis or Interpretation: H.A., S.E., Literature Search: H.A., S.E., Writing: H.A., S.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Darmas B, Mahmud S, Abbas A, Baker AL. Is there any justification for the routine histological examination of straightforward cholecystectomy specimens? Ann R Coll Surg Engl 2007;89:238-41.
2. Björk D, Bartholomä W, Hasselgren K, Edholm D, Björnsson B, Lundgren L. Malignancy in elective cholecystectomy due to gallbladder polyps or thickened gallbladder wall: a single-centre experience. Scand J Gastroenterol 2021;56:458-62.
3. Shrestha R, Tiwari M, Ranabhat SK, Aryal G, Rauniyar SK, Shrestha HG. Incidental gallbladder carcinoma: value of routine histological examination of cholecystectomy specimens. Nepal Med Coll J 2010;12:90-4.
4. Lundberg O, Kristoffersson A. Open versus laparoscopic cholecystectomy for gallbladder carcinoma. J Hepatobiliary Pancreat Surg 2001;8:525-9.
5. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. Clin Epidemiol 2014;6:99-109.
6. Gourgiotis S, Kocher HM, Solaini L, Yarollahi A, Tsiambas E, Salemis NS. Gallbladder cancer. Vol. 196, American Journal of Surgery. Elsevier; 2008. p. 252-64.
7. Lundgren L, Muszynska C, Ros A, Persson G, Gimm O, Valter L, et al. Are Incidental Gallbladder Cancers Missed with a Selective Approach of Gallbladder Histology at Cholecystectomy? World J Surg 2018;42:1092-9.
8. Emmett CD, Barrett P, Gilliam AD, Mitchell AI. Routine versus selective histological examination after cholecystectomy to exclude incidental gallbladder carcinoma. Ann R Coll Surg Engl 2015;97:526-9.
9. Koppatz H, Nordin A, Scheinin T, Sallinen V. The risk of incidental gallbladder cancer is negligible in macroscopically normal cholecystectomy specimens. HPB (Oxford) 2018;20:456-61.
10. Dix FP, Bruce IA, Krypcyzk A, Ravi S. A selective approach to histopathology of the gallbladder is justifiable. Surgeon 2003;1:233-5.
11. van Vliet JL, van Gulik TM, Verbeek PC. Is it necessary to send gallbladder specimens for routine histopathological examination after cholecystectomy? The use of macroscopic examination. Dig Surg 2013;30:472-5.
12. Bazoua G, Hamza N, Lazim T. Do we need histology for a normal-looking gallbladder? J Hepatobiliary Pancreat Surg 2007;14:564-8.
13. Siddiqui FG, Memon AA, Abro AH, Sasoli NA, Ahmad L. Routine histopathology of gallbladder after elective cholecystectomy for gallstones: waste of resources or a justified act? BMC Surg 2013;13:26.
14. Zhang WJ, Xu GF, Zou XP, Wang WB, Yu JC, Wu GZ, et al. Incidental gallbladder carcinoma diagnosed during or after laparoscopic cholecystectomy. World J Surg 2009;33:2651-6.
15. Kalita D, Pant L, Singh S, Jain G, Kudesia M, Gupta K, et al. Impact of routine histopathological examination of gall bladder specimens on early detection of malignancy - a study of 4,115 cholecystectomy specimens. Asian Pac J Cancer Prev 2013;14:3315-8.
16. Aloia TA, Járufe N, Javle M, Maithel SK, Roa JC, Adsay V, et al. Gallbladder cancer: expert consensus statement. HPB (Oxford) 2015;17:681-90.
17. Renshaw AA, Gould EW. Submitting the entire gallbladder in cases of dysplasia is not justified. Am J Clin Pathol 2012;138:374-6.
18. Goldin RD, Roa JC. Gallbladder cancer: a morphological and molecular update. Histopathology 2009;55:218-29.
19. Patel S, Roa JC, Tapia O, Dursun N, Bagci P, Basturk O, et al. Hyalinizing cholecystitis and associated carcinomas: clinicopathologic analysis of a distinctive variant of cholecystitis with porcelain-like features and accompanying diagnostically challenging carcinomas. Am J Surg Pathol 2011;35:1104-13.
20. Yamamoto H, Hayakawa N, Kitagawa Y, Katohno Y, Sasaya T, Takara D, et al. Unsuspected gallbladder carcinoma after laparoscopic cholecystectomy. J Hepatobiliary Pancreat Surg 2005;12:391-8.