J Surg Med. 2018;2(2):127-129.
DOI: 10.28982/josam.414185

Research article
Araştırma makalesi

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Incidental gallbladder cancer: Review of 3856 cholecystectomies

İnsidental safra kesesi kanseri: 3856 kolesistektominin incelemesi

Kemal Tekeşin [1], Abdullah Şişik [1]

[1] Department of General Surgery, University of Health Science, Umraniye Education and Research Hospital, Istanbul, Turkey

Abstract

Aim: Gallbladder cancer (GBC) is a rare but fatal disease that causes more than 5000 new cases per year in the United States. In the pre-operative period, it is diagnosed in less than 20% of the cases of GBC. The remaining cases are diagnosed after laparoscopic cholecystectomy or intraoperative. Following the 0.25-3% of laparoscopic cholecystectomy, GBC is incidentally detected during histopathology. However, the incidental GBC constitutes 74-92% of all GBCs. The most important step in this disease is the correct staging. Staging determines disease management and treatment options and predicts survival. Curative surgeries in the treatment of GBC are limited to local resectable disease. In this study, it was aimed to present cases of GBC which was diagnosed incidentally after cholecystectomy and premalignant gallbladder lesions (BillIn: Biliary intraepithelial neoplasia).

Methods: 3856 patients who underwent cholecystectomy between 2009 and 2017 constituted the study universe. Patients who were diagnosed as incidental GBC (eight patients (0.21%)) and BillIn (five patients (0.12%)) were examined as a result of histopathological examination. The patients were recorded in terms of demographic data, histopathology, surgical reports and follow-up.

Results: A total of 13 (0.33%) patients were detected in the study group, including GBC and BillIn. The mean age of patients was 54.8±14.3 (age range 33-83), seven male and six women. Although cholecystectomy was performed more frequently in women (72.7%) as determined in the study universe, GBC was seen more frequently in male gender ($p<0.05$). Distribution of tumor stage in malignant patients was identified; four patients were observed in T2, three patients T1a and T3 GBC in one patient, BillIn in five patients.

Conclusion: GBC and BillIn are rare histopathological findings which are detected after cholecystectomy performed due to gallstone disease. Mean survival time of GBC is lower than other gastrointestinal cancers. The recent pre-operative examinations and a frozen-section examination in case of malignancy suspicion has been suggested in the literature, therefore surgeons should be prepared for advanced therapies.

Keywords: Gallbladder, Incidental cancer, Cholecystectomy

Öz

Amaç: Safra kesesi kanseri (SKK), ABD'de yılda 5000'den fazla yeni vakaya neden olan ender görülen ancak ölümcül bir hastalıktır. Ameliyat öncesi dönemde SKK olgularının %20'sinden azında teşhis konulur. Kalan olgular laparoskopik kolesistektomi sonrası ya da intraoperatif olarak teşhis edilir. SKK, laparoskopik kolesistektomilerin %0,25-3'ünü takiben tesadüfen histopatoloji sırasında saptanır. Bununla birlikte insidental SKK, tüm SKK'ların %74-92'sini oluşturmaktadır. Bu hastalıkta en önemli adım doğru evrelendirilmedir. Evreleme, hastalık yönetimi ve tedavi seçeneklerini belirler ve sürviyi öngörür. SKK tedavisinde küratif ameliyatlar, lokal rezektabl hastalık ile sınırlıdır. Bu çalışmada kolesistektomi sonrası insidental tespit edilen SKK ve premalign safra kesesi lezyonu olan biliyer intraepitelial neoplazi (BillIn) (safra kesesi displazisi) olgularını sunmak amaçlanmıştır.

Yöntemler: Çalışma evrenini 2009-2017 yılları arasında kolesistektomi gerçekleştirilen 3856 hasta oluşturdu. Histopatolojik inceleme sonucunda insidental olarak saptanan SKK (sekiz hasta (%0,21)) ve BillIn (beş hasta (%0,12)) tanısı alan hastalar irdelendi. Hastalar demografik veriler, histopatoloji, ameliyat raporları ve takipler açısından kayıt edildi.

Bulgular: Çalışma grubunda SKK ve BillIn olmak üzere toplam 13 (%0,33) hasta tespit edildi. Hastaların ortalama yaşı 54,8±14,3 (yaş aralığı 33-83), yedisi erkek ve altısı kadın idi. Çalışma evreninde tespit edildiği kadarıyla kolesistektomi kadınlarda (%72,7) daha sık yapılmasına rağmen, SKK erkek cinsiyette daha sık görüldü ($p<0,05$).

Sonuç: SKK ve BillIn safra taşı hastalığına yönelik kolesistektomi sonrası tesadüfen rastlanan histopatolojik bulgulardır. Diğer gastrointestinal kanserlere göre, SKK sağkalımı düşük olan kanserlerdendir. Literatürde önerilen ameliyat öncesi yakın zamanda gerçekleştirilecek görüntüleme tetkikleri, gereğinde frozen inceleme yapılması ve gerekebilecek ileri tedavilere hazırlıklı olmaktır.

Anahtar kelimeler: Safra kesesi, İnsidental kanser, Kolesistektomi

Corresponding author / Sorumlu yazar:
Kemal Tekeşin
Address / Adres: Genel Cerrahi Kliniği, Ümraniye Eğitim ve Araştırma Hastanesi, Ümraniye, İstanbul, Türkiye
E-mail: ktekesin@yahoo.com

Ethics Committee Approval: Ethics committee approval was not received because of retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 10.04.2018
Accepted / Kabul Tarihi: 12.04.2018
Published / Yayın Tarihi: 12.04.2018

Copyright © 2018 The Author(s)
Published by JOSAM
This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite / Atıf için: Tekeşin K, Şişik A. Incidental gallbladder cancer: Review of 3856 cholecystectomies. J Surg Med. 2018;2(2):127-129.

Introduction

Laparoscopic cholecystectomy is the gold standard for the treatment of benign gallbladder diseases in all over the world, with decreased postoperative pain, premature oral intake, premature discharge and better cosmetic results, with low morbidity rates for the last 20 years. Although developments in imaging techniques are promising, especially with the widespread use of techniques such as abdominal tomography (CT) and ultrasound (USG), early detection of gallbladder cancer (GBC) that does not cause specific symptoms in the early period may not be possible. In general, only 30% of the patients have doubts in the preoperative period and the remaining 70% are revealed in postoperative pathological examination [1-3]. In other words, in the literature, approximately 1 of each 100 laparoscopic cholecystectomy could be diagnosed with cancer [4].

For the first time, Maximillian Stoll mentioned GBC in Vienna in 1777 [5]. After many years, Nevin et al. [6] revealed the first GBC staging and the survival rates following the open cholecystectomy. Drouard et al. [7] showed the port location metastases in 1991. The GBC is a very aggressive disease and 5-year survival rates 3-13%, the mean survival time is 3-11 months. The underlying cause of these ratios is the very late occurrence of the symptoms such as pain, jaundice and the disease is in very advanced stages when diagnosed (T3, T4) [1,8]. The incidental GBC is a cancer diagnosed with postoperative pathological examination that is not diagnosed in the preoperatively period. There is no effective treatment method except for the surgical resection of the GBC, and the complete resection appears as a single curative method [9-11].

The aim of our study is to determine the incidence of incidental GBC in patients who underwent laparoscopic cholecystectomy due to symptomatic gallbladder stone in our clinic, compare with the rates in our country and the world in light of literature information, clinical and to investigate their pathological characteristics, to determine the prognostic factors affecting survival, and to detect recurrence rates.

Materials and methods

We designed a retrospective cohort study. The records of 3856 patients who underwent laparoscopic cholecystectomy due to symptomatic gallbladder stone between 2009 and 2017 at our general surgery clinic were retrospectively examined. In the postoperative period, the demographic characteristics of patients who were diagnosed as GBC and biliary intraepithelial dysplasia (BillIn) with histopathological examination and survival rates were determined, and compared with literature information. In the preoperative period, physical examination, anamnesis, laboratory or radiological examinations were not suspicious for malignancies in any of the patients. All surgeries were performed by specialist general surgeons, with 14 mm-Hg CO2 with standard 4 ports and pneumoperitonium. Tumor staging were recorded according to the criteria in American Joint Committee on Cancer (AJCC) [12]. The postoperative follow-up and treatment of the patients were performed according to international guidelines.

Statistical analysis

Categorical variables are expressed as the frequency and percentage, parametric data with normal distribution are expressed as mean ± standard deviation, parametric data that does not conform to the normal distribution are expressed as median, inter quartile range and value range. In comparison, Fisher's exact test was used for categorical data; the T-Test is used for parametric data. If the value of p is 0.05 or lower than 0.05 in the confidence range of 95%, the differences were considered statistically significant.

Results

A total of 13 (0.33%) patients were detected in the study group including GBC (n=8, 0.20%) and BillIn (n=5). Flow diagram of the study is shown in figure 1. The mean age of patients was 54.8±14.3 (age range 33-83), seven male and six women. Although cholecystectomy was performed more frequently in women (72.7%) as determined in the study universe, GBC was seen more frequently in male gender ($p<0.05$). Distribution of tumor stage in malignant patients was identified; Four patients were observed in T2, three patients T1a and T3 GBC in one patient, BillIn in five patients. Patients with T3 were diagnosed during surgery. Advanced surgical resection was not possible due to poor patient's overall condition. The patient deceased at the postoperative first month. Both extended hepatectomy and lymphatic dissection were performed in patients with T2 GBC; while these patients were alive and followed (the average follow-up period was 18 months). Surgery was not performed due to the detection of metastasis in one patient, the patient deceased at six months after the first surgery. In one patient, no additional surgery could be performed because a patient did not approve the surgery. No additional treatment was applied to patients who were diagnosed with T1a GBC and BillIn.

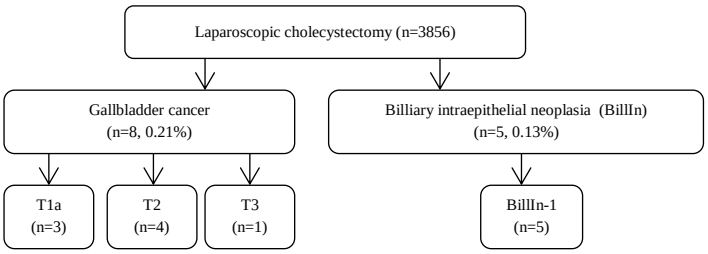

Figure 1: Flow diagram of the study

Discussion

GBC is a rare cancer and is seen at 3 percent in 100,000 worldwide. The incidence is a geographical distribution and is most commonly seen in Chile, Japan and Northern India. The most frequent cancer of the bile pathways is the gastrointestinal tract's most frequent cancer [1,13]. Gallbladder stones, advanced age, sclerosing cholangitis, porcelain pouch factors such as GBC's best known risk factors. In general, the prognosis of GBC is relatively weak and the presence of the tumor's penetration depth and lymph node metastasis was determined as the most important prognostic factors. After cholecystectomy, the unexpected GBC was first reported in 1961. Nowadays only one third of the GBC can be diagnosed in preoperative period [3,14,15]. It is diagnosed with histopathological examination

following laparoscopic cholecystectomy which is performed due to benign pathologies. In the normal population, the risk of women getting to the GBC is 2-6 times higher and the incidence increases with age. However, the male gender is a distinct bad prognostic factor in the GBC and is associated with shorter survival rates [16]. In our study, the prevalence of male patients was significantly higher, but the limited follow-up makes lower the significance of this outcome.

The most important risk factor for gallbladder cancer has been reported to be chronic inflammation. The presence of inflammation is also associated with peroperative perforation and the spread of saffron to the body, which affects the prognosis negatively. In 70-98% of patients, calcium is found in the pouch [16,17]. In our study, no perforation has been reported during the peroperative period, with the determination of the calcium detection rate in the gallbladder. Curative surgical resection improves the survival rate of GBC. Simple cholecystectomy is adequate for T1a GBC and 5-year survival rates for these tumors have been reported as 90-100% [18]. The incidental GBCs are usually found in the early stage (T1) tumors.

Following the laparoscopic cholecystectomy, the port location metastases were determined as 10-30% in the literature for a period of 10 months. In cases without peroperatively perforation, the rate of the port location metastasis is significantly lower [19]. In our study, we did not detect any port metastasis in the study patients.

The detection of a relatively different proportion of the random detected GBC is linked to various reasons. The characteristic of these reasons is that in the prospective studies, especially in situ carcinoma ratio is higher compared to the retrospective studies. Because of the standard pathological examination, there is not enough sampling of the fundus and corpus sections of the cancer [20]. In some countries, gallbladder cancer is endemic, so rates in these regions increase the overall average [3]. In other words, in our country, it is expected to detect the incidence GBC at lower rates than in some parts of the world, but still multi-centered and prospective studies with high volume of patients should be conducted. In our study the ratio of incidental GBC was 0.20%, and that was lower compared to the previously published studies in the literature [15,18]. However, in other studies conducted in the Turkish population, we have determined that these ratios are lower than the literature in accordance with ours [19,20].

We think that one of the limited aspects of our study is the retrospective design of the study and length of the follow-up. The impossibility of additional surgical resection and early adjuvant treatment were also other restrictive problems. The most important reason for these adverse consequences is that laparoscopic cholecystectomy has been performed with low complication rates. To be seen as a trivial initiative, so we think that the pathology results in the postoperative period should not be given the need for follow-up and evaluation.

In our study, the adverse effects of advanced stage of tumors have been detected and positive effects of additional surgical resection in the early period have been observed in the survival. Our incidence GBC rates were determined to be lower than other studies in the literature. Following the cholecystectomy, the pathology results should be followed carefully, without loss of communication with the patients.

Acknowledgements

Authors would like to thank the department of pathology and general surgery.

References

1. Jha V, Sharma P, Mandal KA. Incidental gallbladder carcinoma: Utility of histopathological evaluation of routine cholecystectomy specimens. South Asian J Cancer. 2018 Jan-Mar;7(1):21-23.
2. Aydın OU, Tihan ND, Sabuncuoğlu MZ, Dandin Ö, Yeğen FS, Balta AZ, et al. Assessment of lateral to medial dissection of Calot's triangle in laparoscopic cholecystectomy: A case-control study. J Surg Med. 2018;2(1):27-31.
3. Zaidi MY, Maithel SK. Updates on Gallbladder Cancer Management. Curr Oncol Rep. 2018 Mar 2;20(2):21.
4. Shirai Y, Yoshida K, Tsukada K, Muto T. Inapparent carcinoma of the gallbladder. An appraisal of a radical second operation after simple cholecystectomy. Ann Surg. 1992;215:326-31.
5. Stoll M. Rationis medendi in nosocomio practico Vindobonensi. Pars prima; Sumtibus August Bernardi, Wien, 1977. p. 254.
6. Nevin JE, Moran TJ, Kay S, King R. Carcinoma of the gallbladder: staging, treatment and prognosis. Cancer. 1976;37:141-8.
7. Drouard F, Delamarre J, Capron JP. Cutaneous seeding of gallbladder cancer after laparoscopic cholecystectomy. N Engl J Med. 1991;325:1316.
8. Tatli F, Ozgönül A, Yucel Y, Yalcin HC, Ciftci R, Gümer M, et al. Incidental gallbladder cancer at cholecystectomy. Ann Ital Chir. 2017;6:399-402.
9. Egger B, Maurer CA, Bartels C, Baer HU. Primary carcinoma of the gallbladder. "A Swiss center's experience". Dig Surg. 1997;14:169-74.
10. Kondo S, Nimura Y, Kamiya J, Nagino M, Kanai M, Uesaka K, et al. Five-year survivors after aggressive surgery for stage IV gallbladder cancer. J Hepatobiliary Pancreat Surg. 2001;8:511-7.
11. Shih SP, Schulick RD, Cameron JL, Lillemoe KD, Pitt HA, Choti MA, et al. Gallbladder cancer: the role of laparoscopy and radical resection. Ann Surg. 2007;245:893-901.
12. Edge SB, Compton CC. AJCC cancer staging manual. 7th ed. New York: Springer, 2010;347-77.
13. Basak F, Hasbahceci M, Canbak T, Sisik A, Acar A, Yucel M, et al. Incidental Findings and Unexpected Cancers during Routine Pathologic Evaluation of Gallbladder Specimens: A Review of 1747 Elective Laparoscopic Cholecystectomy Cases. Ann R Coll Surg Engl. 2016 Apr;98(4):280-3.
14. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, et al. Cancer statistics, 2004. CA Cancer J Clin. 2004;54:8-29.
15. Marcial-Rojas RA, Medina R. Unsuspected carcinoma of the gallbladder in acute and chronic cholecystitis. Ann Surg. 1961;153:289-98.
16. 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 Apr;42(4):1092-9.
17. Scott TE, Carroll M, Cogliano FD, Smith BF, Lamorte WW. A casecontrol assessment of risk factors for gallbladder carcinoma. Dig Dis Sci. 1999;44:1619-25.
18. Yasui K, Shimizu Y. Surgical treatment for metastatic malignancies. Anatomical resection of liver metastasis: indications and outcomes. Int J Clin Oncol. 2005;10:86-96.
19. Copher JC, Rogers JJ, Dalton ML. Trocar-site metastasis following laparoscopic cholecystectomy for unsuspected carcinoma of the gallbladder. Surg Endosc. 1995;9:348-50.
20. Genç V, Onur Kirimker E, Akyol C, Kocaay AF, Karabörk A, Tüzüner A, et al. Incidental gallbladder cancer diagnosed during or after laparoscopic cholecystectomy in members of the Turkish population with gallstone disease. Turk J Gastroenterol. 2011;22:513-16.