

Araştırma Makalesi– Research Paper

**COMPARISON OF CANCER OR DYSPLASIA FREQUENCY BY AGE GROUPS IN PATIENTS WHO HAD CHOLECYSTECTOMY
KOLESİSTEKTOMİ YAPILAN HASTALARDA KANSER VEYA DİSPLAZİ SIKLIĞININ YAŞ GRUPLARINA GÖRE KARŞILAŞTIRILMASI**

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Özet

Safra kesesi karsinomları, safra yollarında görülen en sık görülen malignitedir. Spesifik belirti ve semptomları olmaması nedeniyle çoğu kez safra kesesi taşı nedeniyle yapılan kolesistektomi sırasında saptanmaktadır. Bu doğrultuda biz de çalışmamızda benign safra kesesi hastalıkları nedeniyle kolesistektomi yapılan olgularda displazi ve karsinom sıklığını göstermek amacıyla çalışmamıza dahil edilen 530 hastanın 74'ünde displazi, 3 hastada ise safra kesesi karsinomu saptanmıştır. Bu durum safra kesesi kanserlerinin erken evrede yakalanmasına ve tedavi başarısının oldukça yükseklere çıkarılmasında oldukça önemlidir. Bu nedenle benign nedenlerle bile olsa yapılan operasyon sonrası patoloji analiz raporlarını özenle takip etmek gerekmektedir.

Anahtar Kelimeler: Kolesistektomi, displazi, safra kesesi karsinomu

Abstract

Gallbladder carcinomas are the most common malignancy of the biliary tract. Since it does not have specific signs and symptoms, it is mostly detected during cholecystectomy for gallstones. In this direction, we also found dysplasia in 74 of the 530 patients included in our study, and gallbladder carcinoma in 3 patients, to show the frequency of dysplasia and carcinoma in patients who underwent cholecystectomy due to benign gallbladder diseases. This is very important in catching gallbladder cancers at an early stage and increasing the success of treatment. For this reason, it is necessary to carefully follow the pathology analysis reports after the operation, even for benign reasons.

Keywords: Cholecystectomy, dysplasia, gallbladder carcinoma

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1. INTRODUCTION

Gallbladder carcinomas are the most common malignancy seen in the biliary tract and the third most common gastrointestinal system malignancy according to United States data (Lau et al., 2017). It is a rare but aggressive malignancy that usually occurs in the elderly. It is 2-3 times more common in women than in men, especially in the seventh decade (Lazcano-Ponce et al., 2001, pp. 349-364; Pandey et al., 2002, pp. 365-368).

Although modern imaging methods are widely used, early diagnosis is rare due to the lack of specific signs and symptoms, and many gallbladder carcinomas are not diagnosed preoperatively (Levy et al., 2001, pp. 295-314). Gallbladder cancer is present in approximately 0.3-2% of patients who undergo cholecystectomy, mostly due to gallstones (Pandey et al., 2002, pp. 365-368; Dix et al., 2003, pp. 233-235; Grobmyer et al., 2004, pp. 47-49; Kalita et al., 2013, pp. 3315-3318)

In this study, we also; tried to show the incidentally detected dysplasia and carcinomas according to age groups in patients who underwent cholecystectomy for benign gallbladder diseases in our clinic.

2. MATERIAL AND METHODS

The study protocol was approved by the local ethical committee (IRB:2021-267-26).

530 patients who underwent cholecystectomy for benign gallbladder diseases between 01.01.2019 and 31.01.2020 in Eskişehir Osmangazi University Medical Faculty Hospital General Surgery Clinic were retrospectively scanned. Age, gender, additional disease, surgical procedure, hemogram, some biochemical tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin and direct bilirubin levels) and pathology analysis reports of these patients were examined. The patients were evaluated in two groups those aged 75 and over (older) and those aged 75 years. In addition, the surgical procedure performed, started laparoscopically; They were grouped as patients who ended laparoscopically or switched to open surgery. Patients who underwent open surgical procedures due to previous abdominal surgery were not included in the study.

Statistical Analysis

Data analysis was done with SPSS 25.0 package program. For quantitative data, Normal Distribution was analyzed by Shapiro Wilk. Median, 25%-75% Percentile values were used for data that did not show normal distribution. Continuous quantitative variables that did not show normal distribution were analyzed with the Mann-Whitney U test, Kruskal-Wallis test, and qualitative data using the Chi-square test.

3. RESULTS

Of the 530 who underwent cholecystectomy for cholelithiasis, 288 (54.3%) were female and 187 (45.7%) were male. The median age of the patients was 58, and there were 475 patients under the age of 75, and 55 patients aged 75 and over (elderly). Seventeen (30.9%) of 104 patients with diabetes as a comorbid disease were in the elderly patient group, and there was a significant difference when compared with the group under 75 years of age ($p < 0.05^*$).

Seventeen (30.9%) of 67 patients with coronary artery disease were in the elderly patient group, and there was a significant difference when compared with the group under 75 years of age ($p < 0.001^{***}$). 5 (9.1%) of 34 patients with a history of asthma/ Chronic Obstructive Pulmonary Disease were in the elderly patient group, and no significant difference was found when compared with the group under 75 years of age ($p = 0.382$). Thirty-two (58.2%) of 147 patients with known hypertension were in the elderly patient group, and there was a significant difference when compared with the group under 75 years of age ($p < 0.001^{***}$) (Table.1).

Table.1. Demographic characteristics and comorbid diseases		n, %			p
		<75 age	≥ 75 age	Total	
Gender n=530	Female	288 (%60.6)	32 (%58.2)	320 (%60.4)	
	Male	187 (%39.4)	23 (%41.8)	210 (%39.6)	
Comorbidities	Diabetes Mellitus	87 (%18.3)	17 (%30.9)	104 (%19.6)	<0.05*
	Hypertension	115 (%24.2)	32 (%58.2)	147 (%27.7)	<0.001***
	Coronary Artery Disease	50 (%10.5)	17 (%30.9)	67 (%12.6)	<0.001***
	Chronic Obstructive Pulmonary Disease	29 (%6.1)	5 (%9.1)	34 (%6.4)	n.s (p=0.382)

In the elderly group, a significant difference was found in the differentiation of leukocyte values from chronic cholecystitis and acute cholecystitis, with $p = 0.027^*$ as the leukocyte value increased. Again, leukocyte values and open surgery increased significantly in the elderly group ($p = 0.025^*$) (Table.2).

Table.2. Age distribution and studied blood parameters		median	%25	%75
Age		58	47	67
Laboratory tests	Hemoglobin (g/dL)	13	11.45	14.1
	Leukocyte (/uL)	7400	5750	9450

	Thrombocyte (/uL)	230000	176000	265500
	AST (U/L)	25	17.5	45.5
	ALT (U/L)	18	12	27
	ALP (U/L)	74	65	112
	T.Bilirubin (mg/dl)	0.6	0.4	1.3
	D.Bilirubin (mg/dl)	0.2	0.1	0.5

Twenty (36.4%) of 83 patients who underwent open cholecystectomy were in the patient group aged 75 years and above, and open surgery was significantly higher compared to the group under 75 years of age ($p < 0.001$ ***). probability was found to be significantly increased ($p < 0.05$ *).

After the pathology analysis of the patients who underwent cholecystectomy; Chronic cholecystitis was found in 417 patients, acute cholecystitis in 36 patients, dysplasia in 74 patients, and gallbladder carcinoma in 3 patients. No significant difference was found between the pathology results according to age groups (Table.3).

Table.3. Surgical procedure and Pathological diagnosis		n , %			p
Surgical procedure	Laparoscopic surgery	412 (%86.7)	35 (%63.6)	447 (%84.3)	<0.001***
	Open surgery	63 (%13.3)	20 (%36.4)	83 (%15.7)	
Pathological diagnosis	Chronic cholecystitis	379 (%79.8)	38 (%69.1)	417 (%78.7)	n.s
	Acute cholecystitis	30 (%6.3)	6 (%10.9)	36 (%6.8)	n.s
	Dysplasia	63 (%13.3)	11 (%20)	74 (%14)	n.s
	Carcinoma	3 (%0.6)	0	3 (%0.6)	n.s

n.s: non-specific



4. DISCUSSION

Gallbladder cancer is the most common malignancy of the biliary tract, which is rare but has a very aggressive course (Lau et al., 2017). The incidence of gallbladder carcinoma, which is known to be more common in the elderly, is gradually decreasing due to the increasing frequency of early cholecystectomy for benign gallbladder diseases. As in our study, the incidence of accidental carcinoma in cases performed for cholelithiasis was found to be 0.6%, which is consistent with the literature, and the cases with carcinoma were in the group of patients younger than 75 years of age (Lazcano-Ponce et al., 2001, pp. 349-364; Pandey et al., 2002, pp. 365-368; Levy et al., 2001, pp. 295-314; Dix et al., 2003, pp. 233-235).

The role of chronic inflammation caused by gallstones in the etiology of gallbladder cancers has been shown in many studies (Grobmyer et al., 2004, pp. 47-49; Kalita et al., 2013, pp. 3315-3318; Akyürek et al., 2004, pp. 357-361). In our study, 78.7% of patients with known cholelithiasis were found to have chronic cholecystitis findings after pathology analysis, which is consistent with the literature (Kalita et al., 2013, pp. 3315-3318; Hart et al., 1971, pp. 1151-1153; Serra et al., 1996, pp. 1515-1516). However, it is known that the presence of gallstones is between 54-97% in patients with known gallbladder cancer (Levy et al., 2001, pp. 295-314).

Two patterns have been identified in the development of gallbladder carcinoma: metaplasia-dysplasia-carcinoma and adenoma-carcinoma development (Levy et al., 2001, pp. 295-314). The progression from metaplasia to carcinoma in the gallbladder epithelium has been studied (Levy et al., 2001, pp. 295-314; Grobmyer et al., 2004, pp. 47-49; Akyürek et al., 2004, pp. 357-361; Basak et al., 2016, pp. 280-283; Siddiqui et al., 2013, pp. 1-5). When the pathology analysis reports of the patients who underwent cholecystectomy were evaluated in our study, there were chronic inflammation caused by gallstones in 417 (78.7%) cases, and chronic cholecystitis cases with occasional dysplasia in 74 (14%) cases. This suggests that it is similar to the chronic inflammation and dysplasia pattern caused by gallstones involved in the development of gallbladder carcinoma.

In our study, the rate of conversion to open cholecystectomy was 36.4% in patients aged 75 years and older, significantly higher than in other age groups ($p < 0.001$). In the cohort studies of Roslyn et al. and Yamagiwa et al, similar to our study, conversion to open cholecystectomy in elderly patients was quite high (Roslyn et al., 1993, pp. 129; Yamagiwa et al., 1989, pp. 238-243).

It is known that comorbid diseases such as diabetes and obesity are risk factors in the transition from laparoscopic surgery to open cholecystectomy (Orth et al., 2000, 501-508). This situation increased the possibility of comorbidities being a risk factor in the transition to open cholecystectomy since it was significantly more common in the 75-year-old group and those with diabetes, hypertension, and coronary artery disease in our study.



The high rates of conversion from laparoscopic cholecystectomy to open surgery for acute cholecystitis result from the technical difficulty of managing severe inflammatory adhesions around the acutely inflamed gallbladder, making dissection of Calot's triangle and recognizing anatomy more dangerous (Orth et al., 2000, 501-508). In our study, high leukocyte levels in the elderly group were significant in terms of acute cholecystitis in the distinction between acute and chronic cholecystitis, and high leukocyte levels were found to be quite effective in conversion to open surgery ($p < 0.05$).

5. CONCLUSION

In our country, the rate of cholecystectomy performed for benign gallbladder diseases is increasing due to geographical features. Although there is no cancer clinic and radiological findings, it increases the frequency of gallbladder cancer that is detected incidentally in the early period in pathology analysis, especially after cholecystectomy for cholelithiasis, and relatively decreases the incidence of gallbladder cancer, which is more common in the elderly group. This is very important in catching gallbladder cancers at an early stage and increasing the success of treatment. For this reason, it is necessary to carefully follow the pathology analysis reports after the operation, even for benign reasons.

6. REFERENCES

- Akyürek, N., Irkörücü, O., Salman, B., Erdem, O., Sare, M., & Tatlıcioğlu, E. (2004). Unexpected gallbladder cancer during laparoscopic cholecystectomy. *Journal of hepato-biliary-pancreatic surgery*, 11(5), 357–361. <https://doi.org/10.1007/s00534-004-0910-y>
- Basak, F., Hasbahceci, M., Canbak, T., Sisik, A., Acar, A., Yucel, M., Bas, G., & Alimoglu, O. (2016). Incidental findings during routine pathological evaluation of gallbladder specimens: review of 1,747 elective laparoscopic cholecystectomy cases. *Annals of the Royal College of Surgeons of England*, 98(4), 280–283. <https://doi.org/10.1308/rcsann.2016.0099>
- Dix, F. P., Bruce, I. A., Krypczyk, A., & Ravi, S. (2003). A selective approach to histopathology of the gallbladder is justifiable. *The surgeon: journal of the Royal Colleges of Surgeons of Edinburgh and Ireland*, 1(4), 233–235. [https://doi.org/10.1016/s1479-666x\(03\)80023-9](https://doi.org/10.1016/s1479-666x(03)80023-9)
- Grobmyer, S. R., Lieberman, M. D., & Daly, J. M. (2004). Gallbladder cancer in the twentieth century: single institution's experience. *World journal of surgery*, 28(1), 47–49. <https://doi.org/10.1007/s00268-003-7131-4>
- Hart, J., Modan, B., & Shani, M. (1971). Cholelithiasis in the aetiology of gallbladder neoplasms. *Lancet (London, England)*, 1(7710), 1151–1153. [https://doi.org/10.1016/s0140-6736\(71\)91661-8](https://doi.org/10.1016/s0140-6736(71)91661-8)
- Kalita, D., Pant, L., Singh, S., Jain, G., Kudesia, M., Gupta, K., & Kaur, C. (2013). Impact of routine histopathological examination of gall bladder specimens on early detection of malignancy - a study of 4,115 cholecystectomy specimens. *Asian Pacific journal of cancer prevention: APJCP*, 14(5), 3315–3318. <https://doi.org/10.7314/apjcp.2013.14.5.3315>
- Lau, C. S. M., Zywtot, A., Mahendraraj, K., & Chamberlain, R. S. (2017). Gallbladder Carcinoma in the United States: A Population Based Clinical Outcomes Study Involving 22,343 Patients from the Surveillance, Epidemiology, and End Result Database (1973-2013). *HPB*



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surgery: a world journal of hepatic, pancreatic and biliary surgery, 2017, 1532835. <https://doi.org/10.1155/2017/1532835>

Lazcano-Ponce, E. C., Miquel, J. F., Muñoz, N., Herrero, R., Ferrecio, C., Wistuba, I. I., Alonso de Ruiz, P., Aristi Urista, G., & Nervi, F. (2001). Epidemiology and molecular pathology of gallbladder cancer. *CA: a cancer journal for clinicians*, 51(6), 349–364. <https://doi.org/10.3322/canjclin.51.6.349>

Levy, A. D., Murakata, L. A., & Rohrmann, C. A., Jr (2001). Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics : a review publication of the Radiological Society of North America, Inc*, 21(2), 295–555. <https://doi.org/10.1148/radiographics>.

21.2.g01mr16295

Orth, K., & Beger, H. G. (2000). Gallbladder carcinoma and surgical treatment. *Langenbeck's archives of surgery*, 385(8), 501–508. <https://doi.org/10.1007/s004230000178>

Pandey, M., & Shukla, V. K. (2002). Diet and gallbladder cancer: a case-control study. *European journal of cancer prevention: the official journal of the European Cancer Prevention Organisation (ECP)*, 11(4), 365–368. <https://doi.org/10.1097/00008469-200208000-00008>

Roslyn, J. J., Binns, G. S., Hughes, E. F., Saunders-Kirkwood, K., Zinner, M. J., & Cates, J. A. (1993). Open cholecystectomy. A contemporary analysis of 42,474 patients. *Annals of surgery*, 218(2), 129–137. <https://doi.org/10.1097/00000658-199308000-00003>

Serra, I., Calvo, A., Báez, S., Yamamoto, M., Endoh, K., & Aranda, W. (1996). Risk factors for gallbladder cancer. An international collaborative case-control study. *Cancer*, 78(7), 1515–1517.

Siddiqui, F. G., Memon, A. A., Abro, A. H., Sasoli, N. A., & Ahmad, L. (2013). Routine histopathology of gallbladder after elective cholecystectomy for gallstones: waste of resources or a justified act?. *BMC surgery*, 13, 26. <https://doi.org/10.1186/1471-2482-13-26>

Yamagiwa H. (1989). Mucosal dysplasia of gallbladder: isolated and adjacent lesions to carcinoma. *Japanese journal of cancer research: Gann*, 80(3), 238–243. <https://doi.org/10.1111/j.1349-7006.1989.tb02299.x>