ORIGINAL ARTICLE

Short-Term Diagnostic Follow-Up of Patients Undergoing Cholecystectomy for Development of Colorectal Cancer

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ABSTRACT

Background: Colorectal cancer (CRC) incidence is increasing globally, imposing considerable pressure on healthcare systems. The prevalence of colorectal cancer in several studies throughout different areas of Pakistan ranged from 4% to 6%, with an overall incidence of 5%. Cholecystectomy, a prevalent surgical intervention, may result in enduring biochemical alterations, heightening intestinal exposure to bile acids and salts, hence elevating the chance of colorectal cancer (CRC). The incidence of colorectal cancer (CRC) among cholecystectomy patients is 119 per 100,000 person-years, in contrast to 86 per 100,000 person-years for those who did not have the surgery.

Objective: We intended to monitor individuals undergoing cholecystectomy for two years to assess the incidence of future colorectal cancer.

Methodology: This was retrospective research undertaken in the Radiology Department of Fauji Foundation Hospital, Rawalpindi. Imaging and histology records of patients from January 2019 to December 2021 were examined using the Medix online reporting system. Patients who had cholecystectomy were monitored for radiological and histological indications of colorectal cancer during a short-term period of two years.

Results: A total of 370 patients were included, with a predominantly female population (98.1%). The highest proportion of patients (47.6%) was in the 41-50 years age group. Over the two-year follow-up period, no cases of colorectal cancer were detected through imaging or histopathology. The study suggests no short-term association between cholecystectomy and colorectal cancer.

Conclusion: Cholecystectomy is not associated with the short-term development of colorectal cancer.

Keywords: *Gall bladder, cholecystectomy, colorectal cancer, bile acids, follow-up.*

INTRODUCTION

Colorectal cancer (CRC) rates are rising worldwide, exerting a significant strain on the healthcare system. It is ranked as the third most prevalent malignancy globally, with over 1.9 million new cases and an expected 930,000 fatalities in 2020 [1]. The incidence of colorectal cancer in numerous studies throughout different areas of Pakistan varied from 4% to 6%, with an overall incidence of 5% [2]. Comprehending the fundamental risk factors and etiology is crucial for effective prevention, diagnosis, and treatment strategies. Various aetiologies have been linked to the pathogenesis of colorectal cancer (CRC), including genetic predisposition and environmental factors such as tobacco and alcohol consumption, inflammatory bowel disease (IBD), adenomatous polyps, familial history, inadequate nutrition, physical inactivity, and obesity [3]. Cholecystectomy and appendectomy are recognized as risk factors for the development of colorectal cancer (CRC) [4]. Cholecystectomy is recurrent surgical handling used to treat symptomatic gallstones and linked disease. Cholecystectomy was conventionally thought to be an innocuous procedure, but new research has elevated concerns about a possible relation to an enlarged risk of CRC. This connection is currently being researched, and particular procedures are not yet fully understood. Patients and healthcare practitioners must recognize this possible hazard and include it in treatment choices [5]. Colorectal cancer is more likely in those who have had cholecystectomy, with an incidence rate of 119 per 100,000 person-years, against 86 per 100,000 person-years in those who have not had the procedure [6]. This shows a little increase in the risk of colon cancer in cholecystectomy patients, with no associated increase for rectal cancer. However, the complex association between cholecystectomy and colorectal cancer remains poorly understood, demanding more study to reach clear findings [7].

The long-term consequences of cholecystectomy may outweigh severe concerns such as infection, vascular harm, or biliary harm. Biochemical deviations caused by cholecystectomy expose intestinal contents to bile acids and salts, possibly increasing the risk of colorectal cancer and salts, potentially elevating the risk of colorectal cancer. The exposure of the colonic epithelium to deoxycholic acid is thought to begin carcinogenesis. As a result, it is important to identify risk factors and evaluate those with a family history or susceptible diseases [8]. Colorectal cancer is classified into many subtypes, including adenocarcinoma, neuroendocrine, squamous cell, adenosquamous, spindle cell, and undistinguishable carcinomas [9]. Cross-sectional imaging needs a thorough examination of the intestines in those who have had cholecystectomy [10]. Radiological imaging is critical for detecting and

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monitoring colorectal cancer, including local staging with magnetic resonance imaging (MRI) and distant staging with computed tomography (CT) and positron emission tomography (PET) scans. Because of the high incidence of local reappearance and distant metastases, radiography is essential in disease treatment [11].

We wanted to look at the occurrence of colorectal cancer in those who had cholecystectomy during a two-year period.

METHODOLOGY

This is a retrospective study approved by the ethical review committee of Fauji Foundation Hospital, Rawalpindi, Pakistan (Ref. No. 656/RC/FFH/RWP 4/01/2023). The committee tested that the study followed the ethical needs of biomedical research linking both animal and human subjects, and its approval confirms the project's conformism with research ethics. The research studied imaging and histopathological reports of people who had cholecystectomy from January 2019 to December 2021. The inclusion method incorporated all adult patients who endured cholecystectomy during this timeframe, but those having a prior diagnosis of primary malignancies of the gallbladder, pancreas, liver, or colon were omitted from the study. Informed consent was obtained from all participants involved in this study.

We collected radiographic and histological accounts of patients who had cholecystectomy from January 2019 to December 2021, sourced *via* the Medix online reporting system of the hospital. Cross-sectional imaging, comprising computed tomography (CT) and magnetic resonance imaging (MRI), was analyzed to detect any colorectal abnormalities. Histopathology results were scrutinized for the incidence of malignancy.

The primary outcome of the study was to determine the short-term (two-year) occurrence of colorectal cancer in individuals who had experienced cholecystectomy. The study pursued to evaluate the strong connection between cholecystectomy and the later onset of colorectal cancers. Further consequences covered the examination of demographic dispersals, including patterns linked to gender and age, in patients having cholecystectomy.

Statistical software (IBM SPSS Statistics) was utilized to analyze data and determine the occurrence of colorectal cancer among the study population. Descriptive statistics were employed to illustrate the demographic distribution, with stratification by gender and age. Frequency and percentages were computed.

RESULTS

A total of 370 patients who underwent cholecystectomy were included in the study, with a significant majority being female (98.1%). The age distribution showed that the highest number of patients (47.6%) belonged to the 41-50 years age group, followed by 28.9% in the 51-60 years group, 14.9% in the 31-40 years group, 4.9% in the 20-30 years group, and 3.8% in the 61-70 years group **(Table 1)**.

During the two-year follow-up, no cases of colorectal carcinoma were identified in the study population based on imaging and histopathology findings. The absence of colorectal cancer cases suggests that, in the short term, there is no significant association between cholecystectomy and the development of colorectal malignancies. However, due to the study's short duration, a longer follow-up period is recommended to assess potential long-term risks.

Table 1: Frequency distribution of patients' age and gender.

Variables	Groups	Frequency	Percentage (%)
Age groups	20-30 years	18	4.9
	31-40 years	55	14.9
	41-50 years	176	47.6
	51-60 years	107	28.9
	61-70 years	14	3.8
Gender	Male	7	1.9
	Female	363	98.1

DISCUSSION

Cholecystectomy is a common therapy for gallbladder disease; nevertheless, its usefulness has long been debated in terms of its impact on the likelihood of developing other disorders [12]. Patients who have had cholecystectomy have altered bile acid composition, with an increased amount of secondary bile acids in their bile pool [13]. Cholecystectomized patients are constantly exposed to high levels of metabolic chemicals, such as biliary acids, undigested lipids, and other colonic microbiota byproducts, which may increase the risk of colon cancer [14].

Zhao *et al.* observed that cholecystectomy causes a transitory reduction in bile acid production and pool size; however, this effect is not sustained over time [15]. Kullak-Ublick *et al.* discovered a 16% drop in the bile acid pool three months after surgery, but Zhao *et al.* found a fall in synthesis rate and pool size six weeks after surgery, with no significant changes detected nine to twelve months later [15, 16].

Previous research indicates that women have a higher incidence of cholecystectomy; Shaffer (2005) states that women are two to three times more sensitive to gallstone formation, resulting in a higher cholecystectomy rate [17]. Our statistics showed that the bulk of the

population was female (98.1%), with men being a minority (1.9%).

Global research indicates that cholecystectomy may increase the risk of colorectal cancer. Giovannucci *et al.* did a meta-analysis of 33 case-control studies and found a 34% increased risk of colorectal cancer (CRC) [18].

A subsequent meta-analysis of nine cohort studies (Zhang *et al.* 2017) showed a 22% higher risk, primarily for colon cancer. The feminine gender was linked to an increased risk of colorectal cancer (CRC) [19]. Xu *et al.* and Chiong *et al.* discovered an increase in the incidence of colorectal cancer (CRC) after cholecystectomy [20, 21].

Kim *et al.* studied Korean patients after eight years, omitting those who had additional gastrointestinal malignancies or colorectal cancer within a year of cholecystectomy [22]. A statistically significant 108% increase in colorectal cancer risk was found following cholecystectomy, with female patients having a higher risk (154%) than male patients (74%). These results suggest a substantial link between cholecystectomy and the development of colorectal cancer (CRC) [19].

Certain research challenges the idea that gallbladder removal raises the risk of colorectal cancer. A Hungarian retrospective study found an increased incidence of colon cancer following cholecystectomy; nevertheless, the extended latency period encouraged the researchers to investigate if cholecystectomy is an independent risk factor for colorectal cancer (Mándi *et al.* 2021) [23]. Other research, however, revealed no significant link between the two (Zhao *et al.* 2012) [15]. These diverse findings highlight the intricacy of the issue and the necessity for ongoing studies to elucidate the association between cholecystectomy and colorectal cancer.

Although earlier research [18, 19] found a favorable connection, it was only significant in long-term follow-up periods, whereas our study covered a short-term follow-up period. This research shows that screening for colorectal cancer in those who have had cholecystectomy is required, as is a personalized surveillance program. Colorectal cancer (CRC) screening should begin in the 40s when people are most vulnerable [24]. More research is needed to evaluate the potential advantages of colonoscopic surveillance for the early detection of colorectal cancer in persons who have undergone cholecystectomy [25].

CONCLUSION

Over a two-year follow-up period, this retrospective investigation found no evidence associating cholecystectomy with the short-term start of colorectal cancer. Although previous study suggests a link between bile acid consumption and colon carcinogenesis, our findings reveal that any linked risk may arise over time rather than in the early postoperative phase. The study was limited by its short follow-up period and predominantly female sample, necessitating more research with larger, more varied populations and longer follow-up periods. Due to the ongoing debate in the literature, it is recommended to perform long-term surveillance of post-cholecystectomy patients, preferably for 10 to 15 years, to establish a clear association between gallbladder excision and the risk of colorectal cancer.

ETHICS APPROVAL

Ethical approval was obtained from the Ethical Review Committee of the Fauji Foundation Hospital, Rawalpindi (Ref. No. 656/RC/FFH/RWP 4/01/2023). All procedures performed in studies involving human participants were following the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

We confirmed that informed consent was obtained from all participants involved in this study.

AVAILABILITY OF DATA

The data sets collected and analyzed during the study period are available.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

Khalil Hussain: Conceptualization, methodology, data collection, data analysis, writing - original draft.

Kamran Burki: Conceptualization, methodology, writing - review & editing.

Aasma Nudarat Zafar: Conceptualization, writing - review & editing supervision, project administration.

Kiran Fatima Farooq: Supervision, project administration.

REFERENCES

1. Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, *et al.* Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. Gut 2023; 72(2): 338-44.
2. Ahmad Z, Idrees R, Fatima S, Uddin N, Ahmed A, Minhas K, Memon A, *et al.* Commonest cancers in Pakistan-findings and histopathological perspective from a premiar surgical pathology center in Pakistan. Asian Pac J Cancer Prev 2016; 17: 1061-75.
3. Johnson CM, Wei C, Ensor JE, Smolenski DJ, Amos CI, Levin B, *et al.* Meta-analyses of colorectal cancer risk factors. Cancer Causes Control 2013; 24: 1207-22.
DOI: https://doi.org/10.1007/s10552-013-0201-5
4. Wu S-C. Chen WT-L, Muo C-H, Ke T-W, Fang C-W. Sung F-C. Association between appendectomy and subsequent colorectal cancer development: an Asian population study. PLoS One 2015; 10: e0118411.
DOI: https://doi.org/10.1371/journal.pone.0118411
5. Altieri A, Pelucchi C, Talamini R, Bosetti C, Franceschi S, La Vecchia C. Cholecystectomy and the risk of colorectal cancer in Italy. Br J Cancer (2004) 90: 1753-5.
DOI: https://doi.org/10.1038/sj.bjc.6601721
6. Shao T, Yang YX. Cholecystectomy and the risk of colorectal cancer. Am J Gastroenterol 2005; 100: 1813-20.
DOI: https://doi.org/10.1111/j.1572-0241.2005.41610.x
7. Lin OS. Acquired risk factors for colorectal cancer. Methods Mol Biol 2009; 472: 361-72.
DOI: https://doi.org/10.1007/978-1-60327-492-0_16
8. Furlan A, Ferris J, Hosseinzadeh K, Borhani A. Gallbladder carcinoma update: multimodality imaging evaluation, staging, and treatment options. AJR Am J Roentgenol 2008; 191(5): 1440-7.
DOI: https://doi.org/10.2214/ajr.07.3599
9. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: pathologic aspects. J Gastrointest Oncol 2012; 3(3): 153-73.
DOI: https://doi.org/10.3978/j.issn.2078-6891.2012.030
10. Sureka B, Mukund A. Review of imaging in post-laparoscopy cholecystectomy complications. Indian J Radiol Imaging 2017; 27(4): 470-81.
DOI: https://doi.org/10.4103/ijri.IJRI_489_16
11. Kijima S, Sasaki T, Nagata K, Utano K, Lefor AT, Sugimoto H. Preoperative evaluation of colorectal cancer using CT colonography, MRI, and PET/CT. World J Gastroenterol 2014; 20(45): 16964.
DOI: https://doi.org/10.3748/wjg.v20.i45.16964
12 Chen L, Fan Z, Sun X, Qiu W, Mu W, Chai K, *et al.* Associations of cholecystectomy with the risk of colorectal cancer: a Mendelian randomization study. Chin Med J (Engl) 2023; 136(7): 840-7.
DOI: https://doi.org/10.1097/CM9.0000000000002612
13. Berr F, Stellaard F, Pratschke E, Paumgartner G. Effects of cholecystectomy on the kinetics of primary and secondary bile acids. J Clin Invest 1989; 83(5): 1541-50.
DOI: https://doi.org/10.1172/JCI114050
14. Wu Y, Wan J, Choe U, Pham Q, Schoene NW, He Q, *et al.* Interactions between food and gut microbiota: impact on human health. Annu Rev Food Sci Technol 2019; 10: 389-408.
DOI: https://doi.org/10.1146/annurev-food-032818-121303
15. Zhao C, Ge Z, Wang Y, Qian J. Meta-analysis of observational studies on cholecystectomy and the risk of colorectal adenoma. Eur J Gastroenterol Hepatol 2012; 24(4): 375-81.
DOI: https://doi.org/10.1097/MEG.0b013e328350f86b
16. Kullak-Ublick GA, Paumgartner G, Berr F. Long-term effects of cholecystectomy on bile acid metabolism. Hepatology 1995; 21(1): 41-5.
DOI: https://doi.org/10.1002/hep.1840210109
17. Shaffer EA. Epidemiology and risk factors for gallstone disease: has the paradigm changed in the 21st century? Curr Gastroenterol Rep 2005; 7(2): 132-40.
DOI: https://doi.org/10.1007/s11894-005-0051-8
18. Giovannucci E, Colditz GA, Stampfer MJ. A meta-analysis of cholecystectomy and risk of colorectal cancer. Gastroenterology 1993; 105(1): 130-41.
DOI: https://doi.org/10.1016/0016-5085(93)90018-8
19. Zhang Y, Liu H, Li L, Ai M, Gong Z, He Y, *et al.* Cholecystectomy can increase the risk of colorectal cancer: a meta-analysis of 10 cohort studies. PLoS One 2017; 12(8): e0181852.
DOI: https://doi.org/10.1371/journal.pone.0191587
20. Xu YK, Zhang FL, Feng T, Li J, Wang YH. Meta-analysis on the correlation of cholecystectomy or cholecystolithiasis to risk of colorectal cancer in Chinese population. Ai Zheng 2009; 28: 749-55.
DOI: https://doi.org/10.5732/cjc.008.10829
21. Chiong C, Cox MR, Eslick GD. Gallstones are associated with colonic adenoma: a meta-analysis. World J Surg 2012; 36(9): 2202-9.
DOI: https://doi.org/10.1007/s00268-012-1646-5
22. Kim SB, Kim KO, Kim TN. Prevalence and risk factors of gastric and colorectal cancer after cholecystectomy. J Korean Med Sci 2020; 35(42): e354.
DOI: https://doi.org/10.3346/jkms.2020.35.e354
23. Mándi M, Keleti G, Juhász M. The role of appendectomy and cholecystectomy in the pathogenesis of colorectal carcinomas. Ann Med Surg (Lond) 2021; 72: 102991.
DOI: https://doi.org/10.1016/j.amsu.2021.102991
24. Wolf AMD, Fontham ETH, Church TR, Flowers CR, Guerra CE, LaMonte SJ, *et al.* Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin 2018; 68(4): 250-81.
DOI: https://doi.org/10.3322/caac.21457
25. Lee J, Choe S, Park JW, Jeong SY, Shin A. The risk of colorectal cancer after cholecystectomy or appendectomy: a population-based cohort study in Korea. J Prev Med Public Health 2018; 51(6): 281-8.
DOI: https://doi.org/10.3961/jpmph.18.105