

# Incidence of colorectal carcinoma to the time of cholecystectomy

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## ABSTRACT

A prospective study on 193 patients through 3 years from February 2020 till January 2023 patients complain of colorectal carcinoma in different locations. 43 patients (23%) had a history of open or laparoscopic cholecystectomy since a different time ranging from 9 to more than 30 years, who have no family history of colorectal cancer or inflammatory bowel diseases, adenomatous polyps, and no history of familial adenomatous polyposis, (predisposing factors of colorectal cancer). most common location of malignancy for those patients with a history of cholecystectomy in the RT side of the colon 21 patients (48.8%) and the least location in the ano-rectum region one patient (2.4%). The most common time that we diagnosed colorectal carcinoma after 21 to 25 years from the time of cholecystectomy which occurred in 18 patients (41.9%) and the least after 9 years only one patient (2.4). While the microscopic appearance of colorectal cancer in patients with a history of cholecystectomy is, adenocarcinoma occurs in 38 patients (88.4%) and squamous carcinoma occurs in 5 patients (11.6%). While the macroscopic appearance of colorectal cancer occurs most commonly in ulcerative types in 29 patients (67.5%) and least annular type 5 patients (11.6%) and the most common age occur between the age of 60 and 69 years in 24 patients (55.8%) and least occur at the age of 40 to 49 years only 2 patients (4.6%), about the grading of the tumor moderate differentiated type, is the most common type in 67.5%. Aim of the study to know the incidence of colorectal carcinoma after cholecystectomy, locations of tumors, and related time.

**Keywords:** colorectal carcinoma, cholecystectomy, post-operative time, locations of the tumor

## INTRODUCTION

Gallstones are the by far the most common disease that affects the gallbladder. Reports from Autopsies demonstrated that gallstones are present in approximately 10% to 15% of adults [1]. Cholecystectomy is a very common surgical procedure practiced Western & many other countries, and other countries and is done in Western countries, and other countries with over 800,000 being done each year in the United States alone [2]. The gallbladder functions as bile storage, while mealtime stimulation allows for its passage into the duodenum. The normal adult secretes 0.5 L to 1.0 L of bile a day. Bile is composed of 97% water and the rest is bile acids and salts, cholesterol, phospholipids, proteins, and bilirubin, with several minor components. The hepatocytes conjugate these bile acids and then secrete them into the bile to help in fat digestion and absorption in the small intestines upon fasting, 85% of the bile is stored in the gallbladder [3]. The mucosa of gallbladder mucosa acts rapidly to absorb sodium, chloride, and water against significant gradients, leading to bile concentration as much as 10-fold. This concentrating effect changes the composition of the bile significantly [4]. Laparoscopic cholecystectomy is a minimally invasive procedure and is regarded as the procedure of choice for gallbladder diseases, including symptomatic gallstones [4]. The dry fecal weight is approximately 30% bacteria (10<sup>11</sup>–10<sup>12</sup> bacteria/g of feces), the most common class among which is Anaerobes, and Bacteroides species are. Among the aerobic microorganisms, Escherichia coli are the most common (10<sup>8</sup>–10<sup>10</sup> organisms/mL). The colonic microflora are critical for carbohydrates & proteins breakdown and they also participate in bilirubin metabolism [5]. The role of colonic flora is very important in vitamin K production [4]. Colorectal cancer is one of the deadliest cancers in the world. As many as 140,000 new cases are diagnosed annually in the United States, and it is responsible for as many as 50,000 death each year, making it the third most common cause of cancer-related deaths in the United States. Recently, the CRC incidence has been increasing yearly [6]. The role that cholecystectomy (a procedure which was deemed almost harmless) plays in the development of CRC is hard to ignore,

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however, the exact specific mechanism remains unclear. It is thought that cholecystectomy can cause an alteration in the metabolism of bile salts, which are significant in the development of CRC [6].

Bile acids regulate sugar and lipids metabolism via farnesol X receptor pathway [7, 8]. Bile acids can be primary and secondary depending on their source. Primary bile acids (cholic acid and chenodeoxycholic acid) are produced in the liver via cytochrome P450-mediated oxidation of cholesterol in a multi-step process and secreted in bile into the intestine [9]. It has been shown that people with increased levels of fecal bile acids have higher incidence of CRC is higher. Secondary bile acids result from bacterial actions in the colon. In humans, taurocholic acid and glycocholic acid (derivatives of cholic acid) and taurochenodeoxycholic acid and glycochenodeoxycholic acid (derivatives of chenodeoxycholic acid) are the major bile salts. It has also been shown that the secondary acids can exert a wide range of biological toxicities, such as, DNA damage, cytolysis, turnover of the cell and mutagenesis [10,11]. The levels of these secondary acids are related to the occurrence of CRC mainly deoxycholic acid which represents an important carcinogenic agent [12]. DCA causes instability of the genome which arises through many mechanisms, including mitochondrial damage, DNA oxidative damage, and chromosome aneuploid mutations [13]. Continuous contact of high concentrations of SBAs with the intestinal epithelial cells can produce active nitrogen species and Reactive Oxygen Species (ROS) which are responsible for oxidative damage to the DNA of, producing genomic instability and frequent mutations [14]. The Bile acids in the tract of the intestinal lumen of the large bowel play an important regulating function regarding regenerating & the differentiation of the mucosal epithelium of the large intestine. UDCA type of bile can reduce the chemical-induced carcinogenesis. And in patients with primary sclerosing cholangitis, UDCA is considered a chemoprophylactic [15]. The flora of the intestine is the most important and largest micro-ecosystem in the human body. More than 500 species of bacteria are found in Healthy adult intestines [16]. These bacteria play an important role in the production of a biological barrier in the tract of the intestine via the place-holding effects, nutrition competition, and through metabolite secretions [17].

## MATERIALS AND METHODS

All 193 patients diagnosed with colorectal carcinoma through a full history and clinical examination, confirm the diagnosis through specific investigations such as CT abdomen with contrast and colonoscopy with biopsy for histopathology, the

patients who were excluded from the study who have predisposing factors as family history of CRC, IBDs, adenomatous polyps, and history of familial adenomatous polyposis, 43 patients included in this study who have a history of cholecystectomy without the mentioned-above predisposing factors, questioner for patients who have a history of cholecystectomy about the time of the cholecystectomy, age of the patients, any predisposing factors for colorectal carcinoma as mentioned above, classified them according to the time, to the ages of the patients, to the site of locations of the tumors, histopathological types, and macroscopically appearance. Operations were done after preparing the patients for the type of operation according to the site of tumors with most of the patients with primary anastomosis few of them with temporary ileostomy. Eventually, the specimens were sent for histopathological study.

## RESULT

193 patients were diagnosed with colorectal carcinoma through 3 years study from February 2020 till January 2023, the patients excluded from the study who had no history of cholecystectomy or had predisposing factors for colorectal carcinoma as, a positive colorectal cancer family history, inflammatory bowel diseases, adenomatous polyps, and history of familial adenomatous polyposis, 43 patients (22.3%) have a colorectal tumor with a history of cholecystectomy without these predisposing factors which are mentioned above. The most common colorectal carcinoma occurs after 21 years to 25 years after cholecystectomy 41.9% while the least time after less than 9 years of removal of gall bladder 2.3%, while 32.6% of the population with colorectal cancer occurs after 26 to 30 years and only 4.6% occur after 30 years of cholecystectomy, 11.7% of the tumor occur after 16 to 20 years post cholecystectomy as explain in Figure 1. The most common site of the tumor after cholecystectomy occurs in the RT site 48.8% of cases, descending colon 23.2% transverse colon 18.6% sigmoid 7% and the least site is the ano-rectum 2.4% as in Figure 2, adenocarcinoma represents 88.4% while squamous carcinoma 11.6% as Figure 3, according to the macroscopic appearance ulcerative type represent 67.5% while cauliflower type 20.9% and annular 11.6% as Figure 4, 67.5% moderately differentiated tumor according to the grading while mild differentiated 20.9% and well-differentiated 11.6% as in Figure 5. Most of the patients are in the age between 60 and 69 years 55.8% while 21.0 % occur at age more than 70 years, 18.6% occur at the age of 50 to 59 years and only 4.6% occur between age 40 and 49 years as in Figure 5, 6.

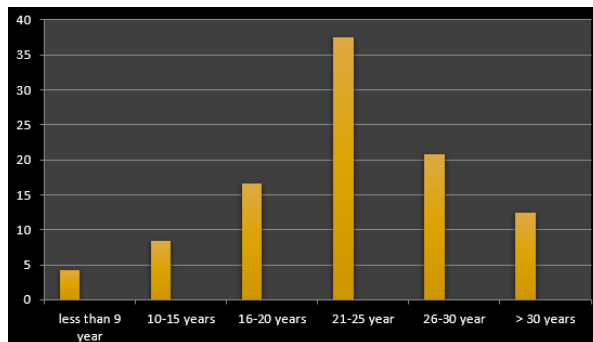


Fig. 1. According to the time of cholecystectomy in percentage

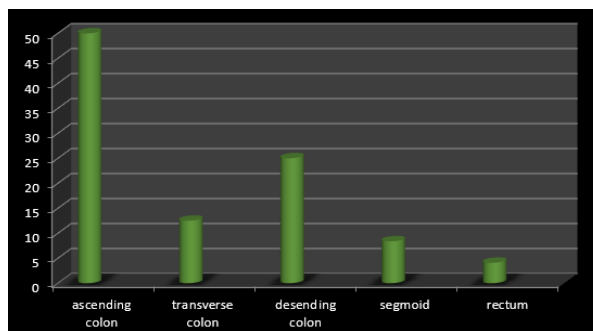


Fig. 2. According to the site location of the tumor in percentage

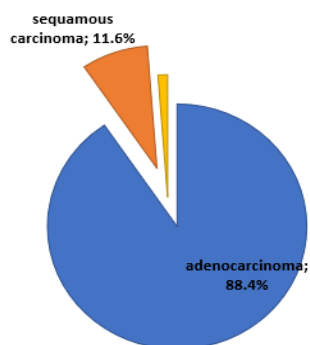


Fig. 3. According to the histopathological finding of the tumor in percentage

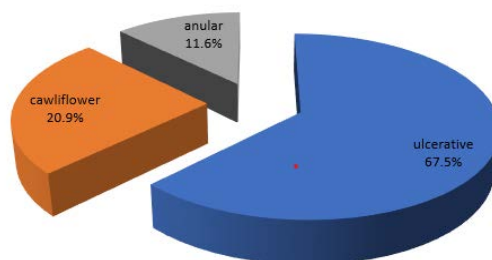


Fig. 4. According to the type of macroscopically finding of the tumor

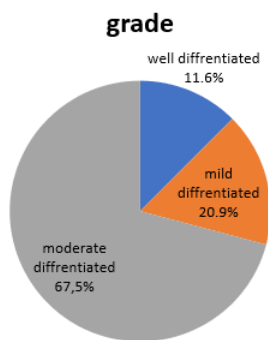


Fig. 5. According to the grade of the tumor

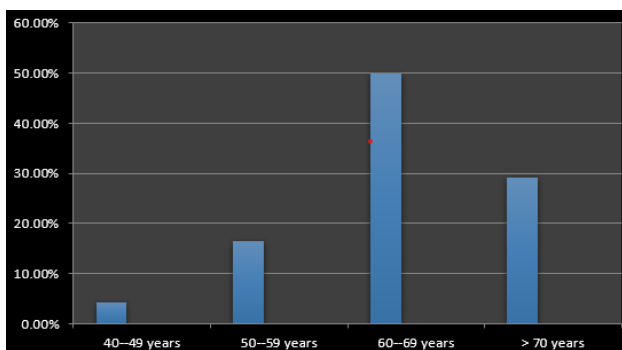


Fig. 6. Incidence according to the age of the patients

## DISCUSSION

The main causes of colorectal carcinoma post-cholecystectomy are the Secondary Bile Acids (SBAs) mainly deoxycholic acid and lithocholic acid which increase in level after cholecystectomy. 43 patients from 193 (23%) in this study have colorectal cancer after cholecystectomy and have no predisposing factors for this cancer as family history, smoking for more than 25 years, or any premalignant conditions or colorectal carcinoma through a formula of questions applied to the patients, this number of patients represent 23% which represent a relatively significant percentage to get a malignant tumor after cholecystectomy with the time which corresponds to the result of E S Schernhammer<sup>1,2</sup>, M F Leitzmann<sup>3,4</sup>, D S Michaud<sup>5</sup>, et al. Cholecystectomy and the risk for developing colorectal cancer and distal colorectal adenomas British Journal of Cancer volume [18]. In regards to the time of diagnosis, cancer after cholecystectomy mainly occurs after 21 years to 25 years in a percentage of 41.9% while 32.6% of cases are diagnosed after 26 to 30 years this result corresponds to the study done by Olov Adami, Olav Meirik, Sven Gustavsson, Olof Nyrén, Ulla-Britt Krusemo (Colorectal cancer after cholecystectomy: Absence of risk increase within 11-14 years) [19]. This explains that most of the cases underwent cholecystectomy at the age between 40 years to 50 years due to gall stones which is the main cause of cholecystectomy so diagnose of the tumor mainly occur between 60 years to 69 years while patients who did the cholecystectomy after age 50 they were died due to other causes before getting the tumor. According to the site or locations of the tumor in those patients mainly occur at the right site in 48.8 % and least occurs in the anorectal area in 2.4% his is due to the high level of secondary bile acid (SBA) secretion

which occur due to changing in the metabolism of bile acid after cholecystectomy and continuing direct effect of SBA on the right site of colon as it's a most proximal part of large bowel in contact with the a new deoxycholic acid and lithocholic acid (SBA) metabolism, but there cause not apply on the transverse colon which affected by the tumor less than descending or left site of colon, this point explained by freely mobility of transvers colon decrease the direct effect of SBA, while incidence of rectum carcinoma appear not affected by this operation. according to the histopathological study, most tumors are adenocarcinoma which is the commonest type this explains that the SBA does not affect the histopathological character of the CRC. 67.5% of cases are an ulcerative type of lesion while annular only 11.6. This explains the SBA metabolism and changes in colonic flora enhancing the ulcerative lesions of colonic mucosa. most cases occur at age 60 years-69 years 55.8% who had done cholecystectomy before at least 21 years- 25 years.

## CONCLUSION

Due to a relatively high incidence of colorectal carcinoma after cholecystectomy so this operation is preferable not done unless to patients with symptoms or complaints from gall bladder disease as symptomatic gall stones while symptomatic patients prefer not to do this operation, but what about asymptomatic multiple small gall stones, is this the surgeons do the operations to prevent obstructive jaundice in futures or leave the gall bladder, we prefer to leave it and if a small stone has slipped into the common bile duct, an ERCP can be done as an outpatient procedure.

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