Abstract

Background: Many studies have investigated the relationship between cholecystectomy and colorectal cancer, and have reported moderately increased risk of colorectal cancer in patients with cholecystectomies. The alteration of bile flow is one possible explanation for this increased risk.

Objective: The aim of this study is to evaluate the possible correlation between cholecystectomy and colorectal carcinoma.

Patients and Methods: Seventy five patients with carcinoma of colon were included in this retrospective study and they include 23 women and 52 men and their ages range from 28 years to 71 years. Those 75 patients with carcinoma of colon were compared to 75 patients with carcinoma of lung, whose ages range from 30 years to 85 years and include 36 men and 39 women.

This entire patient had been selected from those patients admitted to oncology unit in Al-Sadr medical city from July 2010 to March 2012.

Results: The history of cholecystectomy at the time of diagnosis of the carcinoma was significantly higher in the carcinoma of colon group compared to the carcinoma of lung group.

No statistically significant difference was noted in this study between men and women with colorectal carcinoma concerning the history of cholecystectomy.

In our study there was no significant association between time from cholecystectomy to diagnosis carcinoma of colon.

Also in our study there was no significant association between age in cholecystectomised patient and development carcinoma of colon.

Conclusion: We observed a significantly increased occurrence of cholecystectomy among patients with colorectal carcinoma but not related to age, sex and time from cholecystectomy to diagnosis carcinoma of colon.

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Introduction

Cancer of the large bowel is the second cause of cancer death in the United States after lung cancer [1]. Most of colorectal cancers, regardless of etiology, arise from adenomatous polyps [2]. Colorectal cancer is preventable and is highly curable if detected early [2].

By far the two most common and clinically significant neoplastic lesions that appear in the large intestine are adenomatous polyps and adenocarcinoma arising from epithelial cells of the colonic or rectal mucosa. However, the large bowel is also the site of other malignant diseases. Including anal carcinoma (squamous or transitional cell types), lymphoma, leiomyosarcoma, malignant carcinoid tumor, and Kaposi’s sarcoma. Malignant diseases from adjacent sites such as the prostate, ovary, uterus, and stomach may also involve the colon and/or rectum by direct invasion [2].

The prognosis for individuals having colorectal cancer is related to the depth of tumor penetration into the bowel wall and the presence of both regional lymph node involvement and distant metastases. These variables are incorporated into the staging system introduced by Dukes and applied to a TNM classification method [1].

Many studies have investigated the relationship between cholecystectomy and colorectal cancer [4-12], and have reported a moderately increased risk of colorectal cancer in patients with Cholecystectomy [4-9, 12]. The alteration of bile flow is one possible explanation for this increased risk [4, 7, 13, 14].

Two meta-analyses studies showed a modest increase in the risk of developing cancer in the proximal colon after a cholecystectomy [4, 7]. Similarly, three prospective cohort studies also observed an increased risk of proximal cancers, particularly among women [5,8,15].

The association between cholecystectomy and colorectal cancer was plausible due to two possible factors:

(a)- Cholecystectomy can lead to alteration in the bile acid metabolism, thus causing an alteration in the concentrations of bile acids that are delivered to the colon which may act as carcinogens; and/or

(b)- Factors that lead to symptomatic cholelithiasis may be shared with colorectal cancer, and therefore cholecystectomy may act as a surrogate maker for other true contributory factors [36].

However, previous research had shown that the bile of cholelithiasis patients contains a higher amount of secondary bile acids, such as deoxycholic acids, than that of healthy controls [16-19]. Secondary bile acids are thought to be carcinogenic [20-24] and, thus, it is highly possible that
cholelithiasis patients are also at risk for colorectal adenomas.

**Aim of Study**

The aim of this study is to evaluate the possible correlation between cholecystectomy and colorectal carcinoma in al Najaf.

**Patients and Methods**

Seventy five patients with CA(carcinoma) of colon were evaluated in this retrospective study that includes 23 women and 52 men and their ages range from 28 years to 71 years, those 75 patient of CA colon were compared with 75 patients of CA lung, whose ages range from 30 years to 85 years and include 36men and 39 women.

All these patients had been selected from those patients admitted to oncology unit in Al-Sadr medical city from July 2010 to March 2012.

The diagnosis of CA colon was confirmed by histopathological examination of the sample that were taken from patient after surgery or colonoscopy or both, and examined by two expert histopathologists.

The data about age, sex, histopathology of tumor, staging, history of cholecystectomy, and time duration from cholecystectomy to diagnosis CA colon were collected from patient.

The patients in this study were divided into two groups: Those with history of cholecystectomy and those without history of cholecystectomy.

Then those patients with history of cholecystectomy subdivided in two subgroups regarding time from surgery to diagnosis of CA colon: more than 10 year and less than 10 year.

Also the patients in this study were divided in two groups: patient’s age<60years and ≥60 years.

The following patients with CA colon were excluded from this study:
1. Patients who previously diagnosed to have inflammatory bowel disease.
2. Previous diagnosis of FAP(familial adenomatous polyps).
3. Family history of CA colon.

**Statistical analysis**

The chi-square used for categorical variable, p value < 0.05 was considered to indicate statistical significance.

Calculation’s done by interactive chi-square software.

**Results**

During 20 months period of this study, patients 75 patients with CA colon (23 women ,52 men) ages range from 28 years to 71 years with the mean age of 48 years (SD ±15) had been compared with control group of 75 patients with CA lung (39 women,36 men) ages range from 30 years to 85 years with the mean age 53 years (SD ±13), From those patients with CA colon 17 patients had been cholecystectomised (8 women,9 men) while from patient of CA lung only 2 patients were cholecystectomised (2 men) , The elapsed time between cholecystectomy and diagnosis of malignancy was 13.5(SD±10)years for the CA colon group and 15(SD±5.7) years for the CA lung group, as seen in table (1).

The history of cholecystectomy at the time of diagnosis of the carcinoma was significantly higher in the CA colon group compared to the CA lung group (17/75, 23% vs. 2/75, 3%; p-value=0.00023), as seen in table (2).

No statistically significant difference was noted between men and women with colorectal carcinoma concerning the history of cholecystectomy (9/52, 17.3% vs. 8/23, 13%; p-value=0.0956) as seen in table (3).
In this study there was no significant association between time from cholecystectomy to diagnosis of CA colon (6/17, 35% vs. 11/17, 64%; p-value=0.37), as seen in table (4).

Also in this study there were no significant association between age in cholecystectomised patient and development of CA colon (p-value=0.149), as seen in table (5).

**Table 1** Demographic characteristics and incidence of cholecystectomy in patients with colorectal carcinoma and lung carcinoma

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>CA colon (n=75)</th>
<th>CA lung (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female: male)</td>
<td>23 women,52 men</td>
<td>39 women,36 men</td>
</tr>
<tr>
<td>Mean age</td>
<td>48 years (SD ±15)</td>
<td>53 years (SD ±13)</td>
</tr>
<tr>
<td>History of cholecystectomy</td>
<td>17 patient</td>
<td>2 patient</td>
</tr>
<tr>
<td>Elapsed time from cholecystectomy</td>
<td>13.5±10 year</td>
<td>15±5.7 year</td>
</tr>
</tbody>
</table>

**Table 2** the Association between CA colon and cholecystectomy as compare to CA lung (N=150)

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>cholecystectomy</th>
<th>yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA colon</td>
<td></td>
<td>17(89.47%)</td>
<td>58(44.27%)</td>
<td>75(50%)</td>
</tr>
<tr>
<td>CA lung</td>
<td></td>
<td>2(10.53%)</td>
<td>73(55.73%)</td>
<td>75(50%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>19(100%)</td>
<td>131(100%)</td>
<td></td>
</tr>
</tbody>
</table>

P-value=0.00023
Table 3 Association between sex and CA colon (n=75)

<table>
<thead>
<tr>
<th>CA colon</th>
<th>Cholecystectomy</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>yes</td>
<td>No</td>
<td>Total</td>
</tr>
<tr>
<td>male</td>
<td>9(52.94%)</td>
<td>43(74.14%)</td>
<td>52(69.33%)</td>
</tr>
<tr>
<td>female</td>
<td>8(47.06%)</td>
<td>15(25.86%)</td>
<td>23(30.67%)</td>
</tr>
<tr>
<td>Total</td>
<td>17(100%)</td>
<td>58(100%)</td>
<td>75(100%)</td>
</tr>
</tbody>
</table>

P-value=0.096

Table 4 Association between time from cholecystectomy to diagnosis of CA colon (n=17)

<table>
<thead>
<tr>
<th>Time from surgery</th>
<th>Cholecystectomised patient with CA colon</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 10 year</td>
<td>≥ 10 year</td>
<td>Total</td>
</tr>
<tr>
<td>male</td>
<td>4(66.67%)</td>
<td>5(45.45%)</td>
<td>9(52.94%)</td>
</tr>
<tr>
<td>female</td>
<td>2(33.33%)</td>
<td>6(54.55%)</td>
<td>8(47.06%)</td>
</tr>
<tr>
<td>Total</td>
<td>6(100%)</td>
<td>11(100%)</td>
<td>17(100%)</td>
</tr>
</tbody>
</table>

P-value=0.37

Table 5 Association between age and cholecystectomised CA colon (n=17)

<table>
<thead>
<tr>
<th>Age</th>
<th>Cholecystectomised patient with CA colon</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 60 year</td>
<td>≥ 60 year</td>
<td>Total</td>
</tr>
<tr>
<td>male</td>
<td>5(41.6%)</td>
<td>4(80%)</td>
<td>9(52.94%)</td>
</tr>
<tr>
<td>female</td>
<td>7(58.4%)</td>
<td>1(20%)</td>
<td>8(47.06%)</td>
</tr>
<tr>
<td>Total</td>
<td>12(100%)</td>
<td>5 (100%)</td>
<td>17 (100%)</td>
</tr>
</tbody>
</table>

P-value=0.149
Discussion

Multiple clinical studies have demonstrated an association between colorectal cancer and Cholecystectomy [5, 15, 25, 26].

In the current study, cholecystectomy had a statistically significant association with CA colon (p-value=0.00023). This is in agreement with Mannes et al[30] and P. Katsinelos[37] who showed persistent risk of colorectal cancer in patients who had undergone cholecystectomy, and this may be due to there is constant flow of bile into the gut and hence, enhanced exposure of the colon to bile salts[36]. Cholecystectomy leads to an even more increased concentration of primary bile acids in the intestinal lumen, which are transformed through Intestinal bacteria to secondary bile salts[13]. The role of secondary bile acids as an endogenous colon carcinoma has been shown in a number of clinical and experimental studies[28, 29]. Narisawa et al proved that secondary bile salts can promote colonic epithelial cell proliferation in animal models[20].

In the current study, the effect of sex on development of CA colon in the cholecystectomised and non cholecystectomised patient was statistically non-significant (p-value=0.0956). This is in agreement with Reid et al[7] and Ali A. Siddiqui[36] who found that the risk of colon cancer was statistically non-significant in both sexes who underwent a cholecystectomy and this may be due to that sex had no effect on bile flow in colon which regarded as cause for developing CA colon[7, 36].

The effect of age in this study on the cholecystectomised patients with CA colon was a statistically non-significant (p-value=0.149) This is not in agreement with P. Katsinelos [37] and Mannes AG [30] who found that increased risk of CA colon only in patient aged 60-80 years, whereas the younger patient had no increased risk, and this may be due to increased risk of all tumors in old age[30]. In our study we failed to find this relation to age, and this because of limited number of cholecystectomised patients with CA colon that were included in this study.

In the current study, there is statistically non-significant (p-value=0.3733) association between time after cholecystectomy and risk of developing CA colon. This is not in agreement with P. Katsinelos [37] and Mannes AG[30], how found increase risk of developing CA colon after 10 year from cholecystectomy. And this may be due to increase exposure to secondary bile acid lead to increased risk of CA colon[30], also we failed to find this relation to time, and this may related to limited number of cholecystectomised patients with CA colon that were included in this study.

Conclusion and Recommendations

- We observed a significantly increased occurrence of cholecystectomy among patients with colorectal carcinoma but not related to age, sex and time from cholecystectomy to diagnosis of CA colon.
- Since the exact pathogenic association of these conditions has not been fully proved and explained, there is no need for increased surveillance of these patients.

References

20. Narisawa T, Magadia NE, Weisburger JH, et al. Promoting effect of bile acids on colon Cancer after intrarectal instillation of N-methyl-