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Colo-rectal Cancer Risk After Cholecystectomy in Al-Khadymia Teaching Hospital

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Abstract

Background Cholecystectomy is one of the most commonly performed operative procedures, on the other hand, the wide acceptance of laparoscopic cholecystectomy for sure led to the increased rate of cholecystectomies. The data assessing relationship between cholecystectomy and colo-rectal carcinoma is limited; therefore the relationship of whether prior cholecystectomy modifies the natural history of colo-rectal carcinoma is worth assessing in Al-Khdymia Teaching Hospital.

Objective To estimate the risk of colo-rectal carcinoma in cholecystectomized patients and to assess the feasibility of screening in these patients.

Methods Retrospective evaluation of a total of 123 patients with approved colo-rectal carcinoma over a period of eleven years in a wide district drainage referral Hospital (Al-Khadymia Teaching Hospital) in Baghdad-Iraq.

Result The total number of patients included is 123 from June 1999 to June 2010. The whole group approved to have a colo-rectal carcinoma. The age range is from 17-90 years, the females constitute 55 patients of the total and the rest 68 patients were males. The results were not significant regarding the gender of cholecystectomized patients and the risk of colo-rectal carcinoma. While on the other hand there were slightly increased statistically significant relative risk of colo-rectal carcinoma specially involving the proximal colon in cholecystectomized patients.

Conclusions There is an increased risk of incidence of colo-rectal carcinoma in cholecystectomized patients regardless the gender of the patient, and the risk is higher for the proximal colon than the distal colon.

Key words cholelithiasis, cholecystectomy, colo-rectal carcinoma, screening of cholecystectomized patients.

Introduction

Cholelithiasis affects approximately 20% of the female and 10% of the male population. Although most of these patients remain asymptomatic for many years or even for a life time, therefore cholecystectomy is one of the commonly performed operative procedures; in addition to that the wide acceptance of laparoscopic cholecystectomy may have led to the increased rate of cholecystectomies. It is estimated that more than 600,000 cholecysetectomies are performed each year in the United States according to the annual reports issued by the health care services in the US [(1)].

The first clinical report relating the possible correlation between cholecystectomy and colo-rectal carcinoma appeared in 1978 [(1)]. Since then, more than 70 studies have been designed to confirm whether cholecystectomy could increase the risk of colon cancer with controversial or partially inconsistent results. Most of these studies report a slightly increased risk of colo-rectal carcinoma in cholecystectomized patients.

Bile acids are of two types [(2)]:

1- Primary bile acids; formed in the liver from cholesterol. These are the cholic and chenodeoxycholic acids.
2- Secondary bile acids; formed in the distal ileum and colon by bacterial action which causes deconjugation and hydroxylation which convert the cholic acid to deoxycholic acid and the chenodeoxycholic to lithocholic acid.

The proposed pathogenic mechanisms is the increased exposure of the intestinal epithelium to secondary bile acids, which may promote carcinogenesis shown in several clinical and experimental studies [3,4]. However, this possible correlation should lead to screening of cholecystectomized patients for colo-rectal cancer remains questionable. The incidence and risk have never been assessed in major Hospitals in Iraq therefore the incidence is also questionable.

The hypothesis behind the increased risk of colo-rectal carcinoma is that post cholecystectomy changes in the composition and secretion of bile salts affect enterohepatic circulation and exposure of the colon to bile acids [5,6] which may promote carcinogenesis. Some studies suggested the risk of carcinoma is higher in women and mainly at the right side of the colon [7].

The aim of this study is to evaluate the possible correlation between cholecystectomized patients and the risk of colorectal carcinoma in a wide district drainage referral teaching Hospital in Baghdad-Iraq (Al-Khadymia Teaching Hospital) and to answer a question about whether cholecystectomized patients should be put on screening program for early detection of colonic cancer.

Methods

Retrospectively evaluated a total of 123 patients' records with colo-rectal carcinoma that were diagnosed and approved through histopathology study of the specimens obtained after resection of their tumors or through endoscopy if the patient were beyond surgery in Al-Khadymia Teaching Hospital for the period from January 1999 to January 2010.

The following parameters were recorded;

1- The total number of patients.
2- The age.
3- The gender (male or female).
4- Site of the tumor.
5- History of cholecystectomy if present (Yes/No) and the history is approved during staging of the tumor by ultrasonography, CT scan or during the course of surgery. The cholecystectomized groups of patients were further subdivided into a female and a male group.

Results

The total number of patients with colo-rectal tumor is (123). The age range was from 17-90 years and the females constitute (55) patients from the total number and the rest were (68) male patients as shown in the demographic (Table 1).

Table 1. Demographic characteristics of patients enrolled

Patient	Information
Total no. of patients	123
Males	68
Females	55
Age range	17-90 years

According to our results (101) of the patients had colonic tumors and only (22) of the patients had rectal tumors. Patients with colonic tumors are further subdivided to those involving the proximal colon (60 out of 101) and the distal colon (41 out of 101) as summarized in the information (Table 2).

Table 2. Site of Tumor

Site of tumor	No. of patients	%
Colon	101	82.15
Rectum	22	17.85
Ascending colon	60	59.4
Descending colon	41	40.6

The other important parameter is the history of cholecystectomy in which we found that the majority were non cholecystectomized (102 from a total of 123) and the cholecystectomized were only (21 from a total of 123), in addition to that the cholecystectomized patients are categorized according to their gender which showed that only (11) females were cholecystectomized out of (55) and only (10) males were cholecystectomized out of (68) male patients included in the study as shown in (Table 3).

Table 3. Colo-rectal carcinoma and cholecystectomy

History of Cholecystectomy	No.	%
Non-cholecystectomized	102	82.9
Total cholecystectomized	21	17.1
Cholecystectomized Females	11	20
Cholecystectomized Males	10	14.7

Discussion

The relation between cholecystectomized patients and the subsequent risk of development of colo-rectal cancer has been thoroughly studied in recent decades in many parts of the world and the relation has been controversial; therefore we were very much interested to find out the risk and relation of cholecystectomy with colo-rectal carcinoma in our community.

Al-Khadymia Teaching Hospital is a referral hospital draining a wide range of patients from large district in our country, and over an extended period of time from June 1999 till June 2010 which is around eleven years hoping that we end up with real results reflecting the exact nature and the possible risk and relation.

Studying the relation between cholecystectomized patients and colo-rectal carcinoma is a critical issue because cholecystectomy is one of the most commonly performed elective surgeries especially after the introduction of laparoscopic surgery; this is its self raises a reasonable concern if this increase in the number of performed cholecystectomies had led to an increase incidence of colo-rectal cancer. A further concern came after the fact that not only cholecystectomy but also gall stones themselves to a lesser extent have increased biliary and fecal concentration of secondary bile salts[4], this concern came with increased reported missed pathologies of the

Intraperitoneal organs especially the colo-rectal region in laparoscopic surgery over the advantage of open cholecystectomy through which you can see and palpate the whole colon and rectum in the concomitant presence of gall stones, but it seems that the risk is not that important if certain safety rules are followed [3,8,9], which include proper preoperative patient assessment and preoperative careful examination of the colon and rectum prior of removing the gall bladder which should be highly recommended.

The role of secondary bile acids as an endogenous colon carcinogens as we mentioned earlier has been also shown in a number of clinical and experimental studies [9,10]. Narisawa et al also proved that secondary bile salts can promote colonic epithelial cell proliferation in animal models but he did not give much attention to time factor for exposure [11]. Mannes et al, who reported a significantly increased incidence of large bowel adenoma after cholecystectomy [12].

Our data regarding the relation of gender and cholecystectomy with the development of colo-rectal cancer were not significant in accordance to Chi Square ($X2=0.6$, $p < 0.05$). On the other

hand our results regarding the risk of history of having previous cholecystectomy, the possibility of having increased risk of colo-rectal carcinoma and the results regarding the site of predilection in the colon were very close to other large studies and even meta-analysis; therefore we statistically compared our results with those groups and in order to- reach this we applied the t-test for proportions equation that judge about the closeness of results, for the results to be similarthe end figure result should be less than 1.96 and the equation is (t= P1-P2/√P1q1/n1+P2q2/n2) where P1;is sample one;P2;is sample two;q1;is the rest of percentage of first sample;n1;sample size one;q2; rest of percentage of second sample;n2;sample size two.

We applied this method of comparing results for the relation of cholecystectomy and colo-rectal carcinoma risk and for the most common involved site. All our group results were below 1.96 ($p < 0.05$), which means that there is no difference between the results. Our data were compared with very large extended studies and even meta-analysis [7,13,15,20,21,22], they all agree that there is slight increase in relative risk of developing colo-rectal cancer in cholecystectomized patients, further more they noted as we do an increase risk of proximal colon carcinoma over the distal and rectal carcinoma.

We found that there is an increased relative risk of developing colo-rectal carcinoma and increased risk of carcinoma of the proximal colon rather than the distal or rectal regions which is strongly supported by the following large studies; retrospective, prospective and even meta-analysis [13,14,15]. Also we had no significant results between the gender and risk of colo-rectal carcinoma despite the fact that cholecystectomy is performed more in female patients than in male patients supported by our results in which the number of female patients who gave a history of cholecystectomy is higher than in male patients, also we lack the long term follow up for patients with cholecystectomy, however other authors suggested a more than 15 years screening [14,15].

The most reliable evidence we comparing our study with is supplied by Giovanucci who showed slightly increased relative risk for colo-rectal cancer after cholecystectomy with risk slightly higher in women in addition to that he noted a prevalence for the proximal colon [13]. In two large cohort studies, Ekbom et al followed patients up to 23 years after cholecystectomy and he observed only an increased risk among women for right sided colon cancer 15 years after operation [14], while Johansen et al followed up patients for less than 15 years and showed only a border line significant association between cholelithiasis and colon cancer [15].

After all this regarding the question that we raised at the aim of the study about involving cholecystectomized patients in screening program for early detection of colon cancer, almost all authors with results similar to ours agree that there is no evidence to suggest the need for this [4,16,17,18,19].

Conclusion

1- Our study demonstrates a slightly increased relative risk which is statistically significant of colo-rectal cancer after cholecystectomy in the area drained by our referral Teaching Hospital (Al-Khadymia) in Baghdad/Iraq.
2- The site of predilection for carcinoma in cholecystectomized patients is the proximal colon rather than the distal colon and the rectum comes second after the proximal colon.
3- The screening program for the possibility of developing colo-rectal carcinoma after cholecystectomy is not recommended since the elapsed time needed for surveillance is around 23 years.
4- There is no significant relation between the gender of cholecystectomized patient and the future risk of colo-rectal carcinoma.

5- With the increased number of operations for cholecystectomy after the introduction of laparoscope we suggest to follow safety measures and rule to at least inspection of colon and rectal area specially the proximal colon for the fact even cholelithiasis is a relative risk in the incidence of colo-rectal carcinoma.

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