Cholelithiasis, Cholecystectomy and Colorectal Cancer

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Özet: *KOLELİTİYAMİS, KOLİSİSTEKTOMİ VE KOLOREKTAL KANSER*

Kolesistektomiden sonra kolorektal kanser özellikle de sağ kolon kanser insidensinde artış olduğu 1970 den beri yapılan birçok epidemiyolojik araştırmada bildirilmiştir.

Bu çalışmada kolerektal kanser tanısı ile tedavi edilen hastalarda kolesistektomi ve koleliitiazis sıklığı retrospektif olarak araştırılarak aralarındaki ilişki incelendi. Dosyası incelenen 207 hastadan 27 si eksik bilgi nedeni ile çalışma dışı bırakıldı. Geriye kalan 183 hastanın 27 sinde (% 13) koleliitiazis ve 9 da taş nedeni ile daha önce geçirilmiş kolesistektomi (% 4.9) saptandı. Total koleliitiazis oranı % 18 olup sağlıklı kontrol grubunda saptanan % 6 oranından yüksekti (p < 0.01) . Kolesistektomi yapılan hastalarda sağ kalon kanseri % 55.5 iken kolesistektomi olmayanlarda % 20.8 bulundu (p < 0.01).

Bu sonuçlar kolon kanseri ve kolelityomi birlikteliğinin ortak etyolojik faktörlere bağlı olduğunu göstermekle birlikte özellikle sağ kolon kanseri gelişimi için geçirilmiş kolosistektomiini bir risk faktörü olabileceğini düşündermektedir.

Anahtar kelimeler: Kolelitiyamis, kolesistektomi, kolorektal kanser

Summary: *The relation between gallbladder stone and colorectal cancer or increased incidence of colorectal cancer after cholecystectomy has been reported epidemiologically since 1970 in many retrospective studies.*

According to this aspect, we planned a retrospective study to prove the positive correlation between colorectal cancer and cholecystectomy. In principle the history and the sonographic findings of the patients was carefully searched out from their files retrospectively.

Colorectal cancer diagnosed 207 patients were admitted to the study, in whom 24 was ruled out because of insufficient information about gallbladder. Also 100 healthy volunteers were researched of gallbladder stone as a control group. Out of well known 183 patients, 24 were diagnosed of cholelithiasis (13,1%) and 9 has been performed cholecystectomy (4.9%) for the same reason. Overall 33 patients were diagnosed of cholelithiasis (18%). This ratio was 6% in control group and the difference between the groups was determined to be significant (p<0.001).

When the ratio of right colon cancer in cholecystectomy group was 55.5%, this ratio is fixed as 20.8% in noncholecystectomy group. These results were proved to be statistically significant (p<0.001).

As a result we found out that; 1. The coincidence of colon cancer and cholelithiasis are significantly higher supporting the aspect of common etiologic factors effecting both diseases. 2. Cholecystectomy may be a risk factor for right colon cancer that's why the incidence of colon cancer is much higher in this group.

Key words: Cholelithiasis, cholecystectomy, colorectal cancer

The first report in 1978 that cholecystectomy may increase the risk of colorectal cancer, stimulated a number of epidemiyolojical studies. Some showed an increased risk, especially among women and for cancer of the right colon, whereas others failed to establish any association. Nevertheless some reports showed no association between colorectal cancer and cholelithiasis, whereas others suggested an association between cholelithiasis and colorectal cancer among women. The aetiological factors are common both in colon cancer and cholelithiasis and that's way some researchers believe that these two different clinical antites are diagnosed coincidentally more than causing one other. Differences in methodology, limited follow-up and low statisti-

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Table I: Distrubition of colon Ca patients with cholelithiasis and cholecystectomy or none in aspect of female and male.

	Female		Male	
	n	%	n	%
Cholelithiasis	12	50	12	50
Cholecystectomy	5	56	4	44
No cholelithiasis and cholecystectomy	53	35	97	65

cal power due to small numbers of patients are possible reasons for the inconsistent findings.

We therefore planned a retrospective study and investigated relation among cholecystectomy cholelithiasis and colorectal cancer.

MATERIALS and METHODS

A total of 207 patients with colon cancer were treated to Yüksek İhtisas Hospital between 1983-1993. In principle the history of cholecystectomy and the sonographic findings of the patients was carefully searched out from their files retrospectively. Twenty-four patients were ruled out because of insufficent information about gallbladder. Also 100 healty volunteers were researched of gallbladder stone as a control group. Toshıba SAL 77 3,75 MHz sector probe was used to ultrasonographic examination.

The term "carcinoma of the colon" includes carcinomas arising in the caecum, the ascending, transverse, descending and sigmoid colon, and the rectum. Patients who were found to have gallstones at operation or who were subjected to synchronous cholecystectomy were accepted as cholelitiasis. Results were evaluated statistically with student t test.

RESULTS

Out of well known 183 patients, 113 were male and 70 were female. The patients' age ranged from 18 to 88 (mean 51.06) and age of control group ranged 24-82 (mean 49.06). The mean age for female patients was 50.78 and 51.35 for male patients.

Table II: Colon Ca localization.

	Number of cases	%
Right colon	38	20.8
Transvers colon	11	6
Left colon and rectum	134	73.2

Out of 183 colon ca patients, 24 were diagnosed cholelithiasis (13,1 %) and 9 patients had undergone cholecystectomy (4,9 %). Out of 24 cholelithiasis patients 12 were female, and 12 were male. Five patients were female and 4 patients were male out of 9 patients who had undergone cholecystectomy. Ninty seven male and 53 female patients have neither undergone cholecystectomy nor were diagnosed cholelithiasis (Table I).

According to the localization of colonic ca 38 were right sided, 11 were in transvers colon, 134 were localized in left colon and rectum.

As a general consideration left colon and rectum were the most common place for colon ca localization (Table II).

In 8 patients out of 24 cholelithiasis cases colon ca was right sided in 1 patient at transvers colon and in 15 patients of left colon and rectum.

In 30 patients out of 159 non cholelithiasis cases colon ca was localized at right colon and in 129 patients at other segments of large bowel (Table III).

Right colonic ca incidence was more in patients with cholelithiasis than non cholelithiasis group ($p< 0,25$).

In 5 patients (55.5%) out of 9 cholecystectomy cases colon ca was localized at right colon in 4

Table III: Colonic Ca localization in cholethiasis and non cholelithasis group.

	Right colon	Other colon segments and rectum
Cholelithiasis(+) (n: 24)	8 (33.3%)	16 (66.7%)
Cholelithiasis (-) (n: 159)	30 (18.8%)	129 (81.2%)

Table 4: Colonic Ca localization in cholecystectomy and non cholecystectomy group.

	Right colon	Other colome segments and rectum
Cholecystectomy(+) (n: 9)	5 (55.5%)	4 (44.5%)
Cholecystectomy (-) (n: 174)	33 (18.9%)	141 (81.1%)

Table 5: Choletithiasis incidence in colon cancer and control group(including cholecystectomized).

	Colon Ca		Control Cases	
	n	%		
Cholelithiasis (+)	33	18	6	6
Cholelithiasis (-)	150	82	94	94

Table 7: The duration between cholecystectomy and colon

Duration	Number of patients	
0-5 years	2	(28,57%)
6-10	2	(28,57%)
11-15	3	–
16- more		(42,87%)

patients (44.5%) in left colon and rectum. In 33 patients (18.9%) out of 174 noncholecystectomy cases, colon ca was right sided and in 141 patients (81.1%) at rectum and other segments of large bowel (Table IV).

Right colonic ca incidance was more in cholecystectomy group than noncholecystectomy group ($p<0.10$).

6 patients were diagnosed cholelithiasis out of 100 healthy cases of control group 6%. Cohlelithiasis incidence was more in colon Ca patients in comparision to healthy control group ($p<0.10$) (Table V).

When the canser localization was analyzed by sex and with or without previous cholecystectomy: 3 out of 5 female patients with right colon cancer who underwent cholecystectomy and 11 out of 65 without cholecystectomy (60 percent: 17 percent $p<0,25$). The relative risk (RR) for right sided colonic concer in women with previous cholecystectomy was calculated at 3.5. The distrubiton of cancers in the remaing colon in women and also in men was not different from the distrubition in noncholecystectomy group (Tablo 6).

The duration between cholecystectomy and colon Ca is 26 years in one case, 24 years in two cases, 6 years in two cases and 1.5 years in two cases. In two patients duration couldn't be learned. In 3 of 7 cases, whose duration was known, duration between cholecystectomy and colon Ca is more than 15 years (Table 7).

Because the number of patients is low efficient statistical analysis couldn't be made diagnosis between colon cancer and the duration after cholecystectomy.

DISCUSSION

Reports over 60 are established on the hypothesis of cholecysectomy increases the risk of Colon Ca (1–7). These researches gave different results. There are many reports published on the increased risk of right Colon Ca related to cholecystectomy especially in women (1,4,5). In some papers the risk of right colonic cancer are increased after 15 years of cholecystectomy is reported (6). In another research made only in Iceland, it

Table 6: Cancer site women and men with and without chohecystectomy.

Site of Cancer	Female					Male				
	Without cholecysteduy		With cholecystecto			without cholecys.		with cholecys.		
	n	%	n	%	RR	n	%	n	%	RR
Right colon	11	17	3	60	3,54	22	20,1	2	50	2,5
Transvers	3	4.6	1	20		8	3,5			
colon	7	10.7	1	20		19	17,4	1	20	
Left colon	44	67				60	55	1	20	
Rectum	65					109		4		

(RR = Relative risk)

is reported that there is an increased risk of colon Ca after cholesystectomy in men (7).

In 1993 Giovonucci et al. made the metanalysis of 33 clinical trials held (8). Due to this metanalysis, they found significant correlation between cholecystectomy and right colon Ca. The same researchers have drawn the attention to the increasing risk of colon cancer after the years passed from cholecystectomy they also stressed that during the cholecystectomy the possibility of undiagnosed colon cancer is not likely to happen. In many researches, when the cases which haven't passed 15 years over the cholocystectomy are excluded, it is stated that the risk factor will become more. However in some of researches when the common etiologic factors such as cholelithiasis and colorectal Ca, which increase the risk of cancer are found, the doctors emphasize their association rather than forming a risk for each other. However this could happen because of the insufficient time between the studies which have been done previously.

The cancer development mechanism which happen after cholecystectomy was shown through the experiments done on animals. It was reported that in the absence of a gallbladder the bile acids flow continuously into the intestine and these together with intestinal bacteria turn into secondary bile acids, and these bile acids which form too much lead to malign transformation increasing intestinal epithelial proliferation (8–11). But this kind of research hasn't been done on human. Although in one of the research, the attention is concentrated on proximal colonic mucoza, it has been reported that after the cholesystectomy the mitotic index in distal colon increases (8).

In our retrospective study on 183 patients the rate of cholelithiasis was more than the one of the control group. Moreover the causes which get over cholecystectomy the rate of the possibility of right colon cancer was significantly more than the ones who haven't got it over. Especially the difference was greater in females with right colonic cancer (Relative risk: 3.54). Since the number of patients is insuficient, we were unable to make correlation statistically between colon Ca and the duration after cholecystectomy.

As a result when the colon cancer and choleclithiesis are found together it increases the idea that both of the diseases happen due to the common etiologic factors. Furthermore the rate of colon cancer exists more in cholecystectomy it leads us to think that cholecystectomy may cause a risk for colon cancer. The final decision on this subject can only be given after the prospective studies.

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