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Original Article

Sporadic colon cancer in Lebanon: A clinicopathological study

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Abstract

Colon cancer is a heavy public health burden. No data has been previously published on colon cancer epidemiology in Lebanon. The objective of this study was to report the clinical and pathological features of surgically operated colon cancer.

From July 2005 to July 2012, 187 sporadic colonic tumors were operated in Hotel–Dieu de France Hospital (Beirut, Lebanon). Demographic, clinical, pathological and staging data was collected.

The male: female sex ratio was 1.3 and the mean age at diagnosis was 66.0 years. Most tumors occurred at the right colon (54.0%). Histologically, conventional adenocarcinoma had the biggest proportion (88.2%), followed by mucinous adenocarcinoma (9.1%). Most cases operated belonged to stages II, III or IV, leaving only 8.0% of the cases in stage I.

Some characteristics were similar to western countries like the predominance of right tumors while others were similar to developing countries like the sex ratio and the high proportion of stage IV tumors at diagnosis.

This study reports for the first time in the middle–eastern populations a clinico–pathological analysis of surgically operated colon cancer.

Keywords: Colon cancer, Lebanon, developing countries, western countries, clinico–pathological, middle–eastern, epidemiology.

Introduction

Colon cancer (CC) is a heavy public health burden. In the United States of America (USA), it is the second most frequent cancer in women and the third in men. The highest incidences were seen in North America, Australia and Western Europe while the lowest incidences were seen in Africa and Central Asia [(1)]. A progressive decrease of advanced disease incidence and mortality was seen in the USA while an increase of incidence was seen in Spain, East Asia and Eastern Europe [(2)]. A 53% decrease of mortality is seen in the USA from 1975 to 2006, mainly related to screening and more developed treatment options [(3)].

Right and left colon tumors are recently considered different diseases from the same organ [(4)]. Molecular aspects and tumor localization influence survival rates and are essential to predict adjuvant chemotherapy response in metastatic disease [(5)]. In the wild type, left colon cancer (LCC) responds better to cetuximab therapy than right colon cancer (RCC), with better survivor outcomes in different trials (6). RCC is known to have more microsatellite instability (MSI) [(6)]. RCC with MSI has worse outcomes with adjuvant chemotherapy than RCC without MSI [(7)].

The control of risk factors such as consuming red meat, obesity, smoking and physical activity contribute in decreasing incidence and mortality [(8, 9)]. In Lebanon, CC is in fourth position with an incidence of 15.3 per 100,000 habitants in the year 2008 [(10)]. The characteristics of CC are neither reported in Lebanon nor in the Middle East.

The purpose of our study is to elucidate clinico–pathological features of resected colon tumors in our institution as an example of the tumor behavior in Lebanon. Molecular aspect such as the K–ras and the MSI situation were not included in our study due to financial considerations.

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Materials and Methods

This is a retrospective descriptive study conducted in Hotel–Dieu de France (HDF) hospital (Beirut, Lebanon). The study protocol was approved by the ethical committee of the Saint–Joseph University of Beirut. Helsinki declarations of 1963 were taken into consideration: respect, confidentiality and anonymity of the patients. All cases of surgically operated CC between July 2005 and July 2012 were retrieved from the pathology database and hospital records.

Participants

Two hundred twenty (220) colorectal resections were identified in the considered time period. We excluded from the study all patients with missing information and those presenting: an extension of the tumor to the rectum, a hereditary colon cancer syndrome or an inflammatory bowel disease. The eligible population consisted of 187 patients. All patients were operated in HDF for curative or palliative purposes by the same colorectal surgeon specialist. The pathological characteristics were all analyzed at our institute pathology laboratory. Clinical information was retrieved from the hospital records.

Variables

The collected variables were: sex, age, clinical presentation, anemia status, tumor localization, tumor size, histological subtype, tumor grade, vascular invasion, lymphatic invasion and stage at diagnosis. We failed to include tumor molecular characteristics in our study such as the K–Ras type and the mismatch repair status since molecular testing was not done on regular basis for all patients due to financial considerations.

Statistical methods

Statistical analysis was performed using IBM SPSS version 20. Our data was expressed in mean standard deviation (SD), or median, or percentage. Pearson's $\chi 2$, student T and ANOVA tests were used to identify the relationship between variables. A p value <0.05 is considered significant.

Results

Demographic characteristics:

The mean age at diagnosis was 66.0 years and the sex ratio was 1.3. Men and women differed in age in stage I only with a mean age of 59.1 years for women and 77 years for men (p=0.030) (Table 1).

	Stage I	Stage II	Stage III	Stage IV	p-value
Age	66.6 ± 15.4	67 ± 12.6	65.6 ± 14.6	63.3 ± 12.4	p = 0.519
Men	77 ± 5.7#	65.7 ± 12.8	65.9 ±15.6	63.6 ±10.3	p = 0.250
Women	59.1 ± 16.1	68.7 ± 12.2	65.2 ± 13.2	62.9 ± 14.7	p = 0.353

Table 1. The mean age of patients within each TNM stage.

Clinical presentation:

Of all patients, one hundred sixty (85.6%) were symptomatic. Patients most often presented with abdominal pain (78 patients, 42%). Other findings were: anemia 77 (41%), transit disorder 67 (36%), general condition alteration 60 (32%), hematochezia 37 (20%), bowel occlusion 35 (19%) and melena 22 (12%). Among asymptomatic patients n=27 (14.4%), anemia was the only abnormality in 18 patients (67%). Anemia and bowel occlusion were the only clinical presentations to have positive relation with tumor localization. Right tumors had the highest percentage of anemia (67%, p=0.002) and left tumors had the highest percentage of occlusion (65.7%, p=0.001).

Transit disorder was most observed in stage III with a significant result ($p<0.01$). General condition alteration

	Left	Right	Transverse	p-value
Haematochezia	21 (56.8%)	14 (37.8%)	2 (5.4%)	0.070
Abdominal mass	1 (16.7%)	4 (66.7%)	1 (16.7%)	0.352
Abdominal pain	36 (46.8%)	35 (45.5%)	6 (7.8%)	0.208
Transit disorder	32 (48.5%)	32 (48.5%)	2 (3%)	0.143
Occlusion	23 (65.7%)	9 (25.7%)	3 (8.6%)	**0.001**
Perforation	1 (50%)	1 (50%)	0 (0%)	0.916
Anemia	21 (27.3%)	52 (67.5%)	4 (5.2%)	**0.002**
General state alteration	27 (45%)	30 (50%)	3 (5%)	0.636

Table 2. Repartition of different clinical presentations in different localization.

	Stage I	Stage II	Stage III	Stage IV	p-value
Haematochezia	3 (8.8%)	12 (35.3%)	9 (26.5%)	10 (29.4%)	0.728
Abdominal mass	0 (0%)	1 (16.7%)	3 (50%)	2 (33.3%)	0.453
Abdominal pain	2 (2.9%)	27 (38.6%)	22 (31.4%)	19 (27.1%)	0.207
Transit disorder	0 (0%)	21 (33.9%)	22 (35.5%)	19 (30.6%)	**< 0.01**
Dyspepsia	0 (0%)	1 (25%)	2 (50%)	1 (25%)	0.756
Occlusion	0 (0%)	14 (43.8%)	8 (25%)	10 (31.2%)	0.232
Perforation	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0.695
Anemia	4 (5.7%)	31 (44.3%)	17 (24.3%)	18 (25.7%)	0.583
General condition alteration	1 (1.8%)	20 (35.1%)	17 (29.8%)	19 (33.3%)	**0.040**

Table 3. Repartition of each clinical presentation within different stages.

Variables	Number of cases	Percentage (%)
Metastasis at diagnoses	41	
Hepatic	30	73
Pulmonary	8	19.5
Carcinosis	2	5
Scalp	1	2.5

Table 4. Metastatic sites at diagnosis.

was most observed in stage II with a significant result (p=0.04).

Tumor characteristics

Fourteen patients (7.5%) had synchronous tumors; in those patients, the most aggressive one was studied. Overall 101 patients (53%) had a right colon tumor, twelve (6.4%) a transverse colon tumor and 74 (39.6%) a left colon tumor. The biggest proportion at diagnosis is for stage II (40%) followed by stage III (30%), then stage IV (22%) and at last stage I (8%). Curative colectomy was performed in 155 (82%) patients. The liver was the most common metastatic site (73%).

Pathology characteristics

The mean size of tumor per location ranged from 4.8 to 5cm. Most tumors were conventional adenocarcinoma (88.2%) followed by mucinous adenocarcinoma (9.1%), signet–ring cell carcinoma (1.6%) and neuroendocrine carcinomas (1.1%). Most cases of mucinous adenocarcinoma (64.7%) and neuroendocrine carcinomas (100%) were located in the right colon. Vascular or lymphatic invasion was most found in neuroendocrine carcinomas (100%) and signet–ring cell carcinomas (66.7%) compared to conventional adenocarcinomas (31.5%) and mucinous adenocarcinoma (17.6%). Grade 2 tumors had the highest proportion (82.4%) followed by grade 1 (10.9%) and grade 3 (6.7%).

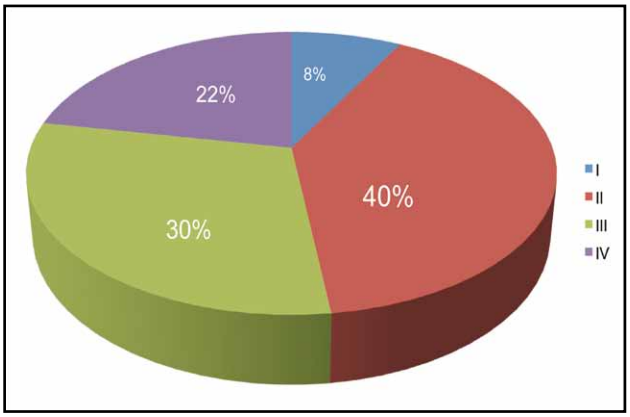


Figure 1. Stage distribution of surgically operated colon cancer.

Discussion

Little is known on colon cancer epidemiology, clinical setting and pathological characteristics in the Middle East and Lebanon. We have therefore launched an international comparison, based on our findings and distinguishing colic from rectal tumors.

Age at diagnosis:

The mean age at diagnosis in our study was 66 years. It is higher than the mean age found in Algeria (53.5 years) [11] and lower than the mean age reported in the USA (71 years) [12]. The sex ratio in our study was 1.3, a result similar to studies conducted in France [13], Malaysia [14], and Algeria [11]. In the USA, the sex ratio reached 1 [12].

Tumor localization and stage at diagnosis:

Most of the tumors in our study were located at the right colon 101 (53%). Since 1990, researchers started to observe a shift of localization of colonic tumors from left to right in the USA and in Sweden [15,16]. A study in California showed an increase of right colon tumors from 50% in 1985 to 54% in 1993 [17]. The recent Wang et al study showed also the same results with 42% for RCC, 30% for LCC and 28% for the rectum [12]. In Algeria, LCC still dominate with 61.8% [11]. The shift of colon cancer localization from left to right is the result of an improved screening system. In addition to this shift the lowest proportion for stage I at diagnosis in our study (8%) and in Algeria (14%) may be an additional indicator of the un–established screening system. Unlike the USA where in a large scale study (n=114,937) stage I came in second position at diagnosis (27.3%)[12]. A conclusion on our screening system cannot be built with this study. Bigger studies need to be done in the future comparing populations from cities and rural places.

Pathology:

Pathology characteristics of tumors in our study were similar to those reported in the literature with the predominance of conventional adenocarcinomas (88.2%) [18]. Mucinous adenocarcinoma followed (9.2%) similarly to Wang et al findings [12]. The proportions of mucinous adenocarcinoma was slightly higher than studies done in Iran, which showed respectively a proportion of 8.5% and 7.5% [19, 20].

Conclusion

Our study is the first to describe tumor behavior of colon cancer in Lebanon. The predominance of right localization, and the mean age at diagnosis above 6o years are similar characteristics found in the western countries. On the other hand, the low proportion of stage

I (8%) at diagnosis and the sex ratio of 1:3 are not similar results compared to developed countries. More studies are needed in order to define the real status of colon cancer, to elucidate the behavior of these tumors, to describe the epidemiological profile and to evaluate the screening system in Lebanon.

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