Journal of BUON **15:** 285-289, 2010

ORIGINAL ARTICLE

Differences between right- and left-sided colon carcinomas

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Summary

Purpose: *Clinical, histopathological, and biological differences between right and left colon carcinomas have been questioned in the literature. The purpose of this retrospective study was to identify possible clinical and histopathological differences between the right and left colon carcinomas.*

Methods: *From 1987-2007, 109 patients with right colon carcinomas (RC group), and 186 patients with left colon carcinomas (LC group) were treated at a single institution. Clinical, histopathological, and biological variables were correlated to tumor location. The endpoint of the study was to see for any relationship between overall survival, recurrences, and their pattern in regard to tumor location.*

Results: *The incidence of distant metastases at initial diagnosis (p=0.049), and poorly differentiated tumors (p=0.001) was higher in right colon carcinomas.*

The 10-year survival rate in the RC group was 63% and in the LC group 66% (p >0.05). Recurrences, sites of recurrence, the in-hospital mortality and morbidity were similar in both groups (p >0.05).

Conclusion: *The biological behavior of right and left colon carcinomas is similar despite minor histopathological differences that do not influence survival and development of recurrences.*

Key words: colon carcinomas, morbidity, mortality, recurrence, survival, tumor location

Introduction

Clinical, histopathological and biological differences between right and left colon carcinomas have been reported in the literature suggesting a difference in the molecular pattern of tumors [1,2]. Differences in regard to clinical presentation, management and outcome have also been reported [3]. Other studies have strongly questioned or even debated the above differences [4-7].

The purpose of this study was to identify possible differences between right and left colon carcinomas. More specifically, to see for any relationship between overall survival, recurrences and their sites in regard to tumor location.

Methods

The files of patients with colon carcinomas treated at the Department of Surgery, Didimotichon General Hospital, from 1987 to 2007 were retrospectively reviewed. Clinical variables such as age, gender, symptoms on presentation, and operative details were recorded. The patients were assessed for ASA (American Society of Anesthesiologists) class. Performance status was assessed according to Karnofsky performance scale. Histopathological details, in-hospital mortality and morbidity, overall survival, recurrences and their sites were also recorded.

All of the tumors located proximally to the splenic flexure were considered as right colon carcinomas and those located distally to the splenic flexure and above the peritoneal reflection were considered as left colon carcinomas. Patients with right colon carcinomas underwent colectomy and immediate reconstruction with ileocolic anastomosis regardless of the symptoms on presentation. Patients with left colon carcinomas treated urgently underwent Hartmann's procedure and those

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Received 28-05-2009; Accepted 04-07-2009

electively treated underwent left colectomy and immediate reconstruction with colorectal anastomosis.

The resected specimens were examined histopathologically and staged according to TNM system.

Stage I and II patients underwent surgery only. Stage III and IV patients received systemic chemotherapy after surgical resection. Patients surviving initial treatment were followed-up every 6 months for at least 5 years with physical examination, hematological and biochemical examinations, tumor markers, abdominal and thoracic CT scanning and colonoscopy. Recurrences and their sites were recorded. Recurrences at the peritoneal surfaces and at the sites of resection were considered locoregional. All the others were considered distant. Tumor location was correlated to clinical, histopathological and biological variables.

Statistical analyses

SPSS (Statistical Package for Social Sciences) was used for statistical analyses. The proportions of patients with a given characteristic were compared by chi-square test, or Pearson's test. The survival curves were constructed using the Kaplan-Meier method and the comparison of curves was calculated using the log-rank test. Cox regression method was used for analysis of survival, recurrences, morbidity, and mortality. A two-tailed p-value < 0.05 was considered statistically significant.

Results

The files of 295 patients with colon cancer were reviewed and analyzed. There were 140 (47.5%) males and 155 (52.5%) females. The RC group consisted of 109 patients and the LC group of 186 patients. The general patient characteristics are listed in Table 1. The mean patient age in the RC group was 70.7±10 years (range 38-91) and in the LC group 71±10 years (range 35-92; p >0.05).

Right colon cancer was more frequently detected in males than in females (p=0.046). Distant metastases were more frequently detected in the RC group (p=0.049) in contrast to well differentiated carcinomas that were more frequently detected in the LC group (p=0.001). In the RC group, 93 (85.3%) patients had undergone right colectomy and 16 (14.7%) transverse colectomy. In the LC group, 176 (94.6%) patients had undergone left colectomy and 10 (5.4%) sigmoidectomy.

Morbidity and mortality

The morbidity rate was 26.5% (78 patients; Table 2). Poor ASA class (p <0.001), poor performance status (p <0.001), and urgent surgery were found to be strongly related with morbidity. There was a trend for advanced age (>65 years) to be related to morbidity but without statistical significance (p=0.056). ASA class was the single predictive factor of morbidity (p=0.018).

The in-hospital mortality rate was 10.8% (32 pa-

Table 1. Patient and disease characteristics

Variable	*RC group (n=109)*	*LC group (n=186)*	*p-value*
Age (years)			NS
<65	31	46	
>65	78	140	
Gender (M/F)	60/49	80/106	0.046
ASA-class			NS
I	52	81	
II	42	82	
III	12	22	
IV	3		
Karnofsky performance status			NS
90-100	95	154	
70-80	13	28	
50-60	1	2	
20-40		2	
Surgery			NS
Elective	80	125	
Urgent	29	60	
Tumor status			NS
T1	1	4	
T2	10	27	
T3	86	129	
T4	11	24	
Nodal status			0.025
N0	53	94	
N1	24	61	
N2	31	28	
Distant metastasis			0.049
M0	80	153	
M1	29	30	
TNM stage			0.054
I	6	21	
II	42	66	
III	31	67	
IV	29	30	
Degree of differentiation			0.001
G1	24	58	
G2	45	100	
G3	24	15	
Residual tumor			NS
R0	89	104	
R1	1	3	
R2	19	18	
Morbidity	28	50	NS
In-hospital mortality	13	19	NS
Recurrence	24	34	NS
Sites of recurrence			NS
Distant	18	27	
Locoregional	6	7	

NS: non significant

Table 2. Postoperative complications

Complications	*No of patients (RC group/LC group)*	*%*
Respiratory	13 (2/11)	4.4
Wound infection	13 (4/9)	4.4
Intra-abdominal abscess	10 (5/5)	3.4
Sepsis	10 (4/6)	3.4
Cardiovascular	9 (5/4)	3
Anastomotic failure	8 (5/3)	2.7
Renal failure	4 (1/3)	1.4
Septic shock	3 (2/1)	1
Intestinal obstruction	2 (2/0)	0.7
Postoperative bleeding	2 (0/2)	0.7
Liver failure	2 (1/1)	0.7
Urinary infection	2 (1/1)	0.7
Total	78 (32/46)	26.5

tients). Poor ASA class (p <0.001), poor performance status (p <0.001), urgent surgery (p <0.001), and the presence of peritoneal dissemination evidenced by high CA-125 serum levels (p <0.001) were found to be strongly related to in-hospital mortality. ASA class (HR=13.421, 95% CI=0.116-0.862, p=0.024), and the presence of peritoneal dissemination (p <0.001) were found to be predictive factors of in-hospital mortality.

Survival

There was no difference in overall survival between RC and LC group (Figure 1). Univariate analysis showed that T, N, M, residual tumor, degree of differentiation, use of adjuvant chemotherapy, stage, ASA class, CEA, CA 19-9, and CA-125 were variables significantly related to survival (Table 3). Multivariate analysis identified that the degree of differentiation (p=0.002), the residual tumor (p=0.006), and CA-125 (p=0.003) independently influenced survival (Table 4).

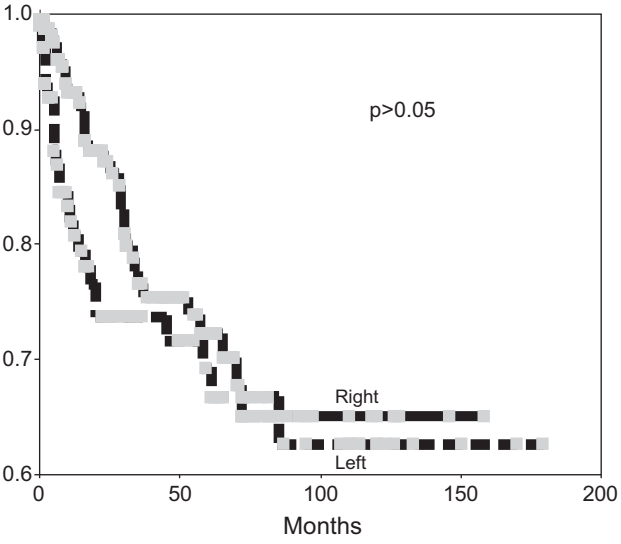

Figure 1. Survival of patients with right and left colon carcinomas.

Follow-up

During follow-up 24 (22%) patients in the RC group and 34 (18.3%) in the LC group recurred (p >0.05). In the RC group 18 patients developed distant metastases and 6 locoregional. In the LC group 27 patients developed distant metastases and 7 locoregional (p >0.05). Univariate analysis showed that nodal status (p<0.001), presence of distant metastases (p=0.014), use of systemic adjuvant chemotherapy (p=0.006), and stage (p <0.001) were variables strongly related to the development of recurrence (Table 5), while multivariate analysis showed that the use of adjuvant chemotherapy (p=0.006) and disease stage (p <0.001) were variables that influenced the development of recurrence (Table 6).

Table 3. Univariate analysis of survival

Variable	*p-value*
Anatomic location	0.209
Gender	0.9981
ASA class	0.0349
Physical status	0.3138
Urgent or elective surgery	0.1089
Tumor depth	0.008
Nodal infiltration	<0.0001
Distant metastasis	<0.0001
Grade of differentiation	<0.0001
Residual tumor	<0.0001
Adjuvant chemotherapy	0.0087
TNM stage	<0.0001
Age	0.434
CEA	0.0023
CA 19-9	<0.0001
CA-125	0.0002

Table 4. Multivariate analysis of survival

Variable	*HR*	*95% CI*	*p-value*
Grade of differentiation	9.361	2.316-47.051	0.002
Residual tumor	7.681	1.436-8.354	0.006
CA-125	8.904	2.669-114.421	0.003

95% CI: 95% confidence interval

Table 5. Univariate analysis of recurrence

Variable	*p-value*
Nodal status	<0.001
Metastasis	0.014
Adjuvant chemotherapy	0.006
Stage of disease	<0.001

Table 6. Multivariate analysis of recurrence

Variable	*HR*	*95% CI*	*p-value*
Adjuvant chemotherapy	7.41	1.332-5.817	0.006
Stage	17.462	0.211-0.568	<0.001

95% CI: 95% confidence interval

Discussion

One of the initially described differences in the literature between right and left sided colon cancer has been the incidence of obstruction. The splenic flexure has been considered as the most frequent site of obstruction [3,5] but this has been strongly questioned by others [8]. Obstructive colon carcinomas have been found equally distributed in both groups. The incidence of urgent surgery is similar for both groups. Most studies about colon obstruction due to carcinomas have shown that these tumors are more advanced and carry worse prognosis compared to non-obstructing ones but this has also been questioned [4,9].

Surprisingly, the incidence of right colon carcinomas has been found to be higher in males than in females. This is partly in agreement with the Nawa et al. study who have reported that right colon carcinomas are more prevalent in male patients under 40 years and over 70 years of age [1].

Morbidity and in-hospital mortality are not influenced by anatomic tumor location. Urgent surgery and performance status remain the most significant variables that influence morbidity and in-hospital mortality [6] despite different opinions [8]. Cardiopulmonary complications have been reported as the most frequent for obstructing carcinomas of the splenic flexure [3]. In-hospital mortality has also been reported to be higher in patients with left-sided obstructing carcinomas [3]. These findings have not been reproduced by this study. As already described in Methods, in right-sided colon carcinomas presented with obstruction one-stage resection and ileocolic anastomosis had always been performed but in left colon carcinomas with obstruction only Hartmann's procedure had been performed. The failure of a left-sided anastomosis associated by major future complications was the principal reason for which one-stage resection with immediate anastomosis was avoided. However, arguments about the integrity of the anastomosis have also been stated in hemodynamically stable patients. It has been reported that the incidence of failures of the left-sided colorectal anastomoses is the same if an elective or an urgent operation has been performed [10].

Analysis of the data has shown that lymph node infiltration and the presence of metastatic lesions at distant sites have been different between right and left colon carcinomas. Aldridge et al. [3], studying a large number of patients have reported no difference in distant or local metastases between right and left colon cancers but the right colon carcinomas were more poorly differentiated and locally advanced. Despite these differences the TNM stage was similar in regard to anatomic tumor location. The degree of differentiation is another variable for which the groups are different. The right-sided colon carcinomas are more poorly differentiated than the left-sided ones.

The majority of studies conclude that right colon carcinomas are usually detected at an advanced stage, in regard to tumor fixation and penetration of the bowel wall [1,2,11]. In addition, advanced carcinomas have been attributed to the development of the flat-type cancer preferentially at the right side of the colon [1,11] or to more advanced stage and poor lesion grade, suggesting a different molecular biology pattern between right and left-sided colon carcinomas [2]. Others conclude that the aggressive right-sided colonic carcinomas are preferentially detected in young patients [12]. Analysis of 17,658 patients presenting as stage IV colorectal carcinomas has definitely confirmed that young patients with right-sided colon carcinomas are more frequently detected at this stage [13].

Despite the above histopathologically recorded differences, the survival rates for right- and left-sided colon carcinomas showed no statistically significant difference. Although 11 variables were identified by univariate analysis to be related to survival, the most significant prognostic variables identified by multivariate analysis were the surgical result as assessed by the residual tumor, the degree of differentiation, and the peritoneal dissemination assessed by serum CA-125 values.

The rate of recurrence for both groups was the same. In addition, the sites of recurrence were the same. Nodal status, presence of distant metastatic lesions, use of systemic adjuvant chemotherapy, and stage of disease were factors related to recurrence. Multivariate analysis identified that the prognostic variables of recurrence were the use of systemic chemotherapy and stage of disease [14].

Conclusions

It appears that there are differences between right- and left-sided colon carcinomas in regard to histopathological variables. These differences are minor and do not influence long-term survival or the development of recurrences. Both, long-term survival and recurrences are similar which means that the biologic

behavior of colonic carcinomas is the same in regard to anatomic tumor location.

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