

RIGHT VERSUS LEFT COLON CANCER- ARE THEY DISTINCT ENTITIES?

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ABSTRACT

Colon cancer is among the most commonly occurring cancers globally and is linked with a poor prognosis. The incidence and prevalence of cancer is expected to rise more in the upcoming years. Right-sided colon cancer reportedly related with poorer survival as compared to the left-sided cancer. This study was conducted to compare both-sided cancers in the Pakistani population. A retrospective analysis of the case files was conducted, including 119 colon cancer patients (i.e. Right colon cancer=41, left colon cancer=78). Left-sided colon cancer showed a lower grade and less rate of metastases. The results showed no significant influence of sidedness on survival outcome, though there was a non-significance difference in favor of right colon cancer. Further studies are required to explore biological differences in cancers arising from both sides of colon.

INTRODUCTION

Colon cancer is among the most commonly occurring cancers around the globe, with a poor prognosis in a majority of patients (1). Anatomically colon and rectum are designed in such a pattern that a large mass can be accommodated for a long time without presenting any specific symptoms. Thus, colon cancer patients are likely to be diagnosed at a late stage. The adult colon is 5 feet long, divided into different sections. The right colon starts with the cecum as first part, then ascending colon, hepatic flexure (under liver where colon makes a turn), then continues as the transverse colon. The middle of the transverse colon demarcates the right and left colon. Therefore, the left half of the transverse colon, splenic flexure, descending colon, and sigmoid colon make the right colon. The rectum is the last part in continuation with the sigmoid colon and ends up with the anal canal. It is suggested that the prevalence of the colon cancer is higher on the left side as compared to the right side (2).

The available literature suggests the influence of colon cancer on clinical outcomes where colon cancer on left side demonstrates better overall survival. In advanced disease, the survival was not influenced by the side of the tumor (3). Similarly, results from the AIO KRK-0104 trial suggested that the left-sided colon was associated with more favorable survival. However, the influence was associated with KRAS mutations, while no influence was seen without taking KRAS into account (4). The NCIC CO.17 trial included metastatic colon cancer and reported that survival in metastatic colon cancer is not influenced by the side of the primary tumor (5). Data also suggested variation in the biological characteristics of colon cancer depending on the location of cancer (6). Thus the survival difference might have multifactorial influencers from essential characteristics to more complex molecular mechanisms.

The right-sided colon cancer presents with advanced stage, thus being associated with poorer survival than the left colon (7). There has been a consideration that the right and left colon might be separate entities. Therefore, this study was conducted to compare basic characteristics of the colon cancer developing on right and left sides of the colon.

METHODS

A total of 119 colon cancer patients were diagnosed and treated during ten years (between 2008-2018) at NIMRA hospital, and their complete clinical information was available. Out of these, 41 were right-sided colon (i.e, Cecum, ascending colon, and right half of the transverse colon and 78 were left-sided colon (i.e, left half of transverse colon, descending colon, and sigmoid colon) were identified from database in recruited in this study. All the patients had surgery after diagnosis or underwent emergency surgery, or in some inoperable cases, only a biopsy was taken. The data were retrospectively collected from case files. Basic histopathological parameters, including primary site, tumor size, metastases status, and histological grades, were recorded. Histological grade was defined as well-differentiated as grade I, intermediately differentiated as grade II, and poorly differentiated as grade III tumors. Demographic characteristics and basic histological characteristics of right sided colon cancer were compared with that of the left-sided colon cancer. Survival was calculated as the time from date of diagnosis to the date of the last follow-up or death and both sides were compared.

Statistical package for social sciences (SPSS version 24.0) was used for data collection and analysis. A comparison was made using the Chi-squared test, and the Kaplan- Meier method was used to compare survival between right and left colon cancer. A p-value <0.05 was considered significant.

RESULTS

The patients (n=119) with complete clinical information available from case files, including 41 right colon and 78 from the left colon were analyzed in this study. Out of which 30.8% of males while 38.9% were females had right-sided colon cancer. Similarly, among left-sided colon cancer, 69.2% were males, and 61.1% were females (Figure 1). On right-sided colon cancer, 19.1% were negative for lymph node metastasis, and 30.8% of left sided had lymph node metastases. Five patients (14.3%) and two (2.6%) were presented with systemic metastases on the right and left-sided colon cancer respectively. Histological grade distribution among right and left colon are shown in Figure 2. Median survival for right-sided colon cancer was 30 months, while 25 months for the left-sided colon. There was no significant difference in the survival of both sides (Figure 3).

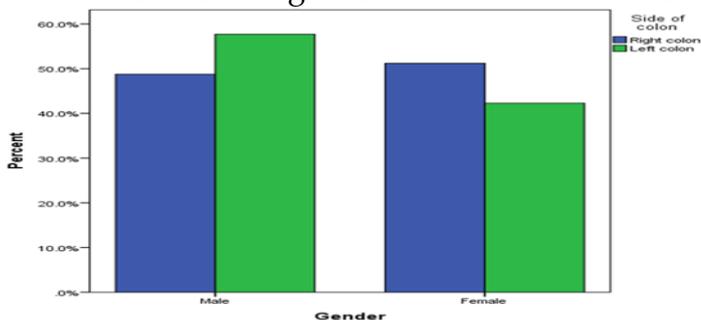


Figure 1. Association of sidedness of colon cancer with gender

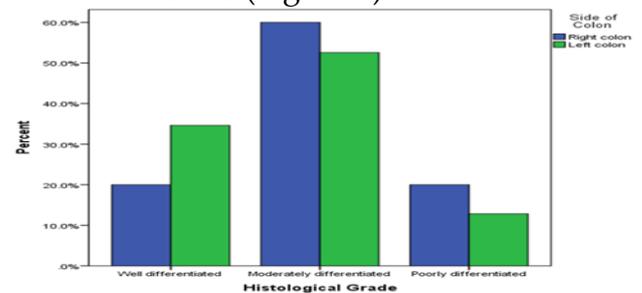


Figure 2. Association of sidedness of colon cancer with histological grade

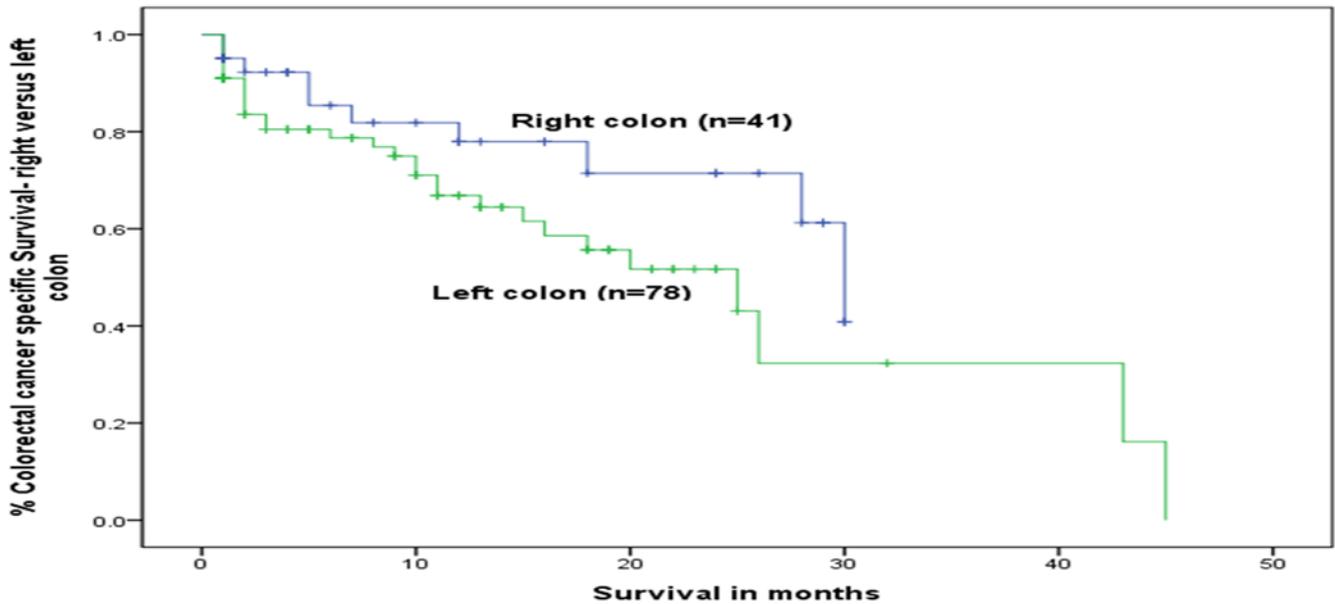


Figure 3: Colon cancer specific survival- Right sided versus left sided

DISCUSSION

The study showed higher rate of left-sided colon cancer in males and presented with a more favorable histological grade. However, the survival difference did not reach a significant level. Left-sided colon cancer reportedly shows better survival in the previously conducted studies. The difference in survival appears to be influenced by biology, which differs according to the location.

Previously reported data suggest that colon cancer in the Pakistani population is associated with a poor prognosis showing shorter survival(8). Biology is also aggressive in the Pakistani population(8). Previously reported studies have suggested that left-sided colon cancer enjoyed better survival, however, this may not be entirely related to the side, but this might influence the development of symptoms. The left-sided colon cancer is nearer to the anal canal; thus, the passing of bloody stool and change in bowel habits develop earlier than the right-sided colon. Obstruction and metastases were more common on the right side, which is most likely attributed to the delay in diagnosis. Cecum has the largest diameter in the entire colon; thus, it can accommodate a large tumor; therefore, the changes of advanced stage at diagnosis are highest. John M Creasy et al. studied 907(3) colorectal cancer patients. They followed them up for 11 years left-sided colon cancer patients showed better overall survival, but there was no significant difference in the disease-specific outcomes. A previously reported study showed that the right-sided colon cancers were significantly more extensive and poorly differentiated than the left colon cancer(9). The same study said that right-sided colon cancer had poor overall and colorectal cancer-specific survival(9). In our study, the survival of both sides was poor, and the sample was even smaller in right-sided colon cancer; thus, it could not reach a significant level. A randomized controlled trial was conducted, including 69 patients, out of which 52 proved to have RAS wild-type metastatic cancer; out of these 84% had left sided disease(10). Though the trial concluded that the sidedness was influencing the disease outcome, actually the mutation was influencing, and wild-type RAS was more prominent on left-sided cancer and showed earlier shrinkage of the tumor and better progression-free survival. In contrast, post-Hoc analysis of the OPTIMOX3 DREAM Phase III study showed better survival in left-sided metastatic colorectal cancer irrespective of KRAS status (11).

The results of the AIO KRK-0104 trial were suggestive of the same finding as reported in other studies where left-sided colon cancer achieved a favorable survival outcome compared to right-sided colon cancer. KRAS mutation and the sidedness of colon cancer were significant factors influencing survival outcomes (12). Yet another study looked at the influence of the primary tumor resection and compared both sides of the colon, and showed no significant difference in survival if the primary tumor was resected (13). The Spanish TTD trial compared KRAS wild type right-sided colon demonstrated lower efficacy than the left-sided colon cancer (14).

This was a single center-based study where pathological reports were retrieved from the same laboratory using the same definitions of the parameters. All patients were treated using the same guidelines at any given time. However, the study's retrospective nature and a small sample size are considered as the study's limitation.

CONCLUSION

This study showed a non-significant difference in the pathological parameters and survival of colon cancer arising from right and left sides. However, cancer arising from right side of the colon showed a lower rate of occurrence, more undifferentiated tumours and inferior survival as compared to the left-sided colon cancer. Further large-scale prospective studies are required to explore the biological differences in the sidedness of the colon cancers.

Conflict of interest

All the authors declared no conflict of interest.

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