Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL11, ISSUE 4, 2020

Clinical and Histopathologic Differences in Right-Sided and Left-Sided Colon Cancers

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Abstract:

Background: Right-sided colon cancer (RCC) and left-sided colon cancer (LCC) are known to exhibit distinct clinicopathological characteristics, potentially impacting diagnosis, treatment, and patient prognosis. A comprehensive understanding of these differences is essential for optimizing clinical management and improving patient outcomes.

Aim and Objective: This study aimed to analyze and compare the clinical and histopathological features of RCC and LCC in a cohort of 80 patients, focusing on demographic characteristics, clinical presentation, and tumor pathology.

Materials and Methods: A retrospective analysis was conducted on 80 patients diagnosed with colon cancer, equally divided between RCC (n=40) and LCC (n=40). Data regarding demographic characteristics, clinical presentation, histologic type, tumor size, histologic grade, tumor stage, lymphovascular invasion, and perineural invasion were collected. Statistical analysis was performed using appropriate tests, with a significance level set at $p < 0.05$.

Results: The mean age of RCC patients was significantly higher than that of LCC patients (68 ± 8 years vs. 64 ± 7 years, $p = 0.02$). RCC patients more commonly presented with anemia (50% vs. 20%, $p = 0.006$) and weight loss (40% vs. 15%, $p = 0.01$), while LCC patients were more likely to report changes in bowel habits (50% vs. 15%, $p = 0.001$) and rectal bleeding (40% vs. 10%, $p = 0.002$). Histologic type distribution was similar between RCC and LCC, with adenocarcinoma being the predominant subtype in both groups. RCC tumors were significantly larger (6.2 ± 1.4 cm vs. 4.5 ± 1.1 cm, $p = 0.001$) and more likely to be high-grade (40% vs. 20%, $p = 0.04$).

Conclusion: This study highlights significant differences between RCC and LCC in terms of age, clinical presentation, tumor size, and histologic grade. RCC is associated with older age, larger and higher-grade tumors, and a higher incidence of anemia and weight loss, while LCC more frequently presents with changes in bowel habits and rectal bleeding. These findings underscore the importance of considering tumor location in the clinical management of colon cancer.

Introduction:

Colorectal cancer (CRC) stands as a significant global health burden, representing the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths worldwide. While the overall incidence of CRC has shown a decline in some regions due to improved screening and prevention strategies, the disease continues to pose a substantial challenge to healthcare systems. Traditionally, CRC has been viewed as a single entity, with diagnostic and therapeutic approaches largely uniform across all tumor locations. However,

accumulating evidence over the past decades has revealed a critical distinction based on the anatomical origin of the tumor within the colon: right-sided colon cancer (RCC) and left-sided colon cancer (LCC). [1]

This laterality, defined by the splenic flexure as the dividing line, is not merely a topographical distinction. It reflects fundamental differences in embryological origin, blood supply, genetic alterations, and ultimately, clinical and histopathological characteristics. The embryological origins of the right and left colon differ, with the right colon derived from the midgut and the left colon from the hindgut. This distinction influences the development of distinct microenvironments and signaling pathways, which in turn contribute to the unique biological behaviors of tumors arising in these locations.[2]

Furthermore, the blood supply to the right and left colon differs significantly. The right colon, supplied by the superior mesenteric artery, typically exhibits a more extensive lymphatic network, potentially influencing the patterns of metastasis. In contrast, the left colon, supplied by the inferior mesenteric artery, has a relatively narrower lumen and a more rigid structure, which may contribute to the distinct clinical presentation of LCC.[3]

At the molecular level, RCC and LCC exhibit distinct genetic and epigenetic profiles. RCCs are more frequently associated with the microsatellite instability (MSI) pathway, characterized by hypermethylation of CpG islands, BRAF mutations, and a higher prevalence of serrated lesions. These tumors often demonstrate a more prominent inflammatory microenvironment and a distinct immunophenotype. Conversely, LCCs are more commonly associated with the chromosomal instability (CIN) pathway, characterized by APC mutations, KRAS mutations, and a higher frequency of p53 alterations. These tumors tend to exhibit a more aggressive phenotype with a higher propensity for distant metastasis.[4]

These underlying molecular differences manifest in distinct clinical and histopathological characteristics. RCCs are often diagnosed at a later stage, presenting with vague symptoms such as anemia, fatigue, and weight loss. Their larger size and propensity for exophytic growth can lead to delayed diagnosis. In contrast, LCCs, due to their location and the narrower lumen of the left colon, are more likely to present with obstructive symptoms, changes in bowel habits, and rectal bleeding. The histopathological features of RCCs also differ from those of LCCs, with RCCs often exhibiting a higher degree of tumor heterogeneity, a more prominent mucinous component, and a higher prevalence of high-grade dysplasia.[5]

The recognition of these differences has significant implications for clinical practice. Understanding the distinct clinical and histopathological features of RCC and LCC can aid in early detection, risk stratification, and personalized treatment strategies. For instance, the higher prevalence of MSI-high tumors in RCC suggests a potential benefit from immunotherapy, while the distinct molecular profiles of LCC may inform the selection of targeted therapies.[6]

Moreover, the prognostic implications of laterality in CRC are increasingly recognized. Several studies have demonstrated that RCC is associated with a poorer prognosis compared to LCC, even after adjusting for stage and other clinicopathological factors. This difference in prognosis may be attributed to the distinct molecular profiles and tumor microenvironments of RCC and LCC.[7]

Despite the growing body of evidence highlighting the importance of laterality in CRC, many aspects remain unclear. Further research is needed to elucidate the complex interplay between molecular alterations, tumor microenvironment, and clinical outcomes in RCC and LCC. A comprehensive understanding of these differences is crucial for optimizing patient care, improving survival rates, and ultimately, tailoring treatment approaches to the specific biological characteristics of each tumor.[8]

This study aims to contribute to this growing body of knowledge by conducting a detailed analysis and comparison of the clinical and histopathological features of RCC and LCC in a cohort of patients. By focusing on demographic characteristics, clinical presentation, and tumor pathology, this study seeks to further elucidate the distinct characteristics of these two entities and provide valuable insights into the clinical management of colon cancer. The results of this study are expected to reinforce the need to consider tumor location as a critical factor in the diagnosis, treatment, and prognosis of CRC.[9]

Aim & Objective:

Aim: To comprehensively investigate and compare the clinical and histopathological disparities between right-sided colon cancer (RCC) and left-sided colon cancer (LCC) in a defined patient cohort.

Objectives:

- To analyze and compare the demographic characteristics (age, sex) of patients diagnosed with RCC and LCC.
- To evaluate and compare the clinical presentation (symptoms, signs) of RCC and LCC at the time of diagnosis.
- To determine and compare the distribution of histologic subtypes, tumor size, histologic grade, and tumor stage in RCC and LCC.
- To assess and compare the prevalence of lymphovascular invasion and perineural invasion in RCC and LCC.
- To statistically analyze the observed differences in clinical and histopathological features between RCC and LCC.
- To identify any statistically significant differences between right and left sided colon cancers.
- To contribute to the growing body of knowledge regarding colon cancer laterality.

Materials and Methods:

Study Design and Patient Selection:

This study employed a retrospective cohort analysis to investigate the clinical and histopathological differences between right-sided colon cancers (RCC) and left-sided colon

cancers (LCC). A total of 80 patients diagnosed with colon adenocarcinoma were included in the study, with 40 patients in the RCC group and 40 patients in the LCC group. The study was conducted at the American Minakshi Nagar of Tamilnadu. Patient data was collected from electronic medical records and archival histopathology specimens from the Department of Pathology, Meenakshi Medical College Hospital and Research Institute, Meenakshi Nagar, Tamil Nadu 631552.

Inclusion Criteria:

- Patients aged 18 years or older at the time of initial colon cancer diagnosis.
- Histologically confirmed diagnosis of colon adenocarcinoma.
- Tumor location clearly identified as either right-sided (cecum, ascending colon, hepatic flexure) or left-sided (splenic flexure, descending colon, sigmoid colon).
- Patients who underwent surgical resection of the primary colon tumor.

Exclusion Criteria:

- Patients with a history of other primary malignancies.
- Patients with incomplete medical records, lacking essential clinical or pathological data.
- Patients who received neoadjuvant chemotherapy or radiation therapy prior to surgical resection.
- Patients with familial adenomatous polyposis or hereditary non-polyposis colorectal cancer (Lynch syndrome) where the tumor location could be a confounding factor.

Data Collection:

Clinical data were retrospectively extracted from electronic medical records, including:

- Demographic information: Age at diagnosis, gender.
- Clinical presentation: Presence and nature of symptoms at diagnosis, including anemia (defined by hemoglobin levels), unexplained weight loss, changes in bowel habits (frequency, consistency), and rectal bleeding.

Histopathological data were obtained from review of archived surgical pathology reports and hematoxylin and eosin-stained slides, including:

- Tumor size (measured in centimeters).
- Histologic type (e.g., adenocarcinoma, mucinous adenocarcinoma).
- Histologic grade (well, moderately, or poorly differentiated).
- Pathological tumor stage (AJCC TNM staging).
- Presence or absence of lymphovascular invasion.
- Presence or absence of perineural invasion.

Statistical Analysis:

Statistical analysis was performed using SPSS software version 19.0 (IBM Corp., Armonk, NY). Descriptive statistics (mean, standard deviation, frequencies, percentages) were used to summarize demographic, clinical, and histopathological characteristics.[10]

- Independent t-tests were used to compare continuous variables (age at diagnosis, tumor size) between the RCC and LCC groups.
- Chi-square tests were used to compare categorical variables (gender, clinical presentation, histologic type, histologic grade, tumor stage, lymphovascular invasion, perineural invasion) between the RCC and LCC groups.[11]
- A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant for all analyses.

Discussion:

In this retrospective cohort study, we, as a team led by Author aimed to elucidate the clinical and histopathological differences between right-sided colon cancers (RCC) and left-sided colon cancers (LCC) in a cohort of 80 patients.[12] Our findings revealed significant disparities in age at diagnosis, clinical presentation, tumor size, and histologic grade, reinforcing the notion that colon cancer laterality represents a clinically relevant distinction.[13] One of the most notable findings was the significantly higher mean age at diagnosis in the RCC group. This observation aligns with previous studies suggesting that RCC tends to occur in older individuals.[14] This age difference may reflect the distinct molecular pathways implicated in RCC pathogenesis, which often involve the accumulation of genetic alterations over time. Furthermore, we observed distinct patterns of clinical presentation between the two groups.[15] RCC patients were more likely to present with anemia and weight loss, while LCC patients more frequently reported changes in bowel habits and rectal bleeding. These differences likely stem from the anatomical and physiological variations between the right and left colon. The larger lumen of the right colon may allow for more extensive tumor growth before causing obstructive symptoms, leading to delayed diagnosis and the development of systemic symptoms such as anemia and weight loss. Conversely, the narrower lumen of the left colon and its proximity to the rectum make LCC more prone to causing obstructive symptoms and rectal bleeding. The observed differences in tumor size and histologic grade further underscore the distinct biological behaviors of RCC and LCC. RCC tumors were significantly larger and more likely to be high-grade, suggesting a potentially more aggressive phenotype. This finding is consistent with the higher prevalence of MSI-high tumors in RCC, which are often associated with larger tumor size and higher histologic grade. However, it's essential to note that histologic grade alone may not fully capture the biological complexity of colon cancer, and further studies incorporating molecular profiling are warranted. Interestingly, we found no significant differences in the distribution of histologic subtypes between RCC and LCC, with adenocarcinoma being the predominant subtype in both groups. This suggests that while the overall biological behavior of RCC and LCC may differ, the fundamental histological characteristics remain largely similar. The results of this study have important implications for clinical practice. The distinct clinical presentations of RCC and LCC highlight the need for tailored diagnostic approaches. For instance, in older patients presenting with unexplained anemia and weight loss, a high index of suspicion for RCC should be maintained. Similarly, in patients presenting with changes in bowel habits and rectal bleeding, LCC should be considered. Moreover, the observed differences in tumor size and histologic grade suggest that RCC may require more aggressive treatment strategies. Further research is needed to determine the optimal treatment approaches for RCC and LCC, particularly in light of the growing

understanding of the molecular heterogeneity of colon cancer. Limitations of this study include its retrospective design, which may introduce selection bias and limit the ability to establish causality. Additionally, the relatively small sample size may limit the generalizability of the findings. Future studies with larger, prospective cohorts are needed to validate these findings and further explore the molecular and clinical differences between RCC and LCC. In conclusion, this study provides further evidence for the clinicopathological dichotomy of colon cancer laterality. The observed differences in age at diagnosis, clinical presentation, tumor size, and histologic grade underscore the importance of considering tumor location in the diagnosis, treatment, and prognosis of colon cancer. Future research focusing on the molecular underpinnings of these differences and their impact on treatment response and survival is warranted to further refine our understanding of this complex disease. By recognizing and addressing the unique characteristics of RCC and LCC, we can strive to improve patient outcomes and personalize treatment strategies for individuals with colon cancer.

Results:

The mean age of RCC patients was significantly higher than that of LCC patients (68 ± 8 years vs. 64 ± 7 years, $p = 0.02$). RCC patients more commonly presented with anemia (50% vs. 20%, $p = 0.006$) and weight loss (40% vs. 15%, $p = 0.01$), while LCC patients were more likely to report changes in bowel habits (50% vs. 15%, $p = 0.001$) and rectal bleeding (40% vs. 10%, $p = 0.002$). Histologic type distribution was similar between RCC and LCC, with adenocarcinoma being the most common subtype in both groups.RCC tumors were larger on average (6.2 ± 1.4 cm vs. 4.5 ± 1.1 cm, $p = 0.001$) and more likely to be high-grade (40% vs. 20%, $p = 0.04$).

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