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Research Article

Impact of Tumor Location on the Clinicopathologic and Oncologic Outcomes of Stage 1-3 Colon Cancer

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Abstract

Objectives: This study aimed to analyze the clinicopathological features and oncologic disparities between stage 1-3 right versus left colon cancer patients treated with surgery.

Methods: In this retrospective study, 220 patients who underwent surgery for stage 1-3 colon cancer between 2014 and 2020 were divided into two groups according to tumor localization: right and left colon tumors. The two groups' demographics, tumor characteristics, and clinical presentation were evaluated comparatively. Oncological outcomes, local and distant recurrence, and overall survival rates were analyzed.

Results: Out of 220 patients, 35% were diagnosed with right colon cancer, while 65% were diagnosed with left colon cancer. Right colon tumors were more prevalent among older women and typically manifested with anemia and bleeding. Conversely, left colon tumors were more common in young men and often presented with changes in bowel habits. Additionally, right colon tumors were linked to unfavorable histopathological characteristics such as poor differentiation and high microsatellite instability. Despite these distinctions, there was no significant variance in the 5-year survival rates between the two groups (83.4% vs. 85%).

Conclusion: This study highlights the critical differences between right and left colon cancers in clinical presentation and tumor characteristics. Although tumor location did not significantly impact early-stage prognosis, right colon tumors were more frequently diagnosed at advanced stages, emphasizing the importance of early detection for better treatment outcomes.

Keywords: Early stage colon cancer, left colon cancer, right colon cancer, clinicopathological differences, survival

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Colorectal cancer stands as the third most prevalent malignancy worldwide, with an estimated 1.9 million new cases and 1 million fatalities in 2020. Projections indicate a substantial rise in both incidence and mortality rates by 2040, underscoring the critical necessity for enhanced research endeavors and more effective treatment modalities. The escalating burden of colorectal cancer underscores the urgency of the situation and the imperative for sustained advancements in the fields of oncology and colorectal cancer.[1]

During embryonic development, the large intestine originates from both the midgut and hindgut, subsequently dividing into the right and left colon based on its location. This unique origin not only lays the groundwork for the distinct clinicopathological features and oncologic outcomes of tumors originating from right and left colorectal cancers but also forms the basis of our study's focus. It has been observed that left colon cancer is more prevalent in men and middle-aged patients, while right colon cancer is predominant in women and young patients.[3-5] These clinicopatho-

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logical variances suggest the potential need for different approaches to diagnosis and treatment.

In our study, we investigated the clinicopathological characteristics and oncologic variances between stage 1-3 right versus left colon cancer patients who underwent surgical treatment. This area of research holds significant potential to impact patient care and outcomes, highlighting the importance of our work in oncology and colorectal cancer. The potential influence of our findings on patient care is substantial, serving as a driving force behind our research.

Methods

Patients

A total of 345 patients with stage 1-3 colorectal cancer who underwent surgery and were followed up in the medical oncology department between 2014 and 2020 were included in this study. Anal and appendiceal neoplasms, lymphoma, or carcinoid neoplasm patients were excluded. Additionally, patients with synchronous and metachronous tumors were also excluded. Patients planned for neoadjuvant treatment were omitted due to the potential impact of treatment on tumor biology. Data, including demographic information (gender, age), clinical characteristics, signs and symptoms related to colon cancer, and operation pathology reports, were collected from the patient's medical files and the hospital database. The patients were then divided into two groups based on the location of the tumor: right-sided and left-sided colon carcinoma. The left colon group includes tumors distal to the splenic flexure (descending colon, sigmoid colon), while the right colon group includes tumors in the cecum, ascending colon, and transverse colon. Of the 345 patients, 220 met the inclusion criteria, and their operation pathology reports were available. These patients were further divided into right-side colon cancer and left-sided colon cancer groups for comparison of clinicopathological characteristics, oncological treatments, treatment responses, and survival analyses (Fig. 1).

Statistical analysis

- Software Used: SPSS Statistics Version 17.0: The statistical analyses were performed using this software package.
- Univariate Analysis of Categorical Data: Chi-squared Test: This test examined relationships between categorical variables.
- Quantitative Variables: Arithmetic Mean/Standard Error: Quantitative data were summarized using the arithmetic mean and standard error. Mann-Whitney U Test: This non-parametric test was used to compare the distributions of two independent groups when the data did not follow a normal distribution.

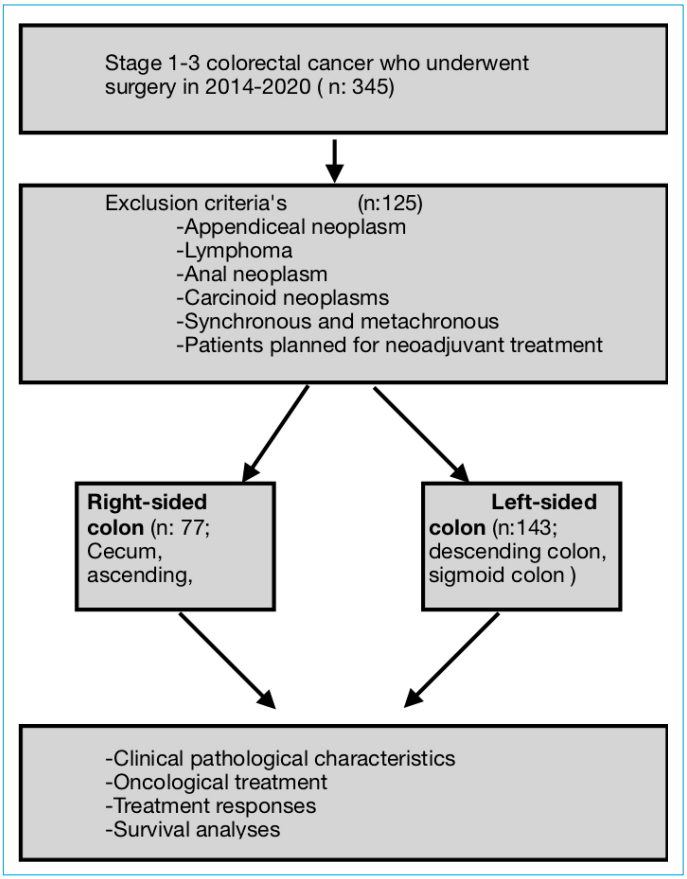

Figure 1. Flowchart of patients.

- Survival Analysis: Kaplan-Meier Method: This method was used to estimate survival functions from the data.
- Significance Level: p-value < 0.05: Statistical significance was determined with a p-value threshold of less than 0.05.

Results

Table 1 summarizes the characteristics and pathological features of all patients. Of the 220 patients, 127(58%) were men, and 93 (42%) were women. The mean age was 65±11.7 years, with over 50% of patients aged above 65. Of all patients, 77 (35%) were located in the right colon, while 143 (65%) were found in the left colon.

We analyzed the clinical characteristics of patients with right colon cancer and left colon cancer. The percentage of women was notably more significant among patients with right colon cancer compared to those with left; female patients with right colon 43 /77 (56%) vs. female patients with left colon 50 /143 (35%), ($p< 0.01$). The patients with right colon cancer were significantly older than those with left colon (67.2 +-10.8 years vs 62.6 +- 10.3 years), ($p<0.01$). In patients aged 40 years or younger, the proportion of right colon cancer was relatively high at 32%.

Table 1. Demographic and pathological data for all patients

Characteristic	Right colon n=77 (%35)	Lenf colon n=143 (%65)	p
Gender			
Male	34 (44)	93 (65)	<0.01
Female	43 (56)	50 (35)	
Age (years)	67.2±10.8	62.6±10.3	
Smoking status			
Active	28 (36)	43 (30)	0.47
Former	13 (17)	34 (24)	
Never	36 (47)	66 (46)	
BMI[a] (mean)	25.8	26.7	0.506
ECOG[b]			
0	35	82	1
1	34	46	0.67
2	8	15	0.58
AJCC[c] Stage			
1	20 (26)	30 (21)	
2	41 (53)	93 (65)	<0.01
3	16 (21)	20 (14)	<0.05
Tumor grade			
G1	12 (16)	20 (14)	
G2	51 (66)	114 (80)	0.072
G3	14 (18)	9 (6)	0.002
Lymphovasculer invasion	24 (31)	28(20)	<0.001
Perineural invasion	13 (17)	25 (18)	0.074
MSI[d]			
Stabil	18 (23)	102 (71)	<0.05
Instable	61 (77)	41 (29)	
Adjuvant chemotherapy	28 (36.6)	63 (44)	0.096
Tumor recurrence			
Distance	15 (19.4)	22 (15.3)	0.876
Local	3 (3.8)	3 (2)	0.673
Disease free survival, mo (mean)	103	110	
Overall survival, mo (mean)	109	120	

[a]BMI: body mass indeks; [b]ECOG: Eastern Cooperative Oncology Group; [c]AJCC: American Joınt Committee on Cancer; [d]Microsatellite instabilite; [e]Calculating using x^2 test and Mann-Whitney U test.

We subsequently compared the primary signs and symptoms reported by patients with right colon cancer to those with left colon cancer. The percentage of patients experiencing symptoms related to bleeding or anemia was significantly more significant in the right colon cancer group compared to the left group (60% vs 45%; p<0.01). On the other hand, intra-abdominal mass and ileus were significantly higher in right colon tumors than in left colon. (%3 vs %1 p<0.05; %20 vs %11, p<0.01 respectively) (Table 2). In patients with left colon, changes in bowel habits were found to be significantly higher than in patients with right colon. (43% vs 26%, p<0.001).

Table 2. Signs and semptoms of patients with right versus left-sided colon cancer

Signs and semptoms	Right colon n=77 (%35)	Left colon n=143 (%65)	p
Bleeding or anemia	46 (60)	64 (45)	<0.01
Abdominal mass	2 (3)	1 (1)	<0.05
Ileus	15 (20)	16 (11)	<0.01
Change bowel habits	20 (26)	62(43)	<0.001
Astenia	20 (26)	33 (23)	0.780
Abdominal pain	22(29)	46 (32)	0.381

Subsequently, we compared the morphological and histological features of right and left colon cancers. The number of patients diagnosed with stage 3 tumors was higher for right colon cancers, whereas stage 2 tumors were more prevalent in left colon cancers. (21% vs 14%; p<0.05, 53% vs 65%; p<0.01, respectively). Histopathological assessments revealed that poorly differentiated adenocarcinomas and lymphovascular invasions were more prevalent in the right colon than in the left (18% vs 6%, p=0.002; and 31% vs 20%, p<0.01, respectively). Right-sided colon cancer predominantly found microsatellite instability compared to left colon tumors (77% vs 29%, p<0.05).

During the 5-year follow-up period, the local recurrence rate was found to be 19.4% for right colon cancer and 15.3% for left colon cancer (p=0.87). The distant recurrence rate was found to be 3.8% for right and 2% for left colon cancer (p=0.67). The difference in recurrence between the two groups was not significant in the 5-year follow-up period. When examining the overall survival, although all risk factors seemed to be against the right colon, no difference in survival was found between right and left colon cancer in the 5-year follow-up (83.4% vs 85%) (Fig. 1).

Discussion

The differences in the behavior of colorectal tumors based on their location have been a subject of interest in previous studies.[8,9] It has been hypothesized that the distinct embryological origins of the right and left colon result in varying behavior patterns of tumors in these regions.[10,11] This has led to the consideration of right and left colon tumors as different entities, influencing the choice of treatment methods. Notably, demographic and clinical features, in addition to histopathological characteristics, also exhibit variations between tumors in the right and left colon. For instance, previous research has indicated that right colon tumors are more prevalent in elderly patients and women, while left colon tumors are more commonly observed in men and younger patients.[12-14] Histopathologically, poorly

differentiated mucinous tumors are more frequently found in the right colon, whereas moderately and well-differentiated tumors are more prevalent in the left colon.[15] These differences also manifest in the clinical presentation of right and left colon tumors, with right colon tumors often presenting with anemia and bleeding, and left colon tumors being associated with passage-related issues.[16-18]

Our study aimed to compare the demographic, clinicopathological characteristics, and clinical presentations of patients with right versus left colon cancer, focusing on 220 patients who underwent surgery for early-stage colon cancer. Consistent with existing literature, our findings revealed a higher proportion of female patients with right colon tumors compared to left colon ($p<0.01$).[18,19] Similarly, older patients were more frequently diagnosed with right colon tumors, aligning with previous research that has also reported the predominance of right colon cancer in the advanced geriatric population (over 80 years).[20-23]

Furthermore, our analysis of symptoms showed that patients with right colon cancer more commonly presented with anemia, bleeding, abdominal mass, and ileus, whereas changes in bowel habits were more frequently observed in patients with left colon tumors (for bleeding and anemia in right colon %60, in left colon %45, $p<0.01$, abdominal mass %3 vs %1 $p<0.05$, ileus %20 vs %11, $p<0.01$; changes in bowel habits 43% vs 26%, $p<0.001$). These findings are consistent with the slower development of right colon tumors and their association with iron deficiency anemia and positive occult blood in the stool, as well as the distal location of left colon tumors leading to bowel passage-related symptoms.[24]

Moreover, our study revealed that right colon tumors were more frequently associated with anemia, abdominal mass, and ileus compared to left colon tumors, contrary to some previous literature.[13,16,18] This discrepancy was retrospectively linked to the lower body mass index of patients with right colon tumors, potentially explaining the higher prevalence of abdominal mass as an early symptom and the earlier onset of ileus, especially in underweight patients.[25,26] Conversely, changes in bowel habits, a common symptom of colon cancer, were significantly more prevalent in patients with left colon tumors, aligning with existing research on the subject.[27,28]

The observed findings indicate that right colon cancer is frequently diagnosed at a more advanced stage, consistent with prior research documenting the tendency for right colon tumors to be detected at later stages.[8,13,18] This may be attributed to the relatively asymptomatic nature of right colon cancer in its early stages, as bleeding from the right colon is often less conspicuous than from the left. Our data revealed a higher prevalence of bleeding symptoms in patients with right colon cancer, along with more severe symptoms such as passage difficulties and abdominal masses typically associated with advanced-stage tumors.

Histopathological analysis unveiled that tumors in the right-sided colon are more poorly differentiated compared to those in the left colon, with a higher frequency of lymphovascular invasion. Moreover, microsatellite instability (MSI-H) was notably higher in right colon tumors,[29] potentially linked to the higher prevalence of hereditary nonpolyposis colorectal cancer in the right colon and inherent defects in DNA repair mechanisms.[30,31] The presence of lymphovascular invasion and poorly differentiated tumors in right colon tumors is associated with a poorer prognosis.[32]

The recurrence and survival rates of right and left colon tumors, which have distinct embryological origins, are anticipated to vary. According to Lee et al., there is no disparity in survival during the early stages (stage 1, 2) between right and left colon tumors. However, they found that stage 3 and metastatic right colon tumors exhibit lower survival rates compared to those on the left sided.[33] In their analysis of 26906 patients, Wang et al. from the Mayo Clinic reported that the survival difference was only evident in the metastatic stage, with no disparity observed in the early stage. Notably, the best prognosis was observed in early-stage rectal cancer, with a median survival of 101 months.[34] The absence of rectal cancer and stage 4 patients in the in our data may have contributed to the failure to observe differences in recurrence and survival rates between right and left colon tumors. The decrease in survival rates as the cancer progresses also reinforces the crucial role of early diagnosis in improving outcomes for colon cancer patients.

Our retrospective study has several limitations. The overall patient numbers were limited, which limited our ability to draw definitive conclusions. Patients with different prognoses (HNPCC patients) were not excluded, and we had no information about the tumors' molecular phenotype. Additionally, the lack of knowledge about the patients' adjuvant treatments is a limitation of the study, as it can affect survival.

In conclusion, our findings confirm that differences exist in the histopathological and clinical features of colon cancers on the left and right sides. This approach may change treatment options and the follow-up process and guide future clinical studies that can be conducted separately for right and left colon tumors.

Disclosures

Ethics Committee Approval: The study protocol was approved by the local ethic committee with 03.06.2024 dated and 2024-03-02 numbered decision.

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Conflict of Interest: The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN | Gut. https://gut.bmj.com/content/72/2/338
2. Kwak HD, Ju JK. Immunological Differences Between Right-Sided and Left-Sided Colorectal Cancers: A Comparison of Embryologic Midgut and Hindgut. Ann Coloproctol 2019;35(6):342-346.
3. Distler P, Holt PR. Are right- and left-sided colon neoplasms distinct tumors? Dig Dis 1997;15(4-5):302-311.
4. Cooper GS, Yuan Z, Landefeld CS, Johanson JF, Rimm AA. A national population-based study of incidence of colorectal cancer and age. Implications for screening in older Americans. Cancer 1995;75(3):775-781.
5. McCashland TM, Brand R, Lyden E, de Garmo P; CORI Research Project. Gender differences in colorectal polyps and tumors. Am J Gastroenterol 2001;96(3):882-886.
6. Gonzalez EC, Roetzheim RG, Ferrante JM, Campbell R. Predictors of proximal vs. distal colorectal cancers. Dis Colon Rectum 2001;44(2):251-258.
7. Tejpar S, Stintzing S, Ciardiello F, Tabernero J, Van Cutsem E, Beier F, et al. Prognostic and Predictive Relevance of Primary Tumor Location in Patients With RAS Wild-Type Metastatic Colorectal Cancer: Retrospective Analyses of the CRYSTAL and FIRE-3 Trials [published correction appears in JAMA Oncol. 2017 Dec 1;3(12):1742]. JAMA Oncol 2017;3(2):194-201.
8. Testa U, Pelosi E, Castelli G. Colorectal cancer: genetic abnormalities, tumor progression, tumor heterogeneity, clonal evolution and tumor-initiating cells. Med Sci (Basel) 2018;6(2):31. Published 2018 Apr 13.
9. Bourakkadi Idrissi M, El Bouhaddouti H, Mouaqit O, Ousadden A, Ait Taleb K, Benjelloun EB. Left-Sided Colon Cancer and Right-Sided Colon Cancer: Are They the Same Cancer or Two Different Entities? Cureus 2023;15(4):e37563. Published 2023 Apr 14.
10. Bauer KM, Hummon AB, Buechler S. Right-side and left-side colon cancer follow different pathways to relapse. Mol Carcinog 2012;51(5):411-421.
11. Yang SY, Cho MS, Kim NK. Difference between right-sided and left-sided colorectal cancers: from embryology to molecular subtype. Expert Rev Anticancer Ther 2018;18(4):351-358.
12. Abancens M, Bustos V, Harvey H, McBryan J, Harvey BJ. Sexual Dimorphism in Colon Cancer. Front Oncol 2020;10:607909. Published 2020 Dec 9.
13. Ra H, Jeong S, Lee H, Chung JW, Kim KO, Lee WS, et al. Clinicopathological Differences between Right and Left Colorectal Cancer by Sex. J Clin Med 2024;13(10):2810. Published 2024 May 10.
14. Brenne SS, Ness-Jensen E, Edna TH, Lydersen S, Laugsand EA. Risk factors for right colon, left colon and rectal cancers differ between men and women: the population-based HUNT study in Norway. Colorectal Dis 2023;25(1):44-55.
15. Rosati G, Galli F, Cantore M, Bergamo F, Banzi M, Zampino MG, et al. Predictive Impact of Mucinous Tumors on the Clinical Outcome in Patients with Poorly Differentiated, Stage II Colon Cancer: A TOSCA Subgroup Analysis. Oncologist 2020;25(6):e928-e935.
16. Vanek VW, Whitt CL, Abdu RA, Kennedy WR. Comparison of right colon, left colon, and rectal carcinoma. Am Surg 1986;52(9):504-509.
17. Rajagopalan A, Antoniou E, Morkos M, Rajagopalan E, Arachchi A, Chouhan H, et al. Is colorectal cancer associated with altered bowel habits in young patients?. ANZ J Surg 2021;91(5):943-946.
18. Missiaglia E, Jacobs B, D'Ario G, Di Narzo AF, Soneson C, Budinska E, et al. Distal and proximal colon cancers differ in terms of molecular, pathological, and clinical features [published correction appears in Ann Oncol. 2015 Feb;26(2):445. doi: 10.1093/annonc/mdu548]. Ann Oncol. 2014;25(10):1995-2001. doi:10.1093/annonc/mdu275.
19. Weiss JM, Pfau PR, O'Connor ES, King J, LoConte N, Kennedy G, et al. Mortality by stage for right- versus left-sided colon cancer: analysis of surveillance, epidemiology, and end results--Medicare data. J Clin Oncol. 2011;29(33):4401-4409. doi:10.1200/JCO.2011.36.4414
20. Nawa T, Kato J, Kawamoto H, Okada H, Yamamoto H, Kohno H, et al. Differences between right- and left-sided colon cancer in patient characteristics, cancer morphology and histology. J Gastroenterol Hepatol 2008;23(3):418-423.
21. Dominguez-Valentin M, Sampson JR, Seppälä TT, Ten Broeke SW, Plazzer JP, Nakken S, et al. Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database [published correction appears in Genet Med 2020 Sep;22(9):1569. doi: 10.1038/s41436-020-0892-4]. Genet Med 2020;22(1):15-25. doi:10.1038/s41436-019-0596-9
22. Dohmen J, Sommer N, van Beekum K, Nattermann J, Engel C, Kalff JC, et al. Geschlechtsspezifische Unterschiede in der Entwicklung kolorektaler Karzinome bei Lynch-Syndrom-Betroffenen – ein systematisches Review [Gender-specific differences in the development of colorectal cancer in Lynch syndrome patients-A systematic review]. Chirurgie (Heidelb) 2024;95(9):696-708.
23. Mirón Fernández I, Mera Velasco S, Turiño Luque JD, González Poveda I, Ruiz López M, Santoyo Santoyo J. Right and Left Colorectal Cancer: Differences in Post-Surgical-Care Outcomes and Survival in Elderly Patients. Cancers (Basel) 2021;13(11):2647. Published 2021 May 28.

24. Kim K, Kim YW, Shim H, Kim BR, Kwon HY. Differences in clinical features and oncologic outcomes between metastatic right and left colon cancer. J BUON 2018;23(7):11-18.
25. Russo A, Franceschi S, La Vecchia C, Dal Maso L, Montella M, Conti E, et al. Body size and colorectal-cancer risk. Int J Cancer 1998;78(2):161-165.
26. Saeed U, Myklebust TÅ, Robsahm TE, Kielland MF, Møller B, Skålhegg BS, et al. Risk and survival in colorectal cancer with increasing body mass index: A nationwide population-based cohort study. Colorectal Dis 2023;25(3):375-385.
27. Adelstein BA, Macaskill P, Chan SF, Katelaris PH, Irwig L. Most bowel cancer symptoms do not indicate colorectal cancer and polyps: a systematic review. BMC Gastroenterol. 2011;11:65. Published 2011 May 30.
28. Baran B, Mert Ozupek N, Yerli Tetik N, Acar E, Bekcioglu O, Baskin Y. Difference Between Left-Sided and Right-Sided Colorectal Cancer: A Focused Review of Literature. Gastroenterology Res 2018;11(4):264-273.
29. Hemminki A, Mecklin JP, Järvinen H, Aaltonen LA, Joensuu H. Microsatellite instability is a favorable prognostic indicator in patients with colorectal cancer receiving chemotherapy. Gastroenterology 2000;119(4):921-928.
30. Boland CR, Goel A. Microsatellite instability in colorectal cancer. Gastroenterology 2010;138(6):2073-2087.e3.
31. Xu Y, Liu K, Li C, Li M, Zhou X, Sun M, et al. Microsatellite instability in mismatch repair proficient colorectal cancer: clinical features and underlying molecular mechanisms. EBioMedicine 2024;103:105142.
32. Zhang L, Deng Y, Liu S, Zhang W, Hong Z, Lu Z, et al. Lymphovascular invasion represents a superior prognostic and predictive pathological factor of the duration of adjuvant chemotherapy for stage III colon cancer patients. BMC Cancer 2023;23(1):3. Published 2023 Jan 3.
33. Lee MM, MacKinlay A, Semira C, Schieber C, Jimeno Yepes AJ, Lee B, et al. Stage-based Variation in the Effect of Primary Tumor Side on All Stages of Colorectal Cancer Recurrence and Survival. Clin Colorectal Cancer 2018;17(3):e569-e577.
34. Wang CB, Shahjehan F, Merchea A, Li Z, Bekaii-Saab TS, Grothey A, et al. Impact of Tumor Location and Variables Associated With Overall Survival in Patients With Colorectal Cancer: A Mayo Clinic Colon and Rectal Cancer Registry Study. Front Oncol 2019;9:76. Published 2019 Feb 19.