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Comparison of Clinicopathological and Survival Features of Right and Left Colon Cancers: Experience of the Medical Oncology Department of Fez

Soukaina El Anssari*, Youssef Elhaitmy, Lamiae Amaadour, Karima Oualla, Zineb Benbrahim, Samia Arifi, Nawfel Mellas

Department of Medical Oncology, University Hospital Center Hassan II, City of Fez, Morocco
Email: *soukainaelanssari21@gmail.com

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Abstract

Right-sided colon cancers (RCC) and left-sided colon cancers (LCC) have different epidemiological, physiological, pathological, genetic, and clinical characteristics, which result in differences in the course, prognosis, and outcome of disease. The objective of our study is to compare right-sided colon cancers and left-sided colon cancers regarding clinicopathological and survival characteristics. This is a retrospective study of 664 patients with colon cancer treated at the medical oncology department of Fez over a period from December 2009 to September 2020. Rectosigmoid, descending colon, and splenic flexure tumors were considered left-sided colon cancers, whereas ascending colon tumors were considered right-sided colon cancers. The Kaplan Meier method was used to estimate median survival. The study included 664 patients (female, 47%) having colon cancer with a median age of 60 years (23 - 83). Of the patients, 78.5% (n = 519) had LCC and 19.36 % (n = 128) had RCC. The rate of patients aged ≥ 65 years and the rate of patients with a family history of colon cancer was higher in the LCC patients. The proportion of poorly differentiated adenocarcinomas represented 3%, of which 63% had cancer of the right colon. There was a significantly higher proportion of higher T stage (T3-4: 62% vs 38%) in right sided tumors as compared to left sided tumors. The rate of metastatic patients was 64.1% in the RCC group and 43% in the LCC group. The median follow-up period was 14 months in the RCC group and 19 months in the LCC group with higher median overall survival in the LCC group (32 vs 21 months). We found histopathological differences between right and left sided colon cancer. Tumors on the right colon were found to be more aggressive, as expressed by poorer differentia-

tion, higher T stage associated with a median overall survival better in left colon cancer.

Keywords

Right-Sided Colon Cancers (RCC), Left-Sided Colon Cancers (LCC), Prognosis, Survival

1. Introduction

Colorectal cancer is one of the most common cancers in the world [1]. There is evidence that right-sided colon cancer (RCC) is different from left-sided colon cancer (LCC) and rectal cancer. There are embryological origins, as well as anatomical, histological, genetic, and immunological differences between RCC and LCC [2] [3]. It has been shown that patients with RCC are older and more often female, and the disease is associated with advanced tumor stages, increased tumor size, more frequent poorly differentiated tumors, and different molecular biological tumor patterns [4] [5] [6]. For the reasons described above, many studies have reported that oncologic outcomes of colon cancer are different according to the location of tumor. Most studies have reported poorer oncologic outcomes in patients with RCC compared with patients with LCC [7] [8] [9] [10] [11]. However, recent studies have reported that the prognosis of localized RCC is better than that of LCC [12]. The present study aimed to compare right-sided colon cancers and left-sided colon cancers regarding clinicopathological and survival characteristics.

2. Methods

A descriptive retrospective study was carried out in the medical oncology department of the Hassan II University Hospital in Fez, collecting 664 patients colon cancer over a period from December 2009 to September 2020. The Rectosigmoid, descending colon, and splenic flexure tumors were considered left-sided colon cancers, whereas ascending colon tumors were considered right-sided colon cancers. The eligibility criteria were an age greater than 16 years, and histological evidence of colorectal cancer.

Epidemiological, clinical and therapeutic data as well as the safety profile were collected from medical files in their computerized form (available in the hosix software) or through files archived in the medical oncology department. The various pieces of information were listed in an exploitation sheet, established after bibliographic research and literature review.

The elements collected were: age at the time of diagnosis, sex, tumor location and size, histological type and grade, tumor stage, surgical treatment of localized forms, adjuvant or palliative chemotherapy, Time to progression, and survival. Survival was calculated by the Kaplan-Meier method.

3. Results

Between December 2009 and September 2020, we included 664 patients colon cancer in the medical oncology department of CHU Hassan II in Fez. The average age of our patients was 60 years, the percentage of patients with an age greater than or equal to 70 years was 17.8%. The majority of patients were male with a percentage of 53% (sex ratio M/F: 1.2). Of the patients, 78.5% (n = 519) had LCC and 19.36% (n = 128) had RCC. The rate of patients aged ≥ 65 years and the rate of patients with a family history of colon cancer was higher in the LCC patients. The proportion of poorly differentiated adenocarcinomas represented 3%, of which 63% had cancer of the right colon. There was a significantly higher proportion of higher T stage (T3-4: 62% vs 38%) in right sided tumors as compared to left sided tumors (Figure 1). The rate of metastatic patients was 64.1% in the RCC group and 43% in the LCC group (Table 1). The median follow-up period was 14 months in the RCC group and 19 months in the LCC group with a higher median overall survival in the LCC group (32 vs 21 months) (Table 2 and Figure 2).

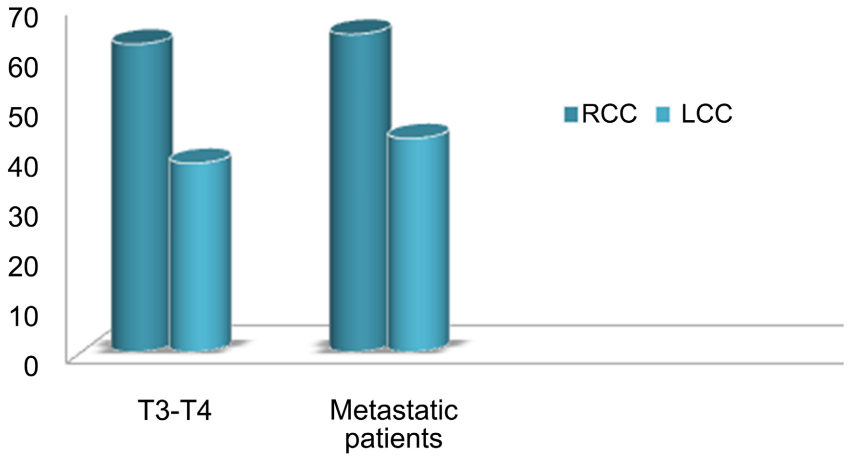

Figure 1. Clinicopathological features.

Table 1. Patients characteristic in the RCC and the LCC group.

Characteristics	RCC	LCC
% patients	19.36%	78%
Stage T3/T4	62%	38%
Metastatic patients	64%	43%
Family history colon cancer	72%	28%

Table 2. Overall survival in the RCC and the LCC group.

Right/left sided colon cancers	RCC	LCC
Median Follow up	14 months	19 months
Overall survival	21 months	32 months

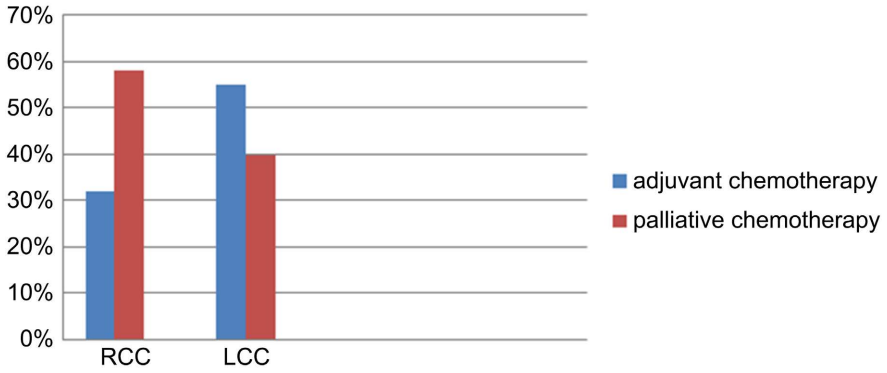

Figure 2. Adjuvant and palliative chemotherapy in the RCC and LCC group.

4. Discussion

Here, we confirm the side of colon cancer (right vs. left) as a distinct parameter that is related to specific histological, molecular and clinical features. RCC is an independent predictor of poor prognosis. In terms of OS, we showed that patients with RCC have a significantly worse prognosis than those with LCC by 34%. Indeed, previous studies have reported poorer oncologic outcomes in patients with RCC compared with patients with LCC [2] [13] [14].

In the present study, LCC (n = 519, 78.5%) was higher than RCC (n = 128, 19.36%) in the same period (2009-2020).The mean age and sex ratio were not significantly different between the LCC and the RCC group. The mean ages were 59.9 years (RCC) and 60.1 years (LCC). Our study reported that the median age at diagnosis was greater for RCC than for LCC. The median age was 71 to 74 years for RCC group versus 66 to 71 years for LCC group. Another study reported that RCC is more common in patients older than 60 years of age compared with LCC [4] [15]. In present study, the distribution of gender was relatively equal with a male predominance. A nationwide Danish cohort study reported a significantly higher proportion of RCC (56.8%) than LCC (46%) in women [10]. The distribution of the T3/T4 stage was higher in the RCC group. Howeve, distribution of the N stage was significantly different between the 2 groups, especially N2b (right side, 10.6% vs left side, 2.4%). In addition, RCC is more poorly differentiated compared with LCC in histological grade. Previous studies have reported higher proportions of poorly differentiated cancers in RCC than in LCC [6].

Colon cancer has different clinicopathological and genetic features between the right side and the left side. Many studies have reported that patients with RCC are older and more often female; moreover, they have more advanced tumor stages, increased tumor size, more often poorly differentiated tumors, and different molecular biological tumor patterns [4] [6]. In addition, MSI-high cancer has been reported to be more frequent in RCC than in LCC [16]. The incidence rate of LCC is higher than that of RCC, and the most recent figures reported by the American Cancer Society confirm a higher proportion of LCC (51%) compared with RCC (42%) in the United States [17]. Several studies have

reported that LCC more often represents an early-stage disease compared with RCC, and these results have affected the disparity in prognoses according to the location of tumors. Similarly, several studies have reported that RCC tends to exhibit a more advanced stage compared with LCC [9] [10] [18].

RCC has shown a reduced prognosis compared to LCC. These findings are consistent with results of other groups [6] [9]. However, there are publications which obtained contradictory outcomes [19] [20] or showed no difference in prognosis between both sides [21]. A meta-analysis on colorectal cancer including 44 studies and over 220,000 patients revealed a higher relative risk for proximal cancers (proximal to the splenic flexure, RR 1.55, 95% CI 1.53 - 1.58) [22], but the underlying mechanisms for this distinctive behavior still remain unclear. Thus, current treatment recommendations are limited to secondary preventive strategies like intensified adjuvant treatment regimens and shorter follow-up periods for patients with RCC [13]. Some studies indicate that the lower mortality risk of LCC is associated with an earlier diagnosis applying endoscopy [13]. Although larger diameters were found for RCC, no difference was detected between RCC and LCC in TNM status.

Gao *et al.* [23] detected tumor location as an independent prognostic factor in mucinous adenocarcinomas, leading to a better outcome for right-sided mucinous adenocarcinomas compared to rectal mucinous adenocarcinomas. Of note, in our study, significantly more mucinous adenocarcinomas were found on the right side and this histological entity was accompanied with a better survival of RCC, too. This effect could be explained by the high amount of MSI RCCs as microsatellite instability is associated with mucinous adenocarcinomas [24] and MSI tumors demonstrate a better prognosis compared to MSS tumors [13]. Thus, analyzing all the patients, the RCC revealed a reduced prognosis despite the higher number of mucinous adenocarcinomas and MSI tumors. The worse prognosis of RCC compared to LCC is thought to be associated with the underlying molecular pathway of cancer development, which, at least in part, may be embryologic determined [13]. Tumors arising from the so-called serrated pathway are characterized by an initial BRAF mutation, subsequently followed by the CpG island methylator phenotype, with either MSS or MSI status, and a reduced prognosis [13] [23] [24] [25]. A significant correlation between BRAF mutations and MSI was revealed, and both characteristics were more often found for RCC. These alterations (*i.e.*, BRAF mutations, MSI) suggest tumor origination from the serrated pathway and therefore could explain the reduced prognosis of RCC [13] [23] [24] [25] [26]. Current treatment recommendations can help to improve the prognosis of colon cancer on a personalized and molecular genetic basis. For example, routine molecular genetic testing for colon cancer, especially if RCC, advises against 5-FU based chemotherapeutic regimens if microsatellite instability is present due to a lack of benefit in this subset of patients [27]. In fact, this study did not reveal a significant difference in cause-specific survival between RCC and LCC for MSS/MSI, KRAS and BRAF status in general or in subgroup analyses. However, due to the lack of cases, these results should be in-

terpreted with caution.

The limit of our study is the limited access to information? also several patients were lost sight of, without knowing their evolution, which biased our survival. We do not know the MSI status of the majority of patients due to a lack of means, and this includes all molecular alterations

5. Conclusion

RCC and LCC show significant differences regarding patient characteristics and long-term outcomes. The reduced prognosis of RCC is assumed to be caused by clinical factors, histopathological factors (poor differentiation, histological tumor subtype) and molecular genetic factors (serrated pathway, MSI, KRAS and BRAF mutations).

Authors' Contributions

All authors have contributed to realizing this study and they have read and approved the final manuscript

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Brenner, H., Kloor, M. and Pox, C.P. (2014) Colorectal Cancer. *The Lancet*, **383**, 1490-1502. https://doi.org/10.1016/S0140-6736(13)61649-9

[2] Hansen, I.O. and Jess, P. (2012) Possible Better Long-Term Survival in Left versus Right-Sided Colon Cancer—A Systematic Review. *Danish Medical Journal*, **59**, A4444.

[3] Bufill, J.A. (1990) Colorectal Cancer: Evidence for Distinct Genetic Categories Based on Proximal or Distal Tumor Location. *Annals of Internal Medicine*, **113**, 779-788. https://doi.org/10.7326/0003-4819-113-10-779

[4] Saltzstein, S.L. and Behling, C.A. (2007) Age and Time as Factors in the Left-to-Right Shift of the Subsite of Colorectal Adenocarcinoma: A Study of 213,383 Cases from the California Cancer Registry. *Journal of Clinical Gastroenterology*, **41**, 173-177. https://doi.org/10.1097/01.mcg.0000225550.26751.6a

[5] Powell, A.G.M.T., Wallace, R., McKee, R.F. anderson, J.H., Going, J.J., Edwards, J., *et al.* (2012) The Relationship between Tumour Site, Clinicopathological Characteristics and Cancer-Specific Survival in Patients Undergoing Surgery for Colorectal Cancer. *Colorectal Disease*, **14**, 1493-1499. https://doi.org/10.1111/j.1463-1318.2012.03048.x

[6] Benedix, F., Kube, R., Meyer, F., Schmidt, U., Gastinger, I., Lippert, H., *et al.* (2010) Comparison of 17,641 Patients with Right- and Left-Sided Colon Cancer: Differences in Epidemiology, Perioperative Course, Histology, and Survival. *Diseases of the Colon & Rectum*, **53**, 57-64. https://doi.org/10.1007/DCR.0b013e3181c703a4

[7] Suttie, S.A., Shaikh, I., Mullen, R., Amin, A.I., Daniel, T. and Yalamarthi, S. (2011) Outcome of Right- and Left-Sided Colonic and Rectal Cancer Following Surgical Resection. *Colorectal Disease*, **13**, 884-889. https://doi.org/10.1111/j.1463-1318.2010.02356.x

[8] Huang, C.W., Tsai, H.L., Huang, M.Y., Huang, C.M., Yeh, Y.S., Ma, C.J., *et al.* (2015) Different Clinicopathologic Features and Favorable Outcomes of Patients with Stage III Left-Sided Colon Cancer. *World Journal of Surgical Oncology*, **13**, Article No. 257. https://doi.org/10.1186/s12957-015-0640-4

[9] Meguid, R.A., Slidell, M.B., Wolfgang, C.L., Chang, D.C. and Ahuja, N. (2008) Is There a Difference in Survival between Right- versus Left-Sided Colon Cancers? *Annals of Surgical Oncology*, **15**, 2388-2394. https://doi.org/10.1245/s10434-008-0015-y

[10] Jess, P., Hansen, I.O., Gamborg, M. and Jess, T. (2013) A Nationwide Danish Cohort Study Challenging the Categorisation into Right-Sided And Left-Sided Colon Cancer. *BMJ Open*, **3**, e002608. https://doi.org/10.1136/bmjopen-2013-002608

[11] Warschkow, R., Sulz, M.C., Marti, L., Tarantino, I., Schmied, B.M., Cerny, T., *et al.* (2016) Better Survival in Right-Sided versus Left-Sided Stage I-III Colon Cancer Patients. *BMC Cancer*, **16**, Article No. 554. https://doi.org/10.1186/s12885-016-2412-0

[12] Moritani, K., Hasegawa, H., Okabayashi, K., Ishii, Y., Endo, T. and Kitagawa, Y. (2014) Difference in the Recurrence Rate between Right- and Left-Sided Colon Cancer: A 17-Year Experience at a Single Institution. *Surgery Today*, **44**, 1685-1691. https://doi.org/10.1007/s00595-013-0748-5

[13] Lee, G.H., Malietzis, G., Askari, A., Bernardo, D., Al-Hassi, H.O. and Clark, S.K. (2015) Is Right-Sided Colon Cancer Different to Left-Sided Colorectal Cancer? A Systematic Review. *European Journal of Surgical Oncology*, **41**, 300-308. https://doi.org/10.1016/j.ejso.2014.11.001

[14] Petrelli, F., Tomasello, G., Borgonovo, K., Ghidini, M., Turati, L., Dallera, P., *et al.* (2017) Prognostic Survival Associated with Left-Sided vs Right-Sided Colon Cancer: A Systematic Review and Meta-Analysis. *JAMA Oncology*, **3**, 211-219. https://doi.org/10.1001/jamaoncol.2016.4227

[15] Christodoulidis, G., Spyridakis, M., Symeonidis, D., Kapatou, K., Manolakis, A. and Tepetes, K. (2010) Clinicopathological Differences between Right- and Left-Sided Colonic Tumors and Impact upon Survival. *Techniques in Coloproctology*, **14**, S45-S47. https://doi.org/10.1007/s10151-010-0622-z

[16] Lim, D.R., Kuk, J.K., Kim, T. and Shin, E.J. (2017) Comparison of Oncological Outcomes of Right-Sided Colon Cancer versus Left-Sided Colon Cancer after Curative Resection. *Medicine* (*Baltimore*), **96**, e8241. https://doi.org/10.1097/MD.0000000000008241

[17] Siegel, R., Desantis, C. and Jemal, A. (2014) Colorectal Cancer Statistics, 2014. *CA*: *A Cancer Journal for Clinicians*, **64**, 104-117. https://doi.org/10.3322/caac.21220

[18] Hussain, M., Waqas, O., Hassan, U., Loya, A., Akhtar, N., Mushtaq, S., *et al.* (2016) Right-Sided and Left-Sided Colon Cancers Are Two Distinct Disease Entities: An Analysis of 200 Cases in Pakistan. *Asian Pacific Journal of Cancer Prevention*, **17**, 2545-2548.

[19] Weiss, J.M., Pfau, P.R., O'Connor, E.S., King, J., LoConte, N., Kennedy, G., *et al.* (2011) Mortality by Stage for Right- versus Left-Sided Colon Cancer: Analysis of Surveillance, Epidemiology, and End Results—Medicare Data. *Journal of Clinical Oncology*, **29**, 4401-4409. https://doi.org/10.1200/JCO.2011.36.4414

[20] Gervaz, P., Bouzourene, H., Cerottini, J.P., Chaubert, P., Benhattar, J., Secic, M., *et al.* (2001) Dukes B Colorectal Cancer: Distinct Genetic Categories and Clinical Outcome Based on Proximal or Distal Tumor Location. *Diseases of the Colon & Rectum*, **44**, 364-372. https://doi.org/10.1007/BF02234734

[21] Verhulst, J., Ferdinande, L., Demetter, P. and Ceelen, W. (2012) Mucinous Subtype

as Prognostic Factor in Colorectal Cancer: A Systematic Review and Meta-Analysis. *Journal of Clinical Pathology*, **65**, 381-388. https://doi.org/10.1136/jclinpath-2011-200340

[22] Nitsche, U., Stögbauer, F., Späth, C., Haller, B., Wilhelm, D., Friess, H., *et al.* (2016) Right Sided Colon Cancer as a Distinct Histopathological Subtype with Reduced Prognosis. *Digestive Surgery*, **33**, 157-163. https://doi.org/10.1159/000443644

[23] Gao, P., Song, Y., Xu, Y., Sun, Z., *et al.* (2013) Does the Prognosis of Colorectal Mucinous Carcinoma Depend upon the Primary Tumour Site? Results from Two Independent Databases. *Histopathology*, **63**, 603-615. https://doi.org/10.1111/his.12190

[24] Nitsche, U., Zimmermann, A., Späth, C., Müller, T., Maak, M., Schuster, T., *et al.* (2013) Mucinous and Signet-Ring Cell Colorectal Cancers Differ from Classical Adenocarcinomas in Tumor Biology and Prognosis. *Annals of Surgery*, **258**, 775-783. https://doi.org/10.1097/SLA.0b013e3182a69f7e

[25] Nitsche, U., Rosenberg, R., Balmert, A., Schuster, T., Slotta-Huspenina, J., Herrmann, P., *et al.* (2012) Integrative Marker Analysis Allows Risk Assessment for Metastasis in Stage II Colon Cancer. *Annals of Surgery*, **256**, 763-771. https://doi.org/10.1097/SLA.0b013e318272de87

[26] Noffsinger, A.E. (2009) Serrated Polyps and Colorectal Cancer: New Pathway to Malignancy. *Annual Review of Pathology*, **4**, 343-364. https://doi.org/10.1146/annurev.pathol.4.110807.092317

[27] Sideris, M. and Papagrigoriadis, S. (2014) Molecular Biomarkers and Classification Models in the Evaluation of the Prognosis of Colorectal Cancer. *Anticancer Research*, **34**, 2061-2068.