Journal of Health Sciences

RESEARCH ARTICLE Open Access

# Anatomical localization and histological gradation of colorectal cancer in General Hospital Tešanj, Bosnia and Herzegovina, in 2013-2022 period

Kenan Galijašević*, Adnan Mujezinović, Amir Denjalić

Department of Anatomy, Faculty of Medicine, University of Zenica, Zenica, Bosnia and Herzegovina

## ABSTRACT

**Introduction:** Carcinomas of the right and left sides of the colon are considered different types of cancer due to their different carcinogenesis, epidemiology, pathology and prognosis. Although several studies have described the prevalence and incidence of colorectal carcinoma (CRC) in the different colonic segments, more epidemiologic data are still needed to better understand the implications and relationship to sociodemographic and clinical variables. The aim of this study is to determine the anatomic location and histologic grade of CRC, to investigate the differences in patient gender and age, and to determine the correlation of gender and age with the anatomic location and histologic grading of CRC.

**Methods:** A retrospective study was conducted covering the period from January 2013 to December 2022. Demographic data (gender and age), histological type and anatomical location of the tumor were observed. The study included all patients in the observed period with a diagnosis of colorectal cancer (CRC) at different anatomical locations and with different grades of histological staging. All patients had adenocarcinoma. Patients were divided into four age groups based on their gender (20-40 years, 41-55 years, 56-65 years and over 65 years old). Tumors of the colon ascending to the splenic flexure are defined as tumors of the right side, and distal to the splenic flexure as tumors of the left side of the colon.

**Results:** A total of 183 patients were included in the study. Patients were between 38 and 82 years old, with a mean age of 64.3 ± 8.9 years. No statistically significant difference was found in the proportion of anatomical localization of CRC ($p > 0.05$). The most common anatomical location of CRC over the 10-year period was found to be the rectum 42.1% and the ascending colon 14.2% and transverse colon 13.1%, with no statistically significant difference in cancer incidence between the right and left sides of the colon. Histologic grade II was predominant in 57.4% of patients. A moderate negative correlation was found between age and histologic grade of CRC ($r = -0.067$), with no statistically significant difference ($p > 0.05$).

**Conclusion:** No statistically significant difference was found in the anatomical localization of CRC between the right and left side of the colon. Histologic grade II CRC was the most prevalent. A moderate negative correlation was found between age and histologic grade of CRC.

**Keywords:** Anatomical localization; histological grade; colorectal cancer

## INTRODUCTION

The length of the large intestine is about 150 cm, and it extends from the ileocecal valve to the anus. Anatomically, the large intestine consists of several parts: the cecum, the ascending, transverse, descending and sigmoid colon, the rectum and the anus (1).

The large intestine is divided into a right and a left side. The difference between the right and left side of the colon lies in its embryologic origin. The cecum, the ascending colon, the hepatic flexure and the proximal two-thirds of the transverse colon develop from the midgut and characterize the right side of the colon. The distal third of the transverse colon, the splenic flexure, the sigmoid colon and the descending colon as well as the rectum originate from the hindgut and mark the left side of the colon (2).

Since 1990, right-sided and left-sided colorectal cancers have been considered distinct cancers due to their different carcinogenesis, epidemiology, pathology and prognosis (2,3). Patients with right-sided cancer tend to be older, female, and have more advanced tumor stages and poorly differentiated tumor cells compared to left-sided carcinomas (4). Most previous studies have shown that right-sided colon cancer was associated with a higher recurrence rate and a lower survival rate than left-sided colon cancer (5,6), although several studies have concluded that right-sided cancer has a better prognosis than left-sided cancer at an early stage (7,8). Tumors on the right and left sides have

Corresponding author: Kenan Galijašević, Department of Anatomy, Faculty of Medicine, University of Zenica, 72000 Zenica, Bosnia and Herzegovina.
E-mail: kenangalijasevic@gmail.com

Submitted: 02 October 2024/Accepted: 16 April 2025

DOI: https://doi.org/10.17532/jhsci.2025.2733

UNIVERSITY OF SARAJEVO
FACULTY OF HEALTH STUDIES

© 2025 Kenan Galijašević, *et al.*; licensee University of Sarajevo - Faculty of Health Studies. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

different histological and molecular characteristics. Right-sided tumors generally have a flat histology. In left-sided tumors, chromosomal instability pathway-related mutations such as KRAS, APC, PIK3CA, and p53 mutations are observed, and these tumors have a polypoid-like morphology (9).

Right-sided tumors arise in the ascending colon and in the proximal two-thirds of the transverse colon, while left-sided tumors arise in the descending and sigmoid colon and in the distal third of the transverse colon (2,10). A recent review of the literature concludes that at least 63% of CRC patients are diagnosed with a tumor on the left side of the colon (11).

Colon tumors not only differ in carcinogenesis, but also in histology. Right-sided tumors have serrated adenomas or are mucinous carcinomas, while left-sided tumors are usually tubular, villous or typical adenocarcinomas (12). Tumors on the left side are easier to detect on colonoscopy due to their polypous morphology, while tumors on the right side usually have a flat morphology and are therefore difficult to detect (13,14).

In terms of histologic tumor grading, a comparison between patients with right-sided stage III and IV carcinoma and left-sided carcinoma showed poor overall survival of patients with right-sided carcinoma, while patients with right-sided stage I and II carcinoma showed better overall survival (15). Similar results were obtained in a cohort study of Japanese patients, which found that the prognosis of stage I and II tumors was statistically significantly better in patients with right-sided carcinoma. However, the prognosis for stages III and IV was worse compared to patients with left-sided carcinoma (16). When it comes to the incidence and prevalence of CRC and other aspects of cancer treatment, rectal tumors are diagnosed and monitored using magnetic resonance imaging, while tumors at other anatomical sites are monitored and diagnosed using computed tomography (17,18). The aim of the study is to determine the anatomical location and histological grade of CRC, to investigate the differences in terms of gender and age of patients, and to determine the correlation of age with anatomical location and histological grading of CRC.

## METHODS

We conducted a retrospective observational study at Tešanj General Hospital in the period between January 2013 and December 2022. The inclusion criteria were patients who were admitted to the surgical department with a diagnosis of CRC, underwent surgery and had a histopathological diagnosis. Exclusion criteria were patients who were not treated surgically and who did not have a pathohistologic diagnosis of CRC. Demographic data (gender and age), histological type and anatomical location of the tumor were observed. All patients had adenocarcinoma. Patients were divided into four age groups based on their gender (20-40 years, 41-55 years, 56-65 years and over 65 years old). Tumors of the ascending colon up to the splenic flexure are defined as tumors of the right side and distal to the splenic flexure as tumors of the left side of the colon, while the tumor of the rectum is considered a separate entity. The criterion used for the classification of CRC is based on the 8th edition of the American Joint Committee on Cancer Handbook (19).

The study was approved by the Ethics Committee of Tesanj General Hospital (01-4-40/22).

The Statistical Package for the Social Sciences (SPSS) software package for Windows (version 21.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel (version 11, Microsoft Corporation, Redmond, WA, USA) were used for statistical analysis of the data obtained. Descriptive analysis was used to present the mean, standard deviation, range (minimum-maximum), frequency and percentage of life expectancy of patients (%). Differences in gender and age of patients with CRC were examined as well as differences in anatomical location (right-sided, left-sided and rectal tumors) and histological grading. The nominal and ordinal variables of the study were analyzed using the $\chi 2$ test. The correlation test (Pearson) was used for the relationship and direction of the relationship between the categories of variables. The value $p = 0.05$ was taken as the limit of statistical significance.

## RESULTS

During the 10-year follow-up period, 183 patients diagnosed with CRC at different anatomical sites and with varying degrees of histologic staging, by type of adenocarcinoma, were included in the study. The patients were between 38 and 82 years old, with a mean age of 64.3 ± 8.9 years. Of the total number of patients, 62.3% were male and 37.7% were female. The dominant age group was patients over 65 years of age with 53.6%, of which 33.9% were men and 19.7% women. In the age group of 20-40 years, two cases of CRC were reported in one male patient (Table 1). There was no statistically significant difference in the relationship between gender and age of the subjects when it comes to the incidence of CRC in the 10-year period ($p > 0.05$).

Regarding the colon side, 12.6% of patients had left-sided carcinoma, of which 7.7% were male and 4.9% were female. Right-sided carcinoma was present in 45.4% of patients, of which 25.1% were male and 20.2% female. Rectal carcinoma was present in 42.1%, of which 29.5% were male and 12.6% female. There was no statistically significant difference in the location of CRC with respect to colon side and gender ($p > 0.05$) (Table 2).

In terms of anatomical localization of CRC, the most common site was the rectum in 42.1% of patients, of which 29.5% were male and 12.6% were female. The second most common location was the right-sided colon, ascending colon, in 14.2% of respondents, of whom 6.0% were male and 8.2% female. The transverse colon was the primary tumor site in 13.1% of subjects, of which 8.7% were male and 4.4% were female. Anatomic localization of CRC on the descending colon was present in one patient, while the sigmoid colon was also a common cancer site at 11.5% (Figure 1). There was no statistically significant difference in the relationship between the anatomical location of CRC and patient gender ($p > 0.05$) (Table 3).

In terms of histologic grading of carcinoma, 57.4% of cases were grade II, of which 25.1% were rectal carcinoma, 9.8% ascending colon, 8.2% transverse colon, 5.5% sigmoid colon, 4.4% flexura hepatica. Grade III was present in 19.1% of patients, including the rectum in 10.4%, cecum,

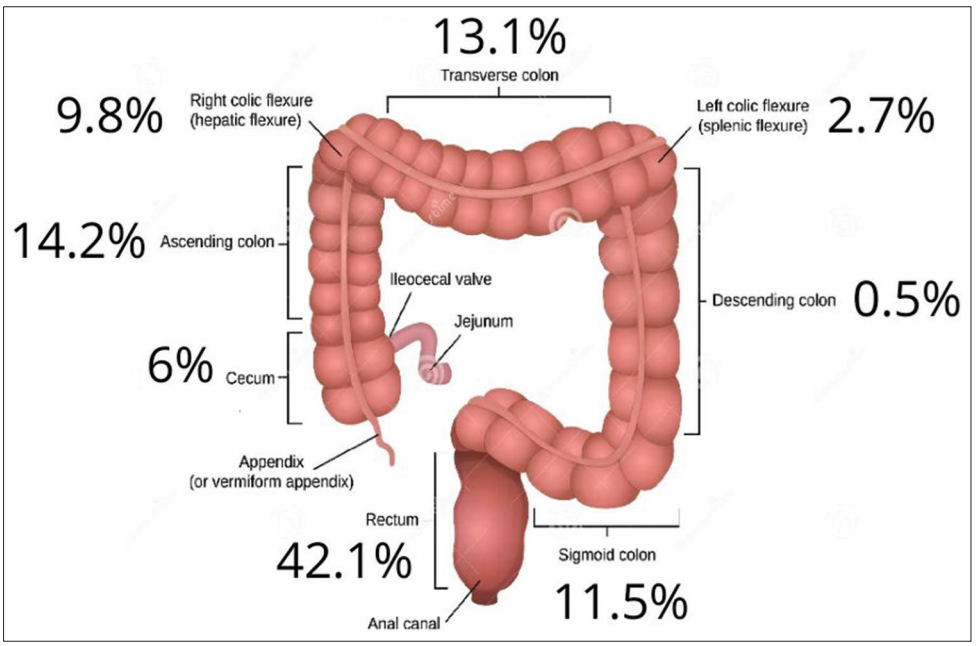


**FIGURE 1.** The colon segments and the percentage of cancer in the study[1]

**TABLE 1.** Gender and age structure of patients

| Lifetime | Gender | | | | | |
|---|---|---|---|---|---|---|
| | Male | | Female | | Total | |
| | n | % | n | % | n | % |
| 20-40 years | 2 | 1.1 | 0 | 0.0 | 2 | 1.1 |
| 41-55 years | 12 | 6.6 | 8 | 4.4 | 20 | 10.9 |
| 56-65 years | 38 | 20.8 | 25 | 13.7 | 63 | 34.4 |
| over 65 years | 62 | 33.9 | 36 | 19.7 | 98 | 53.6 |
| Total | 114 | 62.3 | 69 | 37.7 | 183 | 100.0 |

**TABLE 2.** Cancer location in relation to the side of the colon and gender

| Cancer location in relation to the side | Gender | | | | | |
|---|---|---|---|---|---|---|
| | Male | | Female | | Total | |
| | n | % | n | % | n | % |
| Right side | 46 | 25.1 | 37 | 20.2 | 83 | 45.4 |
| Left side | 14 | 7.7 | 9 | 4.9 | 23 | 12.6 |
| Ca rectum | 54 | 29.5 | 23 | 12.6 | 77 | 42.1 |
| Total | 114 | 62.3 | 69 | 37.7 | 183 | 100.0 |

**TABLE 3.** Anatomy location of colorectal cancer

| Anatomy location of colorectal cancer | Gender | | | | | |
|---|---|---|---|---|---|---|
| | Male | | Female | | Total | |
| | n | % | n | % | n | % |
| Cecum | 4 | 2.2 | 7 | 3,8 | 11 | 6.0 |
| Colon ascendens | 11 | 6.0 | 15 | 8,2 | 26 | 14.2 |
| Flexura hepatica | 13 | 7.1 | 5 | 2,7 | 18 | 9.8 |
| Colon transversum | 16 | 8.7 | 8 | 4,4 | 24 | 13.1 |
| Flexura sinistra | 3 | 1.6 | 2 | 1,1 | 5 | 2.7 |
| Colon descendens | 1 | 0.5 | 0 | 0,0 | 1 | 0.5 |
| Colon sigmoideum | 12 | 6.6 | 9 | 4,9 | 21 | 11.5 |
| Rectum | 54 | 29.5 | 23 | 12,6 | 77 | 42.1 |
| Total | 114 | 62.3 | 69 | 37,7 | 183 | 100.0 |

ascending colon and sigmoid colon in 2.2% and transverse colon in 1.6%. Grade IV was found in 14.8% of patients, including 3.8% in the rectum, 3.3% in the hepatic flexure and transverse colon and 1.1% in the splenic flexure and sigmoid colon. Grade I carcinomas were found in 8.7% of patients, of which 2.7 were found in the sigmoid colon and rectum, 1.6% in the hepatic flexure and 0.5% each in the splenic flexure and descending colon (Table 4).

A moderate negative correlation was found between age and histologic grading of CRC (r = –0.067), with no statistically significant difference (p = 0.365) (Figure 2).

## DISCUSSION

Colorectal cancer is one of the most frequently diagnosed malignant tumors and one of the leading causes of death from malignant diseases in the Western world (20). The median age at diagnosis in industrialized countries is 70 years (21), and in our study the median age was 66 years. In the population of respondents included in this study, there were slightly more men than women (62.3% versus 37.7%), which is consistent with the World Health Organization data for 2020, according to which the percentage of newly diagnosed men worldwide is 54.9% and that of women is 45.1% (22).

Most CRCs are diagnosed in people aged over 50 years, although 5-10% of patients are younger than 40 years (22), which is consistent with the results of our study.

The incidence of CRC increases with age, usually doubling every decade after the age of 40 (23). Men have a higher risk than women of developing CRC (1-1.6 times), rectal cancer (1.5-1.7 times) and cancer of the rectosigmoid junction (1.5-2.0 times), which was also found in our study. It is not yet clear why men develop the disease more frequently. Possible reasons include more frequent abdominal obesity in men, a higher probability of smoking and a difference in hormone status between women and men (24).

The rectum and sigmoid colon are the most common sites of CRC (23). In the United States, one third of CRC patients have rectal cancer (25), and in our study the proportion is even higher (42.1%). In recent decades, the localization of CRC, which used to be predominant on the left side, has tended to shift to the right side of the colon (26), which

1 https://cn.dreamstime.com/

**TABLE 4.** Relation of histological grading and anatomical localization of colorectal cancer

| Anatomical localization | Histological grading | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| | n | % | n | % | n | % | n | % |
| Cecum | 0 | 0.0 | 6 | 3.3 | 4 | 2.2 | 1 | 0.5 |
| Colon ascendens | 1 | 0.5 | 18 | 9.8 | 4 | 2.2 | 3 | 1.6 |
| Flexura hepatica | 3 | 1.6 | 8 | 4.4 | 1 | 0.5 | 6 | 3.3 |
| Colon transversum | 0 | 0.0 | 15 | 8.2 | 3 | 1.6 | 6 | 3.3 |
| Flexura sinistra | 1 | 0.5 | 2 | 1.1 | 0 | 0.0 | 2 | 1.1 |
| Colon descendens | 1 | 0.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Colon sigmoideum | 5 | 2.7 | 10 | 5.5 | 4 | 2.2 | 2 | 1.1 |
| Rectum | 5 | 2.7 | 46 | 25.1 | 19 | 10.4 | 7 | 3.8 |
| Total | 16 | 8.7 | 105 | 57.4 | 35 | 19.1 | 27 | 14.8 |

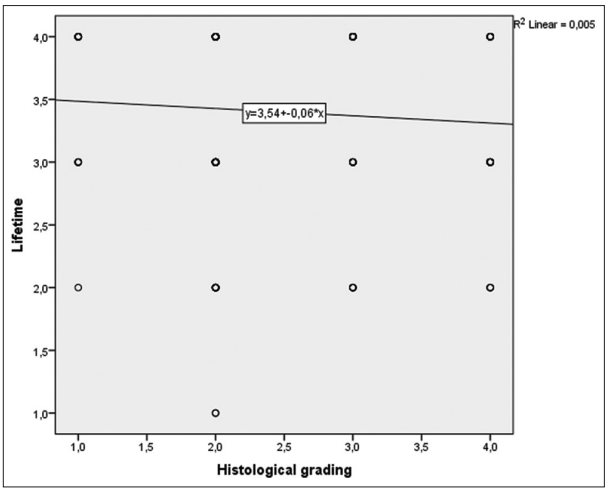


**FIGURE 2.** Correlation of lifetime and histological grading of colorectal cancer.

was also noted in our study, in which there is no statistically significant difference in the localization of CRC when comparing the right and left sides.

Waldron and Donovan found in their 10-year study conducted in Birmingham that 23% of colorectal tumors were right-sided (defined as tumors arising from the cecum, ascending colon, and hepatic flexure) (27). Another study in Dublin found that about 28% of colorectal tumors were right-sided (28). Both studies are over 30 years old and therefore lend themselves well to comparison with our study, in which the number of right-sided CRC was 45.4% of patients, suggesting a general shift of CRC to the right side.

Adenocarcinoma is the most common histologic type and accounts for more than 95% of all colorectal tumors, a finding that is also consistent with our data (29).

Most of our subjects, 105 (57.4%), were diagnosed with stage II cancer. In a study conducted in Pakistan, the authors state that the most common stage in 66.8% of patients was stage II at detection of CRC, which is consistent with the results of our study (30), while in most other studies the most common stage at detection of CRC is grade III (29,31).

## CONCLUSION

No statistically significant difference was found in the anatomical localization of the colon between the right and left side of the colon. All subjects had the histologic type of adenocarcinoma, with grade II being predominant. A moderate negative correlation was found between age and histologic grade of CRC.

## DECLARATION OF INTEREST

Authors declare no conflict of interest.

## REFERENCES

1. Denjalić A, Mujezinović A, Galijašević K. Anatomija Čovjeka. Bosnia, Herzegovina: Univerzitet u Zenici, Medicinski Fakultet; 2020.
2. Iacopetta B. Are there two sides to colorectal cancer? Int J Cancer 2002;101(5):403-8. https://doi.org/10.1002/ijc.10635
3. Bufill JA. Colorectal cancer: Evidence for distinct genetic categories based on proximal or distal tumor location. Ann Intern Med 1990;113:779-88. https://doi.org/10.7326/0003-4819-113-10-779
4. Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H, et al. Comparison of 17,641 patients with right- and left-sided colon cancer: Differences in epidemiology, perioperative course, histology, and survival. Dis Colon Rectum 2010;53:57-64. https://doi.org/10.1007/DCR.0b013e3181c703a4
5. Qin Q, Yang L, Sun YK, Ying JM, Song Y, Zhang W, et al. Comparison of 627 patients with right- and left-sided colon cancer in China: Differences in clinicopathology, recurrence, and survival. Chronic Dis Transl Med 2017;3:51-9. https://doi.org/10.1016/j.cdtm.2017.02.004
6. Bustamante-Lopez LA, Nahas SC, Nahas C, Pinto RA, Marques C, Cecconello I. Is there a difference between right-versus left-sided colon cancers? Does side make any difference in long term follow-up? Arq Bras Cir Dig 2019;32:e1479. https://doi.org/10.1590/0102-672020190001e1479
7. Warschkow R, Sulz MC, Marti L, Tarantino I, Schmied BM, Cerny T, et al. Better survival in right-sided versus left-sided stage I-III colon cancer patients. BMC Cancer 2016;16:554. https://doi.org/10.1186/s12885-016-2412-0
8. Yang J, Du XL, Li ST, Wang BY, Wu YY, Chen ZL, et al. Characteristics of differently located colorectal cancers support proximal and distal classification: A population-based study of 57,847 patients. PLoS One 2016;11:e0167540. https://doi.org/10.1371/journal.pone.0167540
9. 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):264-73. https://doi.org/10.14740/gr1062w
10. Mik M, Berut M, Dziki L, Trzcinski R, Dziki A. Right- and left-sided colon cancer - clinical and pathological differences of the disease entity in one organ. Arch Med Sci 2017;13(1):157-62. https://doi.org/10.5114/aoms.2016.58596
11. Hemminki K, Santi I, Weires M, Thomsen H, Sundquist J, Bermejo JL. Tumor location and patient characteristics of colon and rectal adenocarcinomas in relation to survival and TNM classes. BMC Cancer 2010;10:688. https://doi.org/10.1186/1471-2407-10-688
12. Marzouk O, Schofield J. Review of histopathological and molecular prognostic features in colorectal cancer. Cancers (Basel) 2011;3(2):2767-810. https://doi.org/10.3390/cancers3022767
13. Gualco G, Reissenweber N, Cliche I, Bacchi CE. Flat elevated lesions of the colon and rectum: A spectrum of neoplastic and nonneoplastic entities. Ann Diagn Pathol 2006;10(6):333-8. https://doi.org/10.1016/j.anndiagpath.2006.03.003
14. 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):418-23. https://doi.org/10.1111/j.1440-1746.2007.04923.x
15. Meguid RA, Slidell MB, Wolfgang CL, Chang DC, Ahuja N. Is there a difference in survival between right- versus left-sided colon cancers? Ann Surg Oncol 2008;15(9):2388-94. https://doi.org/10.1245/s10434-008-0015-y
16. Moritani K, Hasegawa H, Okabayashi K, Ishii Y, Endo T, Kitagawa Y. Difference in the recurrence rate between right- and left-sided colon cancer: A 17-year experience at a single institution. Surg Today 2014;44(9):1685-91. https://doi.org/10.1007/s00595-013-0748-5
17. Salmerón-Ruiz A, Luengo Gómez D, Medina Benítez A, Láinez Ramos-Bossini AJ. Primary staging of rectal cancer on MRI: An updated pictorial review with focus on common pitfalls and current controversies. Eur J Radiol 2024;175:111417. https://doi.org/10.1016/j.ejrad.2024.111417

18. Caruso D, Polici M, Bellini D, Laghi A. ESR essentials: Imaging in colorectal cancer-practice recommendations by ESGAR. Eur Radiol 2024;34(9):5903-10.

https://doi.org/10.1007/s00330-024-10645-3

19. Weiser MR. AJCC 8th edition: Colorectal cancer. Ann Surg Oncol 2018;25:1454-5.

https://doi.org/10.1245/s10434-018-6462-1

20. Wu Z, Li Y, Zhang Y, Hu H, Wu T, Liu S, et al. Colorectal cancer screening methods and molecular markers for early detection. Technol Cancer Res Treat 2020;19:1533033820980426.

https://doi.org/10.1177/1533033820980426

21. Brenner H, Kloor M, Pox CP. Colorectal cancer. Lancet 2014;383:1490-502.

https://doi.org/10.1016/S0140-6736(13)61649-9

22. Thomas C, Mandrik O, Whyte S, Saunders CL, Griffin SJ, Usher-Smith JA. Should colorectal cancer screening start at different ages for men and women? Cost-effectiveness analysis for a resource-constrained service. Cancer Rep (Hoboken) 2021;4:e1344.

https://doi.org/10.1002/cnr2.1344

23. Jemal A, Siegal R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. CA Cancer J Clin 2008;58:71-96.

https://doi.org/10.3322/CA.2007.0010

24. Davidović V, Miladinov B, Davidović B. Primarni kolorektalni karcinom u našoj kliničkoj praksi u petogodišnjem periodu. Timočki Med Glas 2017;42(3):139-46.

https://doi.org/10.5937/tmg1703139D

25. Steele GD Jr. The national cancer data base report on colorectal cancer. Cancer 1994;74:1979-89.

https://doi.org/10.1002/1097-0142(19941001)74:7<1979:aid-cncr2820740725>3.0.co;2-j

26. Waldron RP, Donovan IA. Mortality in patients with obstructing colorectal cancer. Ann R Coll Surg Engl 1986;68:219-21.

27. Crerand S, Freely TM, Waldron RP, Corrigan T, Hederman W, O'Connell FX, et al. Colorectal carcinoma over 30 years at one hospital: No evidence for a shift to the right. Int J Colorectal Dis 1991;6:184-7.

https://doi.org/10.1007/BF00341386

28. Bajramagic S, Hodzic E, Mulabdic A, Holjan S, Smajlovic SV, Rovcanin A. Usage of probiotics and its clinical significance at surgically treated patients suffering from colorectal carcinoma. Med Arch 2019;73:316-20.

https://doi.org/10.5455/medarh.2019.73.316-320

29. Kumar S, Burney IA, Zahid KF, Souza PC, Belushi MA, Mufti TD, et al. Colorectal cancer patient characteristics, treatment and survival in oman--a single center study. Asian Pac J Cancer Prev 2015;16:4853-8.

https://doi.org/10.7314/apjcp.2015.16.12.4853

30. Ibrar F, Atiq M, Shafqat F, Khan HM. Early onset colorectal cancer and its association with its histological subtypes. Pak J Med Sci 2024;40(10):2395-9.

https://doi.org/10.12669/pjms.40.10.10143

31. Campo-Sánchez SM, Camargo-Trillos J, Calle-Ramírez JA, Gómez-Wolff LR, Sánchez Patiño LA, García-García HI. Colorectal cancer survival at an oncologic center in Colombia. A historic cohort study. Rev Gastroenterol Mex (Engl Ed) 2019;84:174-84.

https://doi.org/10.1016/j.rgmx.2018.04.002