

CLINICAL STUDY

Is sporadic colorectal cancer more aggressive in young people and should the age of colonoscopy screening be reduced?

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ABSTRACT

OBJECTIVES: The present study aims to report the incidence of colorectal cancer patients under 50 years of age and to compare its aggressiveness with colorectal cancer patients over 50 years of age.

BACKGROUND: Recently, the incidence of colorectal cancer at younger ages has increased, and colorectal cancers in young people have a more aggressive course due to late screening programs.

METHOD: The files of patients who were operated for colorectal cancer were reviewed retrospectively.

Information on the patients such as gender, age, BMI, type and duration of symptoms, location of the tumor, TNM staging, pathology results, operative procedure, morbidity and mortality rates were recorded. Admission complaints, symptom onset time, tumor locations, pathological findings and tumor stages were compared between patients under and over the age of 50.

RESULTS: The incidence of colorectal cancer under 50 was 21 % (56/267). The age group of 40–49 was found to be the most common age range under the age of 50, with a colorectal cancer rate of 68%. In patients under the age of 50, higher invasion of the tumor to the serosa, low differentiation of the tumor in terms of histological findings in a higher number of patients and higher mucin component of the tumors and higher N2 lymph node involvement ratio and the tumor was located more in the lower rectum were statistically significant when compared to patients over the age of 50 ($p=0.026$, $p=0.018$, $p=0.002$, $p=0.042$, $p=0.006$; respectively).

CONCLUSION: The incidence of colorectal cancer has increased at younger ages and has a more aggressive course. Screening programs should be modified (Tab. 4, Fig. 2, Ref. 45). Text in PDF www.elis.sk

KEY WORDS: colorectal cancer, colonoscopy screening, young people.

Introduction

Colorectal cancer (CRC) is the 3rd most common malignant neoplasm in the world. Every year, 1–2 million people get colorectal cancer and around 600,000 people die because of it (1, 2). The incidence of the disease is low under 50 years of age but increases strongly with advanced age. Cases are seen in over 55 years of age, around 90 %. The median diagnosis age in developed countries has been reported as approximately 70. The proportion of cases diagnosed in individuals under the age of 50 in the USA increased from 6 % in 1990 to 11 % in 2013 as a result of the increase in incidence rates of CRC in younger age groups (3–6). This trend shows that young CRC patients need more attention. It is assumed that CRC has different biological behavior in young patients than in older patients, more patients are at an advanced stage when diagnosed and have more aggressive histological fea-

tures (7). In some population-based studies, it has been stated that young colorectal cancers have a better course (8, 9).

Colonoscopy is used for CRC scanning in an increasing number of countries. When a colonoscopy scan is recommended as the primary screening test, it typically begins at the age of 50 or 55 (10–12). Based on the modeling results and the increasing incidence of CRC in the young population, it has been proposed to start screening at the age of 45 in average-risk populations in the recently published American Cancer Association guidelines (13).

The present study aims to report the incidence of colorectal cancer patients under 50 years of age who have been operated in a single center in the last 3 years due to the increase in the incidence of colorectal cancer in recent years and to compare them with patients with colorectal cancer over 50 years of age in terms of locations of tumor, pathology results, and stages.

Material and methods

The files of patients who were operated in elective condition for colorectal cancer in the general surgery clinic between January 2017 and January 2020 were reviewed retrospectively. Patients older than 18 years, who had alarm symptoms during the outpatient clinic admission and who did not have a family history of cancer or a cancer-prone syndrome were included in the

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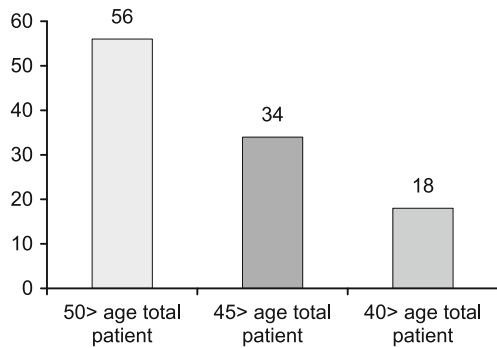


Fig. 1. Number of patient according to age.

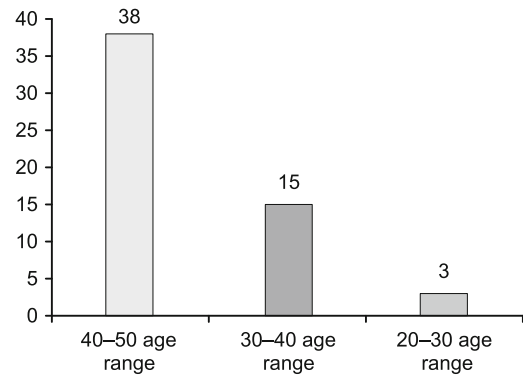


Fig. 2. Number of patient according to age range.

study. Patients under the age of 18 and who had a family history of cancer or a syndrome that could predispose to cancer were excluded from the study.

Information on the patients such as gender, age, BMI, type and duration of symptoms, location of the tumor, stage of the disease in diagnosis (TNM staging), pathology results, histological classification, operative procedure, morbidity and mortality rates were recorded.

Admission complaints, symptom onset time, tumor locations, pathological findings, histological features of tumor and tumor stages were compared between patients under and over the age of 50.

Statistical analysis

The Statistical Package for the Social Sciences 24.0 program was used for the statistical analysis of the variables. Independent Samples t-Test and descriptive statistical methods were used for binary group comparisons of normally distributed parameters. The Pearson Chi-Square test was used in the analysis of qualitative data. The significance was evaluated at $p < 0.01$ and $p < 0.05$ levels.

Tab. 1. Comparison of admission complaints.

Complaints	<50 age (56)	>50 age (211)	p
Rectal bleeding	32 (57.14%)	68 (32.22%)	^a 0.029*
Change in bowel habits	18 (32.14%)	119 (56.39%)	^a 0.032*
Abdominal pain	12 (21.42%)	48 (22.74%)	^a 0.748
Weight loss	6 (10.71%)	28 (13.2%)	^a 0.534
Vomiting	4 (7.14%)	17 (8.05%)	^a 0.796
Symptom onset (month)	4.92	4.70	^b 0.874

^a Pearson Chi-Square, ^b Independent Sample t test, * $p < 0.05$

Tab. 2. Comparison of tumor locations.

Tumor locations	<50 age (n=56)	>50 age (n=211)	^a p
Lower Rectum	20 (35.7%)	39 (18.5%)	0.006**
Middle Rectum	4 (7.1%)	13 (6.2%)	0.789
Upper Rectum	7 (12.5%)	30 (14.2%)	0.741
Sigmoid Colon	9 (16.1%)	63 (29.9%)	0.039*
Left Colon	3 (5.4%)	20 (9.5%)	0.328
Transverse Colon	2 (3.6%)	12 (5.7%)	0.528
Right Colon	11 (19.6%)	34 (16.1%)	0.531

^a Pearson Chi-Square, * $p < 0.05$, ** $p < 0.001$

Results

Between January 2017 and January 2020, 273 patients were operated in our clinic for colorectal cancer. A total of 6 patients were excluded from the study because 2 patients had familial polyposis syndrome, 3 patients had a family history of colorectal cancer and 1 patient developed colorectal cancer on the background of ulcerative colitis. Only one of the 6 patients excluded from the study was under the age of 50.

When the files of 267 patients included in the study were examined, it was seen that 56 colorectal cancer patients who did not have any family history and disease that could cause familial genetic predisposition were under 50 years and 211 patients were over 50 years of age. In the present study, the incidence of colorectal cancer under 50 was 21 % (56/267). The incidence below the age of 45 was 14.23 % (38/267) and the incidence below the age of 40 was 6.74 % (18/267) (Fig. 1). The age range of the patients was between 22–49. The average age was 42.2, while 3 (1.12 %) patients were in the 20–30, 15 (5.63 %) patients were in the 30–40, and 38 (14.23 %) patients were in the 40–50 age range (Fig. 2).

In terms of gender distribution, it was seen that 20 (35 %) patients were female and 36 (65 %) patients were male. The mean BMI of the patients was 27.3 (22–34).

Rectal bleeding was the most common symptom seen in patients. Of the colorectal cancer patients aged 50 >, 32 (57.2 %) had rectal bleeding, 18 (32.1 %) had changes in bowel habits (diarrhea and constipation), 12 (21.4 %) had abdominal pain, 6 (10.7 %) had weight loss and 4 (7.1 %) had vomiting. Compared to patients over 50 years of age, it was significant that rectal bleeding was higher in patients under 50 years of age, whereas more changes in bowel habits were significant in patients over 50 years of age ($p=0.029$, $p=0.032$; respectively) (Tab. 1).

Considering the time between the onset of symptoms and the time of diagnosis, it was found that 6 patients applied 1 month af-

Tab. 3. Surgical and histological findings and complications of patients under 50.

Surgeries performed	
Laparoscopic low anterior resection	14 (25%)
Open low anterior resection	3 (5.35%)
Robotic low anterior resection	1 (1.78%)
Laparoscopic anterior resection	7 (12.5%)
Open anterior resection	7 (12.5%)
Abdominoperineal resection	2 (3.57%)
Laparoscopic left hemicolectomy	3 (5.35%)
Open left hemicolectomy	2 (3.57%)
Laparoscopic right hemicolectomy	7 (12.5%)
Open right hemicolectomy	3 (5.35%)
Low anterior resection + liver metastasectomy	3 (5.35%)
Abdominoperineal resection + liver metastasectomy	1 (1.78%)
Right hemicolectomy + liver metastasectomy	1 (1.78%)
Peritoneal carcinomatosis and loop colostomy due to frozen pelvis	2 (3.57%)
TNM Staging	
1	9 (16.07%)
2	21 (37.5%)
3	19 (33.92%)
4	7 (12.5%)
Histological findings	
Well-differentiated	6 (10.72%)
Moderately differentiated	36 (64.28%)
Poorly differentiated	14 (25%)
Mucinous component	15 (26.7%)
Morbidity	
Superficial wound infection	4 (7.14%)
Anastomosis leakage	4 (7.14%)
Ostomy necrosis	1 (1.78%)
Length of hospital stay (day)	7.36 (5–22)
Local recurrence	2 (3.57%)
Mortality	(1.78%)

Tab. 4. Comparison of Prognostic factors.

Prognostic Factors	<50 age (n=56)	>50 age (n=211)	p
Low differentiation	14 (25%)	26 (12.32%)	<i>^a0.018*</i>
Mucinous component	15 (26.7%)	22 (10.42%)	<i>^a0.002**</i>
Serosa invasion (T4)	15 (26.7%)	30 (14.21%)	<i>^a0.026*</i>
Mean lymph node count	2.071	1.53	<i>^b0.329</i>
Number of patients with lymph involvement	24 (42.8%)	68 (32.2%)	<i>^a0.137</i>
N2 lymph node involvement	14 (25%)	29 (13.74%)	<i>^a0.042*</i>
Stallite deposit	3 (5.35%)	10 (4.73%)	<i>^a0.849</i>
Distant metastasis	7 (12.5%)	14 (6.6%)	<i>^a0.147</i>
TNM Stage 3-4	26 (46.42%)	70 (33.17%)	<i>^a0.066</i>
Local recurrence	2 (3.5%)	5 (2.36%)	<i>^a0.729</i>

^a Pearson Chi-Square, ^bIndependent Sample t test, * p < 0.05, ** p < 0.001

ter symptoms started, 24 patients between 1–3 months, 16 patients between 3–6 months, 6 patients between 6–12 months, and 4 patients 1 year later. In comparison with patients with colorectal cancer over 50 years of age, there was no statistical difference between the mean application times of both groups (p=0.874) (Tab. 1).

Tumors were in the right colon in 11 (19.64%) patients, in the transverse colon in 2 (3.57%) patients, in the left colon in 3 (46%) patients, in the sigmoid colon in 9 (16.07%) patients, 7 (12.5%) in the upper rectum in patients, in the middle rectum in 4 (7.14%) patients and the lower rectum in 20 (35.71%) patients. In the comparison made with patients over the age of 50 with respect

to locations of the tumor, the lower rectal tumors were statistically higher in patients under the age of 50 (p=0.006). Sigmoid colon cancers, however, were significantly more common in patients over 50 years of age (p=0.039) (Tab. 2).

Operations performed on patients under 50 age are detailed in Table 3. No operation-related mortality developed in any patient. Anastomosis leakage occurred in 4 patients, while 2 of these patients were treated with an EndoVac therapy system and 2 patients were treated with a colostomy. Superficial wound infection was performed in 4 patients and ostomy revision in 1 patient. The average length of hospital stay of the patients was 7.36 (5–22) days (Tab. 3).

According to TNM staging, 9 (16.07%) patients were stage 1, 21 (37.5%) patients were stage 2, 19 (33.92%) patients were stage 3 and 7 (12.5%) patients were stage 4. In histological classification, it was seen that 6 (10.71%) patients had well-differentiated, 36 (64.28%) patients had moderately differentiated and 14 (25%) patients had poorly differentiated tumors. Tumors in 15 patients involved the mucin component (Tab. 3).

The follow-up period of the patients was between 3–36 months, and the mean follow-up was 15.7 months. One of the patients with stage 4 peritoneal carcinomatosis died in the 8th month depending on the course of the disease. In 2 patients, local recurrence occurred in the 14th and 22nd months, respectively, and reoperation was performed.

In patients under the age of 50, higher invasion of the tumor to the serosa, low differentiation of the tumor in terms of histological findings in a higher number of patients, and higher mucinous component of the tumors and higher N2 lymph node involvement ratio were statistically significant when compared to patients over the age of

50 (p=0.026, p=0.018, p=0.002, p=0.042; respectively). There was no significant difference between these two age groups in terms of mean lymph node number, the number of patients with lymph node involvement, presence of satellite deposit, distant metastasis, local recurrence during the disease stages, and follow-up periods (Tab. 4).

Discussion

Colorectal cancer (CRC) is one of the main causes of death with high incidence particularly in developed but also in many

other countries. However, there has been an increase in the incidence of the disease in developing countries in recent years (14). Although the incidence increases with age, an increase in incidence has also been reported recently in young individuals. Between 2005 and 2014, the incidence of colon cancer increased by 1.4 % and the incidence of rectal cancer increased by 2.4 % annually in individuals under the age of 50 (15).

While the incidence of colorectal cancer under the age of 50 was 6 % in the 1990s, this rate has increased by up to 10 % in recent years (6, 10–14). The incidence of colorectal cancer under the age of 45 was reported to be 5.7 % (15). In a study by Schellerer et al (16), the incidence of cancer under the age of 50 was 12.4 %, the incidence of colorectal cancer between the ages of 41–50 was 9.1 %, and the incidence of colorectal cancer was 3.2 % in people younger than 40 years. In a recent study by Silva et al (17), cancer incidence was 13.45 % under the age of 50, 5.13 % under the age of 40, and 8.31 % between the ages of 40 and 50. The age range of 40–49 is the period when colorectal cancer is most common under the age of 50 with an incidence rate of 75 % (18, 19). In the present study, the incidence of colorectal cancer was 21.05 % (56/266) under 50, 12.78 % (34/266) under 45, and 6.76 % (18/266) under 40, and these values were high compared to those in the literature. In the patient series of the present study, the age group of 40–49 was found to be the most common age range for colorectal cancer under the age of 50, with a colorectal cancer rate of 68 % (38/56), and was consistent with the results obtained in studies in the literature.

Generally, there are studies reporting that there is no difference in terms of gender distribution in young colorectal cancer patients (19–23). In the patient series in this study, the disease was observed at a higher rate in males than in females (60.7 %, 39.28 %).

Numerous types of cancer are associated with body weight. It has been demonstrated that obesity and an obesogenic diet accelerate the multi-stage transition from normal tissue to invasive malignancy and metastatic disease (24). The increase in colorectal cancer in high-income countries may be caused by an obesity epidemic (25). In the study by Kim et al (26), obesity has been observed to be a risk factor for the development of colorectal cancer in patients under the age of 40. In the present patient series, the BMI average of young patients with colorectal cancer was found to be 27.3, and the patients were found to be overweight.

In the literature, the most common symptoms in patients with colorectal cancer under the age of 50 are rectal bleeding and abdominal pain (19–22, 23). In the study by De Sousa et al (27), rectal bleeding was the most common symptom in patients under 50 years of age with an incidence rate of 77 %, although there was no difference in symptoms between patients under 50 and over 50 years of age. The change in bowel habits was the most common symptom in patients over 50 years old with a rate of 72 % (27). Rectal bleeding was the most common symptom in patients under 50 years of age, with a rate of 57.2 % in the present study, and it was found statistically significant to be seen at a higher rate than in patients over 50 years of age ($p=0.029$). Changes in bowel habits in patients over 50 years of age were found statistically higher than those under 50 years of age ($p=0.032$). The comparison made in

terms of symptom onset time in the study by De Sousa et al (27), the symptom onset times were significantly higher in patients over the age of 50. In this study, the application time under the age of 50 was 4.9 months on average and 4.7 months above the age of 50, and there was no significant difference between the two groups.

The incidence of colorectal cancer for individuals under the age of 50 increased by 22 % from 2000 to 2013. These are mostly due to the increase in distal colon and rectum tumors (14). In the study of Silva et al (17), it was seen that the tumor was in the sigmoid colon and rectum in 65 % of patients under 50 years of age. In another study, it was found that the location of the tumor in the distal colon was found to be statistically significant in patients with colorectal cancer under the age of 50 compared to patients over the age of 50 (20). In the study by Wang et al (21), it was significant that tumors were rather located in the rectum in patients under 50 years compared to patients over 50 years of age. In this study, tumors were in the rectum in 55 % of patients under 50 years of age. In comparison with the patients over 50 years of age, it was statistically significant that the tumors were found more in the lower rectum ($p=0.006$). In patients over 50 years of age, it was significant that tumors were seen more frequently in the sigmoid colon ($p=0.039$).

Considering the histology of the resected samples, it was seen that the prevalence of tumors with mucin component or poorly differentiated tumors was higher in young patients with colorectal cancer (23, 28). In the study by Wang et al (21), poorly differentiated tumor histological types and mucinous components were poor prognostic factors. In the study by Chou et al (29), mucinous component and low differentiation were significantly higher in young patients with colorectal cancer when compared to those in the elderly. In the present patient series, it was statistically significant that the tumors contained mucin components and were low differentiated in patients under 50 years compared to patients over 50 years of age.

Serosal involvement in colorectal cancers is one of the poor prognostic factors associated with decreased survival and may affect additional treatment decisions (30). In a study, the serosal involvement of the tumor was found to be a bad prognostic factor in both univariate analysis and multivariate analysis (21). In a study by Karsten et al (31), it was reported that tumors are at the advanced stage in young colorectal cancer patients and have a high rate of T3 and T4 tumors as 87 % and the tumors in young patients are more aggressive. In the study by Rodriguez et al (9), in a comparison between patients with colorectal cancer under and over 50 years of age, serosal involvement was observed more frequently in patients under the age of 50. In this study, 26.7 % (15/56) of patients under the age of 50 were found to have serosal involvement, and serosal involvement was found to be significant in a higher number of patients compared to patients over 50 years of age.

While 5-year survival is 70–80 % in lymph node-negative patients, this rate is between 30–60 % in lymph node-positive patients (32). There are studies with similar lymph node involvement rates in patients aged 50 years and older (27, 33). Also, there are studies reporting that the number of lymph node-positive patients is higher in young patients and N2 as the lymph node involvement stage is higher in young patients (9, 34). In the present study, there was no

difference between the number of lymph node-positive patients and the average number of lymph nodes with carcinoma metastasis, whereas higher N2 lymph node stages in patients under 50 years of age were found significant.

Many studies have shown that satellite tumor deposits (TDs) are associated with advanced colorectal carcinoma stage and poor prognosis. However, due to the different definitions of TDs, the result data could not be accurately estimated (35). Gopal et al (36) associated TDs with more lymph node involvement, distant metastasis, and decreased survival rates. In this study, satellite tumor deposits in patients under and over 50 years of age were observed at similar rates in both groups.

According to the TNM staging system, the comparison between young and old patients did not differ between tumor stages in most studies (20, 27, 33, 34, 37, 38). In some studies, stages 3 and 4 diseases were observed at a higher rate in young colorectal cancer patients (9, 21, 39). In this study, the grade 3–4 disease rate was 46.4 % in young colorectal cancer patients and 33.17 % in patients over 50 years of age. Although this rate was higher in young patients, it was not statistically significant. There was also no difference between the two groups in terms of distant metastases.

Since the implementation of routine screening for colorectal cancer in the 1990s, there have been significant and persistent general decreases in CRC cases and mortality rates (13, 14, 24). Screening methods such as guaiac test, immunochemical test, DNA tests, and endoscopy are available for colorectal cancer (41). CRC scanning and colonoscopy removal of precancerous lesions is the gold standard (42). In many countries, colonoscopy screening begins between the ages of 50 or 55. In countries developed in terms of the sociocultural economy such as Germany and England, the colonoscopy screening age is 50 (43, 44). Early-onset colorectal cancers are an undeniable health priority that needs to be addressed internationally, as the risk of colon cancer is doubled, and the risk of rectal cancer is quadrupled in those born in the 1990s (45). The recently published American Cancer Association guidelines suggested starting colonoscopy screening for colorectal cancer at the age of 45 in average-risk populations (13). Early diagnosis is one of the factors that increase survival in colorectal cancer. Perhaps the fact that patients under the age of 50 are not included in screening programs in many countries causes the precancerous lesions of these patients to not be detected and to be diagnosed with cancer at a later stage.

Conclusion

The fact that the incidence of sporadic colorectal cancer has increased in young ages in recent years has been revealed in our study. In the present study, the incidence of sporadic colorectal cancer under the age of 50 was found to be around 21 %. Compared to patients over 50 years of age, it was determined that more patients entered the stage of serosa invasion and N2 lymph involvement, and the tumor histology showed a more aggressive course with low differentiation and more mucin components. We think that the aggressive course of the tumor in patients under the age of 50 is still due to the fact that the population under 50 is still not included in screening programs in many countries around the

world. In the present study, 68 % of young patients with colorectal cancer were found to be 40–50 age range. With these findings, it is considered that screening programs should be reviewed, and the population aged 40 years and older should be included in screening programs and we think that rectoscopy should be performed in the presence of alarm symptoms in patients under the age of 40 because the tumor localization was detected in the left colon and distal in about 80 % of these ages in present study.

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