Risk factors for the diagnosis of colorectal cancer

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Abstract

Background: Colorectal cancer (CRC), defined as cancer of the colon or rectum, is one of the most frequently diagnosed cancers, and, according to the World Health Organisation database GLOBOCAN, it accounts for about 1.4 million new diagnoses annually worldwide. There is an association between the occurrence of colorectal cancer and non-modifiable risk factors, including age and hereditary factors, as well as with modifiable factors linked to the environment and lifestyle choices.

Methods: The study included 800 patients, 400 diagnosed with colorectal cancer and 400 within the control group. The research was based on a clinical, direct, individual, structured, in-depth and focused interview. Assessment of activity and BMI was used according to WHO recommendations, as well as the expert system.

Results: The average age of the patients was 64.53 ± 8.86 years, of the control group I - 59.64 ± 9.33 and the control group II - 57.5 (7.83). The association between the incidence of ulcerative colitis and the risk of colorectal cancer was clearly positive ($p<0.001$). Among obese subjects, the colorectal cancer risk was 1.27 (95% CI, 1.06-1.53) in comparison with non-obese subjects. The relative risk for current smokers was 2.17 (95% CI 1.79-2.66). Higher fat consumption and higher red meat consumption were also associated with the higher risk of colorectal cancer ($p=0.01$).

Conclusions: Obesity, low physical activity, active and passive smoking and high salt and red meat consumption have been linked to a higher risk of colorectal cancer. The results give further evidence of the importance of maintaining a healthy lifestyle.

Introduction

For over 40 years, CRC has become an increasing problem in developed countries, where it is one of the leading neoplastic locations. It is now responsible for 655,000 deaths a year worldwide. Incidence rates are highest in the European and American countries and and lowest in developing countries. It is the third most common cancer diagnosed in both men and women in the United States. The estimations of the American Cancer Society indicate 104,610 diagnoses of colon cancer and 43,340 diagnoses of rectal cancer in 2020 in the United States. In the 1960s, Poland was a country with very low mortality from these cancers - the mortality rates were in the range of 5–6/105. Changes in the frequency of colorectal cancer within 30 years made Poland a country with a high risk of dying from colorectal cancer (mortality rate 20/105 in men, 10/105 in women). The time trend of the mortality rates for malignant colorectal neoplasms in Poland, especially in men, is characterised by one of the highest upward trends among European countries. Every year, more than 13,000 Poles develop colorectal cancer, of which over 9,000 dies. The risk of developing colorectal cancer during the lifetime for men is approximately 1 in 23 (4.4%) and for women – 1 in 25 (4.1%) [1–6]. The occurence of CRC worldwide is assumed to increase by 60% to over 2.2 million diagnoses and 1.1 million deaths annually before 2030. This increase will be the result of economic, social, environmental and generational changes in developed countries [7].

The etiology of colorectal neoplasms has not been fully explained and the immediate causes are still unknown, but many years of research have allowed us to distinguish many risk factors. The age of the patient is considered to be the main cause. Although cancer occurs also in young people the chance of developing cancer increases after the age of 50 and 9 out of 10 cancer patients are older than 50 years of age. The peak incidence

occurs after the age of 70. Past inflammatory diseases are another factor that increases the risk for colorectal cancer. The risk of developing the disease increases 20 times in case of ulcerative colitis and in case of Crohn's disease – 3 times Many risk factors are related to lifestyle. Scientific research indicates low physical activity, a low-residue diet rich in fat, high in calories, rich in red meat, but also low in calcium or folic acid. Besides, alcohol consumption and smoking are also mentioned, which in the US are associated with 1/5 of intestinal cancers. Strong scientific evidence shows that obese people develop colorectal cancer more often, and with increasing BMI this risk increases. Elderly people with BMI > 30 have a 5-100% higher risk of the disease in comparison with people with BMI < 23. It is also important to pay attention to the genetic background, especially familial adenomatous polyposis (FAP), which is linked with a 100% lifetime colorectal cancer risk, and hereditary non-polyposis colorectal cancer (HNPCC), where the risk is 70–80% [3, 8–12].

Objective Of The Work

The objective of the study is identification and evaluattion of patient characteristics, demographic and lifestyle factors linked to colorectal cancer at diagnosis.

Method And Data

Study plan

We conducted a multi-area cross-sectional population-based research among patients of the Oncology Center, Clinical Provincial Hospital in 2019–2020. Patients diagnosed with colorectal cancer (shown by histopathology) and the control group without a diagnosis of colorectal cancer received an invitation to take part in the study. As the sample size was small, the proportion of patients with similar characteristics was important.

Qualified patients received an informational pack from a research group member. The information package consisted of a letter describing the objectives of the study and its course, a consent form for patients willing to take part in the study, and a refusal form. Giving their consent, the patient chose to participate in a face-to-face interview conducted in the hospital by a research group member or to fill in the interview form online. The interview lasted approximately 40 minutes. To maintain the physical and mental comfort of the patient, the interview was divided into parts. The online interview could be completed at any time by the patient.

Participant recruitment, inclusion and exclusion criteria

All types of histopathologically confirmed colorectal cancer cases, regardless of their stage, were included in the research. The main indicators to participate in the study were tlife expectancy > 6 months, the diagnosis of cancer at least three months before the study, age of 18 years and more and awareness of the diagnosis. Patients who did not express their willingness to participate in the study, the ones covered by palliative care and those diagnosed within the last three months were excluded from the study as the first months of diagnosis and treatment cause a great psychological burden as well as the need to adapt to the new situation and that could introduce errors. Patients with servere physical symptoms, too stressed, under the age of 18 or unable to read in Polish were also excluded.

Patients with cancer other than colorectal cancer were selected for control group I, and patients of the Provincial Clinical Hospital without a cancer diagnosis, aged 34 to 85 years were in control group II.

Sample
800 patients were included in the study, 400 from the control group and 400 diagnosed with colorectal cancer. The mean age of the patients was 64.53 ± 8.86 years, the control group I 59.64 ± 9.33 and the control group II 57.5 (7.83).

Patient Questionnaire
The research included a clinical, direct, individual, structured interview, in-depth and focused. The initial questionnaire was a standardised measuring tool verified by testing 30 patients for one month. The questions were open-ended, single and multiple-choice and aimed at obtaining demographic, epidemiological, lifestyle and risk behaviour data, as well as risk factors.

BMI assessment
Body mass index (BMI) in kg/m2 was calculated from the baseline height and weight and divided into three categories as per the WHO standard: regular (< 25 kg/m2), overweight (25-29.9 kg/m2) and obesity (>/30 kg/m2).

Assessment of physical activity
Assessment of activity according to WHO recommendations was used: undertaking at least moderate activity for about 30 minutes five times a week, moderate or intense physical effort performed for > 45 minutes on at > 5 days a week, undertaking 18–27 hours of metabolic effort (MET) equivalent per week (hour of jogging, cycling, tennis, swimming – 7 MET, an hour of aerobics, lawn mowing – 6 MET, walking for an hour 6 days a week – 18 MET).

Assessment of covariates
Potential confounders of colorectal cancer risk were selected based on published evidence from EPIC (European Prospective Investigation into Cancer and Nutrition), IARC (International Agency for Research on Cancer) and WCRF (World Cancer Research Fund), which included: smoking (never smoking, passive smoking, active smoking, age at which they started and stopped smoking, number of cigarettes smoked), weekly alcohol consumption based on a relatively safe portion of pure alcohol per day for men (20 g) and for women (10 g), i.e.one glass of wine, a glass of beer, a small glass of strong alcohol. A portion is an equivalent of 30 ml of vodka (40% / vol.), 100 ml of wine (12% / vol.), 285 ml of strong beer (4.9% / vol.) or 375 ml of light beer (3.5% / vol.), compliance with vegetable and fruit consumption guidelines defined as eating more than 2 portions of fruit and 5 portions of vegetables per day or 400–800 g daily, consumption of 600–800 g of fibre per day, consumption of red meat less than 80 g per day or 500 g per week.

Expert system
The research method was an individual analysis of cancer risk performed with the use of a computer application based on an expert system. The tools included a skeleton expert system Jess, allowing formation of decision rules and conclusions. The graphic interface was created with the use of a programming language JavaFx, which allows creation of advanced forms using the CSS styles.

Ethical concerns
The study received an approval from the Ethics Committee. Participants took part in the study voluntarily and anonymously, and the information of the right to refuse or withdraw from the study at any time was provided to

them. Each participant received information about the study objective and the time of study termination.

Data analysis

Prism 4.0 software was used to obtain and analyse data. Confidence intervals and descriptive statistics were used for participant characteristics, demographics and prevalence of needs analysis. Statistical characteristics of continuous variables are presented in the form of arithmetic means, standard deviations, medians. Step and qualitative variables statistical characteristics were presented as numerical and percentage distributions. Cronbach's α composite scales and subscales were used for assessment of internal consistency. Linear regression was used to analyse the relations between unmet needs and quality of life. The repeatability of answers to individual questions was assessed with Kappa Cohen statistics. The correlations were determined using the Pearson test, while χ 2 was used for the comparison between the groups. Significance was assessed at the level of $P < 0.05$. Missing data were removed from analyses.

Results

Demographic data

The study group consisted of 800 people, 400 cases and 400 of the control group. The average age of the patients was 64.53 ± 8.86 years, while in the control group I 59.64 ± 9.33 and in group II 57.5 (7.83). Increasing age was strongly linked to the risk of developing colorectal cancer. The colorectal cancer incidence correlated with the place of residence ($p < 0.0001$) and the level of education ($p < 0.0001$). The general incidence of colorectal cancer was significantly higher for those with low educational attainment and those in the countryside compared to the corresponding groups. Table 1 shows other descriptive statistics obtained from the studied group.

Table 1
Descriptive statistics of the examined group of patiens.

Demographic Information	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	P
Characteristics % (N)				
Sex				
women	40% (160)	37% (74)	88% (176)	0,21
men	60% (240)	63% (126)	12% (24)	
The age of the study group				
SD	64.53 (8.86)	59,64 ± 9.33	57,5 (7,83)	0,12
95%CI	< 34; 82>	< 34; 79>	< 35; 85>	
Place of residence				
city	27% (108)	49% (98)	36% (72)	0,01
village	73% (292)	51% (102)	64% (128)	
Financial situation				
very good	7% (28)	4% (8)	20% (40)	0,19
good	20% (80)	30% (60)	51% (102)	
average	61% (244)	60% (120)	20% (40)	
bad	12% (48)	6% (12)	9% (18)	
Age groups				
34–44	1% (4)	3% (6)	15% (30)	0,07
45–55	6% (24)	11% (22)	12% (24)	
56–66	53% (212)	37% (74)	27% (54)	
67–77	33% (132)	12% (24)	23% (46)	
78–88	7% (28)	37% (74)	23% (46)	
Education of the study group				
higher education	10% (40)	23% (46)	20% (40)	0,01
secondary education	20% (80)	46% (92)	71% (142)	
vocational education	43% (172)	23% (46)	5% (10)	
primary education	27% (108)	8% (16)	4% (8)	
Marital status				
married	19% (76)	54% (108)	65% (130)	0,62
widowed	70% (280)	12% (24)	11% (22)	

Demographic Information	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	P
unmarried	11% (44)	34% (68)	24% (48)	
Source of income				
professionally active	33% (132)	31% (62)	65% (130)	0,59
annuity	13% (52)	20% (40)	12% (24)	
unemployed	7% (28)	18% (36)	9% (18)	
retirement	47% (188)	31% (62)	14% (28)	

Family history of neoplastic diseases

When assessing the incidence of neoplastic diseases in the families of the respondents, it was shown that in the group of patients 47% reported the presence of neoplastic diseases, in the control group I 60%, and in group II 31%. Family history of neoplastic diseases was not clearly associated with the colorectal cancer risk (Table 2,3).

Table 2
The occurrence of neoplasms in the respondents' family.

Family history of diseases	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	RR (95% CI)	P
Characteristics /% (N)					
Family history of polyps					
No	92% (368)	99% (198)	100% (200)	1,0	
Yes	8% (32)	1% (2)	0% (0)	1,03 (0,88 – 1,22)	0,19
Cancer family history					
No	53% (212)	40% (80)	69% (138)	1,26 (0,84 – 1,89)	0,71
Yes	47% (188)	60% (120)	31% (62)	1,15 (0,96 – 1,40)	0,21

Table 3
The occurrence of neoplasms in the respondents' family.

Type of cancer	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	P
Characteristics /% (N)				
Nervous system	0% (0)	1% (2)	3% (6)	0.55
Lung	0% (0)	10% (20)	24% (48)	0.41
Colorectal	15% (60)	9% (18)	15% (30)	0.71
Oral cancer	0% (0)	4% (8)	1% (2)	0.91
Breast	23% (92)	14% (28)	20% (40)	0.88
Ovary	10% (40)	13% (26)	10% (20)	0.54
Prostate	14% (56)	11% (22)	5% (10)	0.91
Pancreas	13% (52)	6% (12)	0% (0)	0.44
Liver	14% (56)	6% (12)	0% (0)	0.91
Skin	1% (4)	0% (0)	2% (4)	0.74

Personal medical history

An important element of the analysis was the assessment of the occurrence of diseases increasing colorectal cancer risk among the studied subjects. There was a clear positive association between the incidence of ulcerative colitis and the risk of colorectal cancer ($p < 0.001$) (Table 4).

Table 4
History of illness among the respondents.

Recognized diseases	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	P
Characteristics /% (N)				
Diabetes	11% (44)	21% (42)	29% (58)	0,99
Ulcerative colitis	71% (284)	1% (2)	4% (8)	0,01
Crohn's disease	18% (72)	0% (0)	0% (0)	0,41
Intestinal polyps	10% (40)	0% (0)	0% (0)	0,55
Hypertension	16% (64)	26% (52)	45% (90)	0,88
Heart arythmia	4% (16)	4% (8)	18% (36)	0,74
Rheumatic disease	0% (0)	0% (0)	4% (8)	0

Bodyweight and physical activity

60% of patients had BMI greater than 25 kg / m2, 20% in control group I, while in group II 35%. Increasing BMI was linked to an increased risk of colorectal cancer (p = 0.01). Among obese subjects, the colorectal cancer risk was 1.27 (95% CI, 1.06–1.53) compared with non-obese subjects. Of the patients, 29% did not meet the guidelines for moderate activity, 47% did not meet the guidelines for energetic activity, while control group II was more likely to follow them. Patients and subjects from the control group I spent more hours a day in a sitting position (Table 5).

Table 5
Life style of the respondents.

Variables	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	RR (95% CI)	P
Characteristics /% (N)					
BMI					
< 25	40% (160)	80% (160)	65% (130)	1,26 (0,84 – 1,89)	0,71
25,0–29,9	25% (100)	14% (28)	23% (46)	1,09 (0,92 – 1,28)	0,59
≥ 30	35% (140)	6% (12)	12% (24)	1,27 (1,06 – 1,53)	0,01
Metabolic equivalent of MET effort per week					
< 10 MET	82% (328)	62% (124)	51% (102)	1,26 (0,84 – 1,89)	0,59
10–17 MET	9% (36)	31% (62)	29% (58)	1,10 (0,87 – 1,39)	0,59
18–27 MET	9% (36)	7% (14)	20% (40)	0,58 (0,36 – 0,95)	0,14
Weekly activity time					
Lack of activity	29% (116)	24% (48)	9% (18)	0,93 (0,63 – 1,38)	0,53
5 days a week for 30 minutes	47% (188)	38% (76)	67% (134)	1,83 (0,52 – 6,50)	0,16
5 days a week for 1 hour	9% (36)	31% (62)	15% (30)	0,63 (0,97 – 1,10)	0,16
7 days a week for 30 minutes	9% (36)	7% (14)	9% (18)	0,60 (0,32 – 1,10)	0,32
Seating hours / day					
1–2	38% (152)	32% (64)	72% (144)	0,81 (0,65 – 1,0)	0,53
3–5	32% (128)	41% (82)	22% (44)	0,93 (0,63 – 1,38)	0,53
6–8	11% (44)	7% (14)	4% (8)	2,07 (1,14 – 3,77)	0,10
> 8	19% (76)	20% (40)	2% (4)	1,26 (0,84 – 1,89)	0,53
Stress					
Acute	31% (124)	9% (18)	27% (54)	1,16 (0,94 – 1,42)	0,73
Chronic	20% (80)	20% (40)	53% (106)	0,70 (0,33 – 1,51)	0,88

Substance Use

30% of patients were smokers, 21% in control group I and 8% in control group II. Only the group among the respondents chewed tobacco leaves (7%). The lowest age at the start of smoking was 14 years in the group of patients (7%). Patients and control group I were significantly more often smokers ($p < 0.0001$), and those groups started smoking at an early age ($p = 0.03$) significantly more often. An association has been noticed between

cigarette smoking and the risk of developing colorectal cancer. The relative risk for smokers was 2.17 (95% CI, 1.79–2.66). The colorectal cancer risk was significant when smoking more than 30 cigarettes per day ($p = 0.01$). There was no significant association between alcohol consumption and the risk of colorectal cancer (Table 6).

Table 6
Life style of the respondents.

Variables	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	RR (95% CI)	P
Characteristics /% (N)					
Smoking					
Never	16% (64)	37% (74)	58% (116)	0,98 (0,75 – 1,28)	0.94
Passive smoking	40% (160)	46% (92)	7% (14)	1,11 (0,80 – 1,54)	0.94
An active smoker	30% (120)	21% (42)	8% (16)	2,17 (1,79 – 2,66)	0,01
Former smoker	47% (188)	31% (62)	27% (54)	0,98 (0,75 – 1,28)	0.94
Age at the start of regular smoking					
10–14 years	7% (28)	0% (0)	0% (0)	1,11 (0,80 – 1,54)	0,03
15–20 years	33% (132)	20% (40)	4% (8)	1,27 (1,06 – 1,53)	0,59
21–25 years	7% (28)	3% (6)	8% (16)	1,05 (0,90 – 1,22)	0,52
> 25 years	53% (212)	77% (154)	88% (176)	2,18 (1,80 – 2,65)	0,94
Burning time					
< 10 years	7% (28)	55% (110)	25% (50)	0,64 (0,30 – 1,35)	0,62
10–20 years	20% (80)	14% (28)	64% (128)	1,16 (0,72–1,87)	0,65
> 20 years	73% (292)	31% (62)	11% (22)	3,42 (1,91 – 6,11)	0,01
Number of cigarettes smoked					
up to 10 cigarettes a day	7% (28)	16% (32)	12% (24)	1,05 (0,90 – 1,22)	0,12
from 10 to 20 a day	20% (80)	43% (86)	70% (140)	1,11 (0,80 – 1,54)	0,59
over 30 a day	73% (292)	41% (82)	18% (36)	2,18 (1,80 – 2,65	0,01
Consuming alcohol					
Abstinent	33% (132)	43% (86)	39% (78)	0,98 (0,75 – 1,28)	0.94
30 ml of vodka daily	14% (56)	3% (6)	4% (8)	0,88 (0,68 – 1,14)	0,12
100 ml of wine daily	14% (56)	9% (18)	7% (14)	3,42 (1,91 – 6,11)	0,52
380 ml of beer a day	0% (0)	9% (18)	10% (20)	1,51 (0,80 – 2,86)	0,94
60 ml of vodka daily	0% (0)	9% (18)	2% (4)	1,20 (0,73 – 1,98)	0,94
200 ml of wine a day	14% (56)	6% (12)	24% (48)	1,33 (0,75 – 2,36)	0,59
700 ml of beer a day	14% (56)	6% (12)	6% (12)	1,64 (0,97 – 2,79)	0,12
More	11% (44)	15% (30)	8% (16)	1,13 (0,83 – 1,56	0,59

Diet

There were no significant associations with the consumption of vegetables and fruits and the way food was prepared. However, the daily consumption of fat in the diet was declared by as many as 87% of the patients, and in control group I by 54% of the respondents, and in group II by 51%. A high salt intake was also observed in the group of patients (89%) and control group I (93%). There was an association between higher fat consumption and higher consumption of red meat and the colorectal cancer risk (p = 0.01) (Table 7).

Table 7
Eating habits among the respondents.

Variables	Cases (n = 400)	Controls I (n = 200)	Controls II (n = 200)	RR (95% CI)	P
Characteristics /% (N)					
Fresh vegetables, fruits					
several times every day	47% (188)	23% (46)	41% (82)	1,06 (0,76 – 1,48)	0,18
daily once a day	20% (80)	37% (74)	29% (58)	0,95 (0,67 – 1,36)	0,21
often several times a week	33% (132)	40% (80)	30% (60)	0,92 (0,65 – 1,29)	0,17
Preparation of dishes					
boiled / steamed	47% (188)	37% (74)	57% (114)	1,30 (0,92 – 1,84)	0,20
fried	20% (80)	30% (60)	18% (36)	1,38 (0,98 – 1,95)	0,55
baked	13% (52)	30% (60)	26% (52)	1,07 (0,74 – 1,56)	0,73
grilled	20% (80)	3% (6)	5% (10)	1,48 (0,76 – 2,87)	0,71
Fatty meals					
daily	87% (348)	54% (108)	51% (102)	1,53 (0,84 – 2,77)	0,01
a few times a week	7% (28)	31% (62)	33% (66)	1,45 (1,19 – 1,77)	0,41
several times a month	6% (24)	15% (30)	16% (32)	1,27 (1,03 – 1,56)	0,37
Consumption of salt					
< 6 g/day	11% (44)	7% (14)	27% (54)	1,07 (0,88 – 1,31)	0,91
> 6 g/day	89% (356)	93% (186)	73% (146)	1,16 (0,94 – 1,42)	0,01
Consumption of red meat					
< 80 g/ day or 500 g/week	13% (52)	46% (92)	66% (132)	1,77 (1,04 – 3,03)	0,82
> 80 g/ day or > 500g/week	87% (348)	54% (108)	34% (68)	2,28 (1,23 – 4,24)	0,01

Discussion

Colorectal cancer, cancer of the colon or rectum, is the third most frequent cancer in men and the second in women, and per the World Health Organization database GLOBOCAN, it accounts for about 1.4 million new diagnoses annually worldwide. The occurrence of colorectal cancer is associated with non-modifiable risk factors, including age and hereditary, and modifiable factors related to the environment and lifestyle [13, 14, 15].

Age is a main risk factor for sporadic CRC. Colorectal cancer is rare among patients younger than 40 years, the incidence increases significantly between 40 and 50 years, and incidence rates increase with each subsequent decade. In people over the age of 50 more than 90% of colorectal cancer cases occur. The incidence is over 50 times higher in people aged 60 to 79 than in people under 40 [15, 16]. The above data were confirmed by our research that shows that a clear peak of incidents occurred in the age groups of 56–66 (53%) and 67–77 (33%), which was emphasized by the results regarding the age of onset in the control groups. More recent data from SEER database suggest that the incidence of CRC is becoming higher in the age group under 50 and it is decreasing in older groups. The incidence of CRC in men and women under the age of 50 in the United States continued to increase at a rate of 2% annually from 1995 to 2016. Registries show an increased incidence of CRC among young adults aged 20–39 years, although the total number of cases in this age group remains significantly lower than that of adults aged 50 years and older [17–26]. Most cases of colorectal cancer occur in people with no family history of colorectal cancer or a predisposing disease, as our research confirms. Family history of cancer was not significantly associated with the risk of colorectal cancer. The incidence of neoplastic diseases in total concerned 47% of the subjects, colorectal neoplasms 15%, and colorectal polyps 8%, and these results were comparable to the results of the control groups. However, up to 30% of people who develop bowel cancer have other family members affected by the disease. People who have history of colorectal cancer or adenomatous polyps in first-degree relatives are at increased risk. About 5 to 10% of colorectal cancer cases are a consequence of known hereditary diseases, eg. familial adenomatous polyposis (FAP) and hereditary colorectal cancer (HNPCC) [15, 16].

Neoplastic colon polyps are precursors of colorectal cancer. The colorectal adenoma risk in the US population is almost 19%. Almost 95% of sporadic colorectal cancers develop as a result of these adenomas. A history of adenomas in a subject increases risk of developing colorectal cancer than patients who had no history of adenomas [15, 16]. Besides, patients with chronic inflammatory bowel disease have a doubled risk of developing CRC. The relative risk of colorectal cancer in IBD patients has been estimated from 4 to 20 times. Patients with ulcerative colitis are more likely to have CRC (HR (hazard ratio) 33.3, 95% CI (confidence interval): 23.1 to 49.1) than patients with Crohn's disease (HR = 5.8, 95% CI: 3.2–10.4) [27–36]. Our research confirms the above results. There was a strong positive association between the occurrence of ulcerative colitis and the risk of colorectal cancer. Compared to control groups, colorectal polyps (10%), ulcerative colitis (71%) and Crohn's disease (18%) were significantly more frequent among patients with colorectal cancer.

Colorectal cancer is considered to be an environmental disease involving cultural, social and lifestyle factors [15, 16]. Low socioeconomic status is linked to an increased risk of developing CRC. In a study by Doubeni et al., it was estimated that the risk of CRC increased by approximately 30% in the lowest socioeconomic status quintile compared to the highest. The overall incidence of CRC was clearly higher among those with low educational attainment or living in low socioeconomic districts [37, 38]. Very similar results were obtained by Kawakatsu et al., who showed that lower socioeconomic status was associated with an increased risk of

gastrointestinal cancer. Compared to people with lower education, people with higher education had a statistically significantly lower risk of developing colorectal cancer 0.52 (0.38–0.71) [39]. Our research confirmed the above results. Colorectal cancer mainly affected people with vocational (43%) or primary (27%) education and with an unsatisfactory economic situation. The differences were significant compared to the control groups.

Possibly modifiable factors such as lack of physical activity and healthy diet, smoking and obesity are thought to account for a significant part (30–50%) of the socioeconomic imbalance in the risk of developing CRC [37, 38, 40]. Diet strongly influences the risk of colorectal cancer. A diet high in fat, especially animal fats, high-temperature meal preparation, red meat, and diets low in fruit and vegetables are major risk factors for colorectal cancer [15, 16]. In 2015, the International Agency for Research on Cancer of the World Health Organization (IARC) studied the evidence linking the consumption of red and processed meat to CRC and classified the consumption of processed meat as carcinogenic to humans and the consumption of red meat as possibly carcinogenic. This was echoed in the 2020 report. In 2018, the World Cancer Research Fund / American Institute for Cancer Research (WCRF / AICR) also concluded that evidence was convincing that consumption of processed meat increased the risk of CRC, while the evidence of the consumption of unprocessed red meat was classified as probable. It has been estimated that for every 50 grams of processed meat consumed daily, the risk of developing CRC increases by about 16%, and for every 100 grams of red meat consumed daily, it increases by about 12%. For colon cancer, these estimates were 23% and 22%, respectively [41, 42]. Prospective studies have shown a relative risk (RR) of 1.22 among those who eat the most red and processed meats [43]. A meta-analysis of 60 studies found that consumption of red meat and processed meat increased the overall risk of developing CRC. The CRC with red meat consumption was 1.12 (95% CI: 1.03–1.21), and the RR with processed meat consumption was 1.15 (95% CI: 1.07–1.24) [44]. While red meat is rich in fats and inflammatory substances such as omega-6, most carcinogens likely come from high-temperature cooking, curing, and smoking [45]. Our research found no significant correlation between fruit and vegetable consumption and the way food was prepared. However, as many as 87% of patients declared daily consumption of fat in the diet. There was an association between higher fat consumption and higher red meat consumption and the risk of developing colorectal cancer ($p = 0.01$).

Both obesity and lack of exercise are the most important behavioural factors in the development of colorectal cancer, and a sedentary lifestyle has been proposed as an independent risk factor in colorectal carcinogenesis. Studies have shown that people with the most sedentary lifestyles have up to a 50% higher risk of developing CRC. Obese men have been found to have a 50% greater risk of colon cancer and a 20% greater risk of rectal cancer [27, 46]. A meta-analysis of 13 cohort studies showed that a 5 kg increase in body weight was associated with a 3% increase in the risk of CRC [44]. In a recent evaluation of observational studies on body obesity and cancer risk, the International Agency for Research on Cancer reported a 30% increased likelihood of developing CRC in those with the highest BMI compared to the lowest [47]. A recent meta-analysis of prospective studies showed a 47% increase in the risk of colon cancer and a 15% increase in rectal cancer, comparing the highest BMI category with the lowest [48]. An analysis by Nunez et al. showed that the group with the highest BMI was associated with an increased risk of colon cancer [49]. Our studies showed that increasing BMI was associated with an increased risk of colorectal cancer ($p = 0.01$). Among obese subjects, the risk of developing colorectal cancer was 1.27 (95% CI, 1.06–1.53) compared with non-obese subjects. Of the patients, 29% did not meet the guidelines for moderate physical activity and spent more hours per day sitting in a class.

In 2009, the IARC concluded that smoking does cause colon cancer. It has been found that the relative risk of CRC with regular smoking is 1.18 [27]. A recent meta-analysis of 14 prospective cohort studies found that prior (HR = 1.12; 95% CI: 1.04–1.20) and current smoking (HR = 1.29, 95% CI: 1.04–1.60) were associated with a worse prognosis in CRC compared to non-smokers and smokers [50]. In a meta-analysis of 106 observational studies, it was estimated that the risk of CRC was increased among cigarette smokers compared to those who had never smoked (RR 1.18, 95% CI 1.11–1.25) [51]. The risk of dying from CRC was also increased among smokers (RR 1.25, 95% CI 1.14–1.37). In both morbidity and mortality, the relationship was stronger in rectal cancer than in colon cancer [52]. In our research, patients and control group I was significantly more often smokers ($p < 0.0001$), and those groups started smoking at an early age ($p = 0.03$) significantly more often.

As with smoking, regular consumption of alcohol may be associated with an increased risk of developing colorectal cancer [15]. People who drink 2–3 alcoholic drinks a day have a 20% higher risk of developing CRC, while those who drink 2–3 drinks a day have this risk increased to 40% [27]. Several studies have found an association between alcohol consumption and an increased risk of CRC. A meta-analysis of 27 cohort studies and 34 case-control studies found that compared to those who never drank, there was a significant increase in the risk of CRC for moderate (two to three drinks a day RR 1.21, 95% CI 1.13–1.28) and heavy drinkers (≥ 4 drinks a day, RR 1.52, 95% CI 1.27–1.81) but not light drinkers (≤ 1 drink a day, RR 1.00, 95% CI 0, 95–1.05) [53]. These results are consistent with other summary analyses [54–56]. However, contrary to previous studies, the dose-response analysis showed a significant 7% increase in the risk of CRC even in light drinkers (RR with 10 g / day ethanol consumption 1.07 [95% CI 1.04–1.10] [57–59] Alcohol consumption was not significantly associated with the risk of colorectal cancer in our studies.

Our study explored the effect of exposure variables on colorectal cancer risk among patients diagnosed with cancer and linked the data to administrative data. The main strengths of this analysis are the use of two control groups in the study and a large number of all cases (n = 800). However, there are some limitations to consider. Exposure variables were derived from self-report, however BMI, physical activity was validated. Our research should be interpreted as exploratory.

Conclusions

1. Much of the socioeconomic difference in the risk of developing colorectal cancer can be attributed to the higher incidence of adverse health behaviours in low-status populations and lower education levels.
2. Obesity, low physical activity, active and passive smoking, and high salt and red meat consumption have been associated with an increased risk of colorectal cancer. These findings provide further evidence of the importance of maintaining a healthy lifestyle.
3. The move from identifying theoretically avoidable causes of colorectal cancer to implementing prevention strategies depends on the determination of exposures deemed to be causally related to disease development.
4. This analysis confirms the importance of independently following strict guidelines for physical activity, achieving and maintaining a healthy BMI, and adhering to dietary recommendations.

Declarations

Funding: This study was supported by our own resources.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by The Bioethics Committee at the University of Rzeszow (Resolution No. 1/12/2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data are not publicly available due to privacy and ethical re-strictions. The data presented in this study may be available conditionally from the correspond-ing author.

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References

1. American Cancer Society. https://www.cancer.org (accessed on 8 November 2020).
2. Polish Oncology Union. http: //www.puo.pl (accessed on 7December 2020)
3. Cancer Statistics Center. https://cancerstatisticscenter.cancer.org (accessed on 22 December 2020).
4. International Agency for Research on Cancer, World Cancer Report 2020. https://www.iarc.fr (accessed on 21 December 2020).
5. US Department of Health and Human Services, US Department of Agriculture. 2015-2020 Dietary Guidelines for Americans. In: US Department of Health and Human Services, US Department of Agriculture, editors. 8th Edition ed. Washington DC, United States of America 2015.
6. World Cancer Researcg Fund. American Institute for Cancer Researcg. Analysing research on cancer prevention and survival. The cancer proces. 2018. https: //www.wcrf.org (accessed on 20 January 2021).
7. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66:683–91.
8. World Cancer Research Fund/American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. AICR, Washington 2018 (accessed on 10 January 2021).
9. World Cancer Research Fund/American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. AICR, Washington 2007 (accessed on 25 January 2021).
10. World Health Organization International Agency for Research on Cancer. Personal habits and indoor combustions. A review of human carcinogens. IARC Monogr. Eval. Carcinog. Risks Hum. 2012; 100: 1-538 (accessed on 20 January 2021).

11. World Health Organization International Agency for Research on Cancer, Smokeless tobacco and some tobacco-specific N-nitrosamines. IARC Monogr Eval Carcinog. Risks Hum. 2007; 89: 1-592 (accessed on 20 January 2021).
12. World Health Organization. Cancer. https: //www.who.int/en/news-room/fact-sheets/detail/cancer (accessed on 27 January 2021).
13. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–E86. doi: DOI: 10.1002 / ijc.29210.
14. Henley SJ, Ward EM, Scott S, et al. Annual report to the nation on the status of cancer, part I: National cancer statistics. Cancer 2020; 126:2225.
15. Haggar FA, Boushey RP. Colorectal Cancer Epidemiology: Incidence, Mortality, Survival, and Risk Factors. Clin Colon Rectal Surg. 2009 Nov; 22(4): 191–197. doi: 10.1055/s-0029-1242458.
16. Macrae FA, Goldberg RM, Savarese DMF. Colorectal cancer: Epidemiology, risk factors, and protective factors. https://www.uptodate.com/contents/colorectal-cancer-epidemiology-risk-factors-and-protective-factors.
17. Brenner DR, Heer E, Sutherland RL, et al. National Trends in Colorectal Cancer Incidence Among Older and Younger Adults in Canada. JAMA Netw Open 2019; 2:e198090.
18. Abualkhair WH, Zhou M, Ahnen D, et al. Trends in Incidence of Early-Onset Colorectal Cancer in the United States Among Those Approaching Screening Age. JAMA Netw Open 2020; 3:e1920407.
19. Meester RGS, Mannalithara A, Lansdorp-Vogelaar I, Ladabaum U. Trends in Incidence and Stage at Diagnosis of Colorectal Cancer in Adults Aged 40 Through 49 Years, 1975-2015. JAMA 2019; 321:1933.
20. Ward EM, Sherman RL, Henley SJ, et al. Annual Report to the Nation on the Status of Cancer, Featuring Cancer in Men and Women Age 20-49 Years. J Natl Cancer Inst 2019; 111:1279.
21. Montminy EM, Zhou M, Maniscalco L, et al. Contributions of Adenocarcinoma and Carcinoid Tumors to Early-Onset Colorectal Cancer Incidence Rates in the United States. Ann Intern Med 2021; 174:157.
22. Howren A, Sayre EC, Loree JM, et al. Trends in the incidence of young-onset colorectal cancer with a focus on years approaching screening age: A population-based longitudinal study. J Natl Cancer Inst 2021.
23. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin 2020; 70:145.
24. Singh KE, Taylor TH, Pan CG, et al. Colorectal Cancer Incidence Among Young Adults in California. J Adolesc Young Adult Oncol 2014; 3:176.
25. Tawadros PS, Paquette IM, Hanly AM, et al. Adenocarcinoma of the rectum in patients under age 40 is increasing: impact of signet-ring cell histology. Dis Colon Rectum 2015; 58:474.
26. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal Cancer Incidence Patterns in the United States, 1974-2013. J Natl Cancer Inst 2017; 109.
27. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Gastroenterol.Review. 2019; 14(2): 89–103. doi: 10.5114/pg.2018.81072
28. Lutgens MW, van Oijen MG, van der Heijden GJ, Frank P Vleggaar, Peter D Siersema, Bas Oldenburg. Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. Inflamm Bowel Dis. 2013;19(4):789-99. DOI: 10.1097/MIB.0b013e31828029c0

29. Olen O, Askling J, Sachs MC, P Frumento 4, M Neovius 3, K E Smedby 3, A Ekbom 3, P Malmborg 5 6, J F Ludvigsson 7 8 9 10. Childhood onset inflammatory bowel disease and risk of cancer: a Swedish nationwide cohort study 1964-2014. BMJ 2017 Sep 20;358:j3951. doi: 10.1136/bmj.j3951.
30. Jenkins MA, Dowty JG, Ait Ouakrim D, et al. Short-term risk of colorectal cancer in individuals with lynch syndrome: a meta-analysis. J Clin Oncol 2015; 33:326.
31. Møller P, Seppälä TT, Bernstein I, et al. Cancer risk and survival in path_MMR carriers by gene and gender up to 75 years of age: a report from the Prospective Lynch Syndrome Database. Gut 2018; 67:1306.
32. Oh M, McBride A, Yun S, et al. BRCA1 and BRCA2 Gene Mutations and Colorectal Cancer Risk: Systematic Review and Meta-analysis. J Natl Cancer Inst 2018; 110:1178.
33. Katona BW, Stadler ZK, Robson ME, Domchek SM. RE: BRCA1 and BRCA2 Gene Mutations and Colorectal Cancer Risk: Systematic Review and Meta-analysis. J Natl Cancer Inst 2019; 111:522.
34. Cullinane CM, Creavin B, O'Connell EP, et al. Risk of colorectal cancer associated with BRCA1 and/or BRCA2 mutation carriers: systematic review and meta-analysis. Br J Surg 2020; 107:951.
35. Ng SC, Lau JY, Chan FK, et al. Risk of Advanced Adenomas in Siblings of Individuals With Advanced Adenomas: A Cross-Sectional Study. Gastroenterology 2016; 150:608.
36. Olén O, Erichsen R, Sachs MC, et al. Colorectal cancer in ulcerative colitis: a Scandinavian population-based cohort study. Lancet 2020; 395:123.
37. Doubeni CA, Laiyemo AO, Major JM, Schootman M, Lian M, Park Y, Graubard BI, Hollenbeck AR, Sinha R. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. Cancer 2012 Jul 15;118(14):3636-44. doi: 10.1002/cncr.26677.
38. Doubeni CA, Major JM, Laiyemo AO, et al. Contribution of behavioral risk factors and obesity to socioeconomic differences in colorectal cancer incidence. J Natl Cancer Inst 2012; 104:1353.
39. Kawakatsu Y, Koyanagi YN, Oze I, Kasugai Y, Morioka H, Yamaguchi R, et. al. Association between Socioeconomic Status and Digestive Tract Cancers: A Case-Control Study. Cancers (Basel) 2020 Nov 4;12(11):3258. doi: 10.3390/cancers12113258.
40. Klabunde CN, Cronin KA, Breen N, et al. Trends in colorectal cancer test use among vulnerable populations in the United States. Cancer Epidemiol Biomarkers Prev 2011; 20:1611.
41. Bouvard V, Loomis D, Guyton KZ, et al. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015; 16:1599.
42. World Cancer Report. Cancer research for cancer prevention. Available at: https://www.iccpportal.org/sites/default/files/resources/IARC%20World%20Cancer%20Report%202020.pdf (Accessed on April 27, 2020).
43. Gillessen S, Templeton A, Marra G, Kuo YF, Valtorta E, Shahinian VB. Risk of colorectal cancer in men on long-term androgen deprivation therapy for prostate Cancer. J Natl Cancer Inst 2010 Dec 1;102(23):1760-70. doi: 10.1093/jnci/djq419.
44. Karahalios A, Simpson JA, Baglietto L, MacInnis RJ, Hodge AM, Giles GG. Change in weight and waist circumference and risk of colorectal cancer: results from the Melbourne Collaborative Cohort Study. BMC Cancer 2016 Feb 25;16:157. doi: 10.1186/s12885-016-2144-1.

45. Robsahm TE, Bjarte A, Hjartåker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev 2013 Nov;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434.
46. Cong Y, Gan Y, Sun H, Deng J, Cao S, Xu X, Lu ZX.. Association of sedentary behaviour with colon and rectal cancer: a meta-analysis of observational studies. Br J Cancer. 2014;110(3):817–26. doi: 10.1038/bjc.2013.709.
47. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K. Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med 2016 Aug 25;375(8):794-8. doi: 10.1056/NEJMsr1606602.
48. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and Risk of Colorectal Cancer: A Systematic Review of Prospective Studies. PLOS ONE 2013; 8(1): e53916. doi.org/10.1371/journal.pone.0053916
49. Nunez C, Nair-Shalliker V, Egger S, Sitas F, Bauman A. Physical activity, obesity and sedentary behaviour and the risks of colon and rectal cancers in the 45 and up studyBMC Public Health (2018) 18:325. doi: 10.1186/s12889-018-5225-z.
50. Ordóñez-Mena JM, Walter V , Schöttker B, Jenab M, O'Doherty MG, Kee F. Impact of prediagnostic smoking and smoking cessation on colorectal cancer prognosis: a meta-analysis of individual patient data from cohorts within the CHANCES consortium. Ann Oncol 2018 Feb 1;29(2):472-483. doi: 10.1093/annonc/mdx761.
51. Botteri E, Iodice S, Bagnardi V, et al. Smoking and colorectal cancer: a meta-analysis. JAMA 2008; 300:2765.
52. Botteri E, Iodice S, Raimondi S, et al. Cigarette smoking and adenomatous polyps: a meta-analysis. Gastroenterology 2008; 134:388.
53. Fedirko V, Tramacere I, Bagnardi V, et al. Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. Ann Oncol 2011; 22:1958.
54. Cho E, Smith-Warner SA, Ritz J, et al. Alcohol intake and colorectal cancer: a pooled analysis of 8 cohort studies. Ann Intern Med 2004; 140:603.
55. Mizoue T, Inoue M, Wakai K, et al. Alcohol drinking and colorectal cancer in Japanese: a pooled analysis of results from five cohort studies. Am J Epidemiol 2008; 167:1397.
56. McNabb S, Harrison TA, Albanes D, et al. Meta-analysis of 16 studies of the association of alcohol with colorectal cancer. Int J Cancer 2020; 146:861.
57. Harnack L, Jacobs DR Jr, Nicodemus K, et al. Relationship of folate, vitamin B-6, vitamin B-12, and methionine intake to incidence of colorectal cancers. Nutr Cancer 2002; 43:152.
58. Giovannucci E, Rimm EB, Ascherio A, et al. Alcohol, low-methionine--low-folate diets, and risk of colon cancer in men. J Natl Cancer Inst 1995; 87:265.
59. Nguyen LH, Liu PH, Zheng X, Keum NN, Zong X, Li X, Wu K. Sedentary Behaviors, TV Viewing Time, and Risk of Young-Onset Colorectal Cancer. JNCI Cancer Spectrum 2018, 2(4), pky073. doi.org/10.1093/jncics/pky073.