ORIGINAL PAPERS

Adv Clin Exp Med 2010, **19**, 6, 723–730
ISSN 1230-025X

Hady R. Hady, Fabian A. Kamiński, Maria Sołdatow, Magdalena E. Łuba, Jadwiga Snarska, Jerzy R. Ładny, Jacek W. Dadan

Risk Factors for Large Intestine Cancer in Clinical Material

Czynniki ryzyka nowotworów jelita grubego w materiale klinicznym

University Hospital in Bialystok, 1st Department of General and Endocrinological Surgery, Białystok, Poland

Abstract

Background. Large intestine cancers are a huge prognostic, diagnostic and therapeutic problem, both in highly developed and developing countries, and their pathogenesis still remains unexplained. Many epidemiological and environmental factors are responsible for the inception and development of cancer of the large intestine.
Objectives, Material and Methods. The aim of the work was to present the cases of large bowel cancer from among 14,543 patients hospitalized in the 1st Department of General and Endocrinological Surgery of the Medical University of Bialystok, Poland, from 1999 to 2008, and to identify the risk factors for large bowel cancer.
Results. Between 1999 and 2008, 14,543 patients aged from 17 to 92 years old were hospitalized in this Department. This group included 704 patients (4.8%) with bowel tumors. Precancerous conditions including polyps and non-specific bowel inflammations were observed in 498 patients (3.4% of the whole group).
Conclusions. Large intestinal tumors frequently coexist with various environmental factors, such as the place of residence, diet and level of physical activity, and with epidemiological factors. Benign tumors and non-specific large intestine inflammations are currently the most important precancerous lesions **(Adv Clin Exp Med 2010, 19, 6, 723–730)**.

Key words: large intestine cancer, epidemiology, risk factors.

Streszczenie

Wprowadzenie. Nowotwory jelita grubego pozostają dużym problemem prognostycznym, diagnostycznym i leczniczym w naszych czasach, zarówno w krajach wysoko, jak i nisko cywilizowanych, a ich patogeneza w dalszym ciągu pozostaje nie do końca wyjaśniona. Za powstanie i rozwój raka jelita grubego jest odpowiedzialnych wiele czynników epidemiologicznych i środowiskowych.
Cel pracy, materiał i metody. Przedstawienie czynników ryzyka nowotworów jelita grubego w materiale klinicznym.
Wyniki. W latach 1999–2008 w I Klinice Chirurgii Ogólnej i Endokrynologicznej Uniwersytetu Medycznego w Białymstoku hospitalizowano 14543 pacjentów. W tej grupie znalazło się 704 (4,8%) chorych z nowotworami jelita grubego. Stany przedrakowe, do których zalicza się polipy i nieswoiste zapalenia jelita grubego zaobserwowano u 498 pacjentów, tj. 3,4% ogółu.
Wnioski. Nowotwory jelita grubego pozostają istotnym problemem diagnostycznym i leczniczym. Często współwystępują z różnymi czynnikami środowiskowymi, takimi jak miejsce zamieszkania, dieta, stopień aktywności fizycznej, oraz czynnikami epidemiologicznymi. Nowotwory łagodne oraz nieswoiste zapalenia jelita grubego pozostają obecnie najistotniejszymi stanami przedrakowymi **(Adv Clin Exp Med 2010, 19, 6, 723–730)**.

Słowa kluczowe: nowotwory jelita grubego, epidemiologia, czynniki ryzyka.

Bowel cancer is one of the main causes of tumors and deaths from cancer. Among the causes of death in Poland, it occupies third place among women (after breast cancer and cervical cancer) and the second place among men (after lung cancer). In 2004, it caused 11.3% of cancer deaths among men and 11.4% among women – almost 5000 men and 4300 women died due to this type of cancer [1].

According to the National Cancer Institute in the USA, it is anticipated that the level of mortality from large intestine cancer in the United States will increase from 510,000 in 2000 to about one mil-

lion in 2050 [2, 3]. The index of mortality in the United States and in Western Europe is 60%; in Poland it is considerably higher [4]. The time from diagnosis to death is longer for women. The five-year survival rate for patients with large intestine cancer in Poland is 30–33%; it is slightly higher than in case of rectum cancer and colon cancer. In Western European countries the five-year survival rates are as high as 50% [5].

It is estimated that in Poland approximately 11,000 cases of large intestine cancer are recognized per year, while in the United States about 160,000 cases are diagnosed per year. In Western European countries 137,000 new cases are noted annually, and in this group about 50% survive for five years. The average rate of increase in new cases in the Polish population is 2.5–3% annually. In 2005, the number of cases registered was 7000 men and 6000 women [7].

The frequency of cancer of the large intestine in the whole Polish population is 6%. The majority of cases are noted among men in Greater Poland, Western Pomerania and Lubuskie Province; among women the highest frequency of large intestine cancers is in Opole Province, Greater Poland and Silesia [1]. In recent years, some changes have been observed in cancer location, with a shift to the right half of the colon, making it necessary to diagnose the whole large intestine. In the United States, 35% of large intestine cancers are located in the sigmoid colon and rectum. In Poland, about 45% are located in the rectum, and about 35% in the sigmoid colon. Multiple tumors are discovered in about 3–5% of patients [1, 5].

In terms of pathomorphological classification, nearly 95% of large intestinal cancers are glandular cancers. The remaining 5% are squamous-cell cancers, mixed glandular-squamous-cell and undifferentiated and unclassified cancers. Thanks to early diagnosis and treatment, a significant reduction of mortality caused by cancers – including large intestine cancer – has been noted since the 1990s. Currently, worldwide large intestine cancer is recognized and treatment initiated in stages I–II of development in about 50–70% of patients, which has led to a long-term recovery rate of 60% [8]. In Poland, 60–70% of large intestine cancers are diagnosed and treated in stages III and IV, which is the reason of success in radical surgical treatment is only 20%.

About 75% of patients with cancer of the large intestine are people who have no known predisposition to develop the illness. The remaining 25% are patients at a higher risk than the average for the whole population [5].

Material and Methods

Between 1999 and 2008, 14,543 patients (aged 17–92 years; average age 48.5 years) were hospitalized in the 1st Department of General and Endocrinological Surgery of the Medical University of Bialystok, including 8554 women (58.8%) and 5989 men (41.2%). The majority of the patients originated from the city: 9652 (64.4% of the whole group), including 5687 women (59%) and 3963 men (41%); while 4888 of the patients (33.6%) lived in the country, including 2865 women (58.5%) and 2023 men (41.5%).

In this time period, 704 patients (4.8% of the patients hospitalized) were treated for malignant tumors; this group consisted of 296 women (42%) and 408 men (58%). Precancerous lesions including polyps and non-specific inflammations of the large intestine were observed in 498 patients (3.4% of the patients hospitalized). Polyps were present in 453 of the patients (3.1%), including 202 women (44.6%) and 251 men (55.4%) (Figure 1).

The locations where malignant tumors of the large intestine were most commonly diagnosed were the rectum (251 cases – 37.8%) and the sigmoid colon (225 cases – 32%). The remaining locations, in decreasing order, were the cecum and

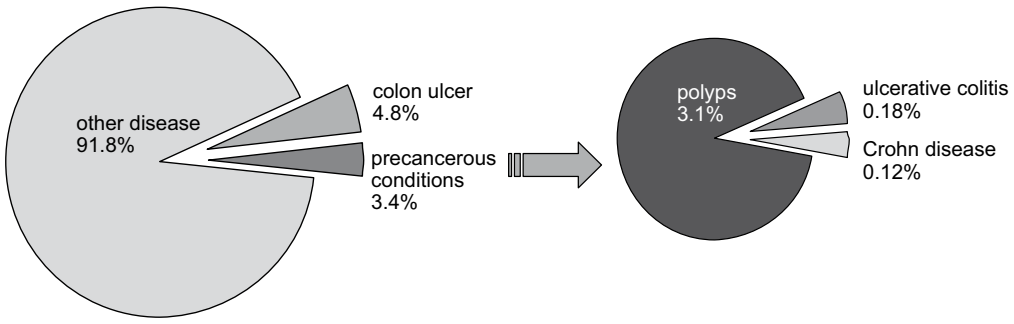

Fig. 1. Frequency rate of precancerous conditions and colon cancer in patients operated on from 1999 to 2008

Ryc. 1. Częstość występowania stanów przedrakowych i raka jelita grubego wśród pacjentów operowanych w latach 1999–2008

ascending colon (117 cases – 16.5%), the descending colon (52 cases – 7.5%), the transverse colon (23 cases – 3.25%) the left hepatic flexure (16 cases – 2.25%) and the hepatic flexure (12 cases – 1.75%); eight cases (1%) were multifocal. The locations of large intestinal polyps were similar: They were diagnosed most commonly in the sigmoid colon (116 cases – 25.5%) and in the rectum (112 cases – 24.8%). Multifocal polyps were observed in 108 cases (24%) cases, in the following locations: the cecum and ascending colon (51 cases – 11.3%), the descending colon (36 cases – 8%), the left hepatic flexure (14 cases – 3%), the transverse colon (11 cases – 2.5%) and the hepatic flexure (5 cases – 1%) (Figure 2).

Among the patients with malignant large intestinal tumors, the following coexisting illnesses were observed: cholecystolithiasis – 24 patients (3.4%); 19 patients (2.7%) had previously undergone a cholecystectomy; diabetes – 29 patients (4.1%); gastric adenocarcinoma – 3 patients (0.5%) patients; malignant kidney tumor – 2 patients (0.3%); and ovarian cancer – 2 patients (0.3%) patients. Among the patients with polyps, cholecystolithiasis was observed in 21 cases (4.6%); 8 patients (1.7%) patients had previously undergone a cholecystectomy; diabetes was noted in 5 patients (1.1%); and malignant kidney tumors in 2 patients (0.5%). Non-specific inflammation of the large intestine coexisted with the following disorders: cholecystolithiasis – 4 patients (8.8%); 2 patients (4.4%) had previously undergone a cholecystectomy; diabetes – 4 patients (8.8%); gastric adenocarcinoma – 1 patient (2.2%) (Table 1).

The frequency of large intestine cancer was related to the age of the patients in the studied group. There were 69 patients under 50 years old, constituting 10%. Patients between 50 and 70 years old suffered from malignant large intestine tumors the most frequently: 338 of the cases (48%). There were 297 patients over 70 years old (42%). The frequency of polyps was similar: The majority of cases (247 patients – 54.5%) were observed in patients between 50 and 70 years old; there were 110 cases in patients over 70 years old (24.3%); and 96 cases among patients under 50 years old (21.2%) (Figure 3).

In anamnesis, familial occurrence of malignant large intestine tumors was noted by 18 of the

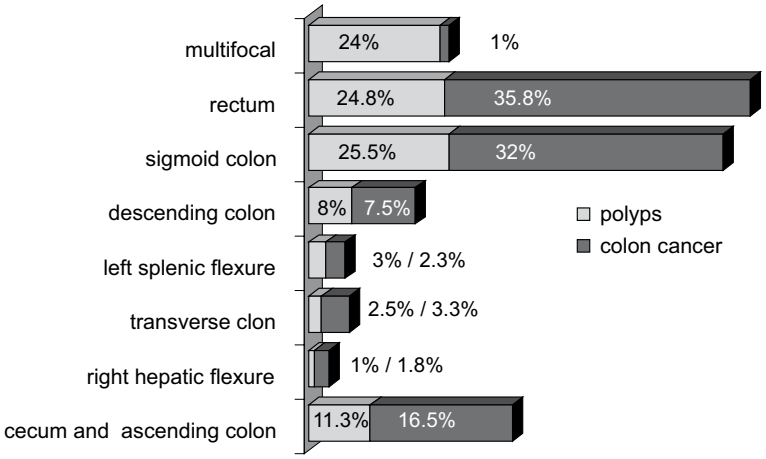

Fig. 2. Frequency rate of polyps and colon cancer by location in patients operated on from 1999 to 2008

Ryc. 2. Częstość występowania polipów i raka jelita grubego w zależności od umiejscowienia wśród pacjentów operowanych w latach 1999–2008

Table 1. Concomitant diseases of patients with precancerous conditions and colon cancer operated on from 1999 to 2008

Tabela 1. Choroby współistniejące u pacjentów ze stanami przedrakowymi i rakiem jelita grubego operowanych w latach 1999–2008

Concomitant diseases (Choroby współistniejące)	Colon cancer (Rak jelita grubego) N = 704	Polyps (Polipy) N = 453	Inflammatory bowel disease (Zespół jelita drażliwego) N = 45
Cholecystolithiasis (Kamica pęcherzyka żółciowego)	24 (3.4%)	21 (4.6%)	4 (8.8%)
Status post cholecystectomy (Stan po przebytej cholecystektomii)	19 (2.7%)	8 (1.7%)	2 (4.4%)
Diabetes (Cukrzyca)	29 (4.1%)	5 (1.1%)	4 (8.8%)
Gastric adenocarcinoma (Rak żołądka)	3 (0.5%)	0	1 (2.2%)
Renal carcinoma (Rak nerki)	2 (0.3%)	2 (0.9%)	0
Ovarian carcinoma (Rak jajnika)	2 (0.3%)	0	0

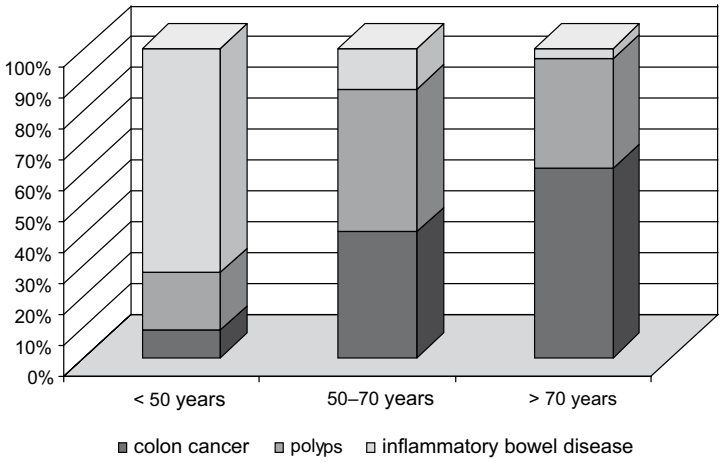

Fig. 3. Frequency rate of precancerous conditions and colon cancer in three age groups of patients operated on from 1999 to 2008

Ryc. 3. Częstość występowania stanów przedrakowch i raka jelita grubego w trzech grupach wiekowych pacjentów operowanych w latach 1999–2008

patients with large intestine cancer treated in the Department; 11 patients noted familial occurrence of polyps and 2 noted non-specific inflammation of the large intestine. This represented 2.6%, 1.6% and 4.4% respectively of the patients hospitalized for the diseases mentioned.

In the group studied, the majority of patients suffering from malignant large intestine tumors, i.e. 419 (59.5%), originated from the city, while 285 patients (40.5%) lived in the country. The presence of polyps was noted in 321 patients from the city (70.8%) and 132 from the country (29.2%); similarly inflammation of the large intestine most frequently affected patients from the city, i.e. 31 patients (68.8%) as compared to 14 patients living in the country (31.2%) (Table 2).

Among the patients with malignant large intestine tumors, 465 (66%) were diagnosed with overweight and obesity. Among the patients with large intestinal polyps, 261 (57.6%) were noted as overweight or obese.

In the group studied, non-specific inflammation of the large intestine was diagnosed in 45 patients (0.3%), among whom ulcerative colitis was differentiated in 27 patients (0.18% of the whole group of examined patients), including 16 women (60%) and 11 men (40%). Crohn's disease was noted in 18 patients (0.12%), including 8 women (44.5%) women and 10 men (55.5%) men. In these groups the majority of patients (37 – 82.3%) were under 50 years old; there were 7 patients (15.5%) between 50 and 70 years old and one patient over 70 years old (2.2%).

Among the cases of large intestine cancer, 162 patients (23%) admitted alcohol abuse and 188 (26.7%) were tobacco smokers. A high-fat diet was declared by 247 patients with malignant large intestine tumors, and 224 of these patients noted low fiber consumption. Similarly, in the group of patients with large intestinal polyps, 179 patients abused alcohol and 124 smoked tobacco; 169 patients had a high-fat diet and 151 had low fiber content in their diet. Among the patients with non-specific inflammation of the large intestine, 5 abused alcohol, 3 were tobacco smokers, 9 had a high fat diet and 9 had low fiber consumption. (Table 3).

Discussion

Large intestine cancers currently remain a huge prognostic, diagnostic and therapeutic problem, both in highly developed and developing coun-

Table 2. The influence of the place of residence on the frequency rate of precancerous conditions and colon cancer in patients operated on from 1999 to 2008

Tabela 2. Wpływ miejsca zamieszkania na częstość występowania stanów przedrakowych i raka jelita grubego wśród pacjentów operowanych w latach 1999–2008

Place of residence (Miejsce zamieszkania)	Colon cancer (Rak jelita grubego) N = 704	Polyps (Polipy) N = 453	Inflammatory bowel disease (Zespół jelita drażliwego) N = 45
Country (Kraj)	285 (40.5%)	132 (29.2%)	14 (31.2%)
City (Miasto)	419 (59.5%)	321 (70.8%)	31 (68.8%)

Table 3. The influence of diet and stimulants on the frequency rate of precancerous conditions and colon cancer in patients operated on from 1999 to 2008

Tabela 3. Wpływ diety i używek na częstość występowania stanów przedrakowych i raka jelita grubego wśród pacjentów operowanych w latach 1999–2008

Diet and stimulants (Dieta i używki)	Colon cancer (Rak jelita grubego) N = 704	Polyps (Polipy) N = 453	Inflammatory bowel disease (Zespół jelita drażliwego) N = 45
Alcohol (Alkohol)	162 (23%)	179 (39.5%)	5 (11%)
Smoking (Palenie tytoniu)	188 (26.7%)	124 (27.3%)	3 (6.6%)
High fat diet (Dieta wysokotłuszczowa)	247 (35%)	169 (37.3%)	9 (20%)
Low fibre diet (Dieta niskobiałkowa)	224 (31.8%)	151 (33.3%)	9 (20%)

tries. Their pathogenesis remains unexplained; for a long time scientists have tried to find and prove a relationship between various genetic, familial, environmental and dietetic factors and the possibility of developing cancer of the large intestine. Many factors are responsible for the inception and development of large intestine cancer, and they can be divided into four groups: epidemiological, intestinal, dietetic and mixed factors [9].

Among the epidemiological factors, age and genetic predisposition are of the highest importance. In both genders, morbidity and mortality increase in particular age groups, and the growth rate is faster in men. Among men with large intestine cancer, 62% of the cases occur in patients over 65 years old; respectively among women it was 66%. Mortality is 70% for men and 77% for women. The frequency decreases in both genders after age 75. The increasing mortality rate among men remains on the same level even after age 65, while among older women the rate of increase halts [1]. The peak morbidity falls in the eighth decade of life. The middle age range (45–64 years old) is alarming, particularly among men: Demises from cancer of the large intestine comprise one third of all deaths caused by cancers.

Genetic and familial predispositions are noted in less than half of all large intestine tumor incidents. Questions asked when taking a family case history are the basis for recognizing such predispositions. Hereditary predispositions can be acknowledged as highly possible in cases where large intestine cancer has occurred in several relatives in at least two generations; has been diagnosed before the patient is 40 years old, even where there is no known familial risk or has occurred simultaneously with other tumors, especially endometrial cancer [10].

Body mass, level of physical activity, geographical factors and level of education are of great importance as well. In the study group the majority of patients with malignant large intestine tumors originated from the city. Similarly, polyps and non-specific inflammation of the large intestine were found more frequently in the urban population. The lower frequency of diseases of the large intestine among the country-dwellers is probably connected with the character of agricultural work. A similar tendency was recorded by scientists from Johannesburg, South Africa [11]. In research provided in Maastricht, Netherlands, where undernutrition during the crisis in the 1930s and World War II has been taken into consideration, no differences were found in the frequency of large intestine cancer in patients from the city as compared with those from the country. Distinctly higher morbidity from large intestine cancer has been noted in patients that are overweight and have a high waist measurement [13, 14]. The relation between obesity and large intestine cancer could originate from the elevated levels of CRP, IL-6, and TNF alfa that can be observed in obese patients. Moreover, fat tissue is able to produce and release proinflammatory cytokines, which are carcinogenic [15, 16]. Obese patients are also at risk for more frequent occurrence of large intestinal polyps, which has also been noted by Bulgarian scientists [17].

It is estimated that a lack of physical activity is the main reason for 14% the cases of cancer of the large intestine in the USA. The results of research carried out in Finland, Norway, Denmark and Iceland do not confirm a protective role for physical activity, but simultaneously indicate a relationship between a sedentary work mode and more frequent occurrence of large intestine cancer [18];

the highest rate of incidence is observed in Northern Europe [19].

Intestinal risk factors include the occurrence of large intestine cancer among close (first-degree) relatives, without genetic considerations and hereditary genetically determined pathological syndromes leading to cancer development. Known mutations of strong predispositional genes are the main cause of about 3% of large intestine cancer incidents [1]. The most commonly recognized syndromes determined by known predispositional genes are Familial Adenomatous Polyposis (FAP) and Lynch syndrome, along with Gardner's syndrome, the Torre-Muir syndrome, FCC and Turcot's syndrome [20].

Other crucial intestinal risk factors for developing cancer of the large intestine are intestinal inflammatory conditions – ulcerative colitis, Crohn's disease [21] or granulomatous colitis, as well as a history of FAP or large intestine polyps especially villous adenoma. The majority of large intestine cancers originate from adenomatous changes, whose main and basic feature is epithelial dysplasia. About 30% of large intestine cancer cases have a hereditary factor in their pathogenesis. The most interesting is the fact that a tendency for developing polypoid adenomas occurs among patients suffering from acromegaly.

It is assumed that the risk of large intestine cancer with ulcerative colitis amounts to about 1–3% after a disease duration of ten years, and it is increasing annually by about 1–2%. The oncological risk is the basis for the necessity of periodic colonoscopy, which should be conducted once every two years during the first decade of the disease, and after that once per year. Similarly, with Crohn's disease the risk of large intestine evolution is 5–6 times higher [22, 23].

Dietetic factors are an important category of factors contributing to the incidence of cancer of the large intestine. High fat content – especially saturated fatty acid – in the diet, extensive consumption of red meat, detrimental substances created during the frying and smoking of food, low amounts of fiber in the diet and alcohol are recognized factors that increase the risk of developing large intestinal cancer [24, 25]. The type of alcohol is also not without significance; the role of hard liquors is acknowledged, while the role of milder alcohol, for instance beer, is still debatable [26, 27]. Besides alcohol, tobacco is a stimulant that elevates the risk of acquiring large intestine cancer [28–32]. The present study also confirms such observations.

The relationship between the risk of developing large intestine cancer and hyperinsulinemia is also worth highlighting. It is connected with the mitogenic effects that are caused by higher level of insulin in blood: An increased risk of cancer is related to the stimulation of IGF-1 and IGF-2 receptors. The hypothesis connecting hyperinsulinemia with large intestine cancer is based on the observation that many of the factors that cause hyperinsulinemia – mainly central obesity and a lack of physical activity – are related to the risk of developing cancer of the large intestine [33, 34].

Among the mixed risk factors for large intestine cancer are ureterosigmoidostomy, which increases the risk of developing large intestine cancer by about 500 times; undergoing cholecystectomy or radiotherapy, although this relationship varies in different geographical regions; and infection with the human papilloma virus, because cancer of the anal margin frequently evolves in association with venereal warts [35–37]. Cancers of the anal margin and canal are found relatively frequently in patients with acquired immune deficiency syndrome. Chronic inflammation is acknowledged as an important cause as well. A high plasma C-reactive protein concentration, the nonspecific inflammation marker, is connected with a higher risk of developing large intestine cancer [38–40]. It has been proved that chronic use of non-steroid anti-inflammatory drugs can decrease the risk of large intestine cancer by 50%, by impeding COX-2 [41, 42]. It has also been established that leucocytosis is the risk predictor for morbidity with this type of tumor [43].

The authors concluded that in spite of advances in medicine, large bowel cancers remain a huge diagnostic and therapeutic issue. Large intestinal tumors frequently coexist with different environmental factors, such as the place of residence, diet, the level of physical activity and epidemiological factors. The authors' observations and world data demonstrate a strict relationship between large bowel tumors and genetic predispositions. Benign tumors and non-specific inflammations of the large intestine currently remain the most important precancerous lesions.

References

[1] **Nowacki M, Bujko K, Krzakowski M, Nowakowska D, Rutkowski A:** Colon cancer. In: Diagnostic and therapeutic recommendations in malignant cancers treatment, Oncology in Clinical Practice, J Pol Clin Oncol Assoc tom 3, supl C, Krzakowski M, Herman K, Jassem J, Jędrzejczak W, Kowalczyk JR, Podolak-Dawidziak M, Reinfuss M, Via Medica Gdańsk 2007, 153–178.

[2] **DeVita VT, Hellman S, Rosenberg S: Cancer:** Principles Practice of Oncology Philadelphia, USA, 2005,7, 217–241.
[3] **Desch CE, Benson AB, Somerfield MR:** Colorectal Cancer Surveillance: 2005 Update of American Society of Clinical Oncology Practice Guideline, J Clin Oncol 2005, 20, 8512–8519.
[4] **Maliszewski D, Jastrzębski T, Drucis T, Kopacz A:** Prognostic factors in colon cancer – what else can we add to the standard? Współcz Onkol 2008,12, 5, 212–216.
[5] **Kordek R, Jassem J, Krzakowski M, Jeziorski A:** Oncology. Students and doctors book. Via Medica Gdańsk, 2004, II, 119–123.
[6] **Pasz-Walczak G, Jesionek-Kupnicka D, Kubiak R, Kordek R:** Basic cancerogenesis mechanisms in colon cancer. Współcz Onkol 2004, 8, 6, 303–307.
[7] **Didkowska J, Wojciechowska U, Tarkowski W, Zatoński WA:** Malignant cancers in Poland in 2004. Oncology Center, Maria Skłodowskiej-Curie Institute, Warsaw 2006.
[8] **Korniluk J, Wcisło G, Nurzyński P, Stec R, Bodnar L, Obrocka B, Szczylik C:** Epidemiology of colon cancer. Współcz Onkol 2006, 10, 136.
[9] **Lin OS:** Acquired risk factors for colorectal cancer. Methods Mol Biol 2009, 472, 361–372.
[10] **Maul JS, Burt RW, Cannon-Albright LA:** A Familial Component to Human Rectal Cancer, Independent of Colon Cancer Risk. Clin Gastroenterol Hepatol 2007, 5, 1080–1084.
[11] **Walker AR, Segal I:** Colorectal cancer in an African city population in transition. Eur J Cancer Prev 2002, 4, 11(2), 187–191.
[12] **Dirx MJ, van den Brandt PA, Goldbohm RA, Lumey LH:** Energy restriction early in life and colon carcinoma risk: results of The Netherlands Cohort Study after 7.3 years of follow-up. Cancer 2003 1, 97(1), 46–55.
[13] **Campbell PT, Jacobs ET, Ulrich CM, Figueiredo JC, Poynter JN, McLaughlin JR, Haile RW, Jacobs EJ, Newcomb PA, Potter JD, Le Marchand L, Green RC, Parfrey P, Younghusband HB, Cotterchio M, Gallinger S, Jenkins MA, Hopper JL, Baron JA, Thibodeau SN, Lindor NM, Limburg PJ, Martínez ME:** Case-Control Study of Overweight, Obesity, and Colorectal Cancer Risk, Overall and by Tumor Microsatellite Instability Status. Natl Cancer Inst 2010, 3, 17, 102(6), 391–400.
[14] **Máchová L, Cízek L, Horáková D, Koutná J, Lorenc J, Janoutová G, Janout V:** Association between obesity and cancer incidence in the population of the District Sumperk, Czech Republic. Onkologie 2007 Nov, 30(11), 538–542. Epub 2007 Nov 8.
[15] **Bradbury J:** A new predictor for colon cancer? Lancet Oncol 2004, 5, 3.
[16] **Marques-Vidal P, Ravasco P, Camilo ME:** Foodstuffs and colorectal cancer risk: A review. Clin Nutr 2006, 25, 14–36.
[17] **Kotzev I, Mirchev M, Manevska B, Ivanova I, Kaneva M:** Risk and protective factors for development of colorectal polyps and cancer (Bulgarian experience). Hepatogastroenterology 2008 Mar–Apr, 55(82–83), 381–387.
[18] **Pukkala E, Martinsen JI, Lynge E, Gunnarsdottir HK, Sparén P, Tryggvadottir L, Weiderpass E, Kjaerheim K:** Occupation and cancer – follow-up of 15 million people in five Nordic countries. Acta Oncol 2009, 48(5), 646–790.
[19] **Coups E, Hay J, Ford J:** Awareness of the role of physical activity in colon cancer prevention. Patient Educ Couns 72, 2008, 246–251.
[20] **Lynch P:** Standards of care in diagnosis and testing for hereditary colon cancer. Fam Cancer 2008, 7, 65–72.
[21] **Jankowski M, Zegarski W:** Crohn's disease and colon cancer. Współcz Onkol 2006, 10, 4, 160–163.
[22] **Freeman H:** Colorectal cancer risk in Crohn's disease. World J Gastroenterol 2008, March 28, 14 (12), 1810–1811.
[23] **Unkart JT, Anderson L, Li E:** Risk factors for surgical recurrence after ileocolic resection of Crohn's disease. Dis Colon Rectum 2008, 51, 1211–1216.
[24] **Bongaerts BW, van den Brandt PA, Goldbohm RA, de Goeij AF, Weijenberg MP:** Alcohol consumption, type of alcoholic beverage and risk of colorectal cancer at specific subsites. Int J Cancer 2008 Nov 15,123(10), 2411–2417.
[25] **Park JY, Mitrou PN, Dahm CC, Luben RN, Wareham NJ, Khaw KT, Rodwell SA:** Baseline alcohol consumption, type of alcoholic beverage and risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition – Norfolk study. Cancer Epidemiol 2009 Nov, 33(5), 347–354. Epub 2009 Nov 22.
[26] **La Vecchia C, Negri E, Franceschi S, D'Avanzo B:** Moderate beer consumption and the risk of colorectal cancer. Nutr Cancer 1993, 19(3), 303–306.
[27] **Enstrom JE:** Colorectal cancer and beer drinking. Br J Cancer 1977 May, 35(5), 674–683.
[28] **Lindor NM:** Alpha-1-antitrypsin deficiency and smoking as risk factors for mismatch repair deficient colorectal cancer: A study for the colon cancer family registry. Mol Genet Metab 99, 2010, 157–159.
[29] **Terry P, Ekbom A, Lichtenstein P, Feychting M, Wolk A:** Long-term tobacco smoking and colorectal cancer in a prospective cohort study. Int J Cancer 2001, 2,15, 91(4), 585–587.
[30] **Paskett ED, Reeves KW, Rohan TE, Allison MA, Williams CD, Messina CR, Whitlock E, Sato A, Hunt JR:** Association between cigarette smoking and colorectal cancer in the Women's Health Initiative. J Natl Cancer Inst 2007 Nov 21, 99(22), 1729–1735. Epub 2007 Nov 13.
[31] **Terry P, Ekbom A, Lichtenstein P, Feychting M, Wolk A:** Long-term tobacco smoking and colorectal cancer in a prospective cohort study. Int J Cancer. 2001 Feb 15, 91(4), 585–587.
[32] **Acott AA, Theus SA, Marchant-Miros KE, Mancino AT:** Association of tobacco and alcohol use with earlier development of colorectal cancer: should we modify screening guidelines? Am J Surg 2008 Dec, 196(6), 915–918.

[33] **Sahra IB, Le Marchand Brustel Y, Tnati J, Bost F:** Obesite et cancers du colon et de la prostate: implication des adipokines. Obes 2008, 3, 72–77.
[34] **Tripkovic I, Tripkovic A, Ivanisevic Z, Capkunc V, Zekanc L:** Insulin Increase in Colon Cancerogenesis: A Case-Control Study. Arch Med Res 35, 2004, 215–219.
[35] **Todoroki I, Friedman GD, Slattery ML, Potter JD, W Samowitz:** Cholecystectomy and the Risk of Colon Cancer. Am J Gastroenterol 94, 1, 1999.
[36] **Wilkes G, Hartshorn K:** Colon, Rectal and Anal Cancers. Semin Oncol Nurs 25, 1, 2009, 32–47.
[37] **Siddiqui AA, Kedika R, Mahgoub A, Patel M, Cipher DJ, Bapat V:** A previous cholecystectomy increases the risk of developing advanced adenomas of the colon. South Med J 2009 Nov, 102(11), 1111–1115.
[38] **Helzlsoner K, Erlinger T, Platz E:** C-reactive protein levels and subsequent cancer outcomes: Results from a prospective cohort study. Eur J Cancer 2006, 42, 704–707.
[39] **Zhang SM, Buring JE, Lee IM, Cook NR, Ridker PM:** C-reactive protein levels are not associated with increased risk for colorectal cancer in women. Ann Intern Med 2005, 142, 425–432.
[40] **Gunter MJ, Stolzenberg-Solomon R, Cross AJ, Leitzmann MF, Weinstein S, Wood RJ, Virtamo J, Taylor PR, Albanes D, Sinha R:** A prospective study of serum C-reactive protein and colorectal cancer risk in men. Cancer Res 2006, 66, 2483–2487.
[41] **Slattery ML, Curtin K, Wolff R, Ma KN, Sweeney C, Murtaugh M, Potter JD, Levin TR, Samowitz W:** PPARgamma and colon and rectal cancer: associations with specific tumor mutations, aspirin, ibuprofen and insulin-related genes. Cancer Causes Control 2006, 17, 239–249.
[42] **Harris R, Beebe-Donk J, Alshafie G:** Similar reductions in the risk of human colon cancer by selective and non-selective cyclooxygenase-2 inhibitors, BMC Cancer 2008, 8, 237.
[43] **Yong-Jae L, Hye-Ree L, Chung-Mo N, Ue-Kyoung H, Sun-Ha J:** White Blood Cell Count and the Risk of Colon Cancer. Yonsei Med J 47, 5, 2006, 646–656.

Address for correspondence:

Hady Razak Hady
University Hospital in Bialystok
1st Department of General and Endocrinological Surgery
M. Skłodowskiej-Curie 24 A
15-276 Białystok
Poland
Tel.: +4885 746 8672
E-mail: klchirog@umwb.edu.pl

Conflict of interest: None declared

Received: 26.08.2010
Revised: 29.10.2010
Accepted: 1.12.2010