Original article

Variability of clinical characteristic of colorectal cancer patients – analysis of selected parameters

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ABSTRACT

Introduction: A steady increase of the incidence of colorectal cancer has been observed for over 30 years, particularly in well-developed countries. Colorectal cancer is one of the lifestyle-related neoplasms and depends on environmental factors.

Aim: Aim of the study was to analyse selected clinical features of colorectal cancer patients.

Material and methods: The study group consisted of 577 consecutive patients with colorectal cancer treated in the Department of Clinical Oncology in Bytom in 2006–2014. The patients were included into the study prospectively. The analysis of selected clinical, pathological and anthropometrical parameters was conducted.

Results: The study group included 237 women and 341 men aged 26 to 86 years (mean age 64.3 ± 9.2 years). Primary tumours were mostly located in the colon and had histological grade 2. The surgical removal of the primary tumour was performed in 540 patients. 65 patients underwent preoperative radiotherapy, 201 – postoperative chemotherapy and 91 – postoperative radio-chemotherapy. 132 of patients obtained the first-line palliative chemotherapy. 88 of patients did not received oncological treatment. KRAS/RAS mutation were determined in 73 patients and the EGFR expression status in 53 patients.

Conclusions: Colorectal cancer patients are a heterogeneous group with differential clinical, pathological and molecular features.

1. Therapeutic management of patients with colorectal cancer largely depends on its location, clinical and pathological stage, patients performance status and comorbidities.

2. Understanding the clinical features of patients with colorectal cancer becomes helpful in designing of screening, which take into account clinical profile of the patient, i.e. age, gender, comorbidities and anthropometric characteristics.

Key words: colorectal cancer, clinical features, epidemiology

INTRODUCTION

Colorectal cancer (colorectal cancer) is one of the most frequent malignancies in the developed countries. The incidence of colorectal cancer in Poland has increased 4-fold in men and 3-fold in women during the last 35 years [1]. In 2015, colorectal cancer was the third most common malignancy in polish females (after breast and lung cancer) and in males (after lung and prostate cancer) [2]. The incidence of colon cancer is more frequent than rectal cancer. In Polish population in 2015, colon cancer represented 7.0% of new registered cancer in males and 6.2% in females, while rectal cancer 4.4% and 2.8% respectively [2]. Furthermore, colorectal cancer was the third cause of cancer-related deaths in women (11.3%) after lung cancer and breast cancer and the second cause in men (11.2%) after lung cancer [2].

In Europe, colorectal cancer is the most common malignancy. The incidence has increased from 376 000 in 2004 to 471 000 in 2012. Colorectal cancer is responsible for 12.3% of deaths from malignant neoplasms in Europe, taking the second position after lung cancer [3]. According to estimates of mortality for selected malignancies in six EU countries (France, Germany, Italy, Poland, Spain, United Kingdom) for 2018, the expected standardized mortality rate for colorectal cancer in Poland is the highest among the surveyed European countries (20/100,000) [4].

Tumours of the colorectal tract are a heterogeneous group varying in the clinical and molecular characteristic. The recommendations for the therapeutic management differs significantly between colon and rectum cancer. The right and left site of colon differ in terms of embryologic processes, microenvironmental and anatomical aspects, i.e. blood supply [5].

The pathogenesis of colorectal cancer is multidimensional. Most of colorectal cancer cases are sporadic and are determined by many factors. Approximately 10–15% of tumours are familial, related to i.e. Lynch syndrome and familial adenomatous polyposis (FAP) [4]. About 10–15% of patients with colorectal cancer have a family tendency unrelated to the aforementioned syndromes, defined as familial colorectal cancer (FCC) [6, 7]. Family occurring colorectal cancer is usually unidentified and not clinically important.

A number of risk factors for colorectal cancer were identified, including environmental, nutritional, genetic factors and the precancerous conditions. Environmental factors include i.a. age over 40 years, family history of colorectal cancer, endometrial cancer, breast, ovarian or prostate cancer. The increased risk of colorectal cancer is observed for people who are overweight, burdened with insulin resistance, diabetes and metabolic syndrome, as well as for the physical inactive persons and smokers. The confirmed risk factors are low-fibre diet rich in animal fats and red meat. Increased incidence of colorectal cancer is also indicated among patients diagnosed with inflammatory bowel diseases (Crohn's disease and ulcerative colitis) and previously treated for colorectal cancer. The risk increases with age and the highest incidence is observed around the age of 70 years. The increasing incidence of colorectal cancer in people younger than 50 has been observed in recent years [8–11], wherein the trend has been noted mainly in developed countries. The percentage of colorectal cancer cases diagnosed before the age of 50 in developed countries is 11–18%, and the growth rate of colorectal cancer diagnoses in this age group is higher than the overall increase in incidence in the general population [12].

Due to the high prevalence and good effect of treatment of early-diagnosed disease, colorectal cancer may be detected by screening programs. The best documented examinations associated with the decrease in mortality caused by colorectal cancer is colonoscopy and the faecal occult blood test. According to the ESMO recommendation, the faecal occult blood test should be performed once a year. On the other hand, NCCN recommends colonoscopy performed every 10 years as the only screening test [13, 14]. The results of a randomized clinical trial demonstrated that screening with the occult blood test reduces the risk of death from colorectal cancer by 25%. The effectiveness of colonoscopy as a screening test has been confirmed by Polish researchers in the study of more than 50 thousand people [15, 16].

Despite the fact that the risk factors for colorectal cancer are relatively well-known, the group of people who should be subject to more intensive screening has not been determined yet. The previous recommendations of international organizations are similar – it is widely accepted that screening (regardless of the method chosen) is carried in the group of people aged 50 to 65 years old, and in the case of family history of colorectal cancer – over the age of 40. Poland is one of four European countries, along with Germany, Italy and Luxembourg, where the program of colorectal cancer early detection is carried by colonoscopy [17].

The observed increase in the incidence of colorectal cancer leads to seeking of new treatment methods that may improve survival rates. It is essential to introduce both screening strategies, in order to improve the detection and implementation of early medical intervention, and the education and health promotion to exclude colorectal cancer risk factors. Distinction of risk groups associated with increased incidence of colorectal

cancer allows the successful planning of screening, and implementation of oncological vigilance and supervision in everyday medical practice.

AIM OF THE STUDY

Aim of the study was the analysis of clinical features of consecutive patients with colorectal cancer treated in the Department of Clinical Oncology in the years 2006–2014.

MATERIAL AND METHODS

The study group included 577 patients with colorectal cancer treated in the Department of Clinical Oncology of the Regional Specialised Hospital No. 4 in Bytom in the years 2006–2014. In all patients, the diagnosis of colorectal cancer was confirmed histologically on the basis of the tissue samples collected during colonoscopy and/or surgery. Patients were included into the study group prospectively, after initial visit in the Oncology Clinic or after the first admission to the Department of Clinical Oncology. The analysis of selected clinical, pathological and anthropometrical parameters was conducted. The data were analysed according to the location of the primary tumour (colon or rectum).

The considered data included: age at time of diagnosis, gender, weight, height and body mass index, the location of the primary tumour (colon, rectum), tumour histological grade, TNM stage according to the UICC/AJCC 2010 recommendation, the course of oncological treatment (radical treatment, palliative treatment or observation), haematological and biochemical parameters of blood and patients' comorbidities.

Medical history, anthropometric parameters and laboratory tests were assessed prior to oncological treatment implementation. The location of the primary tumour was based on the description of colonoscopy or surgical protocol. According to the current Polish Society of Clinical Oncology (PTOK), the rectal location was defined as tumours located in the section of the large intestine to a height of 15 cm from the anal verge.

Clinical stage was assessed on the basis of the report of histopathological examination and imaging studies. Histological grade (G1–G3, Gx) was determined by the pathomorphologist using routine testing of the samples collected during colonoscopy or surgery.

RESULTS

The study group included 237 (41%) women and 341 (59%) men aged 26 to 86 years (mean age 64.3 ± 9.2). The young patients, aged under 50, accounted for 10% all patients (n = 58). 139 patients (24%) were over 70 years old. The age distribution in the whole study group is presented in figure 1. The average age at diagnosis was 62.6 years in women (34.8–86.2 years) and 63.2 years among men (26.2–83.9 years). This difference is not statistically significant (p = 0.49).

FIGURE 1.
Age distribution in the study group.
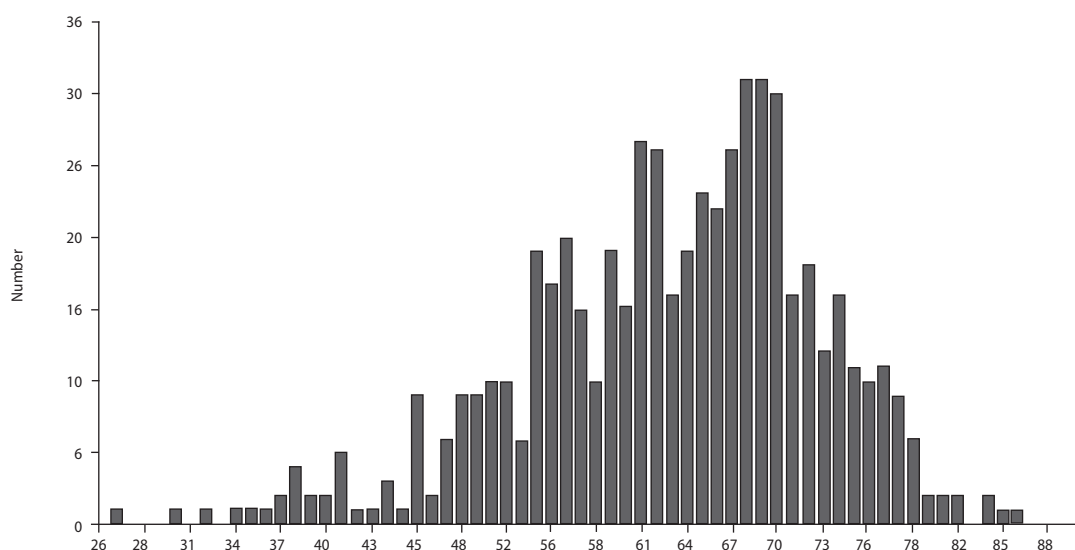
The primary tumour was located in the colon in 60% of patients. Colorectal cancer was the most commonly diagnosed in stage III and 60.3% of tumours were graded as 2 (G2).

The data on the primary tumour location, clinical stage, histological grade and of the implemented treatment are presented in table 1.

The surgical removal of the primary tumour was performed in 540 patients. The other patients underwent laparotomy without tumour removal or were not scheduled for surgery due to previously identified distant metastases and no evidence of bowel obstruction. 65 patients underwent preoperative radiotherapy, 201 – postoperative chemotherapy and 91 – postoperative radio-chemotherapy. 132 of patients obtained the first-line palliative chemotherapy. 88 of patients did not received oncological treatment, including patients who did not require adjuvant treatment due to the low disease advancement (72 patients; all patients with clinical stage I and some of patients with stage II) or patients not qualified for oncological treatment due to the unsatisfactory condition.

The assessment of KRAS/RAS mutation and the expression of membrane receptor for epidermal growth factor (EGFR) was evaluated in the group of selected patients using the tissue samples collected from the primary tumour. KRAS/RAS mutation were determined in 73 patients and the EGFR expression status – in 53 patients. Characteristics of the subgroup with the known RAS status is presented in table 2.

DISCUSSION

Therapeutic management of patients with colorectal cancer largely depends on its location and clinical and pathological stage. The differences in treatment of patients with colon and rectal cancer are a result of many factors, i.e. linked with embryologic development of colorectal tract and anatomical aspects conditioning treatment options.

Our results indicate that the average age of onset in the study group is around 65 years, which is confirmed by numerous epidemiological studies conducted in Poland and around the world [2, 18]. The largest group of 577 patients are individuals aged

TABLE 1.
Characteristics of the study group.

Feature		All patients (n = 577)	Women (n = 237)	Men (n = 340)
Primary tumour location	Colon	346	156	190
	Rectum	231	81	150
Histopathological grade	G1	62	23	38
	G2	348	132	216
	G3	85	44	41
	Gx	82	38	42
Clinical stage according to UICC guidelines 2010	I	62	27	34
	IIA–IIC	152	59	92
	IIIA–IIIC	220	95	125
	IVA–IVB	143	56	89
Type of oncological treatment	Curative treatment	357	161	214
	Palliative treatment	132	60	77
	Observation	88	42	49

TABLE 2.
Characteristics of patients with known RAS status.

Feature		Wild-type RAS (n = 50)	Mutant RAS (n = 23)
Gender	Women	20	9
	Men	30	14
Primary tumour location	Colon	27	10
	Rectum	23	4
Clinical stage according to UICC 2010	I	2	2
	IIA–IIC	6	2
	IIIA–IIIC	12	8
	IVA–IVB	30	11

61–70 years (235 patients, 89 women and 145 men). The second largest group are patients aged 51–60 years, the third one – over the age of 70 years. Patients under 50 years old represented 10% of the study group. Other authors confirm that the percentage of patients under 50 years of age is about 10%, and in the study carried by Schellerer et al. up to 12.4% in the whole group [19].

Colorectal cancer is the most often diagnosed in clinical stage III, which is associated with worse prognosis at the moment of diagnosis. In analysed population, 40% of women and 36.8% of men were diagnosed with colorectal cancer in stage III. They were the largest group. Similarly, in the study conducted by Chinese authors, colorectal cancer was most frequent diagnosed in stage III [20]. In European countries, Dukes' C colorectal cancer is diagnosed in 11% of patients, and Dukes' D – in 21%. The opposite results are noted in the US, where the Dukes' C tumours are diagnosed in 21% patients and Dukes' D – in 11%. This favourable tumours profile is associated with better outcome in these countries [18].

RAS gene status was determined in 73 patients in the study group. Determination of the status of RAS and EGFR gene was not a routine procedure – it is required in clinical practice before the qualification for treatment with panitumumab or cetuximab. KRAS mutation was found in 23 patients (31%). This incidence is similar with data for the Polish population – 40% [21]. RAS mutation is an unfavourable prognostic factor in colorectal cancer. Tumours with RAS gene mutation have more aggressive clinical course and are often associated with the resistance to traditional chemotherapy regimens [22].

CONCLUSIONS

1. Colorectal cancer patients are a heterogeneous group with differential clinical, pathological and molecular features.
2. Therapeutic management of patients with colorectal cancer largely depends on its location, clinical and pathological features.
3. Understanding the clinical features of patients with colorectal cancer becomes helpful in designing of screening, which take into account clinical profile of the patient, i.e. age, gender, comorbidities and anthropometric characteristics.

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