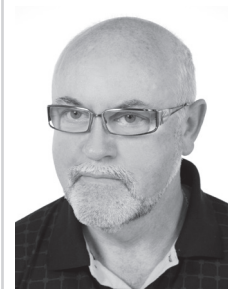


Analysis of 7965 screening colonoscopies and treatment results of detected colorectal cancers – experiences of one center

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ABSTRACT

Introduction: Colorectal cancer is one of the most common cancers in both sexes and is one of the leading causes of death in Poland and the world. An effective method to prevent the development of colorectal cancer (CRC) is the detection of polyps during a screening colonoscopy and their removal.

Objective: The aim of the study was to evaluate results of screening for early detection of colorectal cancer by colonoscopy.

Material and methods: The study was based on analysis of medical records of 7965 patients who underwent colonoscopy as part of the National Screening Program (NSP) for Early Detection of Colorectal Cancer in the 2000–2014 period.

Results: Polyps were removed in 2900 (36.4%) patients, among whom 1885 (23.6%) had adenomas, which were more frequent in men (32.9%). Tubular adenomas were observed in 1685 patients (21.1%), tubulo-villous adenomas were detected in 157 patients (2%) and villous adenomas – in 43 (0.5%) of them. Sixty-three (0.79%) colorectal cancers were detected in various clinical stages, including adenocarcinoma in situ in 3 patients. Probability of 5-year survival rate of colorectal cancer amounted to 74% while 10-years survival was reached in 63% of patients.

Conclusions: The detection rate of polyps, adenomas and carcinomas thanks to screening colonoscopy was 36.4%, 23.6% and 0.79% respectively, while the probability of 5-year survival was 74%. An improvement in the quality of colonoscopy was observed in subsequent years of the NSP, which translated into better detection of adenomas.

KEY WORDS: screening colonoscopy, colorectal cancer, National Screening Program for Early Detection of Colorectal Cancer

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INTRODUCTION

The incidence of colorectal cancer (CRC) is growing at an alarming rate, both in Poland and around the world. Every year, the disease is diagnosed in about 16 thousand Poles and 11 thousand people die for this reason every year [1]. It is estimated that in the next decade, the incidence will rise to about 25 thousand, which is primarily related to the aging population. It was noted that since 1980, the number of cases has increased three times in women and four times in men. Peak incidence occurs after the age of 50, with more than 75% of cases falling on the elderly population over 60 years old in both sexes. CRC is the fourth most common cause of death in the world (8%), with higher mortality observed among men [2].

Primary prophylaxis relies on prevention of the development of the disease by excluding external risk factors or by limiting the exposure to them. In contrast, secondary prevention primarily includes screening examinations, whose main objective is to reduce mortality through early detection and implementation of treatment. Therefore, it consists in detecting the disease in the early, asymptomatic stage, which allows for rapid and often complete recovery. The main cancer prognostic factor is the clinical stage at the time of diagnosis.

The aim of the national colonoscopy programs or screening examinations (SEP) under the CRC screening is early detection and identification of precancerous stages and implementation of appropriate preventive measures. The introduction of these programs has impact on mortality, probably due to the removal of precancerous changes, i.e. adenomatous polyps, during screening colonoscopy. In the USA, since 1998 the prevalence and mortality caused by CRC have been reduced by, respectively, 3% and 2.8% in men and 2.3% and 2.6% in women each year due to screening examinations [3].

SEP is aimed at individuals without clinical signs of disease in the age group 50–65 years old and involves performance of colonoscopy every 10 years. Also younger people are eligible, who are at least 40 years old and have at least one first-degree relative with diagnosed colorectal cancer [2]. Prof. Łukaszczyk Oncology Center in Bydgoszcz has participated in SEP since its inception, i.e. since 2000.

MATERIAL AND METHODS

Retrospective studies were carried out on the basis of the analysis of medical records of 7965 individuals qualified for the Screening Program for Early Detection of Colorectal Cancer

who underwent colonoscopy in the Department of Endoscopy at the Oncology Center in Bydgoszcz in the period from 2000 to 2014. Polyethylene glycol solution (Fortrans) was used to prepare the bowel for the examination in all patients. From 2000 to 2012, examinations were performed in the system of the so-called opportunistic program, and since 2013 – at the invitation. In the years 2000–2012, examinations were performed without the use of drugs or anesthesia, and in 2013–2014 about 20% of examinations were carried out with sedation and an anesthesiologist's involvement. The analysis includes examinations were repeated in cases of incomplete colonoscopy or procedures to remove large polyps performed in the hospital. Medical data were obtained from the SEP database and the hospital databases Med-Inf and CliniNET. The study started once it obtained the consent of the Bioethics Committee operating at the Medical College UMK in Bydgoszcz.

The descriptive analysis of the obtained results involved tables, which show the numbers as well as percentages. The mean and the standard deviation were calculated. Differences between variables were based on the chi-square test for cross tabulation. Student t-test was used for one variable by groups and non-parametric Mann-Whitney U test to assess differences in one characteristic between the two populations. Survival analysis, Kaplan-Meier curves test, and log-rank test were also used for comparative analysis. The null hypothesis (H₀ – there is no difference between groups) was adopted. Statistical significance was set at the level of $p \leq 0.05$. All calculations were performed using Microsoft Excel spreadsheet and Statistica 10.0.

RESULTS

1. The characteristics of screening examination

The number of performed colonoscopies depended on the agreement concluded with the Ministry of Health. The participation of women and men in studies in subsequent years has been on slight increase, with higher rates observed in women ($p < 0.001$) (tab. 1). Availability of the cecum ranged from 91.3% to 96.2% (mean 92.0%).

TABLE 1.

The number of screening colonoscopies in subsequent years.

Year	n/%	Woman (n/%)	Man (n/%)	p
2000	400/5.02	244/61	156/39	< 0.001
2001	250/3.14	156/62.4	94/37.6	< 0.001

2002	150/1.88	76/50.7	74/49.3	0.871
2003	600/7.53	365/60.8	235/39.2	< 0.001
2004	500/6.28	339/67.8	161/32.2	< 0.001
2005	600/7.53	375/62.5	225/37.5	< 0.001
2006	600/7.53	362/60.3	238/39.7	< 0.001
2007	500/6.28	317/63.4	183/36.6	< 0.001
2008	500/6.28	284/56.8	216/43.2	0.002
2009	300/3.77	160/53.3	140/46.7	0.249
2010	615/7.22	349/56.7	266/43.3	< 0.001
2011	950/11.93	569/59.9	381/40.1	< 0.001
2012	500/6.28	289/57.8	211/42.2	< 0.001
2013	1 000/12.55	476/47.6	524/52.4	0.129
2014	500/6.28	251/50.2	249/49.8	0.929
Total	7 965/100.0	4612/57.9	3353/42.1	< 0.001

2. Benign colorectal cancers in the screening examinations

The total number of polyps detected by 7965 colonoscopies amounted to 2900 (36.4%), including 1885 (23.6%) adenomas. The number of people who were found to have polyps in relation to the number of performed colonoscopies was increasing in subsequent years, reaching the highest rate of 50.8% in 2014 (tab. 2). Trajectories of polyps and adenomas detected during screening examinations are shown in Figure 1 and 2. The num-

ber of adenomas detected in the analyzed period increased both in women and men. The average detection rate in the analyzed period amounted to 17% in women and 32.9% in men (overall average 23.7%).

3. Colorectal cancer in screening examinations

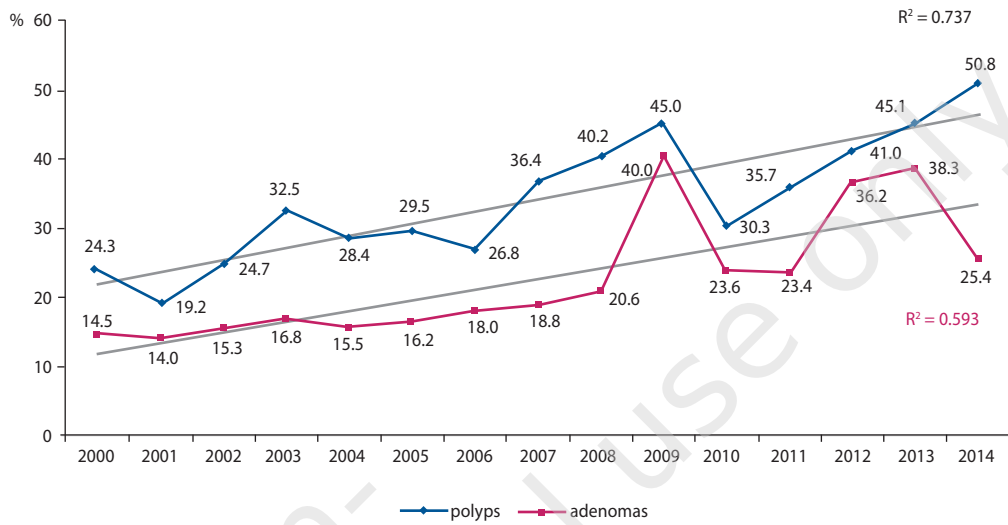
During the screening period from 2000 to 2014 cancer was detected in 63 patients (0.79%). Exceptionally, no cancer was detected in 2002, but only 150 colonoscopies were performed that year. Most of them, 12 (1.26%) cancers, were detected in 2011 during 950 examinations (tab. 3). The majority of cancers were located in the rectum – 34 (54%) and the sigmoid colon – 17 (27%), followed by the transverse colon – 5 (7.9%), ascending colon and caecum – 3 (4.8%) and the descending colon – 1 (1.6%) (tab. 4). Most patients – 15 (23.8%) – suffered from cancer in the clinical stage of T3N0M0, 12 (19%) of them had T2N0M0 stage cancer, 7 (11.1%) – T3N1M and 7 (11.1%) – T3N2M0 (tab. 5). Primary metastases was detected in 10 (15.9%) patients, including 6 patients with cancer located in the rectum, 2 in the sigmoid colon and next 2 in the caecum. Metastases in the liver were detected in 9 patients and additionally, 1 patient had metastases in the bone and the lung, and the another one had metastases in the brain. In one patient we found an isolated metastasis to the ovary.

TABLE 2.

The number of people with detected polyps and adenomas of the colon in subsequent years (n%)

Year	Number of examinations	Number of people with polyps n%	Tubular adenomas	Tubular-villous adenomas	Villous adenomas	Adenomas Total
2000	400	97/24.3	54/13.5	2/0.5	2/0.5	58/14.5
2001	250	48/19.2	33/13.2	2/0.8	0/0	35/14.0
2002	150	37/24.7	21/14	1/0.7	1/0.7	23/15.3
2003	600	195/32.5	89/14.8	10/1.7	2/0.3	101/16.8
2004	500	142/28.4	68/13.6	8/1.6	2/0.4	78/15.5
2005	600	177/29.5	85/14.2	7/1.2	5/0.8	97/16.2
2006	600	221/36.8	104/17.3	12/2	2/0.3	118/18.0
2007	500	182/36.4	86/17.2	4/0.8	4/0.8	94/18.8
2008	500	201/40.2	93/18.6	7/1.4	3/0.6	103/20.6
2009	300	135/45.0	105/35	14/4.7	1/0.3	120/40.0
2010	615	248/40.3	136/22.1	5/0.8	4/0.7	145/23.6
2011	950	339/35.7	199/20.9	21/2.2	2/0.2	222/23.4
2012	500	205/41.0	166/33.2	14/2.8	1/0.2	181/36.2
2013	1 000	451/45.1	339/33.9	35/3.5	9/0.9	383/38.3
2014	500	254/50.8	107/21.4	15/3	5/1	127/25.4
Total	7965	2900/36.4	1685/21.1	157/2.0	43/0.5	1885/23.6

FIGURE 1.
 Trajectories of polyps and adenomas detected during screening.



R² – coefficient of determination.

FIGURE 2.
 Trajectories of adenomas detected in the group of women and men during screening.

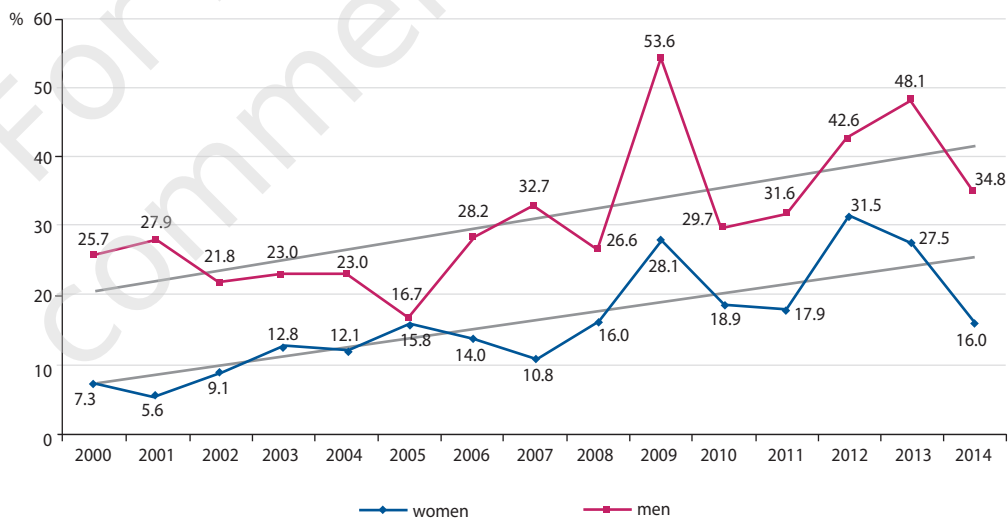


TABLE 3.
 Colon cancers detected in the screening examinations in years 2000–2014.

Years	Number of screening examinations	Cancers n/%
2000	400	1/0.25
2001	250	2/0.8
2002	150	0/0.0
2003	600	2/0.33
2004	500	4/0.8
2005	600	5/0.83
2006	600	6/1.0
2007	500	4/0.8

2008	500	7/1.4
2009	300	2/0.67
2010	615	5/0.81
2011	950	12/1.26
2012	500	6/1.2
2013	1 000	6/0.6
2014	500	1/0.2
Total	7 965	63/0.79

TABLE 4.

Localization of colon cancer.

Localization of cancer	n/%	Women n/%	Men n/%
Rectum	34/54	16/48.5	18/60
Sigmoid colon	17/27	11/33.3	6/20
Descending colon	1/1.6	1/3	0/0
Transverse colon	5/7.9	3/9.1	2/6.7
Ascending colon	3/4.8	2/6.1	1/3.3
Caecum	3/4.8	0/0	3/10
Total	63/100.0	33/100.0	30/100.0

TABLE 5.

TNM classification of colorectal cancers.

TNM Classification	n/%
T1N0M0	1/1.6
T1N1bM0	1/1.6
T2N0M0	12/19
T2N0M1	1/1.6
T2N1M1	1/1.6
T2N2M0	2/3.2
T2NxM0	2/3.2
T3N0M0	15/23.8
T3N0M1	1/1.6
T3N1M1	1/1.6
T3N1M0	7/11.1
T3N2M0	7/11.1
T3N2M1	2/3.2
T3NxM0	2/3.2
T3NxM1	2/3.2
T4N1aM1b	1/1.6
T4N1M0	1/1.6
T4NxM1b	1/1.6
TisN0M0	3/4.8
Total	63/100.0

TABLE 6.

The number of deaths from colon cancer depending on localization.

Cancer localization*	n/%	% in localization	Women n/%	Men n/%
Rectum	7/38.9	20.6	4/40.0	3/37.5
Sigmoid colon	4/22.2	23.5	2/20.0	2/25.0
Transvers colon	2/11.1	40.0	0/0.0	0/0.0
Ascending colon	3/16.7	100.0	2/20.0	0/0.0
Caecum	2/11.1	66.7	2/20.0	1/12.5
Total	18/100.0	28.6	0/0.0	2/25.0
p	0.03	X		0.15

4. Treatment of colorectal cancers detected in the screening examinations

Radical surgery was used in 58 (92.1%) patients, carcinomas in situ were removed during colonoscopy in 3 patients. Two rectal cancers were diagnosed at IV clinical stage, and both these patients received palliative radiotherapy combined with chemotherapy. Preoperative radiotherapy was the option for 14 out of 34 patients with rectal cancer. Postoperative radiotherapy was used in 8 patients: 2 patients had cancer in the sigmoid colon and 6 patients had rectal cancer. Preoperative chemotherapy was administered in only 2 (3.2%) patients with rectal cancer while 43 (68.3%) patients received postoperative chemotherapy. The recurrence after radical treatment of cancer was observed in 9 patients, including 3 patients with rectal cancer, 4 with sigmoid colon cancer, 1 with transverse colon cancer, and 1 with cancer located in the ascending colon. All patients (14.3%) with recurrent cancer underwent another surgery. Complementary postoperative radiotherapy was used in 3 patients with local recurrence. Adjuvant chemotherapy following surgery of recurrent cancer was administered in 5 patients, including 1 patient with cancer located in the rectum and 4 patients with cancer located in the sigmoid colon. Finally, generalization of the disease was observed in 15 (23.8%) patients, including 7 patients with cancer located in the rectum, 2 patients with cancer in the sigmoid colon, 2 with cancer in the caecum, 2 patients with cancer in the ascending colon and 2 patients with cancer in the transverse colon.

The follow-up colonoscopy was performed in 41 (65.1%) patients with diagnosed CRC, including 26 patients with rectal cancer, 13 patients with sigmoid colon cancer, and 2 patients with cancer in the transverse colon. In 48 (76.2%) patients, follow-up examination was performed regularly, among whom 28 patients were diagnosed with carcinoma in the rectum, 13 patients with sigmoid colon cancer, 3 with cancer in the transverse colon, 2 with cancer in the caecum, 1 patient with cancer in the ascending colon and 1 patient with cancer in the descending colon.

In years 2000–2014, 18 (28.6%) patients with diagnosed colorectal cancer in different locations died (tab. 6). The probability of survival was decreasing with time after the disease had been diagnosed and reached 74% after 5 years and 63% after 10 years (fig. 3).

There was no difference in the probability of survival between women and men with CRC detected during screening examinations ($p > 0.656$) and equaled 69% for women and 76% for men 5 years after the diagnosis (fig. 4).

FIGURE 3.
Survival probability in patients who were diagnosed with colorectal cancer during screening tests.

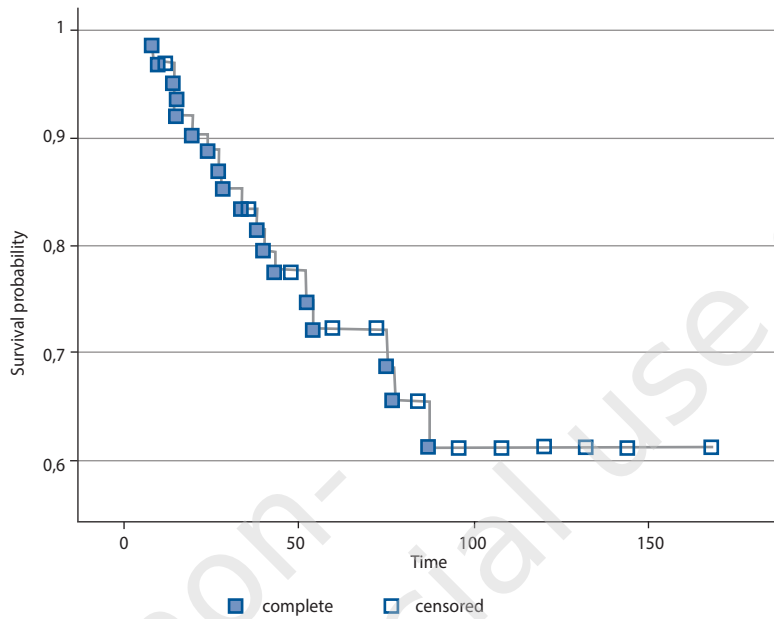
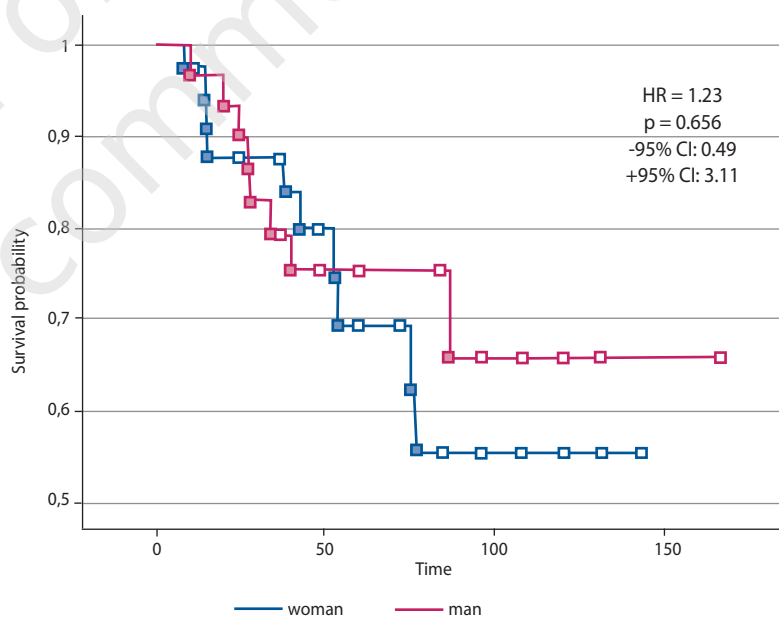


FIGURE 4.
Gender-related survival probability in patients who were diagnosed with colorectal cancer during screening tests.



DISCUSSION

Currently, colonoscopy performed every 10 years is the most effective method of prevention and early detection of CRC. This is confirmed by results of research conducted by a number of centers in the country and in the world [3–5, 7]. In Poland, since 2000, the National Screening Program for Early Detection of

Colorectal Cancer has been implemented and it is a pioneering program on a global scale [6, 7].

The aim of our study was to evaluate the effectiveness of screening examinations using colonoscopy in detecting cancers and precancerous lesions in the colon. During 15 years, screening

colonoscopy was performed in 7965 people, with more examinations conducted in women. During this period, we have also seen a greater overall participation in the Program, with a growing number of men [5–7]. This may indicate increasing awareness of Poles in this respect. It is likely that more examinations performed under the NSP will translate into reduction of the incidence of CRC as well as mortality due to early diagnosis and treatment in the future.

In our study, the tubular adenomas were most frequently observed among all detected polyps. Tubulo-villous and villous polyps were much more rarely found. The analysis does not take into account hyperplastic polyps and serrated adenomas. Adenomatous polyps were diagnosed in men more frequently. Conclusions from other research centers in Poland are similar [5, 6]. Adenomas are removed in every fifth person during screening colonoscopy. Considering their slow growth and transformation into invasive cancer lasting several or even a dozen years, removal of precursor lesions undoubtedly contributes to the reduction of morbidity and mortality from CRC.

Data from the cited centers, among others, reflect the analysis of data from coordinating center to a large extent, which gives a real picture of the obtained data on the basis of performance of screening colonoscopy in the Polish population. Analysis of colonoscopies conducted in Poland in the years 2000–2004 showed that the incidence of adenomas was at 14.1% for both sexes [7]. It has been shown that the incidence of adenomas is greater in men than in women (19.2% vs. 11.4%). These data are comparable with our results made in the same period.

Currently, quality control is a very important element of the NSP. Quality indicators for endoscopic examination of the lower gastrointestinal tract have been strictly defined, with the most frequently cited indicators being: frequency of detection of polyps (called Polyp Detection Rate – PDR), the rate of detection of adenomas (Adenoma Detection Rate – ADR) and the availability of the caecum (Caecal Intubation Rate – CIR) [5–9]. In the published guidelines, the frequency of reaching the caecum in the screening examinations should be at least 95% and the frequency of detection of adenomas should be at least 15% in women and at least 25% in men. In our material, in the subsequent years of the program, ADR significantly increased from 14% to over 30%. The increase in detection of adenomas may be the result of better and better training of doctors performing examinations, accurate viewing of the colon and prolonged withdrawal of the device from the caecum, a better cleansing of the colon for examination, using newer generation of endoscop-

ic equipment in the subsequent years and possibly, anesthesia. Monitoring of the quality indicators for colonoscopy by NSP coordinators seems to be the most important factor.

The results of screening colonoscopies in the United States and the Great Britain were compared in retrospective studies using meta-analysis. Again, there is a slightly higher percentage of women participating in the study. However, the detection of adenomas was about half higher than in our study. In this case, the study was carried out with the participation of people over the age of 65, while 65 years was the upper limit for the study in Poland [9]. Other European retrospective studies show a similar detection of carcinomas and adenomas like in our study, with a slightly higher number of women. Adenomas in male population were also detected more often; however, the participation of people at an older age, up to 75 years, and the incidence of CRC were higher [10].

In the analyzed period, we detected 63 cancers in the colon, in various stages of clinical advancement. In both sexes, rectum was the most common site of cancer. More than half of all detected cancers were located there. Half less cancers were located in the sigmoid colon; cancer in this area was detected in women about 50% more often while rectal cancer was detected more frequently in men. Other cancers, by frequency, were located mostly in the transverse and the ascending colon, with similar percentages in both sexes. Similar results were obtained in a German study covering the same number of colonoscopies, with a slightly smaller percentage of women [11].

In a Polish nationwide study on screening examinations in 2000–2004, colon cancer was detected in 416 people [7]. American studies carried out on a comparable number of participants, with a slightly higher share of men at the similar age, showed a five-fold fewer cases of cancer detected during a screening colonoscopy. Such a large difference compared to our study may be due to the fact, though probably not only, that since the late 80s, the American society has regularly participated in colonoscopic screening examinations. However, similarly to our study, mortality rate among patients diagnosed with cancer reached 25% [12]. Other studies show benefits of screening colonoscopy, based on analysis of the number of patients with CRC brought to the Massachusetts General Hospital, in whom surgery was necessary because of life threatening indications. Symptomatic cancers detected in this way have a better prognosis due to the smaller number of complications that accompany the surgery carried out in emergency conditions and probably due to lower clinical stage at the diagnosis [3]. Basing on meta-analyses,

German researchers indicate risk reduction of morbidity and mortality of CRC from the time of implementation of screening examinations by 40–60% [13]. This is undoubtedly another evidence speaking in favor of screening colonoscopy, which can detect cancer at an early stage.

Only a few patients had metastases detected at the time of diagnosis and liver was the most common place of their location. Radical surgical treatment was used in almost all patients. Palliative chemo-radiotherapy was used in only 2 people with cancer located in the rectum. Three carcinomas in situ were removed with a margin of healthy tissue during the colonoscopy. Pre- and postoperative chemotherapy and radiation therapy were administered in accordance with current standards for the treatment of tumors in a specific location and depending on the clinical stage according to the TNM classification. Pre- and postoperative radiotherapy was given to patients with rectal cancer in most cases. More than half of the patients received postoperative chemotherapy and these were mostly people suffering from cancer of the rectum or the sigmoid colon. This is consistent with current treatment guidelines applied in Poland and in the world [14]. Methods of adjuvant therapies depending on the location of the cancer demonstrate efficacy of preoperative radiotherapy and postoperative adjuvant chemotherapy to prevent metastasis to distant organs [13].

Recurrence after radical treatment was observed in a few patients; they underwent another surgery. Most patients from this group also received a chemotherapy, and radiotherapy was administered in less than half of them. Among patients with detected CRC, generalization of cancer occurred in almost one fifth of them and in the majority of cases they were patients with cancer located in the rectum. However, in the analysis conducted by other researchers, recurrence or generalization was noted in almost half of symptomatic patients with cancer after radical surgery, but as it has already been mentioned, they were not patients who underwent screening examination [16].

The vast majority of patients had regular follow-up examination and more than half of them had a control colonoscopy. Discussions on how postoperative intensive supervision should be conducted and whether it is necessary are still held in Poland and in the world [16]. However, as it is indicated by a group of experts, after analyzing randomized trials conducted by a team from Christchurch Hospital in New Zealand, regular follow-up examinations are justified, particularly in patients with a chance for recovery or long-term survival, in situation when early detection of the recurrence of the disease is possible [4]. In the analyzed period, a dozen or so patients died because of CRC

and most of them were women. Nevertheless, in the Polish epidemiological studies higher mortality is observed among men [1]. In Poland, mortality is higher for all diagnosed CRC compared to other European countries. However, in our study, the probability of five-years survival amounted to 74% for patients who were previously subjected to screening examination.

In the study group, there were no patients who would have another screening colonoscopy performed after 10 years (the need for further examination is questioned by some authors). Perhaps this is because of too short duration of the program or a change in the program system from “opportunistic” to “invited”, in which the coordinating center chooses a person to undergo screening colonoscopy using the Population Registry on the basis of personal numbers PESEL. In contrast, patients with diagnosed and removed polypoid changes were subject to colonoscopic supervision and the time of the examination depended on the type of removed change.

Our research shows that there is a probability of detecting one CRC in 126 colonoscopies, which is comparable to German studies, where one cancer is diagnosed in 121 colonoscopies [17].

In Poland, 5-year survival is still lower by 12%, compared with European Union countries, despite 15 years of the national screening program [18]. However, it is important to say that the rate of 5-year survival of Polish patients with colorectal cancer has increased on average from 44% to 48% in the last decade. On the other hand, compared with the United States, this rate is still low. In the USA, CRC survival amounted to 67% in 2002 [18]. However, it seems reasonable to continue the NSP for the early detection of CRC, taking into account the cost and benefits. Colonoscopy should cover the largest part of the population possible (currently at low reportability), since it is connected with tangible benefits for the health system as well as citizens themselves.

CONCLUSIONS

1. The detection rate of polyps, adenomas and cancers by screening colonoscopy is 36,4%, 23,7% and 0,79% respectively.
2. The probability of 5-years survival is 74% in patients undergoing screening colonoscopy.
3. The improvement in the quality of colonoscopy in subsequent years of the NSP translated into an increased detection rate of adenomas.

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Authors' contributions:

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Marzena Lemanowicz: 15%.