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# BODY MASS INDEX AS A PREDICTOR OF COLORECTAL CANCER

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## ABSTRACT

**INTRODUCTION.** Colorectal cancer is the second most common cancer in the world. Each year in Poland, 16 000 people are diagnosed with colorectal cancer and 9 000 patients die of it. Factors that may increase a chance of developing colorectal cancer include: male sex, advanced age, smoking, and positive family history of this condition. Recently, scientists have discovered that obesity also belongs to the group of risk factors. The present research aims at establishing whether there exists any relationship between BMI and colorectal cancer in Poland.
**METHODS.** This research is based on the analysis of the results of a clinical study conducted in the period from May 2011 to December 2014 in another group of 319 patients undergoing colonoscopy in the district hospital in Wejherowo. Colonoscopy results were compared between 136 patients with colorectal cancer and/or dysplastic polyps and 167 healthy patients.
**RESULTS.** The study revealed that the number of males, elderly people, and smokers was much bigger among patients with colon abnormalities than among healthy people. The multiple factor analysis demonstrates that the body mass index (BMI) was significantly higher among men and women diagnosed with colorectal cancer as compared to healthy patients. Both overweight (BMI reaching from 25.0 to 29.9 kg/m2) and obesity (BMI≥30 kg/m2) were independent risk factors associated with colorectal cancer.
**CONCLUSIONS.** An increased BMI should also be considered as an independent risk factor for colorectal cancer in the Polish population. This may indicate a need for conducting and increasing the frequency of colonoscopic examinations among patients with high BMI in Poland.

*Key words: colorectal cancer, colon polyps, BMI*

## INTRODUCTION

According to the Polish National Cancer Registry, around 16 200 new cases of colorectal cancer are diagnosed each year in Poland (including cancer both in the colon and rectum). In 2005, colorectal cancer affected almost 9 000 men and over 7 200 women. The death rates from this type of cancer are as follows: 5 900 men and 4 800 women. All this indicates that colorectal cancer is the second cause of cancer-related death among men and the third cause of cancer-related death among women (1, 2). In 2007, colorectal incidence rates for women and men were 16.6 and 29.4 per 100 000 respectively and mortality rates amounted to 9.7 (women) and 18.5 (men) per 100 000 (1). Furthermore, since 1995, these rates have significantly increased among men and reached a plateau among women (1). In Poland, colorectal cancer mortality rate for men is higher than the average mortality rate in the member states of the European Union (EU). It was 50% higher than the average level of colorectal cancer mortality for EU member states (according to statistical data from 2009). The number of deaths of women diagnosed with colorectal cancer is slightly bigger than the average mortality level in Europe. Moreover, Poland belongs to one of the few EU member states in which colorectal cancer mortality rate keeps increasing (2).

Most scientific studies show that highly processed foods, unhealthy lifestyle, and increased obesity rates are the major causes of colorectal cancer. Furthermore,

alcohol consumption, smoking, poor consumption of unsaturated fatty acids, high red meat consumption, low level of physical activity, and obesity are considered by many authors of scientific papers as risk factors for colorectal cancer (3, 4). Scientists have also developed prediction models for colorectal cancer incidence based on population studies, that is simple questionnaires asking about the level of BMI being one of possible risk factors for CRC (5). It has been also observed that the patients recovered from colorectal cancer are more likely to develop other types of obesity-related cancers than patients with a healthy weight who are diagnosed with CRC (6). The risk of developing other types of cancer is, however, similar to the risk of developing CRC among obese patients, which indicates that overweight or obesity rates keep increasing and that the level of susceptibility for metachronous cancers after colorectal cancer treatment is not higher when compared to general population.

Dysplastic adenomas of the colon are commonly classified as precancerous changes. Large and advanced adenomas often develop into cancers in the period from 5 to 10 years during the adenoma-adenocarcinoma sequence (7, 8). Even previous studies indicate a positive association between BMI and the risk of colorectal adenomas and colorectal cancer (9-11). The results of the studies were not always unambiguous. The relationship between obesity and colorectal cancer depended on sex and location of polyp in patients from other countries (12-14). Nevertheless, most available data was taken from Asia where the epidemiology of obesity and colorectal cancer is different from medical characteristics in European countries. In Poland, the data about obesity and colorectal cancer relationship is relatively small. Therefore, we decided to carry out the present research based on Polish clinical studies in order to estimate whether such an association really exists. In the study, we also focused on other risk factors for colorectal cancer including age, sex, alcohol consumption, and smoking.

## MATERIAL AND METHODS

The present research is based on a retrospective analysis of medical documents and charts of 319 patients who underwent colonoscopy in the Specialist Hospital in Wejherowo in the period from May 2011 to December 2014. In further stages of the said analysis, 16 patients were excluded because of incomplete data in their medical documentation and due to the lack of possibility to supplement the given data. The results of 116 patients diagnosed with CRC, the results of 20 patients with large dysplastic colorectal adenomas (exceeding 1 cm) were compared to colonoscopy results of healthy patients (n=167). The questionnaire (collecting the data about smoking history, family history of cancer and female hormonal history) that the patients were supposed to fill out on the day of colonoscopy served as the major source of medical information.

**Analysed data.** The analysed data included age, sex, smoking history, alcohol consumption, family history, height, weight, body mass, BMI, and final diagnosis. A current smoker can be defined as a person who smokes at least one cigarette per day for a period of 12 months prior to the examination. A former smoker is a person who has not been smoking for at least 12 months prior to the examination. Non-smokers are a group of people who have never smoked a single cigarette. Alcohol consumption is defined as drinking at least three times a week. The following data was collected on the basis of information provided by patients. A family history may be defined as positive if any first and/or second-degree relative have/has even been afflicted with colorectal cancer. A surgical nurse measured the patients' weight and height. BMI is described as a person's body mass (weight in kilograms) divided by the square of height (expressed in meters) (weight [kg]/height [m2]). BMI is used to classify three different categories in accordance with BMI classification proposed by WHO: normal range from 18.5 to 24.99 kg/m2, overweight from 25 to 29.99 kg/m2, and obesity ≥30,0 kg/m2 (14).

**Statistical methods**.The present research relies on basic methods of descriptive statistics for BMI results of patients from both groups. The average results of a student's t-test used for arithmetic data were compared with the results of a Mann-Whitney test for medians. A ROC (Receiver Operating Characteristics) curve estimated the precision of BMI considered as a risk factor for colorectal cancer and determined a cut-off point. The area under the ROC curve for BMI was measured (based on numerical integration and Wilcoxon signed-rank test). Logistic regression was used to assess the relation between BMI and a risk of developing colorectal cancer on the basis of age, sex, family history, alcohol consumption, and smoking history. Patients suffering from underweight and second-degree obesity were excluded from this analysis because their number was too small, that is limited to four and ten respectively. A multiple logistic regression included variables for which $p<0,2$ in the single factor analysis. A $p$ value below 0,05 was considered as statistically significant.

All statistical calculations were performed in Microsoft Excel 2003 and STATA 11.0. The head of F. Ceynowa Specialist Hospital in Wejherowo and the members of the Bioethics Committee of the Regional Medical Chamber in Gdańsk consented to carry out the said study provided that the prepared database of the study group was fully anonymous.

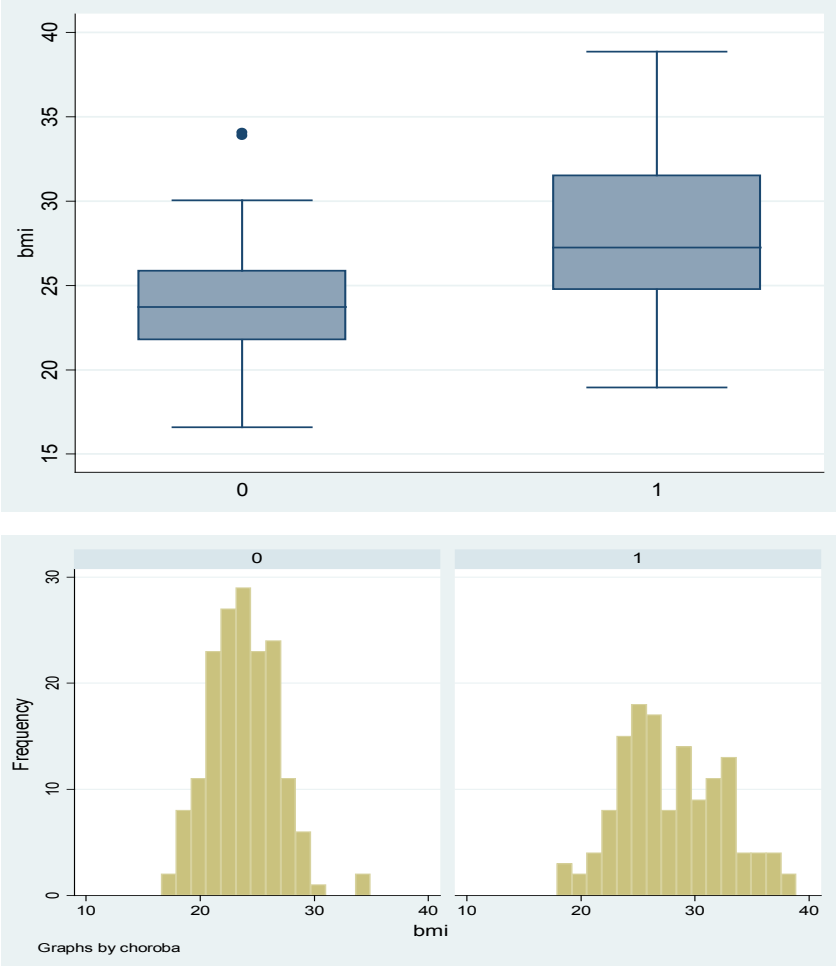


Fig. 1. Summary of BMI in the population of patients and healthy controls

## RESULTS

Table 1 presents the characteristics of patients who underwent colonoscopy. In the group of patients diagnosed with colon abnormalities, the average age of male patients, people with positive family history of colorectal cancer and positive smoking history was statistically higher than in the group of healthy people (Tab. I). BMI level was also 4.18 kg/m2 higher in the group of patients afflicted with colon abnormalities when compared to healthy people (Fig. 1). BMI ranges for each study group are pictured in Table 2. The variables shown above were taken into consideration in the subsequent multiple factor analysis of logistic regression.

Table I. Characteristics of the study population

| variables | control group | polyps and colorectal cancer | P value |
|---|---|---|---|
| **size** | 167 | 136 | |
| **age (years)** | 59.8 ± 7.7 | 64.8 ± 8.77 | <0.001 |
| **gender (male)** | 74 (44.3%) | 77 (66.3%) | <0.001 |
| **positive cancer family history** | 6 (3.6%) | 18 (15.5%) | <0.001 |
| **alcohol consumption** | 18 (10.7%) | 13 (11.2%) | >0.05 |
| **smoking** | 31 (18.5%) | 62 (53.4%) | <0.001 |
| **BMI (kg/m²)** | 23.8 ± 2.95 | 27,98 ± 4,43 | <0.001 |

Table II. Summary of BMI in the population of cancer patients and healthy

| | study group | | control group | |
|---|---|---|---|---|
| | number of patients | percentage of patients | number of patients | percentage of patients |
| **underweight** | 0 | 0% | 4 | 2.4% |
| **norm** | 35 | 25.74% | 112 | 67.07% |
| **overweight** | 58 | 42.65% | 48 | 28.74% |
| **obesity I degree** | 33 | 24.26% | 3 | 1.8% |
| **obesity II degree** | 10 | 7.35% | 0 | 0% |
| **summary** | 136 | 100% | 167 | 100% |

The analysis of sex subgroups reveals significant differences in BMI levels between a control group and a group of patients with colorectal cancer both in men and women (Tab. III). The distribution of BMI was similar in both groups.

The outcomes of the single factor logistic regression demonstrate that a chance of developing adenomas

Table III. Clinical characteristics of patients by gender

| variable | total | | | men | | | women | | |
|---|---|---|---|---|---|---|---|---|---|
| | control group | polyps and colorectal cancer | P*-value | control group | polyps and colorectal cancer | P*-value | control group | polyps and colorectal cancer | P*-value |
| **population** | 167 | 136 | | 77 | 62 | | 90 | 74 | |
| **age (years)** | 59.8±7.69 | 64.±8.76 | <0.001 | 60.3±7.9 | 65.3±7.6 | <0.001 | 50.9±11.6 | 60.1±10.6 | <0.001 |
| **place of residence (town)** | 58 (34.7%) | 45 (33.1%) | 0.76 | 25 (32,4%) | 20 (32,2%) | 0,74 | 33 (33.3%) | 25 (33.7%) | 0.95 |
| **alcohol consumption** | 18 (10.7%) | 15 (11.0%) | 0.92 | 8 (10.4%) | 5 (8.1%) | 0.14 | 10 (11.1%) | 10 (13.5%) | 0.08 |
| **positive cancer family history** | 6 (3.6%) | 20 (14.7%) | <0.001 | 0 (0%) | 14 (22.5%) | <0.001 | 6 (6.67%) | 6 (8.11%) | 0.11 |
| **smoking** | 31 (18.5%) | 72 (52.9%) | <0.001 | 18 (23.4%) | 37 (59.6%) | <0.001 | 13 (14.4%) | 35 (47.3%) | <0.01 |
| **BMI (kg/m²)** | 23.8±2.95 | 27.98±4.4 | <0.001 | 24.0±2.8 | 27.2±2.4 | <0.001 | 23.6±2.2 | 27.2±3.8 | <0.001 |

BMI, body mass index.

and colorectal cancer increases by 8% with each year of age and is 59% higher among men. Moreover, patients with positive family history of this type of condition are more likely to suffer from colorectal cancer than patients with negative family history. Similarly, smokers are 5 times more likely to develop colorectal cancer than non-smokers. The single factor logistic regression also reveals that a chance of suffering from adenomas and CRC is 3.9 times higher among patients with overweight and 35.2 times higher among patients with first-degree obesity when compared to patients having a normal weight. The outcomes of the analysis are presented in Tables IV and V.

Table IV. Odds ratios for adenomas and CRC, depending on demographic factors, smoking, consumption of alcohol, family history and place of residence in univariate analysis

| polyps and colorectal cancer | odds ratio | P>\|z\| | 95% CI |
|---|---|---|---|
| **gender** | 0.41 | 0.000 | 0.25-0.65 |
| **age** | 1.08 | 0.000 | 1.04-1.11 |
| **place of residence.** | 0.93 | 0.764 | 0.58-1.50 |
| **positive cancer family history** | 4.63 | 0.001 | 1.80-11.88 |
| **alcohol consumption** | 0.97 | 0.924 | 0.47-1.98 |
| **smoking** | 4.94 | 0.000 | 2.95-8.26 |
| **overweight** | 3.87 | 0.000 | 2.26-6.63 |
| **obesity I degree** | 35.20 | 0.000 | 10.17-121.80 |

Table V. Odds ratios for adenomas and CRC, depending on demographic factors, smoking, family history and BMI in the multivariate analysis

| polyps and colorectal cancer | odds ratio | P>\|z\| | 95% CI |
|---|---|---|---|
| **gender** | 0.21 | 0.000 | 0.11-0.42 |
| **age** | 1.06 | 0.003 | 1.02-1.10 |
| **positive cancer family history** | 4.18 | 0.013 | 1.34- 13.05 |
| **smoking** | 6.66 | 0.000 | 3.39-13.08 |
| **overweight** | 4.09 | 0.000 | 2.12-7.87 |
| **obesity I degree** | 48.21 | 0.000 | 11.99-193.92 |

The multiple factor regression includes all significant variables of the single factor analysis and indicates that the risk of adenomas and CRC increases with age by 6%. This risk is also 4.2 times higher among patients with positive family history of this condition when compared to the patients with negative family history and 6,6 times higher among smokers when compared to non-smokers. Overweight people are 4 times more likely to be afflicted with adenoma or CRC than patients at a healthy weight and a chance of developing adenoma or CRC in patients with first-degree obesity is 48 times higher when compared to people with a normal weight.

The ROC curve was drawn to assess the prognostic capacity of BMI in terms of adenomas and CRC. The area under the ROC curve amounts to 0,7578 (CI: 0,70719- 0,80844), which means that the prognostic capacity is relatively high. The sensitivity and specificity for obese and overweight patients is 74.26% and 69.46% respectively (Fig. 2).

## DISCUSSION

The present research reveals that the Polish population with an increased BMI is 4 times more likely to develop colorectal cancer. BMI increases the risk of colorectal cancer independently from other risk factors (including age, sex, alcohol consumption, smoking). The results suggest that BMI is a significant risk factor for colorectal adenoma in both men and women. Thanks to weight and height measurements performed by a nurse women could not overestimate their height or underestimate their body mass. Furthermore, CRC is more frequent among smokers and patients with positive family history of this condition. Excessive alcohol consumption is not, however, considered as a risk factor for CRC.

The obtained results confirm that an increasing BMI is a risk factor for colorectal cancer and may lead to the

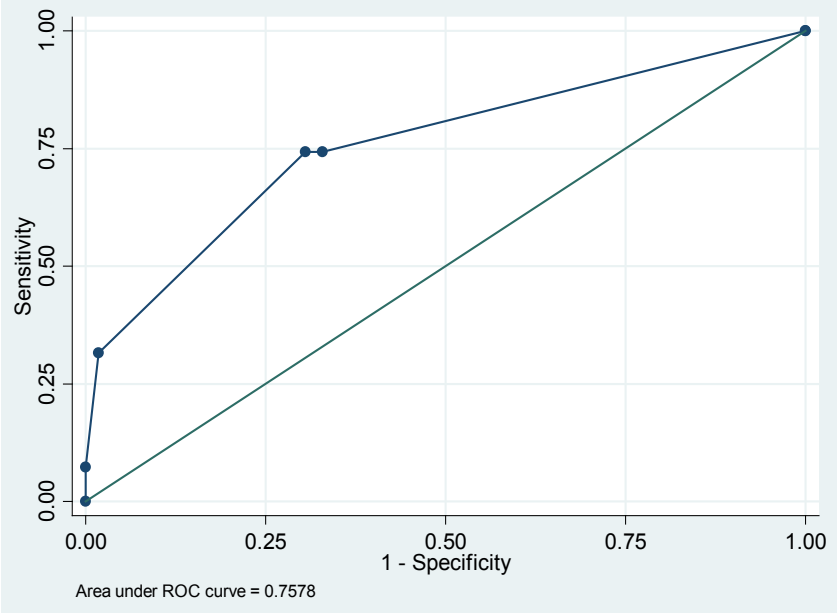


Fig. 2. ROC curve

formation of adenomas in a precancerous state. A meta-analysis, which was published in the past and performed on 29 000 patients, reveals that people who suffer from obesity are 1,33 times more prone to developing CRC than patients with a normal weight (8). Moreover, the data collected in the said meta-analysis suggests that an increased BMI may provoke both colon and rectal cancers. Another systematic review of 141 articles shows that an increase in BMI by 5kg/m2 intensifies the frequency of developing colon cancer and rectal cancer in men by 24% and increases the frequency of developing colorectal cancer in women by 9% (3). Other authors of scientific studies claim that an increasing level of BMI is a risk factor for colorectal adenoma (10). The outcomes of their studies bear witness to the relationship between BMI and a growing risk of developing colorectal adenoma (BMI 25-30 vs. BMI <25 and BMI≥30 vs. BMI <25; OR = 1.32). On the other hand, according to *Anderson* and his associates, the chance of colorectal cancer is higher only among women with an increased BMI level, which means that such a relation does not exist among men. Our study indicates a significant role of obesity in developing colorectal cancer both in men and women (which may, however, result from a small number of clinical studies). Some studies also suggest that risk factors associated with lifestyle, such as smoking, alcohol consumption, age, and small consumption of fatty acids, may contribute to CRC (4, 8, 9). The present research includes all the risk factors mentioned above except for the supply of fatty acids.

There are several hypotheses relating to the development of colorectal cancer induced by obesity (16). Patients with insulin resistance suffer from constant hyperinsulinemia and an increased activity of insulin-like growth factor. Both insulin and insulin-like growth factor are considered as risk factors for colorectal cancer (17). Scientists also discovered that there is a correlation between leptin concentration in fat tissue and colon cancer (18). Furthermore, obese people and people with a healthy weight have a different amount of bacterial flora in the large intestine. Some studies also demonstrate that such a difference may be associated with chronic colitis, which increases the risk of developing colorectal cancer (19).

Previous similar studies reveal the existence of correlation between excessive alcohol consumption and an increased risk of CRC. A meta-analysis of 61 studies confirms that people who drink in moderation (that is 2-3 drinks per day) are more likely to develop CRC than people who do not drink at all. Moreover, the difference in the risk of developing CRC was much more visible in the study comparing heavy drinkers (consuming ≥4 drinks per day) with moderate drinkers and non-drinkers (20). The said meta-analysis provided strong evidence for the existence of correlation between consuming more than 1 drink per day and developing colorectal cancer. Our study did not, however, confirm the relationship between alcohol drinking and the formation of adenomas and CRC in the single factor analysis, which may result from our data collection method (patient's individual declaration is not always reliable).

Smoking is considered as a risk factor for the formation of colorectal polyps. This risk is particularly high in the case of advanced adenomas. A meta-analysis of 42 studies proves that the chance of developing adenomas is greater both in current and former smokers than in patients who have never smoked (21). Moreover, smoking increases the incidence and mortality rates associated with CRC. A meta-analysis of 106 studies demonstrates that smokers are more likely to suffer from CRC than

non-smokers (22). According to some studies, smoking may cause invasive rectal cancer and does not increase the chance of developing cancer of other parts of the large intestine (23). The results of our research reveal, similarly to other scientific publications, that persistent smoking is a risk factor for colorectal cancer irrespective of its location (24, 25).

During our research, we had to face a few significant limitations. Firstly, some parts of our database were collected from a patient questionnaire. Therefore, we cannot be sure about the accuracy of information concerning the smoking or alcohol drinking history of the patients. Secondly, our research does not include other significant risk factors such as other diseases, patient's eating habits, physical activity, and the use of non-steroid anti-inflammatory drugs.

## CONCLUSIONS

Despite the limitations specified above, the outcomes of the present research are significant. In the clinical study, we confirmed the existence of risk factors for CRC such as male sex, smoking, and age. Furthermore, our research reveals a positive association between BMI and colorectal adenomas and colorectal cancer in the Polish population. We believe that the results of our studies may prove useful for future massive screenings. Finally, the specification of risk factors and the construction of prediction models for colorectal cancer may result in a better selection of screening population. Due to the increased frequency of CRC in men with high BMI, which has been also confirmed in the present research, it is recommended to intensify the screening programme, that is increase the frequency of colonoscopic examinations. In order to do so, scientists should create calculators assessing the risk of developing colorectal cancer on the basis of the characteristics, habits, and lifestyles of the Polish population.

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