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## **Simple sugars in fruit and the presence of colorectal cancers and polyps**

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Keywords: colorectal cancer, polyps, fruit, simple sugar

### **Summary**

The current knowledge based on facts provides data regarding genetic and environmental factors relevant for malignancies, including colorectal cancer (CRC) which frequently occurs in well-developed countries. CRC carcinogenesis, a process often lasting 10 to 20 years, has been elucidated.

The aim of the study was to evaluate the role of simple sugars contained in fruit in the development of colorectal cancer and polyps.

The study group consisted of 106 people aged 66 years and older. Colonoscopy screening was used as an opportunistic examination. Among people not qualified for the examination were those with diagnosed disease organic disease of the large intestine, suspected CRC, and people with poor health status due to diagnosed advanced organic diseases of essential organs. Colonoscopy screening was conducted at the Clinic of Gastroenterology and Nutrition Disorders, Collegium Medicum in Bydgoszcz.

The project demonstrated that in the group of 106 elderly people, in whom colonoscopy was conducted as an opportunistic examination under PBP, CRC was detected in 6 subjects, which is significantly more compared to 1 person in the control group. Apart from subjects with CRC, additional 8 subjects had histologically advanced adenomas that due to the high degree of dysplasia and/or presence of a villous

component constituted a real risk of developing CRC in the future. In the control group, whose average age was 10 years younger, only one person was found to have cancer and other two had advanced adenomas, and while more adenomas were detected in the study group, they did not pose a significant risk of CRC.

The results obtained in the study allow us to draw the conclusion that in order to reduce the likelihood of developing colorectal cancer in older age, proper lifestyle habits should be promoted from childhood and based on rational nutrition, safe and functional food products and, inseparably, physical activity, with colonoscopy screening conducted once in ten years starting from the age of 50.

## **Introduction**

Despite comprehensive research conducted at centers equipped with state-of-the-art scientific equipment and employing distinguished scientists, the cause of malignancies is still not known. The current knowledge based on facts provides data regarding genetic and environmental factors relevant for malignancies, including colorectal cancer (CRC) which frequently occurs in well-developed countries. CRC carcinogenesis, a process often lasting 10 to 20 years, has been elucidated. It has been proven that adenoma, and particularly adenoma with advanced characteristics, is the most common precancerous for sporadic CRC (1,2,3,4). According to a broad range of scientific literature CRC is one of nutrition-dependent diseases, therefore one of the more dynamically expanding research areas concerning the environmental factors relevant for CRC is evaluation of the effect of diet and the quality of food consumed on CRC development. In 2011, a panel of experts led by Alan Jackson under the World Cancer Research Fund (WCRF) estimated that introduction of nutritionally favorable changes in the diet of the population could prevent approx. 75% of cases of gastric, colon and rectal cancer (5). Some dietary components can promote the formation of tumors, while other have a protective effect. These components can prevent the development of cancer or intensify it by different mechanisms and at different stages of carcinogenesis. The manner in which dietary factors increase or decrease the risk of cancer development is very complex. They can act directly on the function of genes or their protein products (6). Among the already identified food ingredients to which a protective effect against CRC is attributed are, e.g., calcium, vitamin D, C, E, carotenoids, folic acid, selenium, fiber, polyphenols, saponins, probiotic microorganisms, polyunsaturated fatty acids, curcumin and organic sulfur compounds contained in garlic. Among foods, their components and compounds added to

processed food that promote the development of CRC are, e.g.: heterocyclic amines, polycyclic aromatic hydrocarbons, nitrates from over-fertilized soil and those used for preserving food, excessive consumption of red meat and animal fats, alcohol, tobacco smoking (2,7,8). Moreover, a particularly strong influence of high BMI on the risk of developing CRC is observed. Key phenomenon in these disorders is insulin resistance. Two factors associated with obesity, i.e. high supply of simple sugars and low physical activity, contribute to this phenomenon. Different mechanisms, e.g., postprandial hyperinsulinemia, lead to an increase in the concentration of the biologically active insulin-like growth factor (IGF-1), which stimulates tumor development: intensifies the proliferation and metabolism, and inhibits the apoptosis of various cell types. This results in the generation of abnormal cells that should be eliminated from the body. Thus, insulin and IGF-1 increase the risk of CRC at the early stages of carcinogenesis. Hyperinsulinemia can also result from an excessive stimulation of pancreatic  $\beta$  cells in people consuming high quantities of sweets, among other things (9). The collected scientific evidence warrants identifying physical activity as an important factor reducing the risk of CRC (10).

### **Aim of the study**

The aim of the study was to evaluate the role of simple sugars contained in fruit in the development of colorectal cancer and polyps.

### **Material and methods**

The study group consisted of 106 people aged 66 years and older. Colonoscopy screening was used as an opportunistic examination. Among people not qualified for the examination were those with diagnosed disease organic disease of the large intestine, suspected CRC, and people with poor health status due to diagnosed advanced organic diseases of essential organs. Colonoscopy screening was conducted at the Clinic of Gastroenterology and Nutrition Disorders, Collegium Medicum in Bydgoszcz (hereafter referred to as Clinic), in accordance with the standards described in the national screening program (PBP) for early detection of colorectal cancer financed by the state budget (11). The examinations were conducted by specialists in gastroenterology who had conducted colonoscopy screening procedures continuously since the year 2000 and have high quality ratings for colonoscopy screening documented by the PBP office in Warsaw (12). The control group consisted of 100 consecutive persons aged 40 to 65 years who reported for

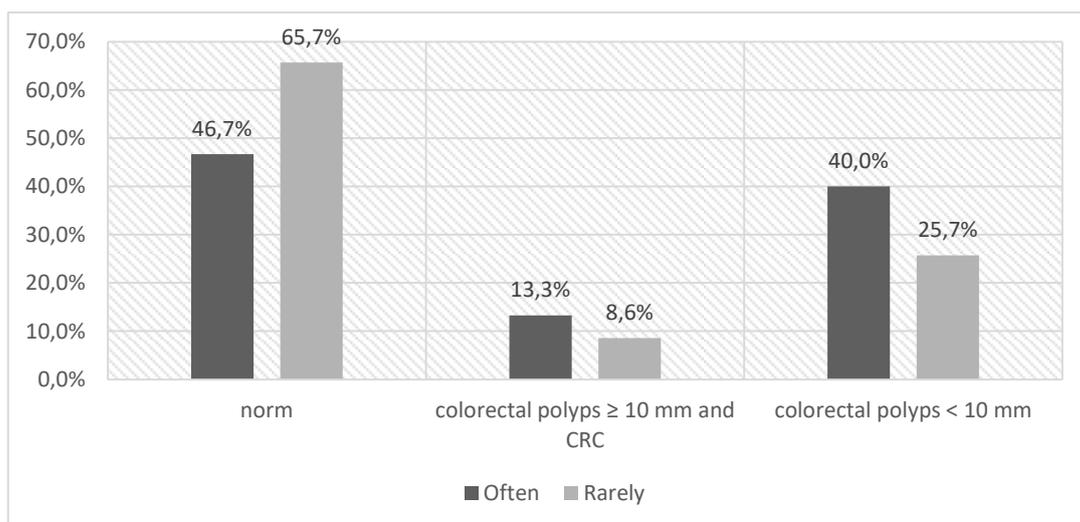
colonoscopy screening under PBP during the period of implementation of the research project titled: “Colonoscopy screening in elderly people”.

The diet and the frequency of consumption of selected products, including fruit and vegetables, were assessed on the basis of a questionnaire prepared by the authors in cooperation with the scientific staff of the Department of Nutrition and Dietetics, Collegium Medicum in Bydgoszcz. The research survey consisted of three parts. The first part consisted of demographic data and questions about the subject’s life style. The second part regarded the subject’s health status and treatment used. The questions in this part referred to the anamnesis predominantly regarding gastrointestinal ailments, past and current diseases, family history of diseases in the first degree of kinship, as well as recreationally used substances and medicines taken. The third part of the questionnaire concerned the current dietary habits and took into account the entire adult life. Questions about the current and past dietary habits regarded the size of portions consumed and the frequency of including selected products in the diet. For practical reasons and for statistical evaluation, consumption of a given group of food products daily or a few times per week was considered as frequent, while consumption a few times a month or more rarely was considered as rare.

## **Results**

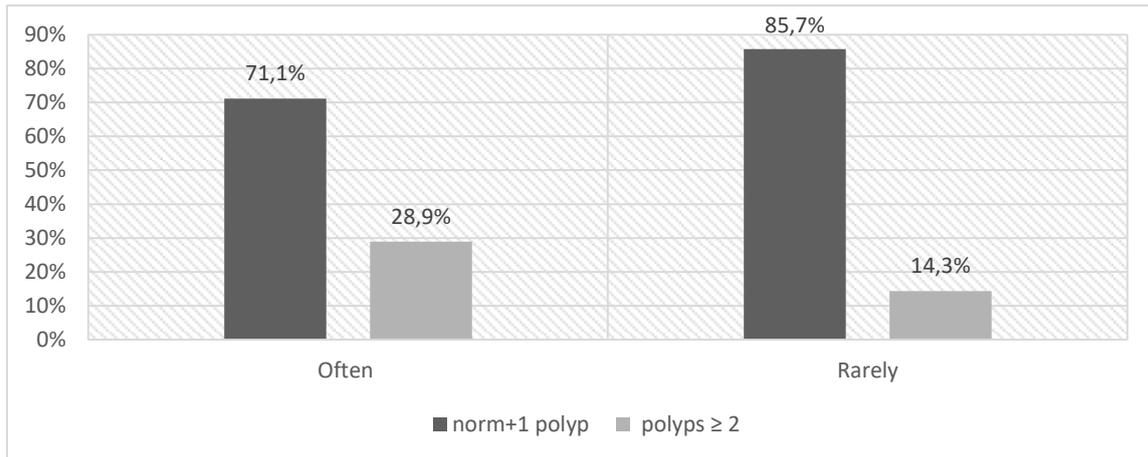
For both the study group and the control group, elderly women living in a large city were the subgroup most frequently filling in the questionnaire and reporting for colonoscopy screening. The largest age groups were people aged 66–70 years in the study group (54%) and people aged 55–59 years (36%) in the control group. In the control group, more than half of people reporting for colonoscopy screening (56.6%) had not been diagnosed with any significant chronic organic diseases, while in the study group this was the case in only 11.1% of subjects. Data regarding previous abdominal surgeries suggested that in the study group there were significantly more people who had undergone abdominal surgeries for various reasons in comparison with people aged 40 to 65 years from the control group. The project demonstrated that in the group of 106 elderly people, in whom colonoscopy was conducted as an opportunistic examination under PBP, CRC was detected in 6 subjects, which is significantly more compared to 1 person in the control group. Apart from subjects with CRC, additional 8 subjects had histologically advanced adenomas that due to the high degree of dysplasia and/or presence of a villous component constituted a real risk of developing CRC in

the future. In the control group, whose average age was 10 years younger, only one person was found to have cancer and other two had advanced adenomas, and while more adenomas were detected in the study group, they did not pose a significant risk of CRC. A very important result of our study, which may provide a real benefit of colonoscopy screening for early detection of CRC in elderly people, is the significantly more frequent detection of adenomas located only on the right side of the large intestine in this age group, as compared with people aged 40–65 years. Poor preparation of the intestine for colonoscopy in our study was statistically more frequent in the study group of elderly people than in the control group. In the group of elderly people, the degree of colorectal cleansing in the 4-step ASGE and ACG scale was very good in 26.4% of subjects receiving the cleansing agent in a single dose and in only 11.5% of subjects prepared using a split dose of PEG with additional bisacodyl. Our study also revealed that elderly people often consuming vegetables had CRC and polyps less frequently than those rarely consuming vegetables.



**Fig. 1. Cancers and polyps  $\geq 10$  mm of the large intestine and the frequency of fruit consumption**

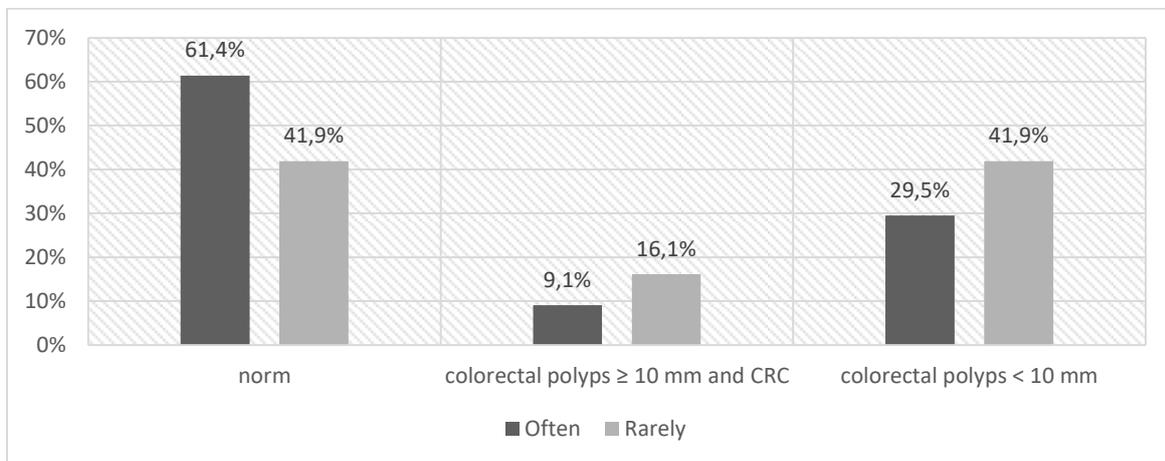
People often consuming fruit much more frequently have colorectal polyps  $\geq 10$  mm and CRC ( $p=0.0027$ ).



**Fig. 2. The number of polyps detected in the large intestine and the frequency of fruit consumption**

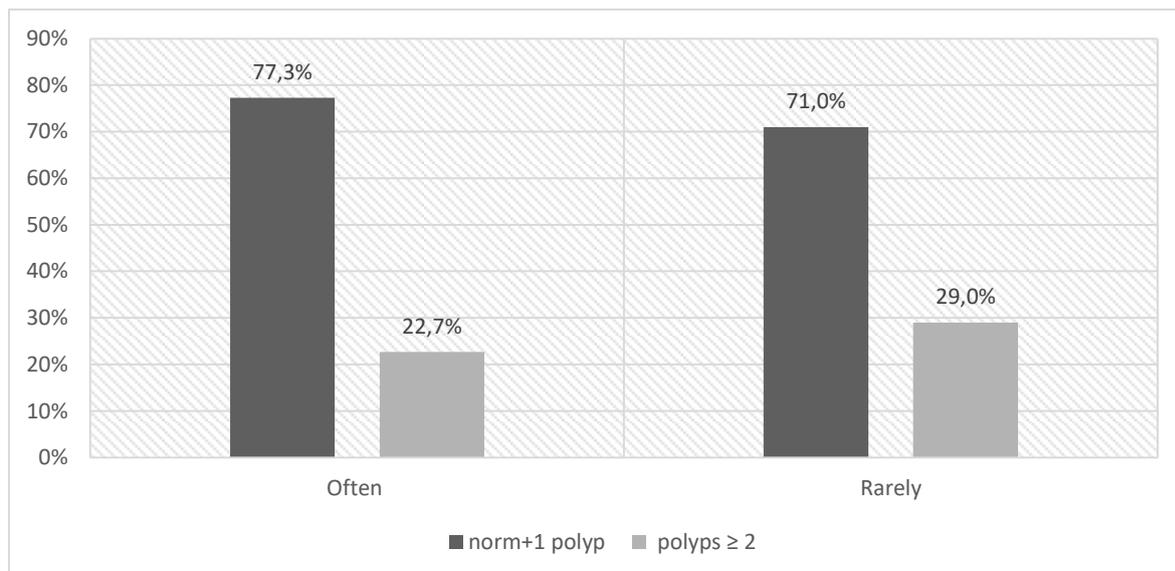
People often consuming fruit constitute a significantly smaller group of subjects with less than 2 colorectal polyps ( $p=0.0098$ ).

### Consumption of vegetables



**Fig. 3. Cancers and polyps ≥ 10 mm of the large intestine and the frequency of vegetable consumption**

Subjects often consuming vegetables much less frequently have colorectal polyps ≥ 10 mm and CRC ( $p=0.0019$ ).



**Fig. 4. The number of detected polyps and the frequency of vegetable consumption**

No statistically significant differences ( $p=0.3343$ ) in the number of polyps detected in colonoscopy screening were found between people eating vegetables often and rarely.

## Results and Discussion

Disease prophylaxis is defined as actions or health programs designed not only to prevent the occurrence of diseases by eliminating risk factors, but also to stop the progress of disease and reduce their negative consequences, such as disability and premature deaths. Primary prophylaxis aims to minimize the exposure to factors that increase the risk of developing a disease or to reduce the likelihood of occurrence of the disease or health disorder, and is focused on the entire population, with particular regard to the so-called risk groups. It predominantly includes education aimed to modify lifestyle and recommends health-promoting behavior (7). Cancers, both in Poland and the rest of Europe, are among the most common causes of premature deaths. The theory of carcinogenesis recognized for several decades is a continuous process which can be divided into three basic steps:

- Initialization, i.e. occurrence of the first irreversible mutation. The original mutant cell is defined as the cancer stem cell. It is characterized by a permanent ability to self-renew and a poor ability to differentiate. Cancer stem cells constitute only a few percent of all cells forming tumor mass. The rest of tumor cells are the so-called descendant cells that in time become incapable of further divisions;

- Promotion, i.e. accumulation of genetic and epigenetic alterations leading to the conversion of the mutated cell into a cancer cell, i.e. a cell undergoing uncontrolled divisions. This step can take up to a few years.

- Progression, during which the tumor develops, acquires the ability to infiltrate tissues and metastasize to distant organs. This process can take a few months to a few years (4).

Some components of diet exhibit a protective effect against CRC, while other components can promote CRC development. This occurs by different mechanisms and at different stages of carcinogenesis. The manner in which dietary factors increase or decrease the risk of cancer development is very complex (2,7,8). Nutritional habits, including the diet and the frequency of consumption of selected products, e.g., fruit and vegetables, were assessed using a questionnaire prepared by the authors in cooperation with the scientific staff of the Department of Nutrition and Dietetics, Collegium Medicum in Bydgoszcz. Questions about the current and past dietary habits regarded the size of portions consumed and the frequency of including selected products in the diet. For practical reasons and for statistical evaluation, consumption of a given group of food products daily or a few times per week was considered as frequent, while consumption a few times a month or more rarely was considered as rare (13). Our study revealed that people aged 66 years and older often consuming vegetables had CRC and polyps significantly less frequently than those rarely consuming vegetables. Vegetables are a valuable source of fiber, which is a mixture of polysaccharidic and nonpolysaccharidic substances, and does not undergo digestion by enzymes in the digestive tract. The concept that high-fiber diet reduces the risk of CRC has a long history that was started in 1969 in a paper by Burkitt. The paper presented a hypothesis that high dietary intake of plant fiber by Africans protects them from developing CRC (130) (14). Howe G. et al. published a meta analysis of 13 clinical studies and concluded that the risk of developing CRC associated with a higher consumption of dietary fiber was 50% lower. Other large prospective cohort studies conducted among American female nurses and Finnish men demonstrated that high-fiber diet does not protect from developing CRC and adenoma (15,16). In several randomized placebo-controlled studies, no beneficial effect of supplementation of plant fiber on the risk of re-development of adenoma was observed. Some researchers have also noted poor tolerance of increased daily uptake of plant fiber by study participants, which may undermine the feasibility of such research projects (7). Aune D. et al., by systematic review and meta analysis of prospective clinical studies, concluded that the risk of developing CRC decreases by 10% with a daily increase of plant fiber consumption by 10 g (17). The panel of experts of the World Cancer Research Fund and the American

Institute for Cancer Research agreed that dietary plant fiber is a factor protecting against the development of CRC because of its biological properties and the results of clinical studies (5). According to our study, elderly people who often eat fruit much more frequently develop CRC and polyps, including synchronous polyps. The results of our study are not in accordance with observations made by most researchers in this topic, although there are published scientific papers declaring no impact of greater consumption of fruit on the reduction of the incidence of CRC. Park Y et al., in a prospective cohort study with 700,000 subjects showed that greater consumption of plant fiber from fruit and vegetables has an opposite effect on the development of CRC than expected (18). Koushik A et al., in their published meta analysis, demonstrated that low fruit and vegetable consumption correlated significantly with a higher incidence of rectal cancer. However, diet rich in these products did not significantly reduce the overall risk of developing CRC (19). Our study is retrospective and includes a small group of people, therefore the obtained results cannot be used to draw long-term conclusions. Nevertheless, it should be noted that it regards an elderly population of Poles. This group of people in Poland until, on average, 40 years of age had access to only a few species of fresh fruit that were available for only a few months per year. Access to vegetables for consumers in Poland before 1989 was better compared to that for fruit, and in the winter many vegetables would additionally be consumed in a pickled form. Most commonly, studies of the impact of food and nutrition on human health consider vegetables, fruit and plant fiber as one food product. In our study, we assessed the impact of fruit and vegetables on the development of CRC separately. Fruit and vegetables differ in, e.g., the content of simple sugars and dietary fiber. Because of the higher content of simple sugars, consumption of fruit should be limited to 1–2 large apples per day. Unlimited consumption of fruit, especially by people with overweight and obesity, can lead to an increase in their body weight. This is not only due to the greater caloric load of fruit, which varies from 40 kcal/100 g to 95 kcal/100 g, but also due to their frequent intake of 300 g and more per day. Fruit should not be substituted with fruit juices. For example, consumption of fruit corresponding to 100 kcal per day includes: half of an avocado, an average banana, 2 small pears, 2 medium-sized apples, 2 kiwi fruit, 4 tangerines, 2 small oranges, 10 plums, 20 strawberries, 30 grapes, 40 cherries and 830 g of watermelon. When arranging diet, one should remember that only fruit with a glycemic index of no more than 50 should preferably be consumed (20).

To increase the quantity of dietary fiber in diet, one should choose Brussels sprouts, cabbage, kohlrabi, broccoli, green peas and prunes. In some people, certain fruit and

vegetables may contribute to discomfort in the abdominal cavity due to tympanites. Such people may consider these fruit and vegetables as unhealthy and eliminate them from their diet. Healthy vegetables are those that contain, e.g., potassium, such as potatoes, beans, tomatoes, beets, soy, zucchini, spinach, lentils. In turn, crucifers are an excellent source of vitamin C, both in the fresh and pickled form. Vegetables from this group contain large quantities of folates, group B and E vitamins, and among primary minerals are sulfur, manganese, molybdenum, iodine, cobalt, selenium and chromium; furthermore: calcium, iron, zinc and potassium. Crucifers also contain proteins constituting a valuable source of the amino acids methionine and lysine (20). There is some evidence linking CRC with consumption of simple carbohydrates. Gnagnarella et al., based on meta analysis of research papers, provided evidence that food products with a high glycemic load and/or glycemic index are associated with a greater risk of development of adenoma and CRC. Insulin is responsible for this phenomenon, not only due to its mutagenic properties, but primarily due to fact that it increases the concentration of bioactive insulin-like growth factor (IGF) 1 (21). In our study, we analyzed the dietary habits regarding the current and past consumption of fruit and vegetables by people reporting for colonoscopy screening at the age of 66 years and older. We also noted that these food products should be assessed separately, not collectively as in many scientific publications, because fruit and vegetables differ significantly in the content of individual nutrients. In our study, we particularly focused on the impact of simple sugars, that are present in greater quantity in fruit than in vegetables, on the development of polyps and CRC. Based on the rich literature and our observations, it can be concluded that an optimal diet with health-promoting, preventive, or even therapeutic properties against CRC is not based on individual nutrients, but rather on reasonably composed menus that include a safe and well-selected set of food products, as well as appropriate methods of their preparation.

### **Conclusions**

The results obtained in the study allow us to draw the conclusion that in order to reduce the likelihood of developing colorectal cancer in older age, proper lifestyle habits should be promoted from childhood and based on rational nutrition, safe and functional food products and, inseparably, physical activity, with colonoscopy screening conducted once in ten years starting from the age of 50.

\*In the control group, PBP subjects could be aged 40 or older if a 1st degree relative had had CRC.

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