Review paper

Primary and secondary prevention of colorectal cancer in the Czech Republic

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Abstract

Colorectal cancer is one of the most frequent malignancies in the Czech Republic and worldwide. Also, a high prevalence of overweight and obesity, a high proportion of smokers in the population, and one of the highest per capita alcohol consumption rates are typical for the Czech population. The role of general practitioners in the prevention of colorectal cancer is crucial. In primary prevention, the doctor should emphasise the importance of a healthy lifestyle – a balanced diet rich in fruits and vegetables, maintaining a normal body weight, adequate physical activity, and non-smoking. In secondary prevention, patients should be informed about the possibilities of colorectal cancer screening and the benefits of early detection of the disease. Participation rates of the target population for colorectal cancer screening are low. Steps leading to increased participation in colorectal cancer screening (including postal invitations) play an important role in influencing the mortality of colorectal cancer.

Introduction

Colorectal cancer (CRC) is one of the most frequent malignancies in the Czech Republic and worldwide. Every year, approximately 1.36 million people throughout the world develop this type of cancer and nearly 700 thousand people die of it [1]. The Czech Republic is one of the countries with the highest CRC incidence and mortality rates, with more than 8000 people developing the condition and nearly 4000 individuals dying of it each year [2]. Czech males and females rank third and tenth, respectively, in Europe in terms of CRC incidence [1]. Mortality due to CRC has not decreased in spite of better diagnostic and therapeutic options.

Colorectal cancer risk factors as key for primary prevention

Knowledge of colorectal cancer risk factors is crucial for both primary prevention and early detection.

Age

Typically, CRC is an age-related condition. The incidence rates tend to increase after 50 years of age, with a peak in the 65–75 age category [2]. Approximately 20% of all patients are younger than 60 years [3].

Gender

Males are affected by CRC slightly more frequently than females. In 2012, a total of 746,298 males and 614,304 females developed the disease worldwide, with mortality rates of 373,639 and 320,294, respectively [1]. In the Czech Republic, males account for approximately 60% of all patients diagnosed with CRC [4].

Race

In the USA, Afro-Americans have higher incidence rates of CRC than Caucasians (by approximately 22% and 23% for males and females, respectively). Afro-Americans tend to develop CRC at a younger age, often under 50 years [5]. The differences may stem from both biological variations [6, 7] and lower use of health care services due to numerous causes [8].

Nutrition

Nutrition plays a role as a source of energy (and thus a factor influencing body weight) as well as through intake of macro- and micronutrients. Individual food components or their culinary use may modify the risk for development of CRC. Increased fruit and vegetable consumption was found to be a protective factor [9–11].

According to World Health Organization recommendations, an adult should consume 400 g (five portions) of fruit and vegetables daily. The protective effect is mainly associated with cruciferous vegetable consumption [12, 13] and increased folate intake [13].

Consumption of processed meat and red meat, particularly if prepared at high temperatures, may be associated with a higher risk for CRC [11, 14, 15]. Lower consumption of red meat and animal fats may be a protective factor against CRC [16]. The protective effects were also observed in fish consumption [17, 18] and may be associated with poultry meat although studies have been inconclusive as yet [13, 18, 19]. Another potential protective factor is increased calcium intake. Large prospective studies have shown a moderate statistically significant inverse association between calcium intake and the risk of CRC [11]. The association was also confirmed by a randomised, controlled study of 913 patients with a history of adenoma receiving calcium supplementation at a dose of 1200 mg (as compared with placebo) [20]. Suitable sources of calcium in food seem to be low-fat dairy products. A study by Aune *et al.*, however, reported their protective effect against colon (but not rectal) cancer only [21]. Many studies have also discussed potential calcium supplementation following the first tumour resection in an attempt to prevent recurrence, but the results have been inconclusive [22]. Nevertheless, calcium supplementation cannot be recommended due to a potentially increased risk of prostate cancer [11].

Epidemiological studies have suggested an inverse association between vitamin D insufficiency and the risk for developing colorectal cancer (CRC). Prospective studies found that circulating 25(OH)-D levels were inversely associated with rectal cancer, CRC, or adenoma [20]; similar results were reported by meta-analyses and placebo-controlled trials [13].

The protective effect of fibre has been confirmed by several studies. However, other studies failed to show a potential association with the amount of fibre consumed. A systematic review and meta-analysis of 25 prospective observational studies found that high fibre intake was associated with a lower risk for CRC [11, 23]. However, fibre-rich foods often contain high amounts of polyphenols potentially modifying carcinogenesis [13, 14].

Body weight

Excess body weight is a well-known risk factor for CRC. The association between excess body weight and the risk for CRC is somewhat stronger for males than for females and is also stronger for colon cancer than for rectal cancer [11, 20]. For every 10 cm increase in waist circumference, cancer risk increases by 33% and 16% in males and females, respectively [20].

Physical activity

Physical activity is a protective factor against numerous malignancies, including CRC [11, 13, 24]. Physical activity should be an integral part of every individual's lifestyle, involving at least 30 min of exercise most days of the week.

Smoking

Tobacco smoking is one of the most important risk factors for malignancies including CRC. Smokers have double the risk for adenoma and death from CRC than non-smokers. More intensive screening of current smokers has been considered [20]. Smoking cessation at an older age does not necessarily result in a decrease in the risk for CRC. Therefore, it is necessary to prevent smoking in adolescents and young adults and or to make them stop smoking as soon as possible [20].

Alcohol consumption

Alcohol consumption is a causal factor in the development of CRC, with a dose-effect relationship [20]. The association between alcohol consumption and the risk of CRC is somewhat stronger in males [11].

Health status

The health status factors that are more likely to be linked with the development of CRC include a personal or family history of polyps or sporadic CRCs and adenomatous polyps. Inflammatory bowel diseases such as ulcerative colitis and Crohn's disease may also play a role. In ulcerative colitis, the risk for CRC is associated with the extent of bowel involvement (the risk for CRC is 5–15 times and 3 times higher in pancolitis and left-sided colitis, respectively) [13].

Other non-modifiable risk factors include genetic predisposition, for instance, hereditary syndromes (familial adenomatous polyposis (FAP) is responsible for less than 1% of CRC cases, and Lynch syndrome or hereditary non-polyposis colorectal cancer (HNPCC) for 3–5% of all adenocarcinomas; FAP and Lynch syndrome are most common, being responsible for a total of approximately 5% of CRC cases) [13].

Diabetes mellitus and insulin resistance have also been associated with CRC. Diabetics have an increased risk of developing CRC [20]. A meta-analysis of 14 studies estimated that in diabetic patients, the risk of CRC was increased by 38% (relative risk (RR) = 1.38, 95% confidence interval (CI) 1.26–1.51) and the risk for rectal cancer by 20% (RR = 1.20, 95% CI: 1.09–1.31) [25]. The observed association may be due to common risk factors such as obesity, low physical activity, nutrition,

or insulin resistance. Studies have also been concerned with the effect of chronic insulin therapy [26].

Medicines and treatments

Prolonged use of aspirin and nonsteroidal anti-inflammatory drugs have been considered as potential protective factors for adenoma, colon cancer, and CRC, with regular use of the drugs being associated with 20% to 40% reduction of the risk. A lower risk for the development of CRC was suggested in a study of hormone replacement therapy in postmenopausal women [13]. Some studies have also indicated protective effects of statins in various types of malignancies, including CRC, but the results have been heterogeneous [13].

A potential effect of androgen deprivation therapy has also been reported, particularly in association with prostate cancer treatment [13], as well as a high risk in patients undergoing cholecystectomy, with some studies suggesting a potential risk in association with right-sided tumours [13].

Secondary prevention and screening for early detection of CRC

In the vast majority of cases, CRC is preceded by adenoma, a clinically detectable precancerous condition gradually developing into cancer. Malignant transformation of adenoma to adenocarcinoma is a slow process lasting several years (10 years on average). As for the location, CRC (adenocarcinoma in 70% of cases) occurs in the rectum in approximately 60% of cases [27]. In half of patients, the tumour remains clinically silent for a long time. When the diagnosis of CRC is made, one in five patients have already developed metastases, most frequently in the regional lymph nodes, liver, lungs, and peritoneum [13]. Given the long lead time, early detection of precancerous and cancerous lesions contributes to early treatment and better survival. Screening tests performed in at-risk individuals prior to clinical manifestation increase the likelihood of early detection of the condition, better patient prognosis, and savings for the health care system.

In the Czech Republic, the CRC screening program was introduced in 2000. Primary colonoscopy was included in the Czech screening program as of January 2009. In the country, CRC screening comprises the faecal occult blood test (FOBT) and screening colonoscopy. These tests are usually offered during a visit to a general practitioner. To cover a larger part of the population, the FOBT has also been performed by gynaecologists since 2009.

Faecal occult blood tests

At present, the FOBT is no longer linked with a regular check-up (in the past, this was a prerequisite for reimbursement). For practical reasons, however, it is offered as part of a regular check-up. In many cases, however, there is considerable delay as patients tend to provide their stool samples up to several months later, if ever.

Starting from 2009, the FOBT should be carried out annually in the 50–54 years age category; regular check-ups are biannual. After 55 years of age, the FOBT is either performed every 2 years or it may be replaced with screening colonoscopy performed every 10 years if the results are negative. The schedule is the same if CRC screening is performed by gynaecologists.

In spite of the above measures, only a small percentage of people eligible for screening undergo the tests, namely approximately 25%, i.e. about 500,000 tests a year. To make the screening effective, at least 45% (preferably 65%) of the target population should participate [28].

In some countries, CRC screening is outside the competency of general practitioners. In the UK, France, or the Netherlands, for instance, the FOBT kit is mailed to people's home addresses and the stool samples are mailed to the laboratory. In Poland, a colonoscopy screening program has been introduced.

Screening colonoscopy

Practitioners should offer screening colonoscopy to asymptomatic patients aged 55 years. Screening colonoscopy may only be performed in accredited centres. In case of negative findings, colonoscopy is repeated every 10 years.

Drawbacks of screening colonoscopy

One disadvantage is that the procedure is costly. Moreover, colonoscopy is an invasive method, posing certain risks. One such risk is perforation, occurring in 0.0029–0.72% of cases; fewer than 5 perforations per 10,000 examinations indicate good quality screening. Heavy bleeding occurs in 0.2–2.67% of procedures. Fewer than 50 cases of bleeding per 10,000 examinations indicate good quality screening. The risk of death from colonoscopy is less than 1 per 10,000 examinations. Also, in some cases total colonoscopy cannot be accomplished. Among the most frequent reasons for incomplete colonoscopy are: pain or uncontrolled loops, stricture or obstruction, poor bowel preparation, cardiorespiratory instability, severe colitis or inflammatory bowel disease, and equipment failure [29].

The referring practitioner should be aware of the requirements of the centre performing colonoscopy as far as the preparation and additional examinations are concerned. The patient's general practitioner must be informed if the patient is referred for colonoscopy by another practitioner.

Patients with normal colonoscopy findings will not undergo the FOBT in the following 10 years.

According to the Czech Gastroenterological Society guidelines, colonoscopy is a follow-up method:

– in patients at risk of CRC – a positive family history of HNPCC (or Lynch syndrome) – colonoscopy every 2 years from 25 years of age; if cancer developed in a younger family member, colonoscopy is recommended 5 years earlier than in the youngest family member affected;
– in case of sporadic CRC before 60 years of age colonoscopy every 5 years, the first procedure performed 10 years earlier than detected in an affected family member, or every 3 years if adenoma was detected;
– in case of ulcerative pancolitis lasting for 8 or more years or left-sided colitis lasting for 15 or more years; colonoscopy is recommended every 1–2 years with biopsies to rule out dysplasia.

Utilisation of CRC screening

The actual participation of the target population in CRC screening and the willingness to undergo the procedure are low due to the discomfort and fear associated with the current methods. To increase the detection rates, adequate participation of the target population is necessary (currently at only 27%) [30]. However, recommendations on the use of FOBT state that at least 45% (preferably 65%) of the target population should participate to achieve optimal results of this type of screening [28].

In CRC screening, the role of general practitioners is of key importance. Nonetheless, only a small percentage of the target population is screened. This is why the decision was made to involve gynaecologists in CRC screening starting from January 2009. At the moment, they examine only a small proportion of patients undergoing screening, but their involvement is beneficial, making the base of screening in primary care stronger. According to the Czech national reference centre, gynaecologists and general practitioners performed the FOBT in 13.3% and 86.6% of patients, respectively, in 2011, as compared with 6.2% and 93.7% in 2009 and 14.1% and 85.1% in 2010 [28].

It is essential to improve communication between gynaecologists and general practitioners caring for the same patients as well as their sharing of examination results. It must be realised that outpatient gynaecologists have a special position in the Czech health care system as they are involved in all three types of screening programs. Increased participation in screening programs could also be achieved by invitations mailed to patients, as introduced in 2014.

Conclusions

The Czech Republic is one of the countries with the highest burden of both cancer and CRC. At the same time, this population is characterised by a high prevalence of excess body weight, high proportion of smokers, and one of the highest per capita alcohol consumption rates. Due to the relatively advanced health care system, there is constantly increasing incidence on the one hand and stagnating mortality on the other hand, mainly resulting from improved therapeutic options, diagnosis, and introduction of organised screening programs.

The benefit of CRC screening as a method leading to a reduction in mortality is limited by low participation of the population in the program. Steps taken to increase participation in screening measures (including the recently introduced postal invitations) play a very important role in affecting CRC mortality.

However, the negative trend in CRC incidence may be effectively influenced through primary prevention (by modifying the exposure to risk factors). The most important primary preventive measures related to CRC are a balanced diet with enough fruit and vegetables, maintaining normal body weight and reducing overweight and obesity, adequate physical activity, non-smoking, and controlled alcohol consumption. The undisputed advantage of primary prevention is that the most important risk factors for CRC are related to numerous other conditions. Thus, their elimination may decrease the incidence of not only CRC but also many other diseases such as cancers or cardiometabolic disorders.

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Conflict of interest

The authors declare no conflict of interest.

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