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Colorectal cancer epidemiology

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Key words: Colorectal Neoplasms; Epidemiology; Incidence; Mortality; Age Factors; Sex Factors; Survival Rate

Colorectal cancer (CRC) is the third most common cancer worldwide after lung and breast cancers with almost 60% of all colorectal cancers occurring in the more developed regions. Nearly 1.2 million new colorectal cancer cases are registered in 2008 (9.7% of the total). CRC is responsible for some 608,845 deaths (8.0 %) worldwide.

There is significant geographical variation in age-standardized and cumulative, 0-74 year incidence and mortality rates. Incidence rates vary tenfold in both sexes worldwide. The highest rates are estimated in Australia/New Zealand (39/100000), Western Europe (33.1/100000) North America (30.1/100000), Eastern Asia (18/100000) and more recently in Japan. The highest incidence rate of CRC is estimated in the Czech Republic (43/100000). The lowest incidence rates are estimated in Africa (3.6/100000 except South Africa) and South-Central Asia (4.5/100000). The highest mortality rates in both sexes are estimated in Central Europe (20.3/100000 for male patients, 12.1/100000 for female patients), and the lowest in the Middle Africa (3.5 and 2.7 respectively).

Current likelihood of risk of developing CRC by the age of 75 is one in 42 male and one in 61 female patients worldwide.

Incidence and mortality rates are higher in men than in women (sex ratio 1.4:1). The incidence of colorectal cancer increases with age beginning at 40 but remains relatively low until the age of 50 and then rapidly accelerates. The majority of deaths of CRC occur in older people, around 80% in people aged 65 and above, and almost two-fifths of deaths appear in the group with age over 80.

In Europe, the incidence of colorectal cancer is increasing, particularly in Southern and Eastern Europe, where rates were originally lower than in Western Europe. In the USA, incidence rose until the mid-1980s but in the last two decades the rates have fallen for both men and women. Countries that have had a rapid 'westernization' of diet, such as Japan, have seen a rapid increase in incidence of colorectal cancer. Consumption of meat and dairy products in Japan increased tenfold between the 1950s and 1990s.

In contrast to incidence trends, CRC mortality has been falling continuously since the early 1990s. Mortality rates have been declining in most European countries from the 1990s onwards and further falls are expected. In the countries of the European Union (EU-27), colorectal cancer was responsible for an estimated 148,000 deaths in 2008.

The five-year relative survival rates for both male and female colon and rectal cancer have doubled between the early 1970s and mid 2000s. In the more developed regions, five-year relative survival for male colon cancer rose from 22% in the early 1970s to 50% in the mid 2000s. For female patients, it rose from 23% to 51%. Five-year survival rates for male rectal cancer rose from 25% in the early 1970s to 51% in mid 2000s and from 27% to 55% for female rectal cancer. These improvements are the result of earlier diagnosis and better treatment but there is still much space for further progress. Ten-year survival rates are only a little lower than those at five-years indicating that most patients who survive five years are cured from this disease.

Colorectal cancer is the second most common cancer in the Province of Vojvodina in all new cancer cases and all cancer deaths. About 1233 new cases (12.76 % of all cancer cases) and 778 deaths (12.69% of all deaths) have been registered in 2007 in Vojvodina. Like worldwide, incidence and mortality rates are higher in men than in women (sex ratio 1.5:1). Age-specific incidence and mortality rates are increasing rapidly from the age of 50, reaching the highest level in the age group of 75 -79.

Time trends have been increasing significantly over the period from 1973 to 2007 in both sexes. In men, incidence increased from 19.81/100000 to 73.6/100000 and mortality from 13.47/100000 to 47/100000. In women, incidence increased from 20.02/100000 to 48.7/100000 and mortality from 15.46/100000 to 31.2/100000.

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Colorectal cancer – risk factors

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Key words: Colorectal Neoplasms; Colonic Neoplasms; Risk Factors; Adenoma; Age Factors; Life Style; Eating; Meat; Pedigree; Obesity; Smoking

Although the exact cause for the development of colorectal cancer is not known, there are factors that increase risk for developing adenomas, polyps and cancer. These include numerous suspect factors.

The first step toward colon and rectal carcinoma appear both. Similar factors appear both for adenomas and for colorectal cancers. The risk of developing colorectal cancer increases with age. About 90 percent of people diagnosed with colon cancer are older than 50. The chance of developing this disease is greater if the patient has had colorectal cancer in the past. Inflammatory diseases of the colon increase the risk of colon cancer. Family history of colorectal cancer and many genetic syndromes such familial adenomatous polyposis and hereditary non-polyposis colorectal cancer are very important for development of this cancer. The emigrant studies showed, 40 years ago, that lifestyle-related risk factors change dramatically the chance for getting the disease. Diet with red and processed meat and without fiber, vegetables, and fruits plays very important role. Researchers have also suggested that methods of cooking meat at very high temperatures generate chemicals that might increase cancer risk. There is evidence that this risk may not be only a related to meat. It may reflect high-fat intake or carcinogens created through various cooking and processing methods. The cancer risk can be modulated by certain genotypes. Cancers associated with high meat consumption may be reduced by the addition of anticarcinogens in the food and especially at the same time as meat preparation or meat consumption, or changing of food preparation methods. Some supplements as folic acid, calcium, vitamin D, and B maybe are linked to a lower risk. Non-steroidal anti-inflammatory drugs reduce risk probably. Cyclooxygenase-2 (COX-2) is an enzyme that regulates prostaglandin synthesis and is overexpressed at sites of inflammation and in several epithelial cancers. Specific inhibitors of COX-2 (coxib) activity could potentially serve as chemopreventive agents. Obesity is associated with an increased risk of colon cancer and regular physical activity may reduce the risk. Smoking was associated with increased risk of CRC and the associated risk was higher for men and for rectal cancers.

There are many factors with controversial and unproven effects on colorectal cancer. Lifestyle-related risk factors must be target of better education and health promotion in order to improve knowledge and primary prevention of this disease.

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Screening for colorectal cancer

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Key words: Colorectal Neoplasms; Risk Factors; Early Detection of Cancer; Mass Screening; Occult Blood; Colonoscopy; Sigmoidoscopy; Immunohistochemistry; Magnetic Resonance Imaging; Tomography, X-Ray Computed; Genetic Testing; Practice Guideline

Colorectal cancer (CRC) is one of the most commonly diagnosed cancers and a leading cause of cancer deaths in the developed regions of the world. CRC screening (secondary prevention of population at average risk of CRC) and case finding (secondary prevention at individuals who have one or more risk factors such as family history of colorectal adenoma/carcinoma, family history of polyposis syndromes, past CRC or adenomatous polyp and inflammatory bowel disease) can prevent the development of colorectal cancer and reduce the risk for death.

Four randomized trials have shown that fecal occult blood testing (FOBT) is effective in lowering colorectal cancer mortality rate (15-33%) and its incidence in individuals who undergo screening. FOBTs available for screening are based on two principal technologies: chemical tests and immunochemical tests. The chemical tests use guaiac to detect the peroxidase activity of heme; so, they react to any peroxidase in feces (e.g. plant foods and heme in red meat) and are affected by certain chemicals (e.g. vitamin C). These tests may detect bleeding from any site of gastrointestinal tract. The fecal immunochemical tests use antibodies specific for human globin; so they are not affected by diet and are highly selective for occult bleeding of colorectal origin. Although the sensitivity of a single FOBT is low, in the range of 30%-50%, a program of repeated annual testing can detect as many as 92% of cancers. After 18 years of follow-up in the Minnesota trial, FOBT screening performed every year was found to reduce colorectal cancer mortality by 33% and every other year by 21%, a rate consistent with the results of the biennial screening in the European trials. Furthermore, in a recent FOBT screening in 478 250 residents of the pilot areas in England and Scotland, the overall positive tests were 1.9% and the rate of detecting cancer was 1.62 per 1000 screened people. The positive predictive value was 10.9% for cancer and 35% for adenoma. Of 552 colorectal cancers detected by screening, 48% of all screen-detected cancers were stage I, and only 1% metastasized at the time of diagnosis. The cost per life year saved by FOTB screening is similar or less to that of breast cancer screening. Despite the cost of FOBT screening, it has been accepted as feasible for national health care. The main disadvantages of FOBT screening being its low compliance rate for the first and repeated screening (20-70%) as well as its moderate sensitivity for detecting colorectal cancer and low sensitivity for polyps.

The FOBT screening performed every year combined with flexible sigmoidoscopy every 5 years is more effective than either of the methods alone. However, despite FOBT may be less sensitive for distal colon lesions, both methods together do not greatly improve the detection rates for proximal lesions. The disadvantage of this type of screening are inconvenience, high cost and complications with an uncertain gain in effectiveness.

Although there are no randomized studies evaluating whether screening colonoscopy alone reduces the incidence and mortality from colorectal cancer, several guidelines have included colonoscopy as a screening option. Colonoscopy has a proven high sensitivity for detecting polyps and carcinomas of the whole colon. One meta-analysis found perforation rates between 0.06% and 0.2% and mortality between 0% and 0.06% for diagnostic colonoscopy. The choice of a 5 to 10-year interval between screening colonoscopies for people at average risk is based on the estimates of the sensitivity of colonoscopy and the rate at which advanced adenomas develop. The disadvantages include vigorous bowel preparation and need for trained examiners. Adequate withdrawal times of colonoscopy from cecum to anus of minimum 6 minutes are required to ensure sufficient neoplastic lesion detection.

Computed tomography colonography and magnetic resonance imaging colonography or virtual colonoscopy have also been evaluated as possible colorectal cancer screening methods. However, due to many disadvantages and higher cost at that time, the use of virtual colonoscopy outside of clinical trials cannot be recommended.

Genetic stool testing (e.g. fecal DNA testing) every 5 years was considered to be effective compared to no screening, but inferior to other screening strategies.

In 2003, the European Commission issued the recommendations for screening for breast, cervical and colorectal cancer valid in all member countries. The Republic of Slovenia adopted this program and national guidelines for colorectal cancer screening were published. After successful pilot phase of screening (using immunochemical FOBT in 10.000 people older then 50 years) in June 2008, a nation wide screening was launched on the 17.4.2009 in population aged 50–79 years. By the end of 2009, 170.217 invitation letters were sent out with compliance of 36%. 43.510 person were tested, 2441 FOBTs were positive. We preformed 1622 colonoscopies and found carcinoma in 118 patients and adenomatous polyps in 772 patients. Therapeutic polypectomies were done in the same procedure. In 118 colorectal cancer cases, 50% were stage I, 21% were stage II.

Organized colorectal cancer screening has greater potential to reduce cancer incidence and mortality due to higher achievable levels of population coverage, follow-up and quality compared with opportunistic screening. However, due to low compliance for colorectal screening in many EU countries, only improved awareness and knowledge of general population about the colorectal cancer risk factors and the benefits of screening can improve compliance.

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Follow up after potentially curative resection of colorectal cancer

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Key words: Colorectal Neoplasms; Diagnosis; Early Detection of Cancer; Colorectal Surgery; Postoperative Period; Neoplasm Recurrence, Local; Neoplasm Metastasis; Practice Guideline; Antineoplastic Protocols

Follow-up serves to identify disease recurrence and early recognize patients in need of additional curative treatment. Disease recurrence is considered as development of distant metastases, local reemerging of tumor at the site of resection, and occurring of metachronous cancer.

Metastatic recurrence of the disease after potentially curative resection of colorectal cancer depends on the stage of the disease at the time of operation. Prognostic values of Dukes and TNM staging are practically identical. The worst prognosis is in patients with Dukes C or TNM III stage of the disease, but the recurrence of illness cannot be completely excluded even in case of patients with Dukes A or T1 stage of the disease. In such situations, new operation can sometimes promise chance for cure. It is very important to recognize development of asymptomatic recurrences as early as possible, because the chance for radical resection depends on the disease extension.

Rules for regular follow up of patients operated for colorectal cancer are based on knowledge of natural history of disease – specific anatomical and time-dependent ways of spreading. These rules are put forth by national (1) and international cancer organization such as ESMO (2,3), in the form of Clinical Practice Guidelines or Minimal Recommendations.

The first appearance of colorectal cancer means that colorectal mucosa express higher grade of proliferation, so there is a chance for emerging of a new adenoma or carcinoma. (4) Endoscopic controls have to be performed periodically, but not too often, due to known timing in adenoma-carcinoma sequence (5). The first control should be done a few weeks or months after operation, to check for presence of missed metachronous adenomas or malignant tumors. All found adenomas have to be transendoscopically removed as the secondary prevention. Further controls are recommended every 3 to 5 years.

After low anterior resection and in the attempt to get anastomosis, resected margins of the healthy tissue can be of not enough distance from the tumor, with a greater chance for remaining of tumor cells in the tissue. For early recognition of locally relapsed disease ESMO guidelines recommend endoscopic controls every six months (3), but ours recommend them every 3 months during the first, and 6 months during the second postoperative year (1). After two years, there is only a chance of metachromous polyp/tumor appearance and endoscopic controls can be performed in 3 to 5 years (1). Endorectal ultrasonography or magnetic resonance examinations are recommended when tumors extend into perirectal tissue.

The possibility of surgical resection in cases of oligometastatic disease induces needs for periodical imaging of potentially most often affected organs – liver and lungs. As the majority of metastases (85%) develop during three years after operation and almost all during 5 years (6), the official recommendations propose imaging of lung and liver (chest and abdominal CT, or chest X-ray plus abdominal US) each 6 months during three year (1,2), and one in years 4 and 5 (1). Other imaging procedures can be performed only in case of suspected symptoms.

Carcinoembryonic antigen testing is contraversal, but some guidelines, as American Society of Clinical Oncology Practice Guideline (2005) recomend CEA test every three months postoperatively for at least three years after diagnosis, if the patient is a candidate for surgery or systemic therapy (7).

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