

Epidemiology And Risk Factors In Carcinomas Of The Large Bowel

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ABSTRACT Colorectal carcinoma (CRC) represents one of the most common types of carcinoma in both males and females, being encountered mainly in developed countries. North America, Australia/New Zealand, Western Europe and Japan represent geographic regions with the highest incidence. Approximately 10% of the CRC appear as a result of inherited genetic defects. Lifestyle is undisputedly an important risk factor which influences the apparition of CRC. Alimentation, both quantitatively and qualitatively; alcohol, by inducing cellular proliferation and inhibiting DNA repair as well as smoking, are closely connected with an increase in the risk for CRC. Ulcerative colitis represents a major cause of CRC. The risk for malignization is 2% after 10 years and 18% after 30 years of inflammatory affect. Many of the symptoms of CRC are vague and non-specific (abdominal pain, constipations or diarrhea), some of them being the same in benign pathologies. Recent progresses gave birth to several national screening programs, having a positive effect on the increase in survival rate for CRC patients.

KEY WORDS *Colorectal Carcinoma, Large Bowel, Risk Factors, Screening*

Introduction

Geographic distribution of colorectal carcinoma.

On a global scale, colorectal carcinoma (CRC) represents one of the most common types of carcinoma in both males and females, being encountered mainly in developed countries. Therefore, in countries such as Canada or France, CRC is the second most frequent death from cancer. [1–3] It is worth mentioning that in males the first place is taken by prostate cancer, while in women by breast cancer. [1,2] In the United States, statistics place CRC as the most frequent cause of death by cancer in non-smoking males and second cause of death in non-smoking women, while in the overall population it represents the third most common cause, following lung and breast cancers. [4, 5]

Geographic regions with the highest incidence are represented by North America, Australia/New Zealand, Western Europe and Japan, while Africa and Asia report much lower incidence rates. [1, 3] This geographic distribution proves that there are notable differences in frequency between countries with different socio-economic statuses. In regards to race, the highest incidence for CRC is found in Afro-Americans. [1–3, 4]

Risk factors and pathogenesis.

Genetic factors.

Although the incidence and annual mortality by CRC increases with age (more rapidly after 50 years of age), [6] it's been noticed an increase in the number of cases in the middle aged population groups. This aspect accounts for a more dedicated research of the risk factors in order to ensure prevention and early detection of CRC, which currently constitutes a major health issue. [6, 7]

The pathogenesis of CRC is complex, both environmental and genetic factors being involved in cancer progression. Numerous CRC cases develop from a chromosomal instability. Therefore it is characterized by a molecular heterogeneity which determines evolutionary differentiation between CRCs, similar in grading and staging. [6]

Approximately 10% of the CRC appear as a result of inherited genetic defects. [6–8] Hence, a comprehensive examination and anamnesis are necessary for identifying risk patients. Genetic studies proved CRC to be a cumulative end-result of sequential genetic alterations, the so-called “step-wise oncogenesis”, which can either be inherited or acquired during the course of some genetic diseases such as familial adenomatous polyposis (FAP), non-polyposic hereditary colorectal cancer (NPHCC) and sporadic colorectal cancer. These can be diagnosed by

molecular studies of the APC gene, RAS oncogenes, study of the peripheral blood DNA, stool and intestinal biopsies. [4, 6–8]

Lifestyle – Dietary factors.

Lifestyle is undisputedly an important risk factor which influences the apparition of CRC. [1, 3–5] Alimentation, both quantitatively and qualitatively, is closely connected with an increase in the risk for CRC. Fruit and vegetable consumption has an anticancerous role, as opposed to a low-fiber, high fat nutrition, which slows bowel movements, alters the intestinal flora and increases the recycling of biliary acids. [1, 3, 5] Alcohol, by inducing cellular proliferation and inhibiting DNA repair, increases up to two-three times the risk for CRC. Other studies showed only a 10% increase for CRC in alcohol consumers. [4, 5, 9]

Lifestyle – Smoking.

Smoking increases the risk, as it enables various carcinogenetic substances (aromatic hydrocarbs, nitrous-amines and aromatic amines). [1–4] Another factor which plays a significant role is physical activity, which lowers the rate of CRC development by stimulating bowel movements and lowering E2 prostaglandins. [4, 5]

Risk factors associated with other diseases.

Studies showed the direct correlation between substitution hormone therapy in menopausal women and CRC development, even though no direct link between the two was ever established. One possible explanation might be that, as the age when hormone therapy is usually administered is usually similar to the age when regular controls are needed, the full body exams detect CRCs at a higher rate. [4, 10]

Also, patients who underwent cholecystectomies, by an alteration of their biliary acids, have an increased risk for CRC development, especially in the proximal colon.

Diabetes mellitus is always quoted as a risk factor for CRC development. [1–5] Acromegalics are more predisposed to CRC through metabolic alterations. [11–13]

Ulcerative colitis as a risk factor.

Ulcerative colitis represents a major cause of CRC. The risk for malignization is 2% after 10 years and 18% after 30 years of inflammatory affect. [10, 11] Extension of the colitis to the pancolitis stage is associated with the malignisation risk. [11, 12] Although the

mechanisms through which the risk for CRC increases were not studied extensively, sclerosant colangitis represents an additional risk factor. Studies did not show an increase of CRC risk in patients with collagenous and lymphocytic colitis. The mechanisms through which neoplasia develops on an inflammatory affection differ from those involved in sporadic cancers, as aneuploidy appears at an early stage in the carcinogenetic process. [1, 5, 13]

Symptoms

Many of the symptoms of CRC are vague and non-specific (abdominal pain, constipations or diarrhea), some of them being the same in benign pathologies. Rectal cancer however displays more specific symptoms. [1–4, 10] Older patients can provide more accurate information regarding their suffering, as they undergo more frequent consults than younger patients. [3, 11, 12] Even though no major results have been obtained so far, many studies tried to promote an examination guide for patients with gastrointestinal symptoms in order to identify the high-risk population. Population should be informed on the symptoms of CRC, in order to be diagnosed promptly and undergo treatment in as low as 14 days. [12–16]

Also, more rarely, one must take notice of the possible osteomas, fibromas, lipomas, dermoid tumors, and thyroid, biliary and liver or adrenal neoplasms in patients with the Gardner syndrome; finding brain tumors in patients with the Turcot syndrome; cutaneo-mucous pigmentations in Peutz-Jeghers syndrome patients; identifying cancers in the female genital area, stomach, skin, larynx in those with non-polypomatous colorectal cancer. [16–19]

Metachronous colon cancer.

Research showed that tumoral adenomas are involved in the development of a metachronous colon cancer (MCC). [14–16, 19]

Although no predictive factor has been discovered so far, patients with CRC have the highest risk to develop MCC. None of the tumoral particularities represents a predictive factor. The insufficient literature data accounts for the low incidence (2-12%) MCC has worldwide. [20] Other explanations are related to the fact the population is rare, and requires constant surveillance over a long period of time. Existence of a synchronous CRC increases the risk for a MCC. Risk is not influenced by the size of the tumor, development rate or existing adenomas. More frequently, the MCC is localized on the right

colon, exists as a vegetant tumor and therefore, gets diagnosed more rapidly. [19, 20]

Screening

When referring to early detection of CRC, classic screening methods include the occult fecal blood test. [12, 15, 17] This method did not bring remarkable progress; it is recommended to all persons above 40 years old, reducing mortality through CRC by 30%. [12, 15] The large display of digestive and extra-digestive manifestations of genetic diseases requires complex screening techniques, such as identifying gastrointestinal polyps, colonoscopy (recommended to all persons above 50 years old each five years and more frequently – at two years intervals – to people who already underwent polypectomy). [15–21]

Conclusion

In conclusion, progresses in the field of identifying and in-depth interpreting of the risk factors gave birth to several national screening programs, while advancing health policies on the globe, having in the end a positive effect on the increase in survival rate for CRC patients.

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