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Review

Adenomas – Genetic factors in colorectal cancer prevention

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ABSTRACT

Colorectal cancer is the second most common type of cancer both in Europe and Poland. During the last 30 years more than a 3-fold increase has been observed in Poland due to environmental and genetic factors. Almost all colorectal malignancies are related to the formation and malignant transformation of colorectal dysplasia and adenoma. Efforts aiming to decrease the number of colorectal cancer deaths are focused on the disease early detection. Genetic diagnosis for hereditary syndromes predisposing to colorectal cancer has been developed and is a part of the routine treatment. Most cancers are sporadic. They often develop from polyps in the colon. In addition to the genetic events described in the 1990s, showing the adenoma transformation into carcinoma that has been a prime example of malignant transformation for a long time, there are also other possibilities of neoplastic transformation. The recognition of colorectal cancer risk factors make sense as their nature is lifestyle- and diet-related. In this review paper those risk factors are presented and the prevention of colorectal cancer is discussed taking into account genetic factors.

1. Introduction

Colorectal cancer is the second most common cancer site both in Europe (Fig. 1) and Poland when analyzing cancer incidence.[1] During the last 30 years, in Poland, more than a three-fold increase in incidence has been observed in women and nearly a four-fold increase in men.[2]

Environmental and genetic factors are basic contributors to this increase. Almost all of the colorectal malignancies are related to the formation and malignant transformation of colorectal dysplasia and adenoma. Colorectal cancer develops through many different pathways, including the serrated pathway and the classical adenoma-carcinoma sequence.[3] Adenomas are classified due to the histopathological structure

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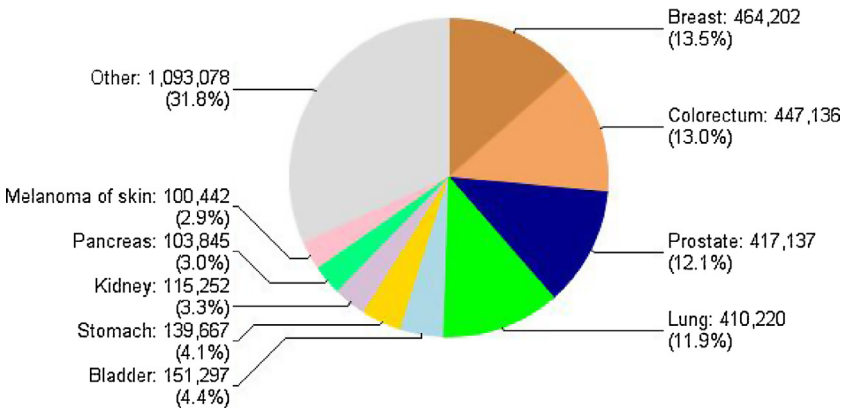

Fig. 1 – Cancer incidence in Europe by site, both sexes 2012.

as: Traditional and Sessile Serrated Adenomas, Tubular, Tubulovillous and Villous. Among the Serrated Polyps, only those having dysplasia (traditional) or sessile type (SSA), even without dysplasia, are classified as adenomas – polyps with potential for carcinogenesis. Among the polyposis syndromes, we identify also those with a predominance of, for example, hyperplastic polyps that do not belong to adenomas, but remarkably increases the risk of developing adenoma, dysplasia and cancer. Juvenille Polyposis,[6] MAP (MUTYH Associated Polyposis)[4] and Peutz Jeghers Syndrome[5] belong to those syndromes. Efforts aiming to decrease the number of colorectal cancer deaths are focused on the disease early detection.[6–8] A reduction of the colorectal cancer incidence can be achieved by proper prevention. Genetic diagnosis for hereditary syndromes predisposing to colorectal cancer has been developed and is a part of the routine treatment of colorectal cancer patients and members of their families. Most cancers are sporadic, they often develop from polyps in the colon. The sequence of genetic events described in the 90s showing the adenoma/carcinoma transformation has been a prime example of malignant transformation for a long time,[9] but there are also other possibilities of neoplastic transformation.[3] Knowledge of the colorectal cancer risk factors is important because of the nature of these modifiable lifestyle and diet-related factors.

In this paper we present the risk factors and prevention of colorectal cancer taking into account genetic factors.

2. Risk factors for adenomas

2.1. *Environmental factors*

The environmental factors are associated with sporadic cancer and are responsible for about 83% of all colorectal cancer cases. Among these patients, the sole influence of the environment is detected in 30%. In 28% of them, cancer is associated with epigenetic mutations such as in DNA repair genes, the remaining 25% have a positive family history. Transcriptional inactivation by promoter CpG island methylation in tumor suppressor genes is an important mechanism which can silence tumor suppressor genes. Epigenetic suppressor gene silencing has commonly been involved in colorectal cancer.[10,11] Epigenetic changes are usually associated with age. The aging process is associated with a wide variety of exposure to risk factors, so its effect is a kind of an accumulation of various processes. A concatenation between the methylation status of genes and a familial tendency to colorectal cancer have been described in several reports.[1,10,11] Polish studies conducted under the National Colorectal Cancer Screening Program emphasize the role of the male sex, because of the lifestyle associated with higher exposure to risk factors that promotes the formation of high-risk adenomas (advanced neoplasia).[12]

Obesity contributes to an increased risk of adenomas and cancer, as does a diet rich in processed products and red meat. Underlying this risk is not only epigenetic disorders associated with abnormal methylation, but also the inflammatory processes.[13] The Metabolic Syndrome is in close connection with these factors which is a consequence of incorrect diet and lifestyle, but also limitation of physical activity. Metabolic Syndrome is associated with weight gain, low levels of high density lipoprotein (HDL), hypertriglyceridemia and hypertension hyperglycemia.[14–16] One of its liver manifestations may be nonalcoholic fatty liver disease (NAFLD) that is an independent colorectal cancer risk factor.[17] All these factors lead to epigenetic changes which, in combination with positive family history, increase the risk of colorectal cancer.

2.2. *Diet and red meat consumption*

No correlation has been found between the total intake of protein and the risk of colorectal cancer development. The focus on the role of eating processed and red meat is increasing. Food preparation methods such as grilling meat causes the formation of carcinogenic polycyclic aromatic hydrocarbons and heterocyclic amines, but also generates the formation of DNA-damaging free radicals.[13]

Protective diet-related factors documented in recent years include the intake of vegetables, fruit and whole grains. The protective effect is related to the content of dietary fiber, which dilutes, absorbs, and removes the cocarcinogens, carcinogens and/or tumor promoters that are present in the gut.[13]