

# LIFE STYLE AND NUTRITIONAL ASPECTS IN THE DEVELOPMENT OF COLORECTAL CANCER IN ELDERLY PATIENTS

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## REZUMAT

Scopul acestui articol îl constituie evaluarea, la vârstnici, a riscului de a dezvolta cancer colorectal în funcție de dietă și stil de viață. Pentru ca această lucrare să ofere o analiză cât mai pertinentă a subiectului, au fost revizuite mai multe studii relevante din literatura de specialitate. În acest context, subliniem faptul că riscul dezvoltării unui cancer colorectal pare să fie legat de cumulara mai multor factori incluzând aici: obiceiurile alimentare (ex. consumul de carne, grăsimi), factorii constituționali (ex. hormonii feminini, timpul tranzitului intestinal), cât și stilul de viață (consumul crescut de alcool, fumatul, obezitatea, sedentarismul). Deși evaluarea impactului fiecărui factor în dezvoltarea acestei forme de cancer este dificilă, putem susține că stilul de viață, cât și obiceiurile alimentare din cursul vieții, constituie principalele premise în dezvoltarea cancerului colorectal la vârstnici. Această revizuire a literaturii subliniază importanța unui stil de viață sănătos cât și a factorilor de nutriție. Un rol protector în dezvoltarea cancerului colorectal este exercitat de către consumul regulat de pește, fructe sau legume proaspete, în timp ce consumul de carne roșie (porc) sau carne procesată (cârnați, șuncă, salam) crește riscul de a dezvolta un cancer colorectal, în special la vârstnici.

**Cuvinte cheie:** cancer colorectal, vârstnic, dietă, nutriție, carne, fructe, legume, stil de viață

## ABSTRACT

The aim of this study was to evaluate the relationship between diet and lifestyle and colorectal cancer risk at elderly patients. In order for this study to provide more comprehensive insights of the process, we reviewed many relevant studies where this correlation has been analyzed. In this context, we claim that colorectal cancer risk seems to be linked with the clustering of various factors, including lifestyle variables (high alcohol consumption, smoking, obesity, sedentary life); dietary habits (e.g., meat, fat intake); or constitutional factors (e.g., female sex hormone, bowel transit time). However, even if it is hard to evaluate the effect of each factor in colorectal cancer development, it can be claimed that dietary habits and lifestyle during youth and middle age of a person constitute the main premises of older age malignancies. This review of the literature emphasizes the importance of a healthy lifestyle and the nutritional aspects such as the consumption of fruits, vegetables, fish, meat, and cereals in decreasing the risk for colorectal cancer. This risk seems to be positively associated with red meat (pork) and processed meat (sausages, ham, salami) intake and inversely associated with the consumption of fish, fruits and raw vegetables.

**Key Words:** colorectal cancer, elderly, diet, nutrition, meat, fruit, vegetables, lifestyle

## INTRODUCTION

Age is an important determinant for cancer development. In support of this claim is the fact that the incidence of malignancies increases with age.<sup>1</sup> Life style and dietary habits (occidental diet type) during youth and middle age constitute the main assumption of older age malignancies, especially related with colon and rectum.

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According to Keighley, colorectal cancer is the most common malignancy in Europe. In Romania, there are approximately 5,889 new cases per year of colorectal cancer and approximately 3,406 deaths per year.<sup>2</sup> The statistical data includes Romania in the group of European countries with a low incidence of colorectal cancer. Countries with a high incidence of colorectal cancer are Norway, Denmark, Netherlands, Sweden, Luxemburg, and Germany, because of the occidental diet type, poor in fiber and rich in red and processed meat, refined carbohydrates, and animal fat.

In Japan, colorectal cancer represents the third cause of death, among the patients with malignancies.<sup>3</sup> The majority of patients who die from gastrointestinal cancer in Japan are older than 65 years, justifying the positive correlation of these malignancies, in particular the colorectal cancer, with age.

## KEY FEATURES OF COLORECTAL CANCER IN ELDERLY

In elderly, the behavior of any malignancy is considered to be more „quiet” because of the well differentiation of the tumor with a slower growth and scant potential for metastasis.<sup>1</sup> In daily clinical practice, this fact is not an absolute rule, because we can also find cases with an aggressive behavior. A low grade malignancy and also a less occurrence of lymph node metastasis are usually found in elderly patients, as compared with younger ones.<sup>4</sup> However, this group of patients has an advanced stage of cancer because of the late presentation to the doctor.<sup>5,6</sup>

In older patients, the most frequent localization of the tumor, found in approximately one-half of patients, is in the proximal part of the colon (proximal to the splenic flexure).<sup>5,7,8</sup> (Table 1) Elderly female patients seem to be more related with this feature as compared with men patients.<sup>9</sup>

**Table 1.** Characteristics of colorectal cancer in elderly.<sup>1</sup>

	<b>Elderly</b>
<b>Locus</b>	Predilection for proximal colon (proximal to the splenic flexures), 30-50% of cases, especially in women
<b>Histology</b>	Frequently poor differentiated adenocarcinoma, especially medullary type, and mucinous carcinoma
<b>Patterns of metastases</b>	Low rate of metastasis, 38% of cases present lymph node metastasis
<b>Multiple colorectal carcinomas</b>	8-15% of cases, which are mostly located in the same or adjacent segments of the colon
<b>Extra-colorectal cancers</b>	25% of cases, which are localized in the stomach (29%), lung (14%), pancreatobiliary systems (10%), hematopoietic system (10%)
<b>Familial</b>	Rare

The carcinogenesis process increases with age. Many factors influence this process. Present data suggests the role of the nuclear and mitochondrial DNA damage, induced by endogenous (oxygen free radicals) and exogenous agents (ultraviolet radiations, pollution).<sup>10</sup> In addition, alteration in metabolism and neuroendocrine systems, alterations in DNA repair, and also the presence of hypermethylation of genes, apoptosis, immunosenescence, telomere shortening and telomere dysfunctions influence the process of carcinogenesis related with age.<sup>11</sup> It is interesting

to notice that, in elderly patients, the presence of apoptosis in the malignant tissue, determine a slower growth of the tumor.<sup>12</sup> This particular aspect explains, in part, the „quiet” behavior of the colorectal cancer in elderly.

## NUTRITIONAL ASPECTS

Diet plays an important role in carcinogenesis process. Many studies have tried to establish a real correlation between nutritional aspects and malignancies onset. It is still very hard to identify the impact of every dietary compound, in singular or combined intake, in the cancer development process.

In 1990, Willett et al. reported for the first time the association between the high intake of red meat and the increased risk to develop colorectal cancer.<sup>13</sup> After this research other studies underlined the same conclusion.<sup>14,15</sup> However, in the medical literature there are also studies who reported no association between meat intake and colorectal cancer development.<sup>16</sup>

In 2005, the European Prospective Investigation into Cancer and Nutrition published the results of the largest European study ever done in this field.<sup>17</sup> This prospective study included 478,040 men and women, with aged between 35 and 70 years, who where without cancer at the moment of inclusion in the study. The patients were recruited from the general population of the ten European countries. One thousand three hundred twenty nine patients developed colorectal cancer after a period of approximately five years. The aim of this laborious study was to evaluate if there is any relation between diet, lifestyle, genetic, and environmental factors and the risk to develop different forms of colorectal cancer. The results of this study have proved the strong association between lifestyle, especially diet and the colorectal cancer development. The risk to develop cancer in the colon and rectum is positively correlated with an increased consumption of red meat and processed meat and inversely correlated with the consumption of fish. (Table 2) From the patients evaluated for the fish intake, the absolute risk to develop colorectal cancer within 10 years was as follows: 1.86% for patients from the lowest category of fish intake (<10 g/day) and 1.28% for patients from the highest category (>80 g/day) of the same group. For the patients with consumption of red and processed meat, the absolute risk to develop cancer was as follows: 1.28% for patients from the lowest category of red/processed meat (<20 g/day) and 1.71% for patients from the highest category (>160 g/day) of the same group.

**Table 2.** Nutritional aspects and the risk to develop colorectal cancer.

		<b>Risk for colorectal cancer development</b>	<b>Locus<sup>17</sup></b>
<b>Meat intake</b>	<b>Red meat</b> - pork,	↑, found in higher consumers (>160 g/day) <sup>17</sup>	Right/left site of the colon and rectum (but not statistically significant)
	<b>Red meat</b> - lamb	↑ <sup>17</sup>	Right/left site of the colon and rectum (but not statistically significant)
	<b>Red meat</b> - beef/veal	Not found <sup>17</sup>	Right/left site of the colon and rectum (but not statistically significant)
	<b>Processed meat</b> (ham, bacon, sausages)	↑, found in higher consumers (>160g /day), but not independently related to colorectal cancer development <sup>17</sup>	Left site of the colon and rectum
<b>Fish</b>	Fish oils or fatty cold water fish	↓, >80g/day for fish intake <sup>17</sup>	Frequently in the left site of the colon and rectum (but not statistically significant)
<b>Poultry</b>	Chicken	Not found <sup>17</sup>	
<b>Cereals</b>	Refined white flour products	↑, but still insufficient data <sup>32</sup>	
	Whole grain	↓, but still considered probable <sup>32</sup>	
<b>Dairy products</b>	Milk, dairy-produce	↓, but still considered probable <sup>32</sup>	
<b>Fruits and vegetables</b>		↑, found in lower consumers (<17 g/day) <sup>17</sup> ↑, found if it is a low consumption (≤ 1.5 servings per day) <sup>26</sup> ↓, if it is a high consumption of raw vegetables and fruits <sup>32</sup>	
<b>Folate (folic acid)</b>		Not statistically significant <sup>17</sup> ↑, found in cases with deficiency of this nutrient (erythrocytes folate <140 ng MI or plasma folate <3 ng MI) <sup>26</sup>	
<b>Other minerals, vitamins and oligo-elements</b>	Calcium, selenium, vitamin D, vitamin E	Insufficient data <sup>32</sup>	
<b>Drinks</b>	Coffee, tea	Not found <sup>39</sup>	
<b>Other factors</b>	Obesity, high alcohol consumption, smoking, and sedentary living	↑, cumulative aspect <sup>26</sup> possible, but insufficient data <sup>17,32</sup>	

The authors did not find any relation between the poultry intake and the colorectal cancer development. It is very important to admit and to recognize that this study has some limitations because of the imprecise estimation of the food intake, who can lead to a possible wrong estimation of the disease risk.

The role of fiber intake was also evaluated in this large study. From the patients with a high intake of red and processed meat, only those with a low (<17 g/day)

and medium (17 to 26 g/day in women and 17 to 28 g/day in men) fiber intake were more strongly associated with the development of colorectal cancer.

The mechanism of colorectal carcinogenesis among the patients with excessive consumption of red and processed meat is still not fully elucidated. Some theories have been launched. For example, the presence of endogenous N-nitroso compounds in gastrointestinal tract, after the ingestion of red and

processed meat could increase the colorectal cancer risk.<sup>18,19</sup> These endogenous nitrosation are formed from heme. The processed meat contains higher amounts of heme as compared with poultry that do not increase the formation of endogenous N-nitroso compounds because it contains lower amounts of heme.<sup>19</sup> Also, the heterocyclic amines could play a role in carcinogenesis.<sup>20</sup> These substances results from the process of cooking, mainly at high temperatures. The main contributor to heterocyclic amines intake is chicken, but there are no studies to reveal a positive association between the intake of poultry and colorectal cancer risk. Other compounds possible involved in the colorectal cancer development are polycyclic aromatic hydrocarbons, who arise also from the process of cooking the meat (grill, barbecue).<sup>20</sup> There are studies focused on the genes who encode the enzymes for the metabolism of heterocyclic amines and polycyclic aromatic hydrocarbons, but the results are unclear.<sup>21,22</sup> Constipation, usually a problem of elderly, increases the exposure of these substances inside the gastrointestinal tract.<sup>23</sup>

The process of cooking meat is very different across the Europe. The processed meat usually contains pork and beef meats. To preserve these meats, a lot of ingredients are added, such as salt, sugar, spices, nitrite, nitrate, water, and fat.<sup>24</sup> Nitrites and nitrates exhibit an association with colorectal cancer risk, because they can expand the exogenous exposure to nitrosamines and their precursors. This fact can partially explain why the processed meat is more strongly correlated with colorectal cancer risk compared with red meat intake.

The benefic role of high fish consumption can be explained by the presence of n-3 fatty acids from the fish oils or fatty cold water fish, which inhibit the carcinogenesis process. Among n-3 fatty acids, the main protective role is exhibit by the long-chain polyunsaturated fatty acids (eicosapentaenoic and docosahexaenoic acids).<sup>25</sup>

Terry et al. studied the link between fruits and vegetables intake and malignancies.<sup>26</sup> It is well known that fruits and vegetables are rich in antioxidants, substances capable to neutralize the DNA-damaging free radicals and to reduce the damage caused by the aggression of modern environmental, like pollution, UV rays, and smoking.<sup>26,27</sup> Fruits and vegetables are also rich in anti-carcinogenic substances like carotenoids, dithiolthiones, glusinolates, indoles, flavonoides, phenols, and protease inhibitors.<sup>28</sup> Diets rich in antioxidants play an important role in cancer prevention, anti-aging process, and also in

cardiovascular protection. We find antioxidants in fruits, derivate product like wine (especially the red wine), vegetables, and in chocolate (from the cocoa bean). Dark chocolate is higher in antioxidants because of its high cocoa content. Fruits and vegetables are inversely associated with the colorectal cancer development.<sup>29,30</sup> A positive correlation is attributed only to the cases with a low consumption of fruits and vegetables.<sup>31</sup> Of interest, the study emphasizes the fact that a consumption of more than 2.5 servings per day is not associated with the development of colorectal cancer. The risk increases with a 1.5 servings of fruits and vegetables per day. Ströhle et al. underline the anticancer properties of the fruits and vegetables, especially in uncooked form.<sup>32</sup>

Other studies emphasize the fact that environmental and constitutional factors play an important role in the development of colorectal cancer, in general population and particularly, in elderly people. These groups of factors includes the consumption of fruits and vegetables, cereals and seeds, red meat and fish, or female sex hormone, bile acid, bacterial flora, and intestinal transit time.<sup>33,34</sup>

The positive or negative influence of cereals intake is mainly correlated with the manufacturing process. There are no sufficient data about the high consumption of the refined white flour products and the colorectal cancer risk, but it is widely believed that these products have carcinogenic properties.<sup>32</sup> Also, the whole grain (seeds) consumption decreases the risk to develop colorectal cancer, but the evidences are still insufficient.

The dairy products, especially milk, are considered to exert an effect of risk reduction for colorectal cancer.<sup>32</sup> On the contrary, the consumption of eggs is considered to have a negative influence, being associated with a higher risk to develop colorectal cancer. Present data suggests that diets with a high content of fat increases the risk of malignancy in an indirect way, because these diets enlarge the odds of obesity, especially the visceral one.

The folate intake and the colorectal cancer risk were intensely debated.<sup>35,36</sup> Giovannucci et al. revealed the inverse correlation between folate intake and colorectal cancer development.<sup>35</sup> Folic acid contributes to the process of carcinogenesis because of its implication in normal DNA synthesis and repair. This fact explained in part, the development of cancer in cases with deficiency of folic acid.<sup>36</sup> Strohle et al. emphasize the lower risk to develop colorectal cancer with the regular intake of higher amounts of folic acid, from the multivitamins supplements.<sup>32</sup>

The correlation between the colorectal cancer development and other minerals and vitamins has been also debated. Further studies need to be performed in order to establish if selenium, calcium, vitamin D, or vitamin E, have a role in the onset of colorectal cancer. The present evidence concerning this aspect is insufficient.<sup>32</sup>

Lifestyle plays also an important role in the process of carcinogenesis. Positive risk factors who contribute to this process are obesity, high alcohol consumption, smoking, and low physical activity. Giovannucci et al. suggested that high recurrent alcohol intake increases the cancer risk and develop so called alcohol-induced colorectal cancer, but the present data underlies just the possible risk to develop this malignancy.<sup>32,37</sup> It is important to recognize that these factors have to be cumulated with dietary and genetic factors to develop colorectal cancer. Willett suggests that approximately 70% of colorectal cancers could be avoided if the patients accepted changes in lifestyle, especially in diet, to improve the quality of life.<sup>38</sup>

## CONCLUSIONS

Carcinogenesis process increases during lifetime, making the age an important risk factor for cancer. Nowadays, the association between nutritional aspects and colorectal cancer risk is intensely debated. It is a fact that diet plays an important role in the onset of malignancies, especially of those related with gastrointestinal tract. However, colorectal cancer risk is related with the clustering of various factors, including life style variables, like high alcohol consumption, smoking, obesity, or sedentary life. Even if it is hard to identify the impact of each factor in the cancer development process, it can be stated that dietary habits and life style during youth and middle age of a person constitutes the main premises of older age malignancies. In this context, diets rich in red meat (pork, lamb), processed meat (ham, sausages, salami), or refined white flour products (bread, brioche, doughnut), or poor in fish (fatty cold water fish), whole grain (seeds), raw vegetables, or fruits accelerate carcinogenesis process.

Further research needs to be carried out in order to establish, to what extent, other dietary compounds, in singular or combined intake, play a protective or rather unprotective role in the development of colorectal cancer.

In this context, the goal is to prevent and to delay the colorectal cancer onset, mainly by encouraging healthy diets as a requirement of improving the quality of life.

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