

# Epidemiologic factors of colorectal cancer in a county hospital in Romania

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**Abstract.** Colorectal cancer is the most common digestive cancer. The aim of this study is to determine the colorectal cancer’s frequency related to age, gender, personal or family history, and also to blood group of the patients operated in the County Emergency Hospital of Baia Mare, Romania. Material and methods: The records of 512 patients with cancer of the colon, rectal cancer and synchronous colorectal cancer were studied retrospectively in a period of 15 years, admitted to The Department of Surgery in The County Emergency Hospital of Baia Mare, Romania. Results: Colorectal cancers have been found to be more frequent in women under the age of 50 and in men above this age ( $p=0.004$ ). In urban environments the right colon cancer (59.62%) and rectal cancer (55.87%) were more frequently encountered. Tumor location had an almost even distribution: 30% right colon, 35.45% left colon, 34.96% rectal cancer and 0.78% synchronous cancers. The association with personal and family history was statistically insignificant, except asthma which was considered a protective factor ( $p<0.001$ ) for colorectal cancer. The abundance in blood groups shows proportional distribution with their representation in the population of our country, but family history of colorectal cancer was found only in O and A groups. Conclusions: The study ascertains the left to right shift of the large bowel cancers, the increasing of medium age of patients and high incidence of colorectal cancer in women under the age of 50 years. Asthma may be a protective factor for colorectal cancer, especially for right colon cancer, and genetic factors are present only in patients with O and A blood groups.

**Key Words:** colorectal cancer, epidemiology, age, asthma, blood groups.

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## Introduction

Epidemiologic arguments indicate the possibility of colorectal cancer prophylaxis by influencing the environment and the lifestyle (Sasieni 2003; Rothman *et al* 2008; Printz 2011). Thereby, it was revealed a great variability for colorectal cancer incidence, which rates vary about 20 times between extremes – India and SUA, economically - developed countries being most affected because of red meat, fat or alcohol intake, sedentary life and smoking (Kirkegaard *et al* 2010; Watson *et al* 2011). But, in the past decades, those countries registered a decline of incidence and mortality of the disease due to screening efficiency and endoscopic resection of colorectal polyps (Phillips *et al* 2007; Lieberman *et al* 2008). In the same geographical areas, different incidences arise, related to ethnic groups, alimentary habits, and different lifestyles, but also because of different economic status, education and access to health care services which are unequal (Shokar *et al* 2007; CDC 2010). The most important argument seems to be the risk of colorectal cancer in immigrants which, beginning with the second generation, strive to have the same incidence with the indigenous population (Shokar *et al* 2008; Mousavi *et al* 2012).

In Romania, the incidence has doubled over the past 20 years, going up to 22.8 per 100,000 inhabitants, according to data

provided by GLOBOCAN in 2008, and becoming the second leading cause of death by cancer, after bronchopulmonary cancer and before gastric cancer. Epidemiology tries to identify the environmental factors that influence the onset and conversion of colorectal adenomas in cancer, and our study tries to study some epidemiological factors in this disease’s prophylaxis.

## Material and methods

We studied the medical records of 512 patients operated on for colon and rectal cancer in the Department of General Surgery of the County Emergency Hospital of Baia Mare, Romania, admitted between January 1994 and December 2008, for which we had the histopathological confirmation of the cancer.

Tumor location was grouped after embryological and vascularization criteria in right colon cancers – from ileocecal valve until the conjunction of the two right thirds with the left third of the transverse colon, left colon cancers – from the limit of the right colon until 15 cm above the anal sphincter, and rectal cancers – distal from this limit. The reinterventions and the recurrences of the tumors were taken out from this study.

We collected data on age, gender, environment, personal or family history, ABO and Rh blood type of the patients. From personal history we recorded the presence of appendectomy,

colectectomy, diabetes mellitus and asthma, as well as cancers related to colon cancer: family history of colorectal cancer and also breast, ovarian, uterine cervix, endometrial, pancreatic, gastric, biliary tract, prostatic cancer or melanoma diagnosed in these patients (Burke *et al* 1997; Brose *et al* 2002; Kadouri *et al* 2007).

Data were analyzed using Student's t-test and  $\chi^2$  (chi-squared) test), considering significant results when  $p < 0.05$ .

## Results

Considering the entire patient population operated in the County Emergency Hospital of Baia Mare, the assembly results show that from 512 patients, 276 were men (53.9%) and 236 were women (46.1%), with a sex ratio of about 7/6. Median age of the entire lot is 64.41 (range: 24-89) years, with variations between 59.92 in 1994 and 68.97 in 2005. Regarding the environment, 308 patients – 60.15% were from urban areas, and 204 (39.85%) from rural surroundings. Tumor distribution in these three locations shows close percentages: right colon – 156 patients (30%), left colon - 181 patients (35.35%), rectal cancers – 179 patients (34.96%) and synchronous cancers – 4 patients (0.78%) (Fig. 1).

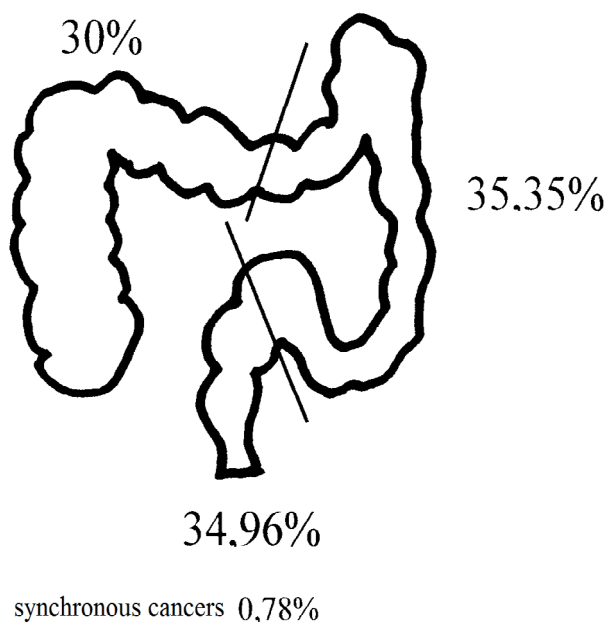


Figure 1. Location of colorectal cancers

We found an increasing of the patients' median age, in both sexes and in all three tumor locations, in the studied period of time (Fig. 2). On the other hand, considering the age of 50 – the age of menopause - we have observed that before this limit colorectal cancers prevail, statistically significant ( $P < 0.004$ ), in women (51.72%: 30 females vs. 28 males) in comparison to the age after 50 when we found more colorectal cancers in men ( 54.84%: 249 males vs. 205 females). Median age is not statistically significant when comparing patients from urban with those from rural areas, patients with appendectomies or

cholecystectomies, with familial or personal history of cancer, with diabetes, asthma, drugs allergies, or based on what kind of blood group they have.

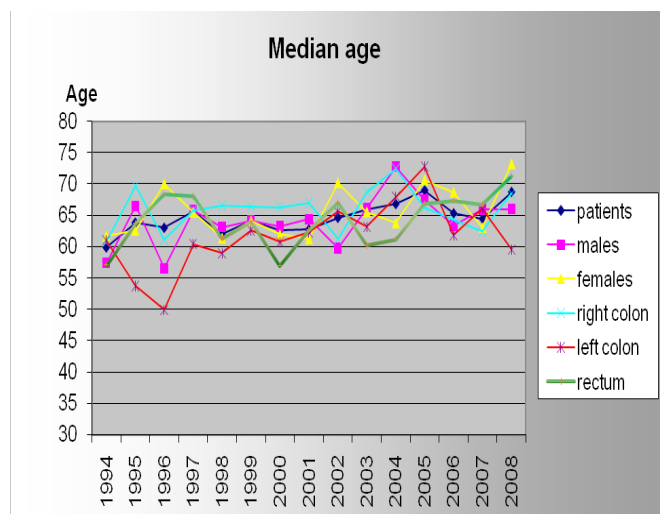


Figure 2. Median age of patients correlated with gender and tumor location

The male predominance of colorectal cancer ( 276 men – 53,9%) it was not found in the entire period of time: there were years with more operated women or both sexes were equally represented (Fig. 3). We observe a slight tendency to decrease the frequency in woman and increase in men ( 1994 – M/F = 41%/59% and 2008 – M/F = 56%/44% ).

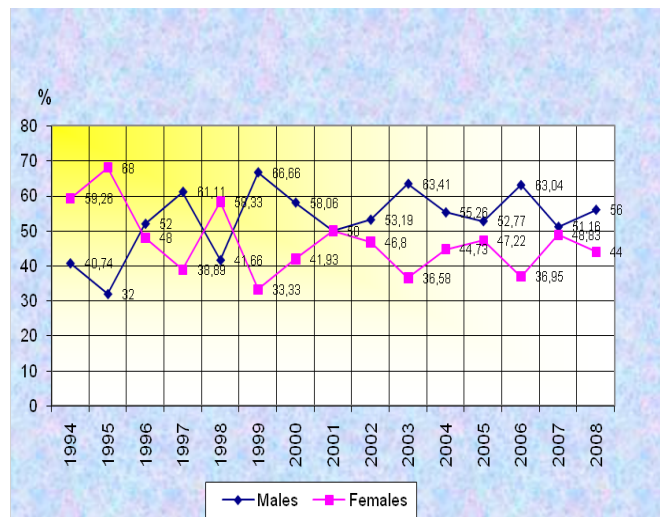


Figure 3. Gender repartition of patients with colorectal cancer between 1994 and 2008

Regarding the entire period of the study, in all three locations, colon and rectal cancers are more frequent among men (Table 1), but on age decades we ascertain female predominance on the grid extremes and male prevailing in 5, 6 and 7 decades of life. Regarding the tumor localization in patients from urban or rural surroundings, we found that right colon cancers and rectal cancers are more frequent in urban than in rural areas, although percentage are not statistically significant.

Table 1. Gender correlated with tumor location in colorectal cancer

|                | 1994-2008 Right colon cancer | Left colon cancer | Rectal cancer |
|----------------|------------------------------|-------------------|---------------|
| <b>Males</b>   | 53.20%                       | 54.90%            | 53.07%        |
| <b>Females</b> | 46.80%                       | 45.09%            | 46.92%        |

Correlations between tumor locations and personal or familial history are heterogeneous. Among all personal histories, only asthma correlates negatively with colorectal cancer: only 4 patients operated for colorectal cancers had bronchial asthma, disease that in Romania has a frequency of 7% in general population (Tudorache 2007):  $P < 0,001$ . Neither patient operated for right colon cancer had associated asthma (Fig. 4).

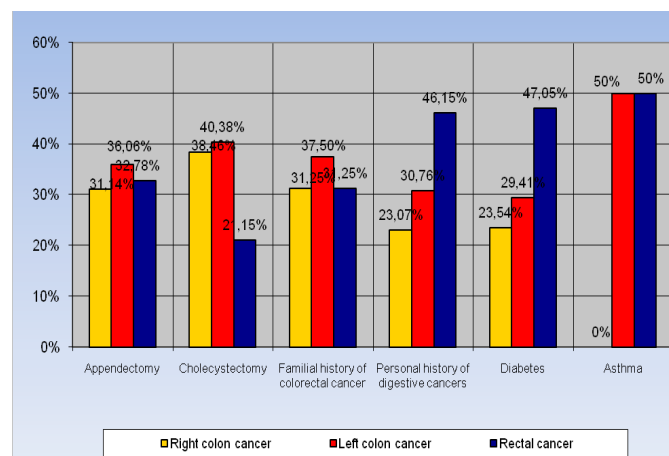


Figure 4. Personal and familial history correlated with tumor location in patients with colorectal cancers

During hospitalization, 365 patients (71,48%) received blood or blood preparations. Patients' distribution in ABO blood groups was similar to their frequency in general population in Romania (Table 2). The same finding is valid for Rh factor.

Table 2. Blood groups ABO and Rh factor of patients with colorectal cancer

| Blood group | General population in Romania | Colorectal cancer and Rh factor | Colorectal cancer |
|-------------|-------------------------------|---------------------------------|-------------------|
| <b>O</b>    | 34%                           | 0+                              | 30.41%            |
|             |                               | 0-                              | 4.93%             |
| <b>A</b>    | 41%                           | A+                              | 35.61%            |
|             |                               | A-                              | 5.20%             |
| <b>B</b>    | 19%                           | B+                              | 14.24%            |
|             |                               | B-                              | 3.83%             |
| <b>AB</b>   | 6%                            | AB+                             | 4.93%             |
|             |                               | AB-                             | 0.82%             |

Tumor location also follows the repartition of the ABO blood types in general population, but is interesting that patients with a family history of colorectal cancer were all in O and A groups, which are, is true, the most frequent among the population.

## Discussions

Epidemiological studies of colorectal cancer indicate a mortality that imposes itself like an important health care issue: 500.000

deaths and the third cause of death from cancer on Earth (Rex *et al* 2000; Parkin *et al* 2005). In Romania, in 2008, 8,696 new cases are discovered and 5178 deaths are registered (GLOBOCAN 2008), an increasing number, as compared to the beginning of the past century, following the changes of socio-economic status, but also due to screening for colorectal polyps.

If we bear in mind that only 5% of colorectal cancer etiology is genetically determined (Burn *et al* 2013), it means that environment factors' adjustment could influence the apparition and malignant transformation of colorectal polyps. The interruption of the pathological chain may have significant results by correcting risk factors and detecting in good time adenomatous polyps - prerequisite in colon and rectal cancer prophylaxis.

In operated patients population, in our hospital, we ascertain an increase of median age (59.92 years in 1994 and 68.72 years in 2008), explained by increased life expectancy but also by high frequency of colorectal polyps in aged persons (Lieberman 2009). Increase incidence with age proves that this is one of the most important risk factors. Median age is not significantly different with gender (M/F = 64, 15/65,55), tumor location, personal or familial history and neither patients' ABO blood groups. Gender repartition of patients differs on age decades: males are more affected between 50 and 79 years, and females have more frequent the disease in early ages and old ages. This finding is congruent with colonoscopy and morphopathologic studies that found a bigger incidence (almost double) of adenomatous polyps in middle aged males (Coode *et al* 1985; Farraye *et al* 2002) and one might speculate that malignization of these polyps is more frequent in women which have a higher incidence of the disease in old age. We ascertain in our patients that women are more affected than men before the age of menopause, as well as other studies that explain the difference by the effect of feminine hormones on p53 gene (McMichael *et al* 1980; Gerhardsson *et al* 1990) or by the smaller levels of physical activity (Gerhardsson *et al* 1986).

Tumor location was found in nearly equal percentages in operated patients and reflects a general tendency of colorectal cancer in the last part of the 20th century: "left to right switch" in all ages and both sexes probably due to high fat diets and sedentary life (McMichael *et al* 1985; West *et al* 1989). The immediate consequence of this finding is the increasing role of colonoscopy in the detection of large bowel cancer.

Higher incidence of colorectal cancer in urban areas confirms one more time the influence of environmental factors in this disease's etiology. There are few studies recorded in the literature about correlation between tumor location and environment and the results vary from region to region (Faivre *et al* 1989). Appendectomy in patients' personal history is not a risk factor for colorectal cancer, data also showed in the literature, but it must be mentioned that a painful syndrome in right lower quadrant in a middle-aged or old person can dissimulate a large bowel neoplasia. On the other hand, it was reported a high incidence of abdominal wall invasion, tumor fixity, distant metastasis and lower differentiation of the tumors in appendectomized patients (Armstrong *et al* 1989).

Cholecystectomy would promote the appearance of colorectal cancer by prolonged contact of biliary acids with the large bowel mucosa, by stimulating the appearance of colonic polyps and their malignant transformation (Giovannucci *et al* 1993), but

this association is not statistically significant in our patients. It would be interesting to verify whether adenomas occur in large numbers after cholecystectomy and if they are influenced by lifestyle changes.

Comparing diabetes' frequency in Romania with the frequency of this disease in patients operated for colorectal cancer, we have not found a significant association. Theoretically, the risk factor for colorectal cancer is represented by hiperinsulinism that precedes with few years the diabetes' appearance and has a proliferative role on large bowel mucosa (Weiderpass *et al* 1997; Magliano *et al* 2012). It was proposed even glucose tolerance test for patients with colorectal cancer for early detection of diabetes mellitus (Suehiro *et al* 2005).

Asthma is quoted as protection factor against large bowel cancer appearance, the mechanism involving the increase of immunocompetence by increased production of immunoglobulins E, interleukins and eosinophils with citotoxic anti-tumor effect (La Vecchia *et al* 1991; Turner *et al* 2005). This hypothesis was verified in our study ( $p < 0.001$ ). Moreover, any patient with right-sided colon cancer has no associated asthma which would explain the preferred distribution of eosinophils (Polydorides *et al* 2008) and T lymphocytes (Kirby *et al* 2003) in the mucosa of the large bowel at this level.

If genetic determinism plays a role only in 5% of colorectal cancers (the percent of familial aggregation found in our series is 1,95% - 10 patients, in the absence of genetic tests), raises the question of the screening for the entire population over a certain age limit, but also the question on patients' sanitary education. Only 29 patients from our study had colonoscopy (emergency operations, diagnosis established by radiologic examination), which explains also the small number of synchronous cancers. In Romania, the average number of colonoscopies is about 197,5/100.000 inhabitants (Sporea *et al* 2005), very small compared to USA (4950 colonoscopies/100.000 inhabitants) or France (1500 colonoscopies/100.000 inhabitants). Also the number of specialized centers in colorectal pathology is very small (Sporea *et al* 2005, 2009).

Our patients operated for large bowel cancer have the same percentage of blood groups as the general population in our country, but we observed the association between family history of colorectal cancer with blood groups type O and A. An association between group O and papillary adenomas was already mentioned in literature and could be due to the prevalence of these blood groups in the population and also because of the small number of patients with family history of cancer (Fleming *et al* 1967). But, if that hypothesis will be verified on large groups of patients, its use in screening would produce notable effects.

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