IMPROVING THE SCREENING OF COLORECTAL NEOPLASIA BY A MATHEMATICAL MODEL. RETROSPECTIVE STUDY

Madalin Munteanu¹, Corina Serban², Alina Popescu³, Ioan Sporea³

ABSTRACT

Introduction: Colonoscopy is a maximum accuracy diagnosis method for colorectal cancer and polyps, allowing multiple and guided biopsy of the observed lesions in the colonic lumen, but also the resection of the polyps. Aim: The purpose of this study was to perform a retrospective analyses of dates obtained from colonoscopy in order to create a mathematical model (risk calculator) which allows the selection of the patients with the highest probability to develop colorectal cancer. Material and methods: Dates from 2780 colonoscopies done in Timisoara County Clinical Emergency Hospital, during the period January 2005 to December 2008 were scrutinized. Results: 321 (11.5%) patients have had cancer. The classification of this group of 321 cancer cases by sex, has shown an increased incidence for men 193 (60.2%) cases. The incidence of colorectal cancer increases with age. Based on our statistic results and other studies developed in the world, we developed a mathematical prediction scheme for the colorectal cancer risk. The mathematical prediction scheme considers: age, sex, weight, height, personal history for polyps, and familial history of colorectal cancer, diet composition, physical activity and obesity. Conclusions: The development of this risk calculator for the colorectal cancer allows the selection of those particular subjects that have the highest probability for a colonic pathology, so that they would be the first to benefit from colonoscopy, without being necessary to use other screening methods. Key Words: colorectal, cancer, model matematic

INTRODUCTION

In the year 2006, in European Union were over two millions (2,288,100) cases of cancer and over one million (1,165,500) deaths.¹ For men, the highest incidence was for prostate cancer, followed by pulmonary cancer, colorectal cancer being the third (163,100 cases, 13% of all cancers).¹ For women, the highest incidence was for breast cancer, while the colorectal cancer was the second (134,100 cases, 12.9% of all cancers).¹
Colorectal cancer is a major problem of public health. It has the second place in oncologic incidence in the developed countries. It has been estimated that in 2006, 413,000 Europeans have been recently diagnosed with colorectal cancer and 207,000 have died. In 2006, in Romania the colorectal cancer incidence rate was 40.7 for men and of 25.4 for women, and the mortality rate was of 23.5 and 14.5, for women, respectively for men.

There are some factors that will increase the chances of a person to develop polyps or colorectal cancer. It is about:

- Risk factors that cannot be influenced: age, personal history of polyps or colorectal cancer, personal history of inflammatory bowel diseases, familial history of colorectal cancer, syndromes genetically transmitted, race and ethnicity.

- Risk factors which are related to the life style: diet, physical activity, obesity, smoking, drinking alcohol, diabetes.

- Risk factors with a controversial role: cholecystectomy, Barrett’s esophagus, subtotal gastrectomy, acromegaly, night shift, radiation.

Age is considered to be the main risk factor. Chances to develop colorectal cancer grow considerably after the age of 50, more than 90% of patients diagnosed being over 50 years old. Men have a higher risk than women.

Personal history of colorectal cancer or polyps: probably over 85% of colorectal cancers develop from colonic polyps, which leads to the idea that for colorectal cancer there is a premalignant lesion well defined and that is the adenomatous polyp. The potential malignity of polyps is different from the point of view of size and histological type. For an adenomatous polyp, 20 mm or more, the malignancy risk is about 50%, while for a 10 mm villous polyp the risk is of 30%. The estimated risk for a polyp bigger than 10 mm to become malignant is 3% at 5 years, 8% at 10 years and 24% at 20 years.

Familial history of colorectal cancer: for a person with affected first-degree relatives, the relative risk for colorectal cancer is two to three times higher. The risk is greater if the adenoma or carcinoma has appeared at a young relative, or when more than one person in the family had cancer.

Diet: many studies have shown differences of dietary patterns for person with small, medium and high risk for colorectal cancer. Table 1 shows the relative risk of colorectal cancer associated with consuming red meat and processed meat.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study years</th>
<th>Relative risk for red meat</th>
<th>Relative risk for processed meat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larson</td>
<td>1966 – 2006</td>
<td>1.22</td>
<td>1.09</td>
</tr>
<tr>
<td>Norat</td>
<td>1973 – 1999</td>
<td>1.24</td>
<td>1.36</td>
</tr>
<tr>
<td>Sandhu</td>
<td>1980 – 1999</td>
<td>1.17</td>
<td>1.49</td>
</tr>
<tr>
<td>Oba</td>
<td>1992 - 2000</td>
<td>-</td>
<td>1.98</td>
</tr>
</tbody>
</table>

Material and Methods

This retrospective study was based on colonoscopic reports gathered from a four year period. Data from 2780 colonoscopies done during January 2005 to December 2008 in the Gastroenterology and Hepatology Clinic, Timisoara County Clinical Emergency Hospital, was analyzed.

Patient’s age, gender, size and location of all polyps and tumors discovered were recorded. The anatomic location of all tumors was estimated based on anatomic landmarks and by the length of colonoscope insertion.

The location of carcinomas was categorized into three groups: left colon (sigmoid, descending colon, rectosigmoid junction and splenic flexure), right colon (cecum, ascending colon, hepatic flexure and transverse colon), and rectum. Informed consent was obtained from all patients, and the study was approved by the ethics committee of our Hospital.

Results

From the total of 2780 patients, 1484 (53.4%) were women and 1296 (46.6%) were men.
The age groups that have participated in this study were between 7.8% (216 patients) – lowest incidence – met at group age <40 years and 29.1% (810 patients) – highest incidence – met at group age 50-59 years. (Table 2)

By all 2780 patients examined by colonoscopy, 321 (11.5%) of them have had cancer (4.6% were women and 6.9% were men).

The sex repartition of these patients indicate an increase incidence at men 193 (60.2%) cases comparative to women 128 (39.8%).

Table 2. Group distribution by age.

<table>
<thead>
<tr>
<th>Group age (years)</th>
<th>Patients (number)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>216</td>
<td>7.8</td>
</tr>
<tr>
<td>40 – 49</td>
<td>308</td>
<td>11.1</td>
</tr>
<tr>
<td>50 – 59</td>
<td>810</td>
<td>29.1</td>
</tr>
<tr>
<td>60 – 69</td>
<td>721</td>
<td>25.9</td>
</tr>
<tr>
<td>≥70</td>
<td>725</td>
<td>26.1</td>
</tr>
</tbody>
</table>

Depending on the anatomical location of cancer we have observed that patients have had the following types of cancer:

- 110 patients (34.3%) rectal cancer;
- 116 patients (36.1%) left side colon cancer;
- 83 patients (25.9%) right side colon cancer;
- 12 patients (3.7%) mixed colon cancer.

After age and sex criteria, we noticed that the most affected group of age was the one ≥ 70 years. (Table 3)

Table 3. Number (%) of patients, grouped by age and sex.

<table>
<thead>
<tr>
<th>Group age (years)</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>6 (1.9%)</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>40 – 49</td>
<td>13 (4%)</td>
<td>12 (3.8%)</td>
</tr>
<tr>
<td>50 – 59</td>
<td>26 (8%)</td>
<td>35 (10.9%)</td>
</tr>
<tr>
<td>60 – 69</td>
<td>24 (7.5%)</td>
<td>47 (14.7%)</td>
</tr>
<tr>
<td>≥70</td>
<td>59 (18.4%)</td>
<td>96 (29.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>128 (39.8%)</td>
<td>193 (60.2%)</td>
</tr>
</tbody>
</table>

68 (21.2%) of all colon cancer patients have had colorectal polyps, also.

Based on our statistic results and on various studies quoted in introduction, we developed a mathematical prediction scheme for colorectal cancer risk. The prediction scheme considers: age, sex, weigh, height, personal history for polyps, a positive familial history of colorectal cancer, diet composition, physical activity and obesity.

The formula is:

\[ r[i] = v[i] + s[i] + k \cdot a[i] \]

where:

- \( v[i] \) = the coefficient for age;
- \( s[i] \) = the coefficient for sex;
- the \( k \) vector = \( k_1, k_2, k_3, k_4, k_5, k_6 \);
- \( k_1 \) = the coefficient for personal history;
- \( k_2 \) = the coefficient for family history;
- \( k_3 \) = the coefficient for the meat intake;
- \( k_4 \) = the coefficient for vegetables/fruit intake;
- \( k_5 \) = the coefficient for physical activity;
- \( k_6 \) = the coefficient for obesity (body mass index);
- body mass index = weight in kg/(height in cm/100)^2;
- \( a[i] = [0 | 1 | 0 | 0 | 1 | 0] \) - the negative or positive influence of vector \( k \), were 0 = no influence and 1 = positive influence;
- * means to multiply the \( k \) vector with \( a[i] \) vector.

Based on this formula, we have developed a risk calculator computer program, where patients can fill up a questionnaire, available online on line on the Gastroenterology and Hepatology Clinic Cluj-Napoca website [http://www.gastrotm.ro](http://www.gastrotm.ro).

**DISCUSSION**

Colorectal cancer is a major problem of medical world, being in the same time both a curable malign pathology and preventable. Implementing viable screening programs for colorectal cancer has become a concern for medical systems due to the positive impact on the quality of life and on medical costs. On the other hand, there is no ideal screening method for colorectal cancer.

Colonoscopy, the method with the highest sensibility, is expensive for all medical systems, requires high tech devices, trained personnel and it is not without complications. Plus, we don’t know the real compliance for this method.

The most frequently used tests are the hemocult tests; when are performed regularly, they have a pretty good sensibility for the diagnosis of colonic pathology, but they cannot be compared up with colonoscopy. However, a positive test, requires a colonoscopy.

The incidence of colorectal cancer in the present study increased with age (from 7.8% for the 40-49 years study group to 48.3% for the study group aged over 70 years. Other observation from our study was the increased incidence of proliferative processes in men (60.2%).

Romania, like other European countries, has started a screening program for colorectal cancer, using two methods: hemocult test and colonoscopy. A multicentric study made by Gastroenterology and
Hepatology Clinic - Timisoara, concluded that we don't have the means - financial and human - in order to face this kind of program.

Currently there are few models which calculate the colonorectal cancer risk. An example is the one from National Cancer Institute of U.S National Institutes of Health. The prediction scheme considers: race, age, sex, weigh, height, vegetable consumption, personal history for polyps, medications that contain aspirin, NSAIDs, hormones, smoking cigarettes – for males, periods – for females, a positive familial history of colorectal cancer, physical activity and obesity.

The risk calculator developed by us for colorectal cancer is the first made in Romania. It allows the selection of those particular subjects that have the highest probability for a colonic pathology, so that they would be the first to benefit from colonoscopy, without being necessary to use other methods. In this way the existing resources could be used properly in order to improve the quality of life. There would be a reduced number of unnecessary colonoscopies, complications related to this method, all of these increasing the compliance of patients. This website for patients, where they can fill up a questionnaire, will increase the possibility to establish their risk for a malignant colonic pathology and the population will be informed about this matter and they will have a greater compliance for screening.

CONCLUSIONS

- Sex and age are related to the development of proliferative processes.
- Left-side colon seems to be the most affected part of bowel by proliferative processes.
- The estimation of the mathematical prediction scheme presented in this paper is a fast and simple way to determine the necessity of further examination.
- The methodology involved in creating the formula can be applied to any other disorder, but must be adequately adjusted.

REFERENCES