SCREENING FOR COLORECTAL CANCER WITH FECAL OCCULT BLOOD TESTING AND COLONOSCOPY: CORRELATION OF CLINICAL DATA, SITE, SIZE AND DISEASE'S STAGE

Iuliana Taraşi[1], Gabriela Florența Dumitrescu[2], Anca Indrei[3], P. Plămădeală[4], Anca Trifan[5], C. Stanciu[5],
1 Departament of Gastroenterology, „St. Spiridon" Emergency Clinical Hospital Iaşi
2 Department of Pathology, „Prof. Dr. N. Oblu" Emergency Clinical Hospital Iaşi
3. Department of Anatomy and Embriology,
„Gr.T. Popa" University of Medicine and Pharmacy Iasi
4 Department of Pathology, „St. Mary" Emergency Clinical Hospital Iaşi
5 Institute of Gastroenterology Iaşi

SCREENING FOR COLORECTAL CANCER WITH FECAL OCCULT BLOOD TESTING AND COLONOSCOPY: CORRELATION OF CLINICAL DATA, SITE, SIZE AND DISEASE'S STAGE (Abstract): *Aim*: We present the main results from a combined screening study for colorectal cancer carried out in an asymptomatic population from Iaşi, Romania, during 2004-2007, adopting a combination of faecal occult blood testing (FOBT) and full colonoscopy. The primary aim of the current study was to determine the location of polyps and cancers and the prevalence of advanced histologic features in colorectal lesions removed by polipectomy followed or not by surgery. Secondary aim was to determine whether there were any risk factors for advanced histology in each patient group. *Material and methods*: Overall, 1291 asymptomatic subjects were screened. Patients were divided into groups, based on age: 50-59 yr, 60-69 yr, and ≥70 years, which were statistically analyzed. *Results:* Using FOBT and full colonoscopy with polypectomy as combined screening tools we were able to identified 38 cases (2.94%) of polypoid lesions (non-neoplastic and neoplastic) and colorectal cancers. 1.85% subjects from all eligible subjects were found to have advanced neoplasia and 43.75% of them had advanced histology. Taking into consideration colorectal adenomas, there were a predominance of male subjects in 50-59 age group (31.25%), but their histology was not an advanced one. As age increases to ≥70 years old, the tendency is for women subjects with villous architecture with high-grade dysplasia to predominate (18.5%). Proximal site was associated with smaller size of neoplastic polyps (<40 mm), and tubular architecture with or without non-invasive low-grade dysplasia. Distal colon expressed all histopathological types with all kind of grades of dysplasia, but 12.5% of cases were associated with greatest sizes (≥40mm), villous architecture with non-invasive high-grade dysplasia. We detected 8 (21.05%) cancers from all positive FOBT and colonoscopic detected lesions. The mean age of subjects with colorectal cancers was greater than that of subjects with colorectal adenomas (64.125 vs 61.125 years old). We found a male predominance and a predominant 50-59 years age group affected by the disease. There was an equal distribution on the left and right sided cancers. Most subjects, especially those in 50-59 group age were in stage II (87.5%), but there was a stage I colorectal cancer detected in a 60-69 years age group male. On histopathological examination adenocarcinoma was the commonest type (87.5%). *Conclusions:* Some aspects like the older age at presentation (mean age 64.125 years), equal right to left site location, and 12.5% cancers showing early stage (I) can be consider similar to that reported in Western countries. Some others epidemiological features like delayed presentation of the disease in an advanced stage (87.5%) make our population similar to that from developing countries. Our study prove that colonoscopy can be a useful screening tool when is applied to average-risk people who had a positive FBOT. We support the urgent need to screen asymptomatic subjects as high percentage of locally advanced tumors was detected.

KEY WORDS: POLYP, CANCER, COLORECTAL, COLONOSCOPY, FBOT

Correspondence to: Iuliana Taraşi, MD; e-mail: iulianatarasi@yahoo.com*

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INTRODUCTION

Colorectal carcinoma is one of the most common types of cancer throughout Europe, with about 250,000 cases annually in Europe, about half of whom die [1,2].

While colon cancer in an advanced and incurable stage often produces clinical findings, premalignant adenomatous polyps and early, highly curable, colon cancer are often asymptomatic. This phenomenon renders adenomas or early cancers difficult to detect by clinical presentation and provides the rationale for mass screening of asymptomatic adults over 50 years old for early detection and prevention of colon cancer [2,3].

It is believed that more than 50% of colorectal deaths may have been prevented through the use of screening tests [3,4]. Screening of asymptomatic individuals for colon malignancy has been advocated for the past 30 years in the hopes of reducing colon cancer mortality [5]. With technological advances in recent years it is now feasible to screen asymptomatic individuals so that, with early diagnosis through screening and appropriate follow-up and treatment, both morbidity and mortality from colorectal cancer may be decreased. Fecal occult blood tests (FBOT) and flexible sigmoidoscopy were used in many screening programs, but in the last years colonoscopy has become the primary screening test because of its high sensitivity and specificity, and the ability to perform polypectomy [2,4,6-9].

In the present study a combined screening investigation (FOBT and full colonoscopy) of 1291 asymptomatic subjects was conducted in a three years period (2004-2007) for identification of the distribution of colorectal adenomas and carcinomas by age at diagnosis, gender, and sub-site of the tumor. These factors also are evaluated in conjunction with size and grade of dysplasia in case of adenomas, or with disease stage and tumor differentiation at the time of diagnosis in case of colorectal cancers.

MATERIAL AND METODS

Participants - 1291 participants (702 males, and 589 females), from metropolitan area of Iaşi, a city of about 500,000 inhabitants, were enrolled in a prospective colorectal cancer screening at Ambulatory of „St. Spiridon" Clinical Emergency Hospital Iaşi from February 1^{-st}, 2004 until December 31^{-st}, 2007. Participants were recruited by random selection on the basis of age ($\geq$ 50 years old) and were eligible for screening if they had none of the following: history of inflammatory bowel disease, active rectal bleeding or positive FOBT in the past 12 months, history of colon polyps or colon cancer, colonoscopy or sigmoidoscopy within the past 5 years, family history of colon cancer with either a single affected first-degree relative aged 55 years or older or at least two affected first-degree relatives of any age.

Study protocol - Asymptomatic subjects provided stool specimens from three consecutive days for fecal occult-blood testing (Hemoccult Sensa). The two stool samples for FOBT were collected from two different parts from the same stool. The participants were instructed to abstain from red meat, poultry, fish, and certain raw vegetables and fruits and to stop taking vitamin C tablets and aspirin for 24 hours before and during the collection of the samples; adherence to this regimen was not verified. The slides were tested at the Clinical Laboratory of the „St. Spiridon" Clinical Hospital Iaşi according to a standardized, controlled procedure. The FOBT test was judged to be positive if one of the 3 samples per patient yielded a positive test reaction. 89 subjects (48 males, and 34 females) with a positive result detected were referred for a full colonoscopy.

A complete video colonoscopic examination was performed by experienced gastroenterologists from Institute of Gastroenterology Iaşi. During the examination, the location and size of all polypoid lesions were noted on a standardized report form. Unless medically contraindicated, any tumoral mass was resected or biopsied and sent to the Department of Pathology for analysis. When the histopathological report identified a cancer, the patient was sent to surgical department.

Tumoral masses were considered to be located in the right colon (proximal location) when arising in the cecum, ascending colon, hepatic flexure, and transverse colon. Distal location included lesions found in the left colon (splenic flexure, descending colon and sigmoid) and rectum (intestinal portion located no more than 15 cm from the anal verge).

Table I
Vienna Classification of gastrointestinal epithelial neoplasia [12]

Category 1	Negative for neoplasia / dysplasia (normal, reactive, regenerative, hyperplastic, atrophic, and metaplastic epithelium)
Category 2	Indefinite for neoplasia / dysplasia
Category 3	Non-invasive low-grade neoplasia (low-grade adenoma / dysplasia)
Category 4	Non-invasive high grade neoplasia 4.1. High grade adenoma / dysplasia 4.2. Non-invasive carcinoma (carcinoma in situ) 4.3. Suspicion of invasive carcinoma
Category 5	Invasive neoplasia 5.1. Intramucosal carcinoma 5.2. Invasive carcinoma

Histologic evaluation - All the retrieved colonic lesions were sent to Pathology Department for histologic evaluation. Polypoid lesions and carcinomas were fixed in buffered 10% formaldehyde solution. Multiple semiserial sections were cut to assess questionable examples of microinvasive carcinoma. The pathologist noted the histological type and grades of epithelial dysplasia for adenomas using the World Health Organization International Classification of Intestinal Tumors criteria. Colorectal adenomas can be defined as well demarcated, circumscribed lumps of epithelial dysplasia (atypia) with or without a stalk, usually polypoid but occasionally flat, which can be classified into three histological types: tubular, tubulovillous and villous. If the tubular pattern occupied more than 80% of the tumor it was classified as tubular; with a villous pattern of more than 80% it was classified as villous; the remainder were classified as tubulovillous. Subjects were assigned to groups based on the histology of polyp(s) and of the stage of the carcinoma found at colonoscopy.

A lot of studies defined advanced colonic neoplasia as two entities: invasive cancer and advanced adenoma. Advanced adenoma was defined as a lesion of adenomatous histology that meets at least one of the following criteria: a size of 10 mm or more, the presence of a villous component of at least 25%, or the presence of high-grade dysplasia [10,11].

Non-invasive indicates absence of evident invasion. Intramucosal indicates invasion into the lamina propria or muscularis mucosae [12]. As all resected tumoral polyps in our study had a size of more than 20 mm, the pathologist wanted to avoid confusion concerning the terms adenoma, dysplasia, and carcinoma, and used *The Vienna classification of gastrointestinal epithelial neoplasia* which graded the intestinal

epithelial neoplasia into five categories (Table I). Carcinomas were histopathologically characterized by tumoral type, grade of cell diferention, blood vessels infiltration, lymphatic vessels infiltration, and extent of tumor penetration and then were grouped in stages according to tumor-node-metastasis (TNM) classification of the Union Internationale Contra le Cancer (UICC) and the American Joint Committee on Cancer (AJCC).

The histologic grade of the pure adenocarcinomas was based on a survey of the tumor architecture and cytologic features, and tumors were categorized according to the predominant growth pattern. The well differentiated tumors were characterized by well-formed glands composed of relatively uniform cells distributed in an orderly manner abut a central lumen. The moderately differentiated tumors were characterized by less orderly, more complex gland formation with foci of cribriform and papillary growth patterns. Adenocarcinoma with colloid features (AD/CF) was defined as adenocarcinoma with an intermediate morphology (both ordinary gland-forming and colloid growth patterns, the former predominating) and less than 15% of the colloid pattern present. Colloid carcinoma was defined as an adenocarcinoma growing largely (more than two-thirds) in a colloid pattern. The TNM system compartmentalizes carcinomas according to the depth of invasion of the primary tumor, the absence or presence of regional lymph node metastases, and the absence or presence of distant metastases.

Table II
Characteristics of subjects enrolled in screening study

Subjects enrolled	Number (percents)	Male	Female
Positive FOBT	**89 (6.89%)**	**48 (53.93%)**	**41 (46.06%)**
Negative FOBT	**1202 (93.10%)**	**654 (50.65%)**	**548 (49.34%)**
Asymptomatic (Total)	1291 (100%)	702 (54.37%)	589 (45.62%)

RESULTS

During 2004-2007, 1291 asymptomatic subjects ≥ 50 years old had three FOBT; 89 (6.89%) – FOBT screened patients (48 males and 41 female) had at least one positive Hemoccult Sensa test and 82 (92.13%) – positive FOBT-subjects (46 males and 36 females) received full colonoscopy (Table II).

The overall rate of any colonic neoplasia (adenoma or carcinoma) was 1.85% (24 of 1.291 subjects) and the overall rate of colorectal lesion with advanced histology (category 4 and 5 in Vienna Classification) was 1.16% (15 of 1291 subjects) (Table III). FOBT detected 17.07% cases of reactive and hyperplasic epithelium (polyps ≤ 10mm) and 29.26% cases of adenomas with advanced neoplasia (polyps ≥ 20mm) and cancers (Table IV). Combined screening using colonoscopy in positive FOBT subjects revealed reactive and hyperplasic epithelium (polyps ≤ 10mm) in 36.84% participants and adenomas with advanced neoplasia (polyps ≥ 20mm) and cancers in 63.16%. Adenomas with advanced histology were detected in 7 cases (18.42%) and colorectal cancer in 8 (21.05%) subjects (Table IV).

The histopathological diagnosis of the colorectal lesion detected in the 38 subjects with positive FOBT and positive full colonoscopy revealed 14 (17.07%) negative cases for neoplasia / dysplasia (Category 1) as there were 6 cases of reactive

epithelium and 8 cases of hyperplastic epithelium. 46.33% of the 82 positive FOBT subjects were diagnosed during colonoscopy as having either polypous lesion or cancer (Table IV).

There were 16 (42.10%) adenomas 20 mm or larger in diameter and 8 (21.05%) colorectal cancers (Category 5). 39.47% (15 cases) of all detected lesions were advanced neoplasia (Category 3, 4 and 5) (Table IV).

Table III
The overall rate of colonic neoplasia correlated with screening tools

Asymptomatic subjects	1291 (100%)
Subjects with positive FOBT	89 (6.89%)
Subjects with positive FOBT and positive full colonoscopy	38 (2.94%)
Subjects with advanced neoplasia detected by FOBT and full colonoscopy	24 (1.85%)
Subjects with advanced histology detected by FOBT and full colonoscopy	15 (1.16%)

Table IV
Colonoscopic and histological results of subjects with at least one positive FOBT

		Histologic results			
Patients with positive FBOT followed by colonoscopy (n=82)		Category 1	Category 2	Category 3, 4	Category 5
Positive colonoscopy	38 (46.34%)	14 (36.84%)	9 (23.68%)	7 (18.42%)	8 (21.05%)
Negative colonoscopy	44 (53.65%)	-	-	-	-

Table V
The cumulative age, sex and histology distribution of colorectal adenomas

		Tubular adenoma	Tubular adenoma with low-grade dysplasia	Villous adenoma	Villous adenoma with high-grade dysplasia	Total
50-59	Male	4	-	1	-	5 (31.25%)
	Female	2	-	-	1	3 (18.75%)
60-69	Male	1	1	-	-	2 (12.5%)
	Female	2	-	1	-	3 (18.5%)
≥ 70	Male	-	-	-	-	-
	Female	-	1	1	1	3 (18.75%)
Total		9 (56.25%)	2 (12.5%)	3 (18.75%)	2 (12.5%)	16 (100%)

The most affected asymptomatic subjects by any colorectal adenoma were those included in 50-59 years-age-group (56.25%). Mean age was 61.125 years (range 50-75). Tubular adenomas were the most frequently encountered 68.75% (11 cases), the dysplasic subtype representing 12.5% (2 cases). Villous adenoma was diagnosed in 5 cases (31.25%) the dysplasic subtype representing 2 cases (12.5%) from all the colonoscopic detected adenomas (Table V).

We examined risk factors associated with advanced histology (Category 3 and 4) within each age group, location and size of adenomas. 50-59 years–age group was strongly associated with tubular adenoma without dysplasia (37.5%). Only 12.5% (2

cases) of adenomas were detected in 70-75 years age group, but correspond to villous adenomas with or without dysplasia (Table V).

The majority of polyps detected by colonoscopy (56.25%) was 20-29 mm in size and had a tubular architecture. There is an overlap between tubular adenoma with low-grade dysplasia and villous adenoma at 30-39 mm sized polyps. As polyp sizes increased to ≥ 40 mm all the lesions were villous adenoma with high-grade dysplasia, but there were only a minority of cases (12.5%) (Table VI).

Table VI
Correlations between histological types of adenomas and their sizes

Size of adenomas	Tubular adenoma	Tubular adenoma & dysplasia	Villous adenoma	Villous adenoma & dysplasia	Total
20-29 mm	9 (56.25%)	-	-	-	9 (56.25%)
30-39mm	-	2 (12.5%)	3 (18.75%)	-	5 (31.25%)
≥ 40mm	**-**	**-**	**-**	**2 (12.5%)**	**2 (12.5%)**
Total	9 (56.25%)	2 (12.5%)	3 (18.75%)	2 (12.5%)	16 (100%)

Table VII
Correlations between site and histological type of colorectal adenomas

	Tubular adenoma	Tubular adenoma with non-invasive low grade dysplasia	Villous adenoma	Villous adenoma with non-invasive high grade dysplasia	Total
Proximal Colon	1 (6.25%)	1 (6.25%)			2 (12.5%)
Distal Colon	8 (50.00%)	1 (6.25%)	3 (18.75%)	2 (12.5%)	14 (87.5%)
Total	9 (56.25%)	2 (12.5%)	3 (18.75%)	2 (12.5%)	16 (100%)

Proximal location was identified as the site for development of colorectal adenomas in 12.5% of the subjects and was associated only with tubular adenomas with or without non-invasive low-grade dysplasia (Category 3). 87.5% of total adenomas were in the distal colon (14 out of 16) and expressed all histopathological types with all kind of grades of dysplasia, but 31.25% of cases were associated with villous adenomas with or without non-invasive high-grade dysplasia (Table VII).

Colorectal carcinomas represented 21.05% (8 cases) of all colonoscopic detected lesions in asymptomatic subjects with positive FOBT. Mean age was 64.125 years (53 years to 78 years). 6 cases (75%) were found to be pure adenocarcinomas, with well-differentiated tumors constituting the largest group (4 cases). Adenocarcinoma with colloid features (AD/CF) occurred in 1 case (12.5%). Colloid carcinoma was seen in 1 subject (12.5%) (Table VIII).

The distribution of tumors by site for the entire group was: proximal colon - 4 cases (50%) and distal colon - 4 cases (50%). Pure adenocarcinomas were distributed

equally in proximal and distal colon. Colloid carcinoma encountered in proximal colon, and adenocarcinoma with colloid features appeared in distal colon (Table VIII).

There were 5 males and 3 females subjects. The age was not a differentiating factor but more frequent colorectal cancer appear in equal percentage (37.5%) in 50-59 age group and 60-69 age group. The distribution of all 8 invasive carcinomas by stage (S) showed a larger number of S II colonoscopic detected colorectal cancers (75%), most of them developing in males, 50-59 age group (Table IX).

Colorectal cancers detected by colonoscopy were situated in equal percentages in proximal colon (50%) and distal colon (50%). Half of the colonoscopic derected proximal colon cancers developed in 60-69 years group, but 50% of distal colon cancers was associated with 50-59 years group. ≥70 group presented the same distribution of cancers in both colonic segments.

Table VIII
Degree of differentiation of colorectal carcinoma (histological grading)

Degree of differentiation	Proximal colon	Distal colon	No. subjects
Well differentiated (G1)	2	2	4 (50%)
Moderately differentiated (G2)	1	1	2 (25%)
Poorly differentiated (G3) with colloid areas		1	1 (12.5%)
Colloid carcinoma (G3)	1		1 (12.5%)
Total	4 (50%)	4 (50%)	8 (100%)

TableIX
The cumulative age, sex and colorectal cancer stage distribution

Demographic characteristics	Number (%)	Stage I	Stage II	Stage III	Stage IV
Male	5 (62.5%)	1	4	-	-
Female	3 (37.5%)	-	2	1	-
50-59	3 (37.5%)	-	3	-	-
60-69	3 (37.5%)	1	2	-	-
≥70	2 (25%)	-	1	1	-
Total	8(100%)	1 (12.5%)	6 (75%)	1 (12.5%)	-

DISCUSSIONS

Colorectal cancer is the second leading cause of cancer death in the United States. In women, it ranks third after lung and breast cancer, and in men, it ranks third after lung and prostate cancer. Incidence and mortality from colorectal cancer are similar in both men and women [3].

Death from colorectal cancer can be prevented by the detection of early-stage disease that has not metastasized. The concept of the early detection of colorectal cancer appear in the late 1960s, but technical means by which this concept could be implemented clinically developed in 1970s [5]. The American Cancer Society, The US Preventive Services Task Force, and a number of surgical and gastroenterological associations have established guidelines for colorectal cancer screening and

surveillance. A variety of screening options are recommended for average-risk, asymptomatic individuals beginning at about age 50 years. These include FOBT, flexible sigmoidoscopy, double–contrast barium enema, or colonoscopy and are associated with a decrease in colorectal mortality. Each of these tests has different features and none clearly emerges as the "gold standard." FOBT is the least invasive test, whereas colonoscopy is the most accurate. Colonoscopy is routinely used to follow-up positive results obtained from other less invasive tests and also used for surveillance after the detection of polyps or cancer [13-18]. Recently, there has been increasing interest in using colonoscopy as a screening test because of its sensitivity in detecting precancerous polyps or lesions and its ability to remove such lesions as part of the same procedure.

Several expert panels have recommended combined screening with sigmoidoscopy and a fecal occult-blood test as they argue that advanced neoplasia could be detected in more patients by both tests than by one [16,17,19].

American Cancer Society, for instance, recommends that average-risk individuals obtain an annual take-home multiple-sample fecal occult blood test (FOBT), a flexible sigmoidoscopy every 5 years (or both FOBT and flexible sigmoidoscopy), double-contrast barium enema every 5 years, or a colonoscopy every 10 years (13). Annual and biennial serial FOBT screening reduces colorectal cancer incidence by 17% to 20% [20], but also produces a 33 percent decline in mortality in the annually screened group as compared with the control group [21]. The reduction in mortality demonstrated in the FOBT screening studies is attributable to the performance of follow-up colonoscopy. Recent cross-sectional colonoscopy screening studies indicate that colonoscopy is more sensitive than flexible sigmoidoscopy or sigmoidoscopy plus FOBT for the detection of large adenomas and cancers [13].

Using FOBT and full colonoscopy with polypectomy as combined screening tools we were able to identified 38 cases (2.94%) of polypoid lesions (non-neoplastic and neoplastic) and colorectal cancers in 1291 asymptomatic subjects ($\geq$ 50 years old). 1.85% subjects from all eligible subjects were found to have large colorectal lesions (greater than 20 mm in diameter), the so-called advanced neoplasia, and this percentage corresponds with those from other studies [5,17,22-24]. On the other hand, FOBT and full colonoscopy identified advanced histology in 43.75% of these large polyps that is two-three times higher than the percentage reported by Regula et al [24] and Fukami and Lee [25]. We observe that the endoscopic description of a lesion as a „tumor" may not necessarily reflect the presence of cancer. Although most patients (64.8%) had lesions with advanced histology including cancer (21.05%), we note that 35.7% did not have such features.

In our study, bleeding polyps of 10-20 mm weren't neoplasic and polyps of 20-29 mm were tubular adenomas without any sign of malignity, but all the colonoscopic detected lesions greater than 30 mm showed advanced histology. Anyway, we can conclude that the larger the size of the colorectal lesion, the more likely it is to harbor advanced histology.

The number of male subjects predominates in 50-59 group age (31.25%), but the histology of their adenomas was not an advanced one. As age increases to $\geq$ 70 years old, the tendency is for women subjects to predominate (18.5%). Their detected adenomas expressed a villous architecture with or without high-grade dysplasia. By the contrary, Konishi and Morson found in their study that the number of younger women patients slightly predominates, or is about the same as that of younger men patients but

as age increases from 50 years old to over 80 years old, the tendency is for men patients to predominate [26].

Our results show that the most frequent detected type was the tubular one (68.75%) while villous adenomas appear more rarely (31.25%) but frequently was associated with high-grade dysplasia. Though our study is a small one (38 positive FOBT and full colonoscopic colorectal lesions), the histopathological results are similar with those of Liebermann et al (949 patients whose largest polyp was ≥10 mm) [10] and Konishi and Morson (1118 adenomas) [26].

In our study, more than a half of colonoscopic detected polyps expressed advanced neoplasia (≥ 20 mm) and 64.8% of them harbored advanced histology. It is worth worthy to specify that polyps < 30 mm didn't present any dysplastic features. Our results confirm a progressive increase in the proportion of advanced histologic features with increasing polyp size above 30 mm as all polyps greater than 40 mm harbour high-grade dysplasia. So, we can conclude that as the size of adenomas increases so does the grade of dysplasia. The influence of the size of adenomas on grade of dysplasia shows a similar trend to that previously reported. Loeve et al reported that 10.9% of patients who had a polyp of any size with high-grade dysplasia developed an advanced neoplasm within 5 years, compared with only 0.6% of those with small polyps that did not harbor high-grade dysplasia [27].

Liebermann et al. found that polyp histology was neoplastic in 82.0%, with advanced histology in 30.6%. There was a progressive increase in the proportion of polyps with advanced histology with increasing size above 10 mm. The proportion of polyps with advanced histology was 18.9% in 10-14 mm polyps, 31.7% in polyps 15-19 mm, 42.3% in polyps 20-24 mm, and 75% in polyps ≥25 mm [1]. Severe dysplasia in colorectal adenomas appears to be a selective histopathological marker for increased colorectal cancer risk. It is closely linked with increasing age, with the larger adenomas and particularly those with a villous component in their histology [26].

We identified proximal colon as the site for 12.5% adenomas and distal location for 87.5%. Proximal site was associated with smaller size of neoplastic polyps (< 40 mm), and tubular architecture with or without non-invasive low-grade dysplasia (Category 3). Distal colon expressed all histopathological types with all kind of grades of dysplasia, but 12.5% of cases were associated with greatest sizes (≥ 40 mm), villous architecture with non-invasive high-grade dysplasia (Category 4). Our findings corresponds with other studies [10,26] as for larger polyps, distal location was associated with a higher likelihood of advanced histology compared with proximal location.

Konishi and Morson found that small adenomas (mostly with mild dysplasia) were evenly distributed throughout the colorectum but that adenomas showing severe dysplasia (mostly the larger tumours, > 10 mm diameter) were concentrated in the left colon and rectum, particularly the sigmoid, part which is also the segment with the highest risk of colorectal carcinoma in high risk populations. In the right colon and in the transverse colon, 67% of adenomas were < 5 mm diameter excluding a small number of large irremovable ones. They were intrigued about the high percentage (9.5%) of severe dysplasia of adenomas situated in the left colon and about the unexpectedly small percentage of severe dysplasia in the right colon. They consider that these percentages could be due to biased selection of patients [26].

We examined risk factors associated with advanced histology within each group. We detected strong correlation between histological types and the age of asymptomatic

subjects enrolled in our screening study. 50-59 group age was strongly associated with tubular adenoma without dysplasia (37.5%). Only 12.5% (2 cases) of adenomas were detected in female 70-75 yr age group, but correspond to villous adenomas with or without dysplasia. Liebermann et al didn't find any risk factors associated with advanced histology within each group [10]. Age, sex, and race were not associated with advanced histology within any of the groups. Only distal location of the ≥ 10 mm polyps was associated with a higher likelihood of advanced histology compared with proximal location [10].

Konishi and Morson found also a greater percentage of villous adenomas in patients older than 70 yr compared to younger age groups, the difference being statistically significant. The percentage of severe dysplasia in patients older than 70 years old was greater than that in the younger age groups [26].

Sato et al reported that adenomas are more often found in a high colorectal cancer risk community than in a low risk community. These authors also showed that the adenomas found in the high risk community more often exhibited severe dysplasia than in the low risk community [28]. As we identified a great percentage (31.25%) of villous adenomas most of them being associated with high-grade dysplasia (40%) we can assume the hypothesis that the community of Iaşi is one with high risk. Our results have shown that the larger adenomas with severe dysplasia are mostly concentrated in the left colon and rectum. It is well known that there is a higher colorectal cancer risk with increasing age. We have confirmed previous reports of a relation between age and severe dysplasia which, although not statistically significant, demonstrates a trend. Persons over 70 years old are particularly prone to a high incidence of severe dysplasia and consequently can be considered to be those with the highest cancer risk.

Using both screening methods, we detected 8 (21.05%) cancers from all advanced neoplasia. The mean age of subjects with colorectal cancers was greater than that of subjects with colorectal adenomas (64.125 vs 61.125 years old). We found a male predominance and a predominant 50-59 years age group affected by the disease. There was an equal distribution on the left and right sided cancers. Most subjects, especially those in 50-59 group age, were in stage II (87.5%), but there was a Stage I colorectal cancer detected in a 60-69 years age group male. Making an extensive study (1694 colorectal hungarian patients), Fuszek et al reported also that 75.7% of the colorectal cancers were in T3-T4 at diagnosis and lymph node metastases could be detected in 47.7% [29].

On histopathological examination adenocarcinoma was the commonest type (87.5%) as was found in all studies dealing with colorectal malignancies (30-34). On histological grading well differentiated adenocarcinomas were the most frequent (50%), but from distal part to proximal part of the colon there was an increase of colloid in detected cancers.

This study reveal that the subjects enrolled in our screening programme shares a mixture of epidemiological features of Western countries and USA on one side and those of developing countries on the other side for colorectal carcinoma. Some aspects like the older age at presentation (mean age 64.125 years), equal right to left site location, and 12.5% cancers showing early stage (I) can be consider similar to that reported in Western countries and United States of America [24,30]. Some others epidemiological features like delayed presentation of the disease in an advanced stage (87.5%) make our population similar to that from developing countries (36). Anyway, quite a similar profile as ours seems to be that reported by Celestino et al in Peru [31].

CONCLUSIONS

Although there is now general agreement that average-risk adults aged 50 and older should be screened for colorectal cancer, in Romania few eligible adults have ever been screened for this disease. Our study prove that colonoscopy can be a useful screening tool when is applied to average-risk people who had a positive occult blood test. We support the urgent need to screen asymptomatic subjects as high percentage of locally advanced tumors were detected and it is clear that it can be obtain not only a reduction in cancer mortality but also a reduction in its incidence.

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