ORIGINAL PAPER

Predictive parameters for advanced neoplastic adenomas and colorectal cancer in patients with colonic polyps – a study in a tertiary medical centre in the South-West region of Romania

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Abstract

Although many papers had described the role of colo-rectal adenomas and the risk for colon cancer, there is a lack of data about epidemiological factors, the histological type, the pit-pattern and type of polyps in Romania. In polypoid adenomas the risk of malignant transformation is well known and is increasing over time, with size and villous architecture. In this paper we evaluate the predictive parameters that allowed us to establish a correlation between the macroscopical aspect and histological architecture of adenomas in our geographical area (South-West region of Romania). Two predictive parameters of cancer characterize early neoplastic lesions: their size and their surface elevation (elevated, flat or depressed). The morphology of adenomas and multiplicity of polyps also have a prognostic value. In our study the main localization of polyps was in the left colon, while the main histological type was tubulo-villous adenomas. We consider that the significant parameters for dysplasia and malignant lesions are the size of lesions, multiplicity of polyps and villous architecture.

***Keywords*:** colonic adenomas, colorectal cancer, morphology, macroscopically view.

Introduction

Adenomatous polyps are the most frequent neoplasm found during colorectal cancer screening programs [1, 2]. Removal of these lesions has been shown to reduce the risk of future colorectal cancer and advanced adenomas [3, 4]. Thus, it is very important to establish from the beginning which type of lesions has a high risk for cancer development. The histopathological findings, the macroscopic view and localization are key factors for establishing the cancer risk. It is very important also to distribute the patients by groups of stratification risk. The macroscopical and histological parameters associated with a high risk for developing of colorectal cancer has been described in various studies. Thus, the multiplicity, the size of adenomas and the villous and tubulo-villous architecture are the most frequent parameters involved in the advanced neoplasia. On the other hand, there are few non-morphological parameters which seem to be associated with a high risk (increasing age, man, personal or familial history of adenomas or colorectal cancer).

The aim of our study was to assess the predictive parameters that allowed us to establish a correlation between the macroscopical aspect and histological architecture of adenomas, in a population of consecutive patients diagnosed with colorectal polyps during colonoscopy in a tertiary gastroenterology center.

Patients and methods

We evaluated 309 patients (191 males and 118 females) with 464 polypoid lesions examined by consecutive colonoscopies in a period of five years (2001–2005). We have used initially a conventional colonoscopy system (Olympus EXERA type 145) with different colonoscopes (CF–Q160AL, CF–Q145L). Only fourteen polyps were evaluated until now by high magnifying colonoscopy (CF–Q160ZL) up to 100 times. To enhance the pit pattern we have used an association of blue methylene chromoendoscopy and magnification endoscopy.

Three patients with familial adenomatous polyposis were excluded. We compared the correlation between the size, the number of lesions per patient, the morphology of adenomas, the histological architecture of polypoid lesions and the risk for dysplasia (high-grade and low grade of dysplasia).

In a small lot of 14 polyps the correlation between pit pattern and dysplasic lesions was evaluated also. The colonoscopist was blinded to the results of pathology during the index examination and the characteristics of polyps noted above were written on a separate sheet and introduced in an on-line database. After the pathology result was available, the correlation between endoscopic characteristics and pathological features was established.

Results

From 309 patients, 193 had singular adenoma and 116 multiple adenomas. We analyzed 464 polypoid lesions: 399 adenomas, 59 hyperplasic polyps and 6 other types of lesion (inflammatory lesions and hamartoma).The main localization of polypoid lesions was the left side of colon (63.78%), mainly in the sigmoid (33.62%), while in the cecum we found only 6.25% of lesions (Figure 1).

We found 41 polyps with low grade dysplasia (Figure 2) and 56 polyps with high grade dysplasia (Figure 3). The distribution of dysplasia is represented in Table 1.

Table 1 – *Distribution of dysplasia as a function of localization*

	Cecum	Ascending colon	Transverse colon	Descending colon	Sigmoid	Rectum	Entire colon
No. of polyps	29	48	86	73	156	72	464
Low grade dysplasia	0	3 (6.25%)	12 (13.95%)	3 (4.11%)	12 (7.69%)	11 (15.28%)	41 (8.83%)
High grade dysplasia	4 (13.79%)	4 (8.33%)	10 (11.63%)	8 (10.95%)	19 (12.18%)	11 (15.28%)	56 (12.07%)
Total dysplasia	4 (13.79%)	7 (14.58%)	22 (25.58%)	11 (15.06%)	31 (19.87%)	22 (30.56%)	97 (20.90%)

Dysplasia has been found in the entire colon but most frequently in the rectum (where 22.22% from lesions have dysplasia) and most rare in the cecum.

We observed that the majority of polyps (64.87%) and the majority of lesions with dysplasia (65.98 % of total lesions with dysplasia) were placed in the left side of the colon. Our histopatological findings are described below in Table 2.

Table 2 – *Distribution of dysplasia as a function of histology*

	Adenomas		
	Tubular	***Tubulo-villous***	***Villous***
No. of polyps	93	271	35
Low grade dysplasia	11 (11.83%)	26 (9.59%)	7 (20%)
High grade dysplasia	10 (10.75%)	32 (11.81%)	11 (31.42%)
Total dysplasia	21 (22.58%)	58 (21.40%)	18 (51.42%)

Thus, from the total number of 399 adenomas, 93 (23.30%) were tubular adenomas, 271 (67.91%) tubulo-villous adenomas and 35 (8.77%) villous adenomas. There were 97 adenomas with dysplasia (24.31%), 41 lesions with low grade dysplasia (10.27%), 56 lesions with high grade dysplasia (14.03%), 59 hyperplasic polyps (12.71%) and other histological findings six lesions (five inflammatory lesions and one hamartoma). Dysplasia was associated with adenomas (22.58% from tubular adenomas, 21.40% from tubulo-villous adenomas and 51.42% from villous adenomas (Figures 2 and 3).

In hyperplasic polyps we did not find dysplasia.

An obvious correlation between the size of adenomas and dysplasia has been found: 7.84% of lesions less than 1 cm have dysplasia while the lesions over 2 cm 67.21% have dysplasia (Table 3).

Table 3 – *Distribution of dysplasia as a function of size*

	≤ 1 cm	1–2 cm	≥ 2 cm
No. of polyps	255	148	61
Low grade dysplasia	16 (6.27%)	18 (12.16%)	5 (8.20%)
High grade dysplasia	4 (1.57%)	18 (12.16%)	36 (59.01%)
Total dysplasia	20 (7.84%)	36 (24.32%)	41 (67.21%)

Regarding the multiplicity of polyps and the risk for high grade dysplasia and advanced neoplastic lesions, our study concluded that 23.31% from patient with unique polyps had dysplasia and 44.82% of patients with more that two polyps had dysplasia (Figure 4).

From the fourteen polyps assessed by high magnifying colonoscopy we find follow results: two polyps II pit pattern, three polyps IIIs, seven polyps IIIL (Figure 5), and two polyps IV pit pattern (Figure 6).

The correlation between the pit pattern and dysplasic lesions is described in the Table 4.

Table 4 – *The correlation between pit pattern and dysplasic lesions*

		Type I	Type II	Type IIIs	Type IIIL	Type IV	Type V
Adenomas	*Low grade dysplasia*	0	0	0	4 (57%)	2 (100%)	0
	High grade dysplasia	0	1 (50%)	1 (33%)	3 (43%)	0	0
	No dysplasia	0	0	1 (33%)	0	0	0
Hyperplasic lesions		0	1 (50%)	1 (33%)	0	0	0

Because of the small number of polyps and our low experience regarding the magnifying colonoscopy we can not conclude about the correlation of pit pattern and histological findings, but we will extend our study in the future by increasing of the number of patients examined by magnifying colonoscopy. We will complete the study regarding the learning curve also.

Discussions

The adenomatous polyps are the most frequent neoplastic lesion found in the patients examined in endoscopy laboratory.

It is very important to establish from the beginning what are the parameters which allow us to prevent the colorectal cancer. It is well known that the adenomatous polyps are high risk lesions for developing of colorectal cancer.

The baseline colonoscopy needs to be of high quality for the based adenoma characteristics to be used for planning surveillance intervals. Consequently, a low incidence of colorectal cancer can be achieved in postpolypectomy patients [3, 5, 6].

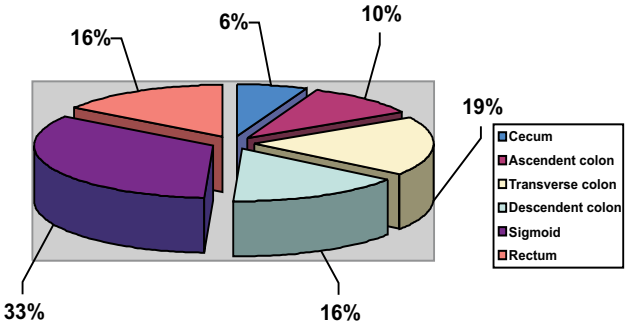

Figure 1 – *Distribution of polyps*

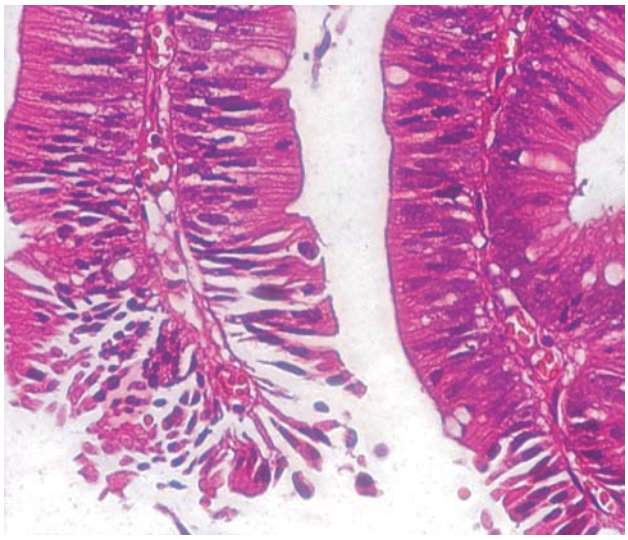

Figure 2 – *Low grade dysplasia villous adenoma (HE staining, ob. ×20)*

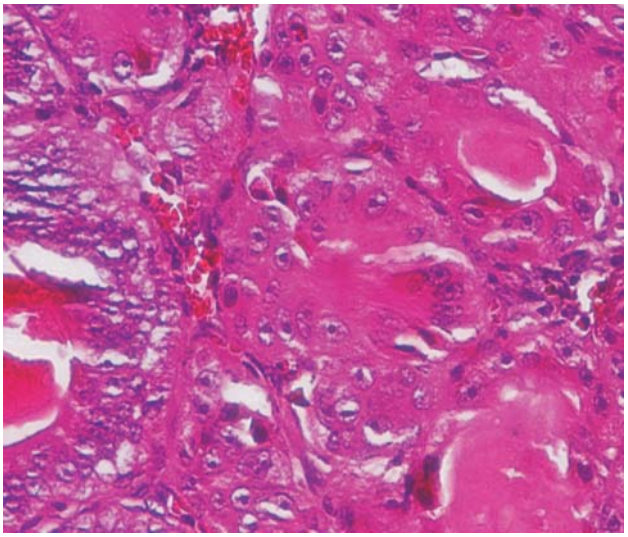

Figure 3 – *High grade dysplasia adenoma (in situ carcinoma, HE staining, ob. ×20)*

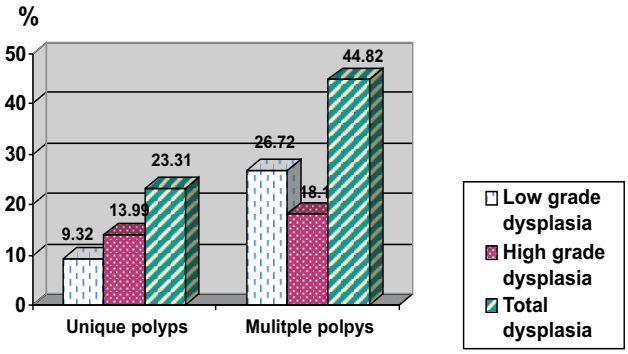

Figure 4 – *Distribution of dysplasia in patients with unique and multiple polyps*

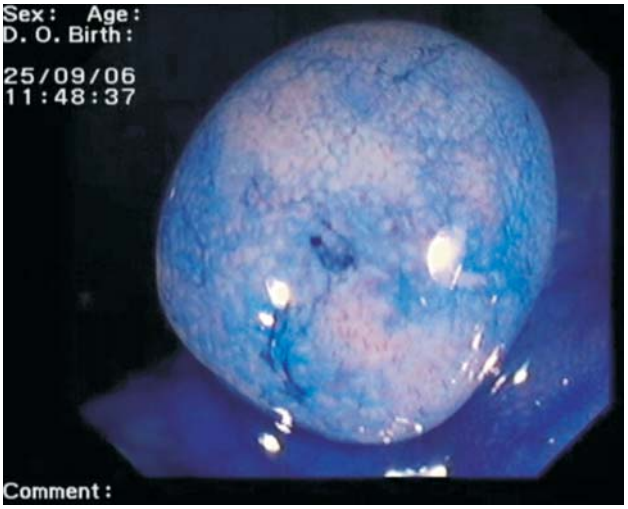

Figure 5 – *IIIs pit pattern of a colonic polyp (examination by high magnifying colonoscopy in association of methylene blue chromoendoscopy)*

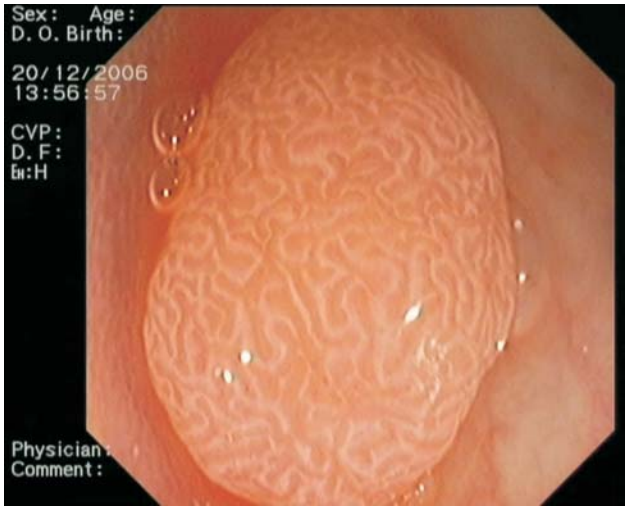

Figure 6 – *IV pit pattern of a colonic polyp (examination by high magnifying colonoscopy)*

Incomplete removal of large sessile polyps, particularly by piecemeal polypectomy, could contribute to a higher subsequent incidence of a colon cancer [7, 8]. Inadequate removal of sessile rectosigmoid adenomas is also associated with an increased risk for rectal cancer [9].

Regarding the macroscopic appearance few findings are associated with an increased risk for advanced neoplasia: the multiplicity of adenomas [5, 7, 10] and the size of adenomas. Lesions over 1 cm can predict a metachoronous advanced adenoma [11]. The risk of advanced neoplasia in patients with small adenomas is lower than in large adenomas: SIR (standardized incidence ratios) for adenomas less than 1 cm is 1.5, although it reaches 2.2 for 1–2 cm adenomas, and 5.9 for adenomas over 2 cm [12]. In another study the relative risk for advanced neoplasia is 2.4 for size 0.6 to 1 cm and 4.4 for polyps over 1 cm [13].

Regarding histological findings few types of adenomas have a high risk for advanced neoplastic lesions: villous and tubulo-villous adenomas [13, 14]. In the present, dysplasia is classified into low grade and high grade dysplasia. In the subset of high-grade dysplasia are included severe dysplasia and carcinoma in situ, while low grade dysplasia includes mild and moderate dysplasia. During a five years surveillance period 10.9% of patients with high-grade dysplasia had advanced neoplasia compared with 0.6% in patients with tubular adenomas less 1 cm without high-grade dysplasia [15].

Other risk factors for advanced adenomas include increasing age, male sex, history of polyps [10, 11], family history for colorectal cancer and adenomas at a young age [16]. Proximal adenomas are also associated with family history of colorectal cancer [17].

In our study the majority of polyps were placed in the left size of colon, and we found few significant parameters for dysplasia: the size of lesions over the 2 cm, the villous architecture and the multiplicity of polyps. The results are useful for the assessment for the risk of development of colorectal cancer, and moreover, for the detection of early malignant lesions. The adenocarcinoma sequence suggests that colorectal cancer develop from benign adenomas, thus it is very important to find and recognise these lesions. The resection of these lesions could prevent the appearance of colorectal cancer. These parameters are very important for establishing the assessment of patients and the follow up period. Thus, the *US Multi-Society Task Force on Colorectal Cancer* and the *American Cancer Society* elaborated "Guidelines for colonoscopy surveillance after polypectomy" [12].

During colonoscopy every effort should be made to obtain a tissue diagnosis but many authors tried to find the right way to detect the high risk lesions without pathological exam. New endoscopic techniques are currently developed to improve the accuracy of polyp detection. Many studies tried to establish whether mucosal crypt patterns are feasible to distinguish non-neoplastic polyps from neoplastic polyps. Magnifying colonoscopy with chromoendoscopy seems to provide a higher diagnostic accuracy than that obtained by conventional colonoscopy or chromoendoscopy [18].

Surface analysis of colorectal lesions by magnifying colonoscopy in addition to chromoendoscopy has been established by Kudo S *et al.* [19–21]. The mucosal crypts patterns were divided into six groups: type I, II, IIIL, IIIS, IV and V. In other study, Kato S. *et al.* re-categorized the polyps into three groups in accordance with treatment decisions: non-neoplastic (types I and II), non-invasive (type IIIL, IIIS, IV) and invasive (type V). First group does not need biopsy and treatment, the second one need endoscopic removal and the third group should be referred to surgery [18].

The combination of colonoscopy and magnified chromoendoscopy thus seems to represent the most reliable non-biopsy method for distinguishing non-neoplastic from neoplastic lesions, while it also allows an easy detection of mucosal lesions in the colon and facilitates visualization of the margins of flat lesions [22–24].

This procedure is safe and can be used routinely. The procedure usually takes about 10–20 seconds for one polyp, and is less troublesome and time wasting than conventional colonoscopy (it is not necessary to take biopsies from all lesions) [22]. For experienced endoscopists, the inter- and intra-observer reproducibility of the classification of colonic pit pattern is good [25].

Many other techniques are currently under development for the detection of neoplastic lesions: real-time Doppler capabilities have now been added to endoscopic optical coherence tomography; the results of large-scale testing of narrow-band imaging endoscopy in the colon are being awaited; and fluorescence imaging has recently been added to the facilities available in video endoscopy. Most importantly, endomicroscopy now for the first time allows single-cell subsurface imaging during ongoing colonoscopy procedures, opening the way to in-vivo molecular and functional imaging [26].

The precise role of these techniques, cost and time per procedure need to be evaluate in future studies. However, by using a precise delineation of polyp characteristics, combined with an accurate follow-up after polyp resection, most of the authors hope to prevent colorectal cancer in high-risk patients.

Conclusions

The findings of our study are similar to the literature, the most important morphological parameters correlated with a high risk of colorectal cancer being the size of adenomas, the multiplicity of adenomas and the villous structure.

Regarding the pit pattern of polyps, we studied a small lot of patients, and we need to have experience for a correct assessment of the macroscopic aspect in high magnifying colonoscopy. We plan to extend our studies regarding the correlation of the pit pattern and histological features. Future prospective studies should investigate the learning curve for endoscopic diagnosis with magnifying colonoscopy or with chromo-endoscopy.

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