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ORIGINAL ARTICLE

Large bowel endoscopy and management of colorectal cancer and its premalignant forms – endoscopy survey

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Summary

Purpose: *To estimate the relationships between patients' clinical variables like age and sex with the endoscopical and histological findings of colorectal lesions and to assess the efficacy of endoscopy in diagnosing and treating polyps and early forms of colorectal cancer (CRC).*

Patients and methods: *Analyzed were patients included in our database who were subjected to lower gastrointestinal tract endoscopy at our department for the last 15 years.*

Results: *5107 patients were examined. In almost 1/5 (955) of them, the examination was for surveillance purposes. Women/men: 55%/45%. The number of patients with polyps was 1180. Polyps were diagnosed most frequently in patients aged 51-60 years and were located mostly in the sigmoid colon (43%). Patients with CRC were 613 and were diagnosed predominantly in the age group of 60-70 years (32%), most frequently in the rectum (38%), followed by the sigmoid colon (32%). 128 patients were diagnosed with early CRC. In 52 (40.62%) of them successful endoscopic therapy was carried out.*

No serious complications were observed except one case of late perforation after polypectomy, with a successful outcome.

Conclusion: *Lower gastrointestinal endoscopy is a highly efficient method for screening, diagnosis and therapy of colorectal polyps and early forms of CRC. It is still underused for screening purposes in patients after the age of 50 years.*

Key words: colorectal cancer, endoscopy, polyps

Introduction

A considerable part of all cancer-related mortality is due to gastrointestinal cancers. In 2004 in Europe 2,886,800 incident cases of cancer were diagnosed and 1,711,000 cancer deaths were registered. The most common type was lung cancer (13.2%), followed by CRC (13%). Lung cancer was also the main cause of death (20%) in all cancer patients, while CRC was second (11.9%), gastric cancer was third (8.1%) and breast cancer fourth (7.6%) [1]. The majority of colorectal lesions develop from benign adenomatous polyps. Almost 90% of CRC develop over a protracted period of time along the polyp-cancer sequence [2,3]. Early detection and removal of precancerous polyps with subsequent surveillance has the potential to reduce future CRC incidence as well.

There are several histological types of polyps, each with different clinical significance and malignant potential. Thus the patient management depends on the accurate polyp diagnosis: after endoscopic biopsy of the lesions, the clinician is faced with the therapeutic dilemma – will the polypectomy only be adequate therapy, or does the patient need surgical resection, and what the follow up period should be after successful endoscopic removal.

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The purpose of this study was to draw conclusions from the clinicopathological relationships in patients with colorectal neoplasia examined, diagnosed and treated at our department and give recommendations for screening and surveillance in relation with the latest world standards.

Patients and methods

The technical equipment of the department consists of 3 Olympus endoscopes - a digital (video) colonoscope CF-Q-160L, a light (fiber) colonoscope CF-1T20L and one light (fiber) sigmoidoscope CF-P-20S.

Additional devices: light sources - CLV-160, CLE 10, CLV- U20, a transmitter - OTV-F3, an electrosurgical unit - PSD-10, a video transmitter CV-160 and a monitor OEV - 203. A Berchtold electrotom 620 and argon plasma coagulation equipment are used.

Patients

During the period 1991-2005 5107 endoscopic examinations of the large bowel were performed. Patients were referred to the department due to various reasons – positive fecal occult blood testing (FOBT) or anemia, intestinal discomfort, abnormal radiological findings or palpable abdominal mass, liver infiltration of unknown origin etc.

The patients' preparation for the examination was: Day 1: ingestion of 1 sachet Fortrans diluted in 1L water till midday, and additionally 2L water only till the evening. Patients were asked to eat easily digestible food. Day 2: 2 sachets Fortrans in 2L water till midday and 1L water till the evening. On that day the patients were asked to drink only clear fluids and avoid any food. Patients with contraindications were considered for enema preparation.

Examinations were performed on an outpatient basis. Though patients were not required to stay, we insisted that they should not be left without supervision at home and be off work, especially in cases where polypectomy was performed. In most of the cases we performed sigmoidoscopy and less frequently colonoscopy.

Sigmoidoscopy was performed with a 65 cm long endoscope, while for colonoscopy we used 1.5 m colonoscope. For practical purposes the following segments were defined: rectum - 18 cm, sigmoid colon - up to 35 cm, descending colon - 35-65 cm, transverse colon 65-85 cm, ascending colon 85 cm to coecum. When possible, we used also other anatomical marks to locate the lesions. General anesthesia was used only on rare occasions, mostly in colonoscopies. Only a small number of sigmoidoscopies were performed under sedation.

Diagnostic work up

When a lesion was found one or several biopsies were taken and decision over the appropriate treatment was made after the histological result. All biopsied lesions were divided into 3 grades of epithelial dysplasia (atypia) - mild, moderate or severe. The latter was used synonymously with carcinoma *in situ* or early CRC, according to the foci of the part in which the most advanced grade was identified. Severe degree was characterized by marked pleomorphism, less mucin present, distorted glandular structures with frequent bridging and fusion - back-to-back arrangement. The term "early CRC" doesn't describe a specific stage in the histogenesis of CRC, but cancer that is curable endoscopically and is analogous to the Japanese term "early gastric cancer" - an adenocarcinoma limited to the mucosa or submucosa [4]. According to this classification CRC means the invasive type and "early CRC" means either carcinoma *in situ* or grade III dysplasia.

When a lesion was found on sigmoidoscopy, the decision for colonoscopy was considered on the basis of the size and histological type of this lesion, clinical sings and family history for CRC.

Treatment

Polyps and early CRC were treated according to the type, size, localization and histological type. Endoscopy techniques used were: electrocoagulation, electroresection and argon-plasma coagulation. The latter was applied mostly on sessile lesions, usually in 2-3 successive attempts before complete cure.

To reach the best treatment decision, the most important factor to consider was the degree of dysplasia of the lesion. Patients whose lesions had grade III dysplasia or carcinoma *in situ* were dealt with the highest level of caution - as high-risk patients.

Before the endoscopic polyp removal, hematology readings - especially blood group and coagulation parameters - should be available. The biopsy was taken from the top and the basis of pedunculated polyps when possible, but never from the necrotic surface.

During polypectomy we aimed at removing the polyp completely with its stalk, while preventing from bleeding or perforation. For this reason adrenaline solution was injected at the basis of the stalk. If the polyp was too large we used piece-by-piece excision. When

the lesion was 5 mm or smaller in size, we removed it directly during the biopsy. In case of obstruction, when a biopsy was not possible to obtain, we referred the patient for double contrast barium examination and/or urgent surgical intervention.

Surveillance

If the examination did not detect any abnormal findings, the patient was not scheduled for follow up. This was our recommendation also for patients with hyperplastic and small (less than 1 cm) tubular polyps. Further screening in 5-yearly intervals was advised only if the patient was 50 years of age or older, without family history of CRC.

In case of polyp removal, we requested the patient to come for surveillance in a period defined according to the degree of dysplasia, the size and the number of the removed polyps. Patients with high-risk polyps were asked to come for follow up in 3 months initially. If the examination was normal, the next one was in 6 months. Further follow up periods in case of normal examination were the 1st, 3rd and finally 5th year.

Close surveillance was also needed for patients operated for CRC in the postoperative period. Those treated surgically for rectal cancer were put on surveillance every 3-6 months for the first 2-3 years. Patients operated for colon cancer needed colonoscopy 1 year after the resection, then at the 3rd and 5th year [5].

Patients with ulcerative colitis and Crohn's disease were examined once monthly during the acute phase, when biopsy was also obtained. After remission, these patients were also subjected to surveillance every year.

Results

Examination

Our data included the period from 1991 to 2005 during which 5107 endoscopies of the large bowel were carried out. For most of the patients, these were single examinations. In 366 of patients we performed more than one examination for surveillance purposes. This accounted for 955 from the total examination number.

Most of the patients were examined by sigmoidoscopy (4260; 83.41%). In 225 (4.40%) of them we had to limit the examination to flexible rectoscopy due to various difficulties (malignant obstruction, perisigmoid adhesions or simply due to lack of cooperation). The number of total colonoscopies was 622 (12.20%) (Table 1).

Table 1. Number of endoscopies by large bowel segment

Endoscopy	*Patients, n*	*%*
Rectoscopy	225	4.40
Sigmoidoscopy	4260	83.41
Colonoscopy	622	12.17
Total	5107	100.00

Patients

The age of the examined patients ranged from 10 to 92 years. More examinations were performed in women (55%) than in men (45%). According to age, the greatest numbers of the examined patients was in the age group of 60-70 years, followed by the 40-50 and 70-80 year-old groups (Table 2).

Findings

Polyps group

The number of patients with endoscopically detected polyps was 1180. According to sex, patients were mostly affected if they were women (54.23%) aged 50-60 years (30.87%; Tables 3, 4). They were affected slightly more frequently than those aged 40-50 years, but twice as frequently compared to patients before the age of 40. The least affected were patients after the age of 70 (2.4%).

Table 2. Number of examined patients by age

Age (years)	*Patients, n*	*%*
< 20	158	3.09
20-30	179	3.50
30-40	454	8.88
40-50	927	18.15
50-60	579	11.33
60-70	1944	30.06
70-80	774	15.15
> 80	91	1.78
Total	5107	100.00

Table 3. Number of patients with polyps by sex (n = 1180)

Sex	*Patients, n*	*%*
Women	640	54.23
Men	540	45.76

Table 4. Number of patients with polyps by age groups

Age (years)	*Patients, n*	*%*
<20	15	1.28
21-30	59	5.06
31-40	165	14.15
41-50	313	26.84
51-60	360	30.87
61-70	226	19.38
71-80	28	2.40
Total	1166	100.00

Number and segmental distribution of polyps

Most of the polyps were localized in the sigmoid colon (43.05%), followed by the rectum (33.39%) and the descending colon (15.65%; Table 5).

Patients with only one polyp only prevailed (71%; Table 6). The rest of them had various numbers of polyps, between 3 and 20. Thirty-eight of the patients who had 20 or more polyps were categorized as having multiple polyps. Twenty of them had hundreds of polyps, typical for familial adenomatous polyposis.

Registered histological results were available for 661 polyps (Table 7). 96.7% of the polyps were of adenomatous type. However, only 46.22% of the polyps found were additionally specified in their subgroups – tubular, villous and adenovillous (mixed) type. The majority of them was found in the sigmoid colon (297) and rectum (194). The least frequently diagnosed were tubular and hyperplastic polyps (3.4%).

Table 5. Segmental distribution of adenomas

Segment	*Patients, n*	*%*
Rectum	453	33.93
Sigmoid	581	43.05
Descending	209	15.65
Transverse	51	3.82
Ascending	41	3.07
Total	1335	100.00

Table 6. Number of polyps per patient

Patients, n	*%*	*Number of polyps*
843	71.40	1
153	12.90	2
65	5.50	3
49	4.10	4
9	0.76	5
7	0.59	6
5	0.42	7
1	0.08	8
2	0.16	9
1	0.08	10
1	0.08	11
2	0.16	12
2	0.16	13
1	0.08	15
1	0.08	17
38	3.22	> 20 (multiple)

Colorectal cancer group

The total number of patients with endoscopically or histologically defined diagnosis of CRC was 613 (Table 8). The number of patients diagnosed on endoscopy first was 586 (95%). 429 (70%) of them were histologically confirmed. In 63 (10.26%) patients with lesions defined as malignant on endoscopy were finally diagnosed as benign on histology. The rest 94 (15.33%) patients diagnosed with CRC on endoscopy were referred to their regional hospitals and the histological result is absent in our database. On the other hand there were 27 (4%) patients whose lesions that appeared benign on endoscopy, the histological examination revealed CRC.

Table 7. Number of polyps by segment and histological diagnosis

Segment	*Adenomatous*	*Tubular*	*Villous*	*Adenovillous*	*Hyperplastic*	*Total*
Rectum	85	5	37	60	7	194
Sigmoid	161	13	21	94	8	297
Descending	73	4	22	37	4	140
Transverse	8	1	1	3	2	15
Ascending	6	0	1	7	1	15
Total, n (%)	333 (50)	23 (3.47)	81 (12.25)	202 (30.5)	22 (3.32)	661 (100.00)

Table 8. Number of patients with colorectal cancer (CRC)

	Patients, n (%)
Diagnosed endoscopically as CRC	586 (95.6)
Histologically confirmed	429 (70)
Histologically defined as benign on biopsy, though malignant endoscopically	63 (10.26)
Absent histological report	94 (15.33)
Histologically malignant, endoscopically benign	27 (4.40)

Age and sex distribution of CRC (Table 9)

According to the patients' age, CRC was diagnosed most frequently in the group of 60-70 year-old patients (45.60%). Looking at the incidence by decades, a sharp increase of CRC after the age of 50 was observed, when the number of cancers tripled in comparison to the previous decade. Though the examined men were less than women, they were diagnosed more frequently with CRC (332; 54%) than women (282; 46%).

Segmental distribution of CRC (Table 10)

CRC was diagnosed most frequently in the rectum (38%) and the sigmoid colon (32%). Both ascending and descending colon were equally affected by colorectal cancer (11.90% and 10.11%, respectively), while the transverse colon and the coecum were the least affected segments.

Table 9. Patients with colorectal cancer by age

Age (years)	*Patients, n*	*%*
< 30	9	1.29
30-40	16	2.30
40-50	56	8.06
50-60	147	21.18
60-70	280	40.34
70-80	162	23.34
> 80	24	3.45

Table 10. Segmental distribution of colorectal cancer

Segment	*Patients, n*	*%*
Rectum	234	38
Sigmoid	196	32
Ascending	73	11.90
Descending	62	10.11
Transverse	36	5.87
Coecum	23	3.75
Total	613	100.00

Carcinoma in situ

128 patients were histologically diagnosed with early CRC, defined as carcinoma *in situ* or polyps with severe (III) degree of dysplasia. Seven of these patients were unsuitable for endoscopic treatment and were referred for surgical treatment. However, 52 of them, suitable for endoscopic therapy, were treated successfully at our Department. The rest of the patients (69) chose to be treated elsewhere and data of their clinical outcome are lacking. Patients with invasive CRC were referred directly for surgical treatment.

Discussion

The presented summary of endoscopic examinations for the last 15-year period included patients referred to the Endoscopy Department with various complaints of the lower gastrointestinal tract. These findings, however, demonstrate that, though using a symptom-oriented approach, the number of diagnosed CRC (661 in 5107 examinations; 12.94%) is similar to the annual incidence rate of CRC in Europe (13.2%) [1]. Owing to the frequent symptoms colorectal lesions produce, patients were motivated to seek medical examination.

The pioneering work of Muto, Bussey and Morson revealed that the majority of CRCs develop from adenomatous polyps [2,3]. They concluded that this polyp-to-carcinoma sequence is based on the following findings: adenomatous polyps have bowel distribution similar to that of CRC; polyps are frequently found at the edge of the malignant tissue and that endoscopic removal of polyps decreases the risk of CRC by 76-90%. The transition time from polyp to carcinoma is approximately 10 years [6]. This was demonstrated in the USA National Polyp Study, where the cancer incidence in 1120 postpolypectomized patients was only 0.4% after 10 years of follow up [2,6,7]. This evidence of reduction of CRC incidence was present for up to 10 years from the last follow up examination. It supports the understanding of 5-year interval between screening

examinations for average risk population, including surveillance patients after removal of a hyperplastic or tubular adenoma [8].

Our endoscopic examination protocol follows the world standards. In most of our patients we performed sigmoidoscopy. Colonoscopy was indicated for high-risk patients and those with symptoms of right-sided pain or palpable mass, dark stools, weight loss, or radiographic findings for lesion in the proximal colon, or positive family history. Some of the examinations were restricted to the rectum only, due to difficulties on further insertion of the endoscope, like adhesions or lack of patients' cooperation. In this case, patients were advised on some other type of examination, such as double contrast barium enema (DCBE).

The ratio of patient with polyps to patients with CRC in this study was 3:1. Polyps were diagnosed most frequently in 50-60 year-old patients, while CRC was diagnosed mostly after the age of 60. This is in support to the 10-year difference in relation to the polyp-carcinoma sequence. We diagnosed mostly adenomatous type of polyps. This is opposite to the prevalence of hyperplastic type of polyps in the general population (90%), which remain asymptomatic. Polyps were mostly solitary. The greatest number was found in the sigmoid colon, while CRC affected mostly the rectum and then the sigmoid colon. Although the male group of our patients was smaller, they were affected more frequently by CRC.

Special attention was paid to high-risk patients - those with early CRC (carcinoma *in situ*) and polyps with grade III dysplasia. High-risk patients with polyps include: those with 3 or more adenomas, high-grade of dysplasia or carcinoma *in situ*, villous features or adenoma $\geq$ 1 cm in size.

During the period 1991-2005 we diagnosed 128 high-risk patients with early CRC or polyps with grade III dysplasia. Fifty-two of them were treated successfully at our Department. The most important issue about these patients was the histopathologic evaluation of the removed lesion, especially in its basis.

Carcinoma *in situ* is called also early CRC, implying a cancer that is still endoscopically curable, limited to the mucosa or muscularis mucosae, but not beyond the submucosa [2]. It could be cured by endoscopic resection. Malignant adenoma and polypoid carcinoma form a spectrum ranging from pedunculated adenoma with a mixture of adenomatous and malignant glands to a lesion solely composed of malignant glands without remnants of adenoma. Microscopic foci of carcinoma can be found in these lesions.

Colorectal adenomas are common but most of them never become malignant. To estimate the risk, patients' history and polyps' histopathological features should be considered.

In some countries there are screening guidelines for early detection of CRC and its premalignant lesions. The strategies are not equal with regard to evidence of effectiveness, magnitude of effectiveness, risk or up-front cost. In the USA for example, recommendations for people after the age of 50 being at average risk include FOBT or fecal immunohistochemical testing (FIT) annually, or sigmoidoscopy every 5 years or in combination with FOBT, or colonoscopy every 10 years, or DCBE every 5 years. For people at increased risk, colonoscopy is the only method of surveillance.

The decision to perform colonoscopy after detection of a neoplasm during sigmoidoscopy is controversial and should be individualized. Prevalence of proximal advanced adenomas in patients without distal adenomas is about 2-5% [9]. People at increased risk of CRC have only the option of colonoscopy as method of surveillance [10]. Those are people with some of the following criteria: they have been diagnosed and treated for colorectal neoplasia or have a first degree family member diagnosed with CRC before the age of 60; or two first degree relatives diagnosed at any age. Single relatives to people diagnosed after the age of 60 should be considered as average risk individuals [11].

FOBT was not routinely recommended to our patients for screening purposes, due to the low sensitivity of the test (30-50%) and the benefit for decreased incidence of CRC only after 10 years of annual use [12].

Reports prove that sigmoidoscopy reduces the CRC mortality by 75% within the reach of the endoscope [7]. If combined with FOBT, sigmoidoscopy will identify 76% of patients with advanced dysplasia or invasive cancer [9]. If a polyp was found on flexible sigmoidoscopy, subsequent colonoscopy would identify 70-80% of patients with advanced proximal neoplasm.

From the imaging techniques DCBE and virtual colonoscopy (CT) have received greater acceptance, due to their lower association with patients' discomfort and complication rates. DCBE leads to 33% reduction of CRC-related deaths. Its sensitivity varies from 33-100% for polyps and 62-100% for CRC due to selection bias [13]. DCBE is not recommended for all patients with positive FOBT, because it is less accurate than colonoscopy for the detection of both small cancers and adenomas [14].

Virtual colonoscopy (VC) has sensitivity of 70% and specificity more that 90% for detecting CRC and large polyps, but only 82% for polyps between 6-9 mm [15]. For the average-risk people VC detects 60% of the 1-1.9 cm polyps and 43% of polyps 0.6-0.9 cm

[16]. Its sensitivity for cancer is 85% in comparison to colonoscopy which is 95% [17]. VC is accurate for medium and large colorectal polyps and cancer [18]. Its advantages, however, over colonoscopy include visualization of the colon next to the obstructing lesion and inspection of both sides of the haustral folds [19].

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