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Colonoscopic findings of symptomatic patients aged 50 to 80 years suggest that work-up of tumour suspicious symptoms hardly reduces colorectal cancer-induced mortality

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Summary

Questions under study: The risk of colorectal cancer (CRC) starts to increase at the age of 50 years in average persons without special risk factors. The significance of clinical symptoms and frequency of endoscopies done at this age are hitherto unknown. We do not know the stage of colorectal cancers nor the distribution of advanced neoplasms in symptomatic persons above 50 years. These data are of interest to validate the necessity of screening programmes, to define the target population and to interpret results of screening studies in asymptomatic people.

Methods: Endoscopies of the colon performed from 1991 to 2000 in symptomatic patients aged 50 to 80 in the well-defined area of Uri were analysed retrospectively, focusing on symptoms leading to the endoscopy and the occurrence of neoplastic lesions.

Results: Sixteen percent of the population at the age of 50–80 years had a colonoscopy for work-up of symptoms. A CRC was found in 5.5% of all patients (83 of 1514 patients), in 12.3% of patients with tumour suspicious symptoms, but only in 0.3% of patients with unspecific pain. Stage of tumours was often advanced (82% T3/T4, 38% N1–3, 21% M1). In 2.6% of patients a colorectal cancer was found before the age of 60, mostly in men. Advanced lesions were more frequent in men, increasing with age.

Conclusions: A substantial part of the population above the age of 50 had an endoscopic work-up of the colon for symptoms, what has to be considered when defining the target population and the necessary manpower of screening programmes. Tumour-suspicious symptoms were significant predictors for the presence of a CRC, but tumours were often already advanced. This underlines the importance to screen persons before developing symptoms.

Key words: colonoscopies; colorectal cancer; adenomas; advanced lesions

Introduction

Colorectal cancer (CRC) is an increasing problem in industrial countries, especially in the elderly population. In Europe, CRC has become the number one amongst the cancers afflicting both sexes [1, 2]. In Switzerland, 2,000 to 2,600 new cases of colon cancer and 1,100 to 1,700 of rectal cancer are diagnosed every year [3]. CRC ranks third in incidence after prostate cancer and lung cancer in smoking men and second after breast cancer in women [3]. This immense public relevance prompted different countries to introduce regional or national screening programmes to prevent CRC. The risk of contracting CRC for the average population without special risk factors such as genetically determined family tumour syndromes or chronic inflammatory bowel disease increases after the age of 50 [4–6]. Screening for CRC is therefore recommended to start at the age of 50 [7] but the optimal strategy is still disputed.

There is strong but mainly indirect evidence for the effectiveness of colonoscopic screening. Tumours are found at an early stage by screening of asymptomatic persons [6, 16, 21, 22] and adenomas as precursor lesions of CRC, can be re-

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moved at endoscopic screening preventing development of CRC in a substantial part [14, 15, 17, 21, 22]. However, no population-based randomised screening data using colonoscopy has been available up to now. Studies have been confined to highly selected groups of people only.

In Switzerland screening for CRC is neither recommended nor paid for by the insurance. Rapid work-up of tumour suspicious symptoms is strongly advised instead. The impact of this recommendation is unknown, however. The aim of our study was to evaluate the relevance of symptoms to detect CRC at an early stage. The number of endoscopies done in symptomatic patients at the age above 50 is important to define the target population of screening programmes and to identify the necessary manpower for screening. Since CRC screening trials in asymptomatic persons have been done in selected patient groups only, population based findings in symptomatic people help to validate results of the screening studies of the same age group.

Methods

The canton of Uri is a well-defined mainly rural area with little migration served by one endoscopic centre mainly. This unselected population is therefore ideally suitable for evaluation of the endoscopic findings of symptomatic persons in the relevant age group. The area has 35,500 inhabitants; approximately 10,000 are aged 50 to 80 (data of year 2000) [18]. Endoscopies of the colon performed in Uri from 1.1.1991 to 31.12.2000 in patients aged 50 to 80 years were analysed retrospectively with special attention for neoplastic lesions. Included were persons referred to colonoscopy because of abdominal symptoms. Only patients with their first colonoscopy in life were evaluated. Endoscopies in asymptomatic persons, persons with increased risk for CRC (surveillance after resection of a CRC, surveillance after polypectomy, known inflammatory bowel disease, FAP, HNPCC) and patients with performed colorectal surgery were excluded. Incomplete colonoscopies were excluded as well.

A database for endoscopic findings was created in Excel 2000 with the following data: name, age, gender, symptoms, date of endoscopy, indications for endoscopy and findings.

Indications for endoscopy were classified into the following groups: altered bowel habits, anorectal bleeding, anaemia, weight loss (defined as loosing more than ten percent of body weight in the last six months before colonoscopy), signs of bowel obstruction, unspecific abdominal pain, chronic diarrhoea, chronic constipation, work-up of extracolonic abdominal tumour. Tumour suspicious symptoms were defined as altered bowel habits, weight loss, anaemia, anorectal bleeding and signs of bowel obstruction.

In cases where patients presented with more than one indication for colonoscopy the most important indication was recorded for analysis. Tumour-suspicious symptoms were defined as a major indication.

Findings were classified into the following groups: colorectal cancer, polyp, ulcerative colitis, Crohn's disease, infectious colitis, diverticulosis, angiodysplasia, "others" and endoscopy without any pathologic findings. The three most important endoscopic findings were registered. Location of findings was given as rectosigmoid and proximal colon (defined as proximal to the sigmoid colon).

In cases where patients presented with more than one finding at colonoscopy the histological most advanced lesion was recorded.

Polyps were evaluated for histology (neoplastic or non-neoplastic), number, location and size. Adenomas with high-grade dysplasia (carcinoma in situ) were recorded specially. Advanced lesions were defined as tubular adenomas measuring 10 mm and more in maximum diameter, polyps with villous features, polyps with high-grade dysplasia and colorectal cancer. Colorectal cancer was defined as T1 to T4. Where endoscopic reports were unclear, the patient files were consulted in addition.

Statistics

Results are expressed as mean, median, standard deviation and ranges. Hypothesis testing for independent numerical data was performed with the Wilcoxon rank sum test, the exploration of the association between binary variables was performed with the Chi-squared test (2×2 table) using a statistical package programme (SPSS 12.OG for Windows, version 12.0.1). Factors with $p < 0.05$ were considered statistically significant.

Results

From 1991 to 2000 2658 colonoscopies were performed. 1144 endoscopies were excluded from evaluation due to lack of symptoms, increased CRC risk, earlier colonoscopy, colonic surgery or incomplete examination. Finally 1514 patients fulfilled the inclusion criteria (54% women, mean age 65 years, median 65, SD 9 and 46% men, mean age 65 years, median age 65, SD 9), 263 women and 197 men at the age of 50 to 59 years, 260 women and 249 men at the age of 60 to 69 and 290 women and 255 men at the age of 70 to 80 years. Indications for endoscopies are shown in table 1.

Of the 1514 patients 603 (40%) had diverticulosis, 484 (32%) had polyps, 83 (5%) had colorectal cancer, 48 (3%) had angiodysplasias, 15 (1%) had inflammatory bowel disease, 16 (1%) infectious colitis, 10 (0.7%) ischaemic colitis, 352 (23%) had an endoscopy without any pathologic finding. 71 patients were submitted to the group of "other findings" including 17 patients with microscopic colitis, 15 patients with radiation proctitis, 13 patients with an extracolonic malignancy, 11 patients with undefined colitis, 9 patients with ulcers of the colon, 3 patients with volvulus of the sigma or cae-

Table 1

Indications for endoscopies (n = 1514).

Indication for endoscopy	Women (n = 813)		Men (n = 701)	
Tumour-suspicious symptoms (altered bowel habits, weight loss, anaemia, anorectal bleeding, signs of bowel obstruction)	448	55%	435	62%
Unspecific abdominal pain	265	33%	197	28%
Chronic constipation	22	3%	16	2%
Diarrhoea	52	6%	39	6%
Work-up of extracolonic tumour	26	3%	14	2%
Total	813	100%	701	100%

Table 2

Findings in work-up of tumour suspicious symptoms compared to unspecific symptoms (data given in raw numbers and %, up to two indications in every patient recorded).

Finding	Tumour suspicous symptoms (n = 946)					Unspecific symptoms (n = 713)
	Altered bowel habits (688)	Weight loss (67)	Anorectal bleeding (95)	Anaemia (77)	Signs of bowel obstruction (19)	Unspecific abdominal pain (512), chronic diarrhoea (96), constipation (65), work-up of extracolonic tumour (40)
Colorectal cancer	74 (7.8%)	33 (3.5%)	3 (0.3%)	5 (0.5%)	2 (0.2%)	2 (0.3%)
Polyps	111 (11.7%)	7 (0.7%)	5 (0.5%)	8 (0.8%)	0 (0%)	54 (7.6%)
Infectious Colitis	4 (0.4%)	1 (0.1%)	0 (0%)	1 (0.1%)	0 (0%)	15 (2.1%)
Ischaemic lesions	3 (0.3%)	0 (0%)	3 (0.3%)	0 (0%)	1 (0.1%)	6 (0.8%)
Inflammatory bowel disease	3 (0.3%)	0 (0%)	2 (0.2%)	0 (0%)	0 (0%)	14 (2%)
Diverticulosis	220 (23.3%)	10 (1%)	23 (2.4%)	23 (2.4%)	2 (0.2%)	261 (36.6%)
Angiodysplasia	7 (0.7%)	3 (0.3%)	4 (0.4%)	5 (0.5%)	0 (0%)	11 (1.5%)
Others	63 (7%)	7 (0.7%)	42 (4.4%)	6 (0.6%)	6 (0.6%)	49 (6.9%)
Normal findings	203 (21%)	6 (0.6%)	13 (1.4%)	29 (3.1%)	8 (0.8%)	301 (42.2%)

cum, 2 patients with malrotation of the colon and 1 patient with carcinoma of the appendix.

In 83 patients (5.5%) a colorectal cancer was found, 55 in men (66%) (mean age 67, median 66, SD 8) and 28 in women (34%) (mean age 70, median 72, SD 7) (difference of age: p = 0.099). 3 persons had a second synchronous CRC. CRC was found significantly more frequent (p <0.001) in patients presenting with tumour suspicious symptoms (12.3%) than in patients with unspecific symptoms (0.3%) (table 2).

The distribution of cancer according to site, gender and age is shown in table 3 and figure 1.

52% (45) of colorectal cancer were found in the rectosigmoid (17 in women, mean age 69 years, median age 71, SD 7, 28 in men, mean age 66 years, median age 65 years, SD 7) and 48% (42) in the proximal colon (12 in women, mean age 72 years, median age 73, SD 6, and 30 in men, mean age 69 years, median age 67, SD 8).

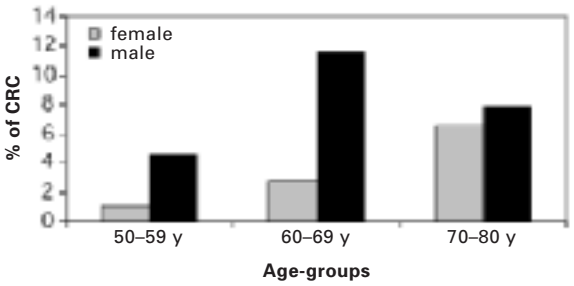

Figure 1

Distribution of cancer according to site, gender and age.

Tumour stage (classification of UICC 2002) was T1 in 6%, T2 in 12%, T3 in 58%, T4 in 24% (Tx = 7 excluded). Lymph node stage was N0 in 62%, N1 in 22%, N2 in 14%, N3 in 2% (Nx = 6 excluded). 79% had no distant metastases, 21% were M1 (Mx = 6 excluded). The following characteristics of cancers were identified (n = 87 colorectal cancer, 10 excluded for incomplete staging): T1NOM0 5 (6% of 77 CRC), T2NOMO 8 (10%), T2N1M0 2 (3%), T3NOM0 26 (34%), T3N1/2M0 12 (15%) T3N0M1 2 (3%), T3N1/2M1 4 (5%), T4N0M0 6 (8%), T4N1M0 2 (3%), T4N1-3M1 8 (10%), T4NxM1 2 (3%). The mean diameter of cancer at diagnosis was 4.8 cm, median 5 cm, SD 1.5.

We counted 955 polyps in 484 patients (32%), (40% in women, 60% in men). In 533 polyps a histological work-up was available, 61% of these polyps were in the rectosigmoid (325), 39% (208) in the proximal colon. Of these polyps 48% were tubular adenoma, 19% tubulo-villous adenoma, 0.6% villous adenoma and 32.4% non-adenomatous polyps.

Advanced lesions (AL) were found in 140 patients (9.2%). Distribution according to site, gender and age is shown in table 4. 3% (35) of 1312 patients without a polyp, 6% (3) of 54 patients with a non-adenomatous polyp and 14% (20) of 148 patients with an adenomatous polyp or an advanced neoplasm in the rectosigmoid had an advanced neoplasm in the proximal colon.

Table 3

Distribution of colorectal cancer according to site and age (4 patients with 2 synchronous cancers included, number of cancers = 87, data given in raw numbers and %).

Localisation of CRC	Patients from 50–59 years			Patients from 60–69 years			Patients >70 years		
	F 263	M 197	Total 460	F 260	M 249	Total 509	F 290	M 255	Total 545
Rectosidmoid	2 (0.7)	5 (2.5)	7 (1.5)	5 (1.9)	16 (6.4)	21 (4.1)	10 (3.5)	7 (2.7)	17 (3.1)
Proximal colon	1 (0.4)	4 (2)	5 (1.1)	2 (0.8)	13 (5.2)	15 (3)	9 (3.1)	13 (5.1)	22 (4)
Total	3 (1.1)	9 (4.5)	12 (2.6)	7 (2.7)	29 (11.6)	36 (7.1)	19 (6.6)	20 (7.8)	39 (7.1)

Table 4

Distribution of *advanced lesions* according to site and age (data given in raw numbers and % in gender-specific age-category, n = 156 advanced lesions in 140 patients).

Localisation of CRC	Patients from 50–59 years			Patients from 60–69 years			Patients from 70> years		
	F 263	M 197	Total 460	F 260	M 249	Total 509	F 290	M 255	Total 545
Rectosigmoid	9 (3)	14 (7)	23 (5)	6 (2)	20 (8)	26 (5)	17 (6)	34 (13)	50 (9)
Proximal colon	8 (3)	6 (3)	14 (3)	3 (1)	14 (6)	17 (3)	8 (3)	18 (7)	26 (5)
Total	17 (6)	20 (10)	37 (8)	9 (3)	34 (14)	43 (8)	25 (9)	52 (20)	76 (14)

Discussion

Detection of CRC at an early stage is crucial to improve chances of surviving cancer [20]. Swiss health policy does not yet support any general screening strategy in asymptomatic persons, but encourages people to get a rapid endoscopic work-up in case of warning symptoms. Our retrospective analysis of colonoscopies done in symptomatic persons within the age group at risk (>50 years) accentuated misgivings about this strategy. In 12.3% of patients, a colorectal cancer was found by working up warning symptoms and only in 0.3% if endoscopy was performed for other reasons. Unfortunately, most of these tumours were already advanced: 82% of CRC were T3/4, 38% had lymph node metastasis and 21% had distant metastasis. Our findings are in contrast to tumours detected in selected asymptomatic population groups that have had colonoscopy as part of a screening programme [16, 21, 22]. In these studies, only 20 to 25% of the cancers detected were T3/4, 15 to 20% had lymph node involvement and none to 7% had metastases. These findings strongly indicate that rapid work-up of symptomatic people will hardly be sufficient to reduce mortality from colorectal cancer. We do not believe that the delay of endoscopic work-up in symptomatic patients could explain the advanced tumour stages. Numerous endoscopic units are present in all parts of Switzerland with easy and rapid access, which is not the case in some other industrialised countries [23]. According to a recent survey, one practising gastroenterologist in Switzerland covers 33,000 persons, as is the case in the area of Uri [24]. Patient-induced delay in seeking a doctor in case of bowel problems might hinder rapid work-up since more than 75% of people feel ashamed and are reluctant to discuss their bowel problems with their family doctor in Europe [2]. However, the most likely explanation for our findings is that tumours are already far advanced when they become symptomatic.

Only a few prospective studies on colonosopic screening are available and these have not been done in a population-based setting and could therefore be biased [16, 21, 22]. Up to now, population-based data is not available even from symptomatic people within the age group at risk (>50 years). The few studies [25, 26] done in elderly people evaluated primarily the feasibility and safety of colonoscopies without reporting frequency and findings.

In our study 16% of the population within the age group at risk (>50 years) had a colonoscopy for different reasons, thereby reducing the population eligible for screening. This knowledge is important to calculate the costs of a future-screening programme, or to estimate the manpower sufficient to perform the endoscopies. This frequency of endoscopies done in symptomatic people can influence the demography of findings in screening studies of asymptomatic people as well. More endoscopic work-ups were performed in women than in men. This can influence the gender dependent ratio of pathologic findings in screening studies such as the observed lower prevalence of AL and CRC in women [32, 33].

In accordance with registries of cancer, we found a predominance of colorectal cancer in men [16, 21, 22, 27, 28] and an increase with age [16, 21, 29–31]. CRC was found in the proximal colon, increasing with age mainly. CRC was seldom found in the proximal colon in women before the age of 60 years. This is in agreement with recent findings in screening studies done in asymptomatic patients [32, 33].

Recent results of screening studies in asymptomatic people underline the significance of findings in the rectosigmoid for the occurrence of neoplastic lesions in the proximal colon [32–34]. Our population-based data in symptomatic patients are in agreement with these findings. Similarly, in our analysis, proximal AL were more frequent if polyps were found in the rectosigmoid. The frequency varied according to their histology. 14% of all

patients with adenomatous lesions or advanced neoplasms in the rectosigmoid had a proximal advanced lesion, which was only 3% in patients without a rectosigmoid polyp.

In summary, our data show that early work-up of symptomatic patients can hardly reduce the mortality due to CRC. Therefore, screening programmes of asymptomatic persons are of great importance. Our data help to define the target population and the necessary manpower. In addition, our results are in agreement with findings of screening studies suggesting that tailoring screening according to age, gender, family history and rectosigmoid findings could be reasonable. However such a strategy needs further analysis by prospective population-based studies.

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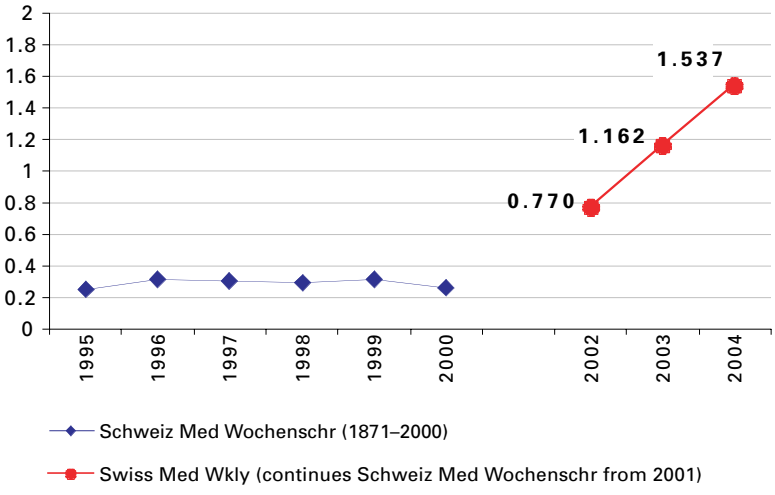

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