WHAT SHOULD WE PROPOSE TO THE AVERAGE RISK PERSON ? PRO COLONOSCOPY. J. F. Riemann, A. Rosenbaum. Klinikum der Stadt Ludwigshafen gGmbH, Medizinische Klinik C (Dept. of Gastroenterology and Hepatology).

In the western industrial countries, colorectal carcinoma (CRC) is one of the leading causes of death from cancer. About 60.000 new diagnoses and 30.000 deaths from CRC per year are the corresponding figures for Germany. It is well known for years, that CRC evolves from premalignant adenomas within a period of approximately 10 years. This process can be stopped by early polypectomy of adenomas. In addition it could be proved that the detection of CRC at an early stage (UICC I) is associated with a significantly higher rate of complete remission and longer survival compared to progressive stages. People at higher risk for adenomas and/or malignant transformation could be identified (e.g. Patients with HNPCC, FAP, family history for CRC or with previous polypectomy). Thus, screening strategies for CRC were developed, and especially the faecal occult blood test (FOBT) proved to be very efficient (Evidence grade I). Since this test only detects bleeding polyps or tumors, and small polyps – although premalignant – usually do not bleed, endoscopic screening methods were introduced : sigmoidoscopy and colonoscopy. Both techniques offer the advantage of immediate polypectomy which combines preventive screening and definite therapy in one step. Numerous studies (Evidence grade II-2) could show that screening colonoscopy combines high rates of sensitivity and specificity with cost-effectiveness. However it must be guaranteed that there are standards concerning the quality of the examination and the technical equipment. Under these conditions, Germany has implemented this procedure into its cancer screening program in 2002. This means screening colonoscopy is now covered by medical insurance. Experiences from the last years show that screening colonoscopy is able to reduce the incidence of the CRC, already existing tumors are diagnosed in an earlier -well treatable- stage, the procedure is cost-effective, and the rate of complications is very low. To date, the most important problem appears to be the very limited acceptance in the wide public – a point that will have to be improved in the future.

Colonoscopy as a screening test for colorectal cancer

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Abstract

Colonoscopy is the current gold standard for the diagnosis and treatment of colorectal neoplasms. Several gastroenterological and/or endoscopical societies recommend screening by colonoscopy in high risk patients for colorectal cancer whilst for average risk patients colonoscopy remains a valid option. In some countries screening colonoscopy is now covered by medical insurance. It is also the final common pathway of all colorectal cancer screening methods. This paper addresses the advantages and also limitations of colonoscopy as the first procedure for colorectal screening and emphasizes the importance of organized training and continuous assessment of competence of gastroenterologists and the necessity to have quality control audits of the endoscopy units. (Acta gastroenterol. belg., **2005**, 68, **251-256**).

Key words : colonoscopy, screening, colorectal cancer.

Introduction

Colonoscopy is the current gold standard for the diagnosis and treatment of colorectal neoplasms (i.e. adenoma and cancer) (1). The American (2), British (3) and French (4) gastroenterological and/or endoscopical societies recommend screening by colonoscopy in high risk patients for colorectal cancer whilst for average risk patients colonoscopy remains a valid option. In some countries (USA, Germany and Italy) screening colonoscopy is now covered by medical insurance (5,6). This paper addresses the advantages and also limitations of colonoscopy as the first procedure for colorectal cancer (CRC) screening.

Prerequisites

A documented discussion about the procedure, its potential risks and benefits, should be done before the patient is medicated (7). Adequate colon cleansing, sedation and endoscopic expertise are the major determinants of quality of colonoscopy (7,8,9). After a 3-5 days low fiber diet, colonic cleansing is performed with either polyethylene glycol or sodium phosphate (7,10). The preparation quality determines not only the completeness and speed of colonoscopy but increases also the yield of endoscopic lesions and the proportion of polypectomies (10). Colonoscopy is usually performed with sedation and/or analgesia, the level of which should be titrated to achieve a safe and compfortable procedure. Benzodiazepines (midazolam) and anesthetic agents (propofol) are currently used,the latter being superior in terms of patient tolerance and satisfaction although increasing the cost and length of hospitalization (11). Deep sedation requires appropriate monitoring by trained doctors or nurses, and the collaboration of an anesthesiologist should be taken into account (11). Colonoscopy without sedation or only on demand, can achieve completeness of the examination in expert hands in more than 90% of patients as well (12,13).

Colonoscopy is a challenging procedure requiring constant training, well organized, well-equipped and well-staffed endoscopic facilities (14). Current guidelines on CRC screening emphasize the importance of colonoscopy adequate training and of continuous quality control audits of competence (15,16). The goal is accurate, painless, safe, rapid and affordable endoscopic testing. It is estimated that, for the initial GI fellows training, a minimum of 100 to 200 supervised colonoscopy procedures are needed before a reach to the cecum is obtained in 90% of the time (11,12). An estimation of an annual volume of at least 200 procedures appear to be required to maintain adequate competence although we are still lacking clear markings of competence (8). Unfortunately, lower endoscopic annual volume rates are associated not only with failure to complete colonoscopy but also with CRC miss rates (9,17).

At the end of the procedure a precise report and safety instructions should be given to patients and their treating physicians. An outpatient visit can be scheduled in order to discuss the pathological results and the cancer risks, need for follow-up colonoscopies and advice regarding appropriate testing of the family members (18). Good collaboration with the general practitionner is mandatory.

Indications of colonoscopy in the context of CRC screening

- **Any positivity of another screening method :**
  1. Positive faecal occult blood tests (FOBT) : in 2% according to recent data (19).
  2. Abnormal sigmoidoscopy : 5 to 16% of patients depending on the criteria used to define a positive screening (20,21,22,23).

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Table 1. — **Diagnostic yield of screening colonoscopy**

Authors	Year	Number of patients	Advanced neoplasia[1]	Cancers[2]	Adenomas
Johnson (USA)	1990	89	Unknown	0	21 (24%)
Lieberman (USA)	1991	105	Unknown	1 (1%)	43 (41%)
Rex (USA)	1993	496	Unknown	3 (0.6%)	128 (26%)
Lieberman (USA)	2000	3196	329 (10.5%)	30 (1%)	1141 (31.5%)
Imperiale (USA)	2000	1994	99 (5%)	12 (0.6%)	453 (23%)
Sung (China)	2003	505	63 (12.5%)	4 (0.7%)	102 (20%)
Erasme (Belgium)	2004	555	46 (8%)	4 (0.7%)	132 (24%)
Okamoto (Japan)	2005	6178	227 (4%)	207 (3.3%)	Unknown
ALL		13118	6%	2%	29%

[1] Advanced neoplasia = Adenoma > 1 cm, or High grade dysplasia or villous content > 25% (35).
[2] Cancer = Invasive cancer, polyp with invasion of malignant cells beyond the muscularis mucosa or macroscopic evidence of adenocarcinoma confirmed histologically.

3. Computed tomography virtual colonoscopy (VC) : 4 to 14%, again depending on the cut-off size of the polyps (10 mm ,8 mm, 6 mm) (24).
4. Double contrast barium enema (DCBE), real data of positivity is lacking except in post-polypectomy surveillance (26%) (25).

- **High risk groups** : familial adenomatous polyposis (FAP), hereditary non polyposis CRC syndrome (HNPCC), familial history of 1-2 1st degree relatives with adenomas or CRC, personal history of long-standing inflammatory bowel disease (IBD), surveillance : post-polypectomy, CRC resection (1-4,26).
- **Alarm signs** : colonoscopy is the first diagnostic method as the risk is high for finding significant lesions with high sensitivity and specificity of colonoscopy in this setting (1).
- **Average risk** (i.e. > 50 years old) persons. Colonoscopy every 10 years or once in life is an alternative to other screening methods, at an individual level, after discussion with the general practitioner or the gastroenterologist (1).

Diagnostic yield

The diagnostic yield of screening colonoscopy in average-risk persons of colorectal neoplasia in the US (27-31), China (Hong Kong) (32), Belgium (33) and Japan (34) is indicated in Table I. Lesions were categorized according to the newly agreed WHO pathological classification (35). We have to emphasize the prevalence of proximal isolated advanced neoplasia, without any distal sentinel lesion ranging from 2 to 5% and increasing with age (33,34,36). As colonoscopy is considered the gold standard for detecting colorectal neoplasia (1), back to back tandem colonoscopy were done in two studies trying to determine the real sensitivity of colonoscopy (37,38). Those studies showed that, although small adenomas (less than 1cm) were missed in almost a quarter of examinations (mainly in the right colon), larger polyps rarely (0 to 6%) went undetected. Recently, VC challenged the sensitivity of conventional colonoscopy,as in one study 12% of large (> 1 cm) adenomas were missed by endoscopy, most of them located behind a proximal fold or near the anal verge (24,39). This emphasizes once more the importance of expertise and experience, of perfect bowel cleansing, the necessity to complete the examination up to the caecum, an adequate colonoscopic withdrawal technique and adherence to quality indicators (40-44). However, an even more recent study, comparing ACBE, VC and colonoscopy, showed that for lesions of 1cm or larger sensitivities were 48%, 59% and 98% respectively, with similar results for smaller lesions (45).

The apparent discrepancies amongst studies comparing VC to colonoscopy lead to a plea for future trials with independent analysis by people with no direct interest in the outcome (46).

VC can be very useful after incomplete colonoscopy and probably should replace ACBE in this indication (47,48).

Overall sensitivity of colonoscopy is considered to be around 90 to 95% (1,49), with even higher specificity per patient and per lesion, with the obvious advantage of polypectomy and detailed pathological analysis of all colonic lesions, as sometimes even small adenomas can harbor high grade dysplasia and/or cancer (4 to 6%) (14,50,51). Colonoscopy is in constant technical improvement, and recent innovations such as the new colonoscope with variable stiffness, the use of video and magnetic endoscope imaging increases the success rate while decreasing pain rate of the patient (40). Chromoscopy with or without magnification, although time consuming could increase the detection yield of diminutive and flat adenomas and may predict neoplastic changes of the adenomas (40).

Complications

Complications related to colonoscopy are, fortunately, quite rare and most often benign but they can sometimes be serious and exceptionnally life threatening. True rates of complications in the commmunity setting or general hospitals are difficult to determine because most reports are retrospective, published by experienced centers (52,53) and may omit late complications, as shown in a study where patients were contacted 30 days after outpatient colonoscopy (54).

Preparation-related complications can occur mainly in old patients with comorbidities. Phosphate preparations can induce renal failure if no adequate hydration is prescribed and electrolytes disturbances (52,55). Electronic monitoring has become standard practice as the main risk is oxygen desaturation and hypotension, and, as already mentioned, the presence of qualified staff is mandatory (11). Perforation, hemorrhage, postpolypectomy coagulation syndrome, and (very rarely) infection are the main complications (52). Most of the above can be managed in a conservative manner but early awareness of a potential complication is vital (56). Perforation rate varies from 0 to 0.32%, mainly after polypectomy and rarely (0.2%) during diagnostic procedures (52,53). In two recent publications, where screening colonoscopy was performed in average risk patients the perforation rates were 0 (3196 procedures) and 0.1% (6066 procedures) (57,58). Polyp size is not always related to the risk of perforation as are right sided sessile polyps (57,58).

Post-procedural hemorrhage, can occur immediately or can be delayed for as long as a month after polypectomy (52,53).The rate of bleeding in 25000 diagnostic colonoscopies was 0.09% and varies from 0.64 to 2.7% during polypectomies (52). In the two screening series mentioned above (57,58) bleeding occurred in 0.2%. Post-polypectomy coagulation syndrome, related to electro coagulation injury to the bowel wall, usually does not require surgical treatment and can occur in approximately 1% of polypectomies, mainly in the right side of the colon (52). Colonoscopy related infection is rare, and is related to diminish host immunity, although short lasting bacteremia has a mean frequency of 4% (59). Death occurs very unfrequently as one study estimated it to be 1 per 16000 patients (52). Finally, we have to emphasize that the complications related to colonoscopy (mainly related to polypectomy), are indirectly at least, also the complications of any screening method with a positive result leading to diagnostic and/or therapeutic colonoscopy.

Acceptability

Acceptability and implementation of CRC screening programs require important educational efforts for both patients and doctors, as there is low level of awareness about CRC and its prevention in the population (60,61). Even gastroenterologists are not often aware of the importance of detecting familial risk factors (7,18). Even in countries like the US, where media are very active to promote CRC screening and colonoscopy reports of the Presidents are available on internet, 60% of the population aged over 50 years were not screened for colorectal neoplasia (62,63,64).

In a recent feasibility study conducted among GP in Belgium, an overall 20% of asymptomatic patients (50 to 70 years old) agreed to undergo screening colonoscopy after 15 minutes of discussion about CRC (65). Some GP succeeded in persuading up to 60% (30 out of 50) of patients to be screened by colonoscopy, reflecting probably a high personal belief and motivation as only 30% of contacted GP participated in the study (65). As expected, women (versus men) and patients with family history were more enclined to be screened (65).

In Australia, acceptability of colonoscopy is around 18% (66), and 29% in a recent US study, this comparing with 15% for sigmoidoscopy and 56% for FOBT (67). In the Australian study mentioned above (66) among screened patients satisfaction for colonoscopy and VC was similar and high, 87% of patients undergoing endoscopy considered it to be less unpleasant than expected. In another American study patients reported that they prefered colonoscopy over VC, as they reported more pain and less respect (?) during VC (68). French data showed that in 2000 CRC screening was the indication for 20% of colonoscopies versus 13% in the year before (increase acceptability ?) (69). Unfortunately, in another study done in 37 health centers in France, even among high risk individuals, acceptability of colonoscopy turned to be low (18%) (70).

Another interesting issue, is the need for reliable data regarding both the current and future capacity for endoscopic screening. Two recent papers have asked this question (71,72). Sufficient capacity exists in the US only for FOBT positive tested patients but the prospect of delivery screening colonoscopy to everyone starting at the age of fifty years is likely to be untenable unless resources are shifted away from excessive surveillance back to screening. It seems impossible to extrapolate figures in Belgium. 100 to 150 more colonoscopies per working day (± 200 a year), reasonably feasible, will produce at the end of the year a total of 20000 to 30000 supplementary colonoscopies, enough to screen high risk individuals (73) and probaly patients positive at FOBT (20000 per 1 million screened by FOBT).

Effectiveness

The ability of colonoscopy to prevent CRC or death from CRC has not been measured in a screening trial. Based on the comparison with historic controls, the National Polyp Study (74) estimated that 76 to 90% of the cancers could be prevented. For FAP and HNPCC, uncontrolled series indicate that mortality from CRC has decreased with proper implementation of screening guidelines (26,75) and a current review confirms that endoscopic surveillance remains the mainstay of preventive management (76). When there is familial clustering of CRC, although no direct data shows a favorable effect of colonoscopic screening, indirect evidence suggests a benefit as cancers arise earlier but has no different distribution or more rapid development than do cancers arising in persons without a familial history (26).

IBD patients are also at risk mainly 10 to 15 years after the start of the disease and surveillance colonoscopy is expected to detect early neoplastic lesions at a curable stage (77).

Table 2. — **PROS and CONTRAS of screening colonoscopy**

PROS	CONTRAS
– High diagnostic yield + histology (1,14,50,51) – Protective effect on CRC (incidence and death) (74,81,83) – Cost-effectiveness established (84-88,90) – Sufficient colonoscopy capacity (62,63,71,72)	– Miss of a certain % of polyps and CRC (17,24,41,42) – Operator dependent (8,15,16) – Risk of complications (52-54) – Not cost-effective (42,89) – Insufficient colonoscopy capacity (62,63,71,72) – Low acceptability (70) – Costly and loss of workday (1)

Surveillance after polypectomy and resection of CRC should be individualized, as clear evidence of surveillance efficacy is unfortunately lacking for the latter, although small survival benefit with routine follow-up was recently observed after CRC surgery (78,79). Screening colonoscopy in average risk persons is an option endorsed by many scientific societies although data from prospective randomized trials are still lacking (1-6,80).

Indirect evidence also supports the case for colonoscopic screening. Sigmoidoscopy is effective in preventing CRC deaths (23) so, logically, a longer scope should also reduce this risk. The efficacy of FOBT followed, in case of positivity by colonoscopy is an indirect argument in favour of the efficiency of the latter method (19). The study by Muller et al, among 32702 veterans, also suggests that endoscopy and polypectomy reduces incidence (by 50%) and mortality of CRC (81). As mentioned above based on comparison with historic controls, the National Polyp Study (74) estimated that 76 to 90% of the cancers could be prevented. Recent articles are in favour of a proximal shift of CRC as well as flat adenomas in the right colon in relation with age (33,82,34). Confirmation of such data will render colonoscopic screening even more efficacious after the age of 60.

Cost-effective analysis

We already know that colonoscpy has been found to diminish the incidence of CRC (74,81) and to protect against death from CRC either directly (83) or indirectly after another screening method (see above, 19,23). For the moment we are lacking firm clinical data indicating that colonoscopy is the most cost-effective screening strategy for CRC. Several articles using mathematical models, studied cost effectiveness of different screening strategies, but we need to remain cautious as all models are approximations (84). The cost of endoscopical procedures is higher in the USA than in Belgium, a factor that can be in favour of cost-effectiveness of colonoscopy in our country (1). In the last 20 years, such articles, using mathematical models, were in favour of colonoscopy as having the highest impact on CRC mortality : one time colonoscopy (for patients aged 55 to 65) (85), colonoscopy every 10 years (patients aged 50) (86),or at the age of 65 (87). In another recent article, (math.-model) extension of life expectancy through screening colonoscopy was two or three time longer than that achieved by sigmoidoscopy or FOBT, mainly among americans aged 50 to 54 years (84).

As always in all studies, compliance was an important determinant of effectiveness (86,87). Some authors in clinical studies, calculated scores (combining variables like family history, gender, age, body-mass index etc) trying to identify individuals best suitable for screening colonoscopy (88). We must emphasize that the "U.S. Preventive Service Task Force" though recognizing the effectiveness of any screening method for CRC, couldn't determine the best screening approach (89). As already mentioned, in Italy and Germany, colonoscopy is now reimbursed for screening as it is considered to be cost-effective by health authorities (5,6,90).

Conclusions

We have summarized in Table II the advantages and disadvantages of colonoscopy for CRC screening. It is the most effective but also the most invasive and costly screening procedure, and thus should mainly targeted on persons who will most likely benefit from it, taking into account familial and personal medical history (91,92). The GP should be actively involved in this process, by identifying persons at risk, and also by explaining the different screening methods available as any screening modality will have an impact on CRC rate reduction. Screening colonoscopy may be advocated in motivated, well informed average risk individuals from age 50. It is the preferred diagnostic investigation after age 65 and in other high risk groups, characterized by a positive personal or family history of colorectal adenomas or cancer and personal history of longstanding IBD. High standards of endoscopy and public awareness of CRC and screening options are mandatory for successful implementation of an endoscopic screening.

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