

Screening of average-risk individuals for colorectal cancer

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Recent developments in screening, diagnosis and treatment of colon cancer could lead to a reduction in mortality from this disease. Removal of adenomas, identification of risk factors, appropriate application of accurate diagnostic tests, and aggressive anatomic-surgical resection of colon cancers may already be having a favourable impact. Screening of average-risk populations over the age of 50 also offers promise in the control of this important cancer. The disease is of sufficient magnitude to deserve detection at an early stage with better prospects of patient survival, since screening tests with moderate sensitivity and high specificity are available. Flexible sigmoidoscopy and faecal occult blood tests are sufficiently acceptable to be included in case-finding among patients who are in the health care system. The results of current controlled trials involving more than 300 000 individuals for evaluating the impact of screening on mortality from colon cancer are needed before this approach can be recommended for general public health screening of the population. Further research is required to develop better screening tests, improve patient and physician compliance, and answer more definitively critical questions on cost-effectiveness. Mathematical modelling using current and new data can be used to determine the effectiveness of screening in conjunction with recommendations for primary prevention.

Introduction

Colorectal cancer has an annual incidence worldwide of more than half a million cases and ranks as the third most common cancer, preceded by only lung and stomach cancers. Countries with a high incidence of colorectal cancer include Australia, Canada, France, Italy, New Zealand, the Scandinavian countries, United Kingdom and the USA (1).

The potential benefit of screening for colorectal cancer is based on: (1) the well-established relationship between survival and stage of disease, and (2) the observation that diagnosis and removal of premalignant adenomas could lead to a decrease in the future incidence of colorectal cancer (2-7).

Several factors influencing the feasibility and effectiveness of screening need to be examined. Those

relating to feasibility include the rate of positive tests, sensitivity, specificity and predictiveness of the tests, and patient compliance. Effectiveness depends on cancer staging, survival, mortality, and cost-effectiveness. Detection of earlier-stage cancers, often associated with improved survival, is critical although bias could influence the results. For example, cancers may be detected earlier but without any real increase in survival (lead-time bias), or only the more favourable cancers may be detected by screening because they are slow-growing cancers (length bias) (2, 3). Overdiagnosis is yet another bias resulting in treatment of cancers that would not have been identified. The validity of screening can be assessed and bias reduced if the mortality from colon cancer can be examined; this is difficult and depends on ascertaining the follow-up of all individuals in a cohort and establishing systematic mortality reviews (2, 3).

Risk factors and screening

Risk factors

Age. Risk for colorectal cancer increases slightly at age 40 and more sharply at 50 years, doubling thereafter with each decade (3). Individuals who are at risk by virtue of age only and who have no other associated high-risk factors are considered at "average or standard risk" for the disease. Several high-risk groups can be identified (Table 1).

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Table 1: Risk for colorectal cancer

Average risk:

Men and women aged 50 years and older

High risk:

1. Inflammatory bowel disease
2. Familial adenomatous polyposis syndromes, including Gardner and Turcot syndromes
3. Juvenile polyposis
4. Hereditary non-polyposis colorectal cancer syndromes
5. Family history of colorectal cancer or adenomas
6. Past history of colorectal cancer or adenomas
7. Past history of breast, endometrial or ovarian cancer

Colorectal neoplasia. Patients who have had one colorectal cancer have a 5–10% risk for a subsequent colorectal cancer (3). Patients with one colorectal cancer have a 1.5–5% risk that an additional colorectal cancer is present at the same time. The prevalence of adenomas in Western countries is as high as 40–50% in older age groups (8), and there is considerable evidence that most colorectal cancers arise from an adenoma or neoplastic polyp (8). Only a proportion of colonic polyps that are detected are true adenomas. In the U.S. National Polyp Study, adenomas accounted for 68% of the polyps removed by colonoscopy in the initial examination. Individuals presenting with one adenoma have a 50% likelihood of additional adenomas and a 30% likelihood of additional adenomas one year after their colons have been cleared of all adenomas (9). The time sequence from a normal-appearing colon through the stage of adenoma and then to cancer has been studied using mathematical models and clinical observations. These studies suggest that the process develops slowly over many years (9).

Genetic predisposition. Genetic syndromes include familial adenomatous polyposis; Gardner, Turcot, and Peutz-Jeghers syndromes; juvenile polyposis and hereditary non-polyposis colorectal cancer syndrome (10). These account for approximately 5% of the colorectal cancer cases each year, and all follow an autosomal dominant mode of inheritance. Until recently, genetic factors were considered to be important only in these syndromes, the majority of colorectal cancer cases being "sporadic". However, several studies have reported a threefold excess of cancer and a high frequency of adenomas among first-degree relatives of patients with colorectal cancer (10). A sizeable proportion of "sporadic" adenomas and colorectal cancers may be genetically determined by an autosomal dominant mode with low penetrance (11). This will be discussed in another paper.

Inflammatory bowel disease. Ulcerative colitis is a risk factor for colorectal cancer (12–14), but accounts for

only a small number of new cases each year. Duration of the disease and its anatomical extent are two factors in the cancer risk, which begins to rise after seven years of disease in patients with involvement of the entire colon and after 15 years when there has been only left-sided colitis. Proctitis alone appears to carry no increased risk (14). This matter will be discussed in another article.

Screening tests

Screening using rapid, simple tests should separate well persons who have a high probability of a disease from those with a low probability (2, 3). The screening test is not intended to be diagnostic, and persons with positive findings should be referred for diagnosis and treatment. Three tests that currently fulfil these criteria are the stool blood test, digital rectal examination, and sigmoidoscopy. The last two can be considered clinically diagnostic in symptomatic people.

The identification of cancer by digital rectal examination is now less frequent as a result of the proximal shift in the site of colorectal cancers. Recent statistics indicate that less than 10% are detectable by digital examination (2, 3). There are several sigmoidoscopes available now: rigid scopes 25 cm in length, 35-cm fibre-optic sigmoidoscopes, 60-cm fibre-optic sigmoidoscopes, and 40–60-cm video endoscopes (15–18). The average depth of insertion of the rigid sigmoidoscope by skilled examiners is 20 cm or less. Studies demonstrated that only the distal 16 cm of the rectosigmoid is well examined by the rigid instrument. The flexible sigmoidoscope has a 2–3 times greater yield for adenomas and cancer as compared to the rigid scope and can adequately examine the entire rectosigmoid, where about 50% of the cancers and adenomas occur (15). The effectiveness of sigmoidoscopy in screening has not been well studied, but some data are available. In one study more than 26 000 asymptomatic patients had 58 cancers detected (6). Of these, 81% were in stages A and B of Dukes' classification and the 15-year survival was 90%. This was an uncontrolled study with follow-up of only the cancer cases. Studies evaluating the efficacy of periodic Multiphasic Health Checkups in the Northern California Kaiser-Permanente programme indicated a reduced mortality from colorectal cancer. Rigid sigmoidoscopy was part of the multiphasic check-up but was not specifically studied. This mortality reduction was reconfirmed in a 16-year follow-up but the precise role of sigmoidoscopy was not clear (19–21). Adenomas are detected by sigmoidoscopy at a higher frequency than carcinomas (15). There are no controlled trials in progress for evaluating the long-term benefit of the flexible scopes.

The testing of stool for occult blood was first

proposed in 1901 (22–24) and the impregnated guaiac slide-test was introduced by Greegor as a screen for colorectal cancer (24). While on a high fibre, meat-free diet, asymptomatic patients were asked to prepare two samples of stool daily for three days on guaiac slides. The slides were tested with a hydrogen peroxide developer and colorectal cancer was detected at an early pathological stage in patients who had positive tests (44). A positive test is caused by the phenolic oxidation of the guaiac to a blue compound, catalysed by the peroxidase-like enzymatic activity of haemoglobin. Other compounds than haemoglobin with a peroxidase-like activity, mainly in certain uncooked vegetables and fruits, can produce a positive test (22, 25). Although dietary factors have not been fully studied, data indicate that diet has little effect on the standard guaiac slide-tests but has a marked effect on the more sensitive guaiac tests, including tests performed after hydration of the slides (25). Elimination of red meat and the small number of peroxidase-rich raw vegetables and fruit will improve the test's specificity and reduce false positives (25). Iron and laxatives have an unpredictable effect on positives and negatives, while vitamin C inhibits the test reaction, causing a false negative in the presence of bleeding (22, 23). Positive stool-blood tests can result from physiological blood loss and benign bleeding lesions, as well as from neoplastic bleeding lesions (22, 23). Isotope studies have shown fluctuation of occult bleeding from colorectal adenomas and cancer, large adenomas bleeding more than the smaller ones. Data also suggest that the blood loss may have to be greater from the right colon than from the left colon to produce a positive test (22, 26, 27). Studies have been carried out on possible improvements in the guaiac test performance.

Hydration of the slides produces a higher positivity rate and leads to more cancers detected, but also a larger number of false positive reactions with resulting unnecessary diagnostic evaluations (26, 28, 29).

Other stool-blood tests have been introduced including: immunochemical tests that are specific for human haemoglobin, a quantitative test for blood (Hemoquant[®]) based on the fluorescence of haem-derived porphyrins, and more sensitive guaiac slide-tests. Some of these tests have been evaluated and compared with the standard guaiac-based slide-test (22, 23, 30).

The immunochemical tests, which utilize antibodies developed against human haemoglobin and depend upon the globin being intact, are not affected by diet, vitamin C or iron. Because globin is digested in the stomach and small intestine, these tests have an extremely low sensitivity for bleeding arising from the upper gastrointestinal tract. Initial experience indicates that the tests have a high sensitivity for colonic bleeding, but more information is needed about their

performance with proximal colonic lesions and after degradation of globin during storage, and about the test's specificity before their ultimate place in screening can be determined.

Non-haem peroxidases, vitamin C and iron do not interfere with the Hemoquant test, which is not affected by degradation of haemoglobin in the intestine or during storage. However, the test is influenced by meat in the diet and by ingestion of aspirin and other drugs that could increase blood loss. Early hopes that Hemoquant could be used to identify the anatomical level of bleeding in the gastrointestinal tract have not been fulfilled. Concerns include questions about its ability to distinguish between physiological and pathological blood loss, interference by diet and drug ingestion, and the relatively high cost of the test. In addition, its increased sensitivity is at the sacrifice of specificity. Maintenance of high specificity with high sensitivity may be possible with the new sensitive guaiac slide-test and with the new immunochemical tests (30).

Several studies and programmes initiated around the world to evaluate screening with the stool-blood tests confirm that this has potential value for colorectal cancer (23, 28, 29, 31–33). A large study is in progress in the Federal Republic of Germany to encourage screening of asymptomatic women and men in doctors' offices on a periodic basis (34). There are five controlled trials now studying the possible usefulness of the stool-blood test in screening for colorectal cancer (Table 2) (28, 35–39). A trial was started in 1975 by the Memorial Sloan-Kettering Cancer Centre and the Strang Clinic to evaluate the stool occult-blood test for detection of colorectal cancer in conjunction with rigid sigmoidoscopy in the setting of comprehensive preventive medical examinations (35). Patients over 40 who presented at the clinic were enrolled and allocated to the study and control group based on the date of enrolment. All 21 756 participants underwent a comprehensive examination which included a general physical examination, a health history questionnaire, and 25-cm sigmoidoscopy. Patients assigned to the study group were also offered stool-blood testing, while control patients were not. Incorporation of the stool-blood test was feasible with approximately 75% of patients who were willing to prepare their slides at the time of their enrolment. The overall rate of positive tests was 1.7% with nonhydrated slides and was strongly age-dependent. The rate of positivity was higher for patients who had not had periodic sigmoidoscopic examinations in previous years. The overall predictive value of the test for adenomas and cancer was 30% and was also greatest on first screening and strongly age-dependent (poor for those under age 50). The majority of patients with a positive

Table 2: Controlled trials of stool-blood testing in screening for colorectal cancer^a

	Cohort size	Positivity rate (%)	Predictive value (%) (adenomas & cancer)	Dukes' A & B stage cancers (%)	
				Screened group	Control group
Göteborg, Sweden	27 000	1.9	22	65	33
Nottingham, England	150 000	2.1	53	90	40
New York, USA	22 000	1.7	30	65	33
Minnesota, USA	48 000	2.4	31	78	35
Funen, Denmark	62 000	1.0	58	81	55

^a This Table is derived from multiple sources and summarizes mainly the data from non-hydrated slides although hydrated slides have also been used in a phase of some programmes. The data are primarily from initial screening. Dukes' A stage cancers accounted for 34–65% in the screened groups compared with 8–24% in the control groups (see text and references for details). Modified from a previously published Table (3).

stool-blood test underwent diagnostic procedures within a year after their tests. The barium enema missed 25% of the neoplastic lesions found through colonoscopy. The sensitivity for the stool-blood test for cancer was estimated at 70% and specificity at 98%. A distinct stage difference was observed with respect to those cancers found on the first (prevalence) screen. The screened group had 65% of their cancers in Dukes' stage A or B, compared to 33% in the control group.

A second controlled trial evaluating stool occult-blood testing was initiated in the USA in 1975 at the University of Minnesota (38). In this study, 48 000 participants aged 50 and older were randomly allocated into one of three study groups: those who were offered stool-blood testing each year, those who were offered testing every other year, and a control group. Compliance with slide preparation was 75% and the initial rate of positivity was 2.4% but has increased markedly, primarily because of use of the hydrated-slide test. Of the 80% of patients with positive tests who underwent diagnostic evaluation, 31% had either adenomas or cancer of the colon or rectum; 78% of the cancers were in Dukes' stage A or B, compared to 35% in the control group. The single-column barium enema had poor sensitivity and was discontinued and colonoscopy was considered extremely important. This study is now in a rescreening and follow-up stage.

A large, controlled, population-based trial was started more recently in England with asymptomatic individuals identified from family doctor registries and allocated randomly to test and control groups (39). Recruitment of 156 000 persons aged 50–74 will be completed in 1990. Screening of the first 107 349 subjects recruited has been completed. In the test

group (52 258 subjects) 53% completed the stool-blood test resulting in 2.3% positive tests for non-hydrated slides with a predictive value for cancer and adenoma of 53% initially and a yield of cancer of 2.3 per 1000 persons screened; 53% of cancers detected were in stage A, compared with 10% in the control group. Estimated sensitivity was 72% and specificity 98%. Rescreening during every other year is planned.

A fourth controlled trial of screening is in progress in Sweden and involves 27 700 inhabitants of Göteborg, aged 60–64 (28). The rate of positivity in the screened group was 1.9% using nonhydrated slides and 5.8% using rehydrated slides. In the initial screen, 65% of the cancers were in Dukes' A or B stage, compared to 33% in the control group. The estimated sensitivity for cancer was 52%, which is much lower than observed in the four other trials. A fifth large population-based, controlled trial has been initiated in Denmark (37). In this study, 62 000 participants aged 50–74 were randomly allocated into either a study group (those who were offered stool-blood testing every other year) or a control group. The first test was completed in 66% of those in the former group with a slide positivity of 1.0%, which is the lowest reported on a first screen.

The trials thus far appear to have similar rates of positive slide-tests for nonhydrated slides (1.0% to 4.0%), similar predictive values for adenoma and cancer (22% to 53%), and a shift to earlier Dukes' staging (65% to 90% in Dukes' A and B). All data indicate an improved sensitivity for cancers but loss of specificity when the slides are hydrated. The sensitivity of the nonhydrated slide has been estimated to be 70–80%, with one study reporting 52% sensitivity (28). Complete evaluation of the colon is clearly necessary and colonoscopy is now being used to establish the

diagnosis. As yet, survival data are not available, except in one programme (35), but can be expected to be favourable given the improvement in staging. Mortality data will be forthcoming within the next few years after complete follow-up so that systematic mortality reviews can be accomplished. It will be important to see whether the early identification of colonic adenomas and their removal will lead to a reduced incidence of colon cancer in these patients.

Diagnosis and treatment

Complete diagnostic evaluation of patients with a positive screening test is essential for effectiveness of the screening programme. Sensitive techniques are now available for accurate clinical diagnosis of colonic lesions (40, 41) but there is debate on whether colonoscopy or barium enema should be the initial test of choice. There are no unbiased controlled studies comparing the independent performance of barium enema with colonoscopy except for the National Polyp Study currently in progress. The double-contrast barium enema is superior to the single column type in most hands for the diagnosis of small adenomas and small cancers. The entire colon can be examined well including the caecum by experienced endoscopists in more than 90% of patients, usually in 15–20 minutes. Colonoscopy has been shown in many studies to have a higher sensitivity than the barium enema for neoplastic lesions of the colon, especially those under 1 cm in size; in addition, biopsies and cytology can be performed and polyps can be removed. Colonoscopy, however, costs more than the barium enema and has a greater risk of perforation (42). The decision to use either or both these diagnostic tests is an individual matter based on the above factors as well as available resources.

Attitudes

Patients' acceptance of stool-blood testing has been good in controlled trials, but was as low as 15% in community programmes (43). Sustained interest in rescreening has been difficult for some programmes. In the New York trial, for example, while acceptance was high for the first screen, the patients were reluctant to return personally or send slides in for rescreening despite intensive efforts. In the English trial, special measures to encourage compliance were found to be very helpful in raising acceptance from 38% to over 50%. Patients with positive screening tests complied with diagnostic studies to a fairly high extent in all of the trials.

Factors influencing patients' acceptance of screening have been studied (44–46). Acceptors are more likely to have had positive attitudes towards preventive health practices, to have had more recent contacts

with medical services, to be better informed about serious illness, and to be more optimistic and less frightened about cancer. An American Cancer Society survey showed that often there were disturbing public misconceptions regarding colorectal cancer (47). Patients have been shown to have a high acceptance of sigmoidoscopy when they present for a general examination (over 90% in the New York programme). However, patients in general have not demonstrated a willingness to return for repeat rigid sigmoidoscopy. This attitude may change with greater use of flexible sigmoidoscopes. Although the American Cancer Society surveys indicate an increasing emphasis on early cancer detection and increased use of stool-blood testing, there is a variable approach by physicians to the diagnostic investigation of patients with a positive screening test (48).

Cost-effectiveness

One cost-benefit analysis suggested a financial savings and a projected increase in life expectancy as a result of stool testing (49). Mathematical models have given us some insights into the range of cost-benefit and cost-effectiveness expectations (50). Although these models do not provide definitive answers, they summarize available data and can provide future research directions.

Treatment of detected cancers

Many reviews of colorectal cancer surgery are available, with extensive discussion of surgical oncology principles and survival statistics (51). Although survival relates clearly to the stage of cancer at the time of resection, aggressive anatomic surgery has been shown to provide the highest chance of cure for each stage. In addition, colorectal cancer provides a unique opportunity for control of the disease because of an identifiable premalignant adenomatous stage. In the past, removal of adenomas above the reach of the rigid sigmoidoscope required laparotomy and colotomy, with the attendant morbidity and mortality. These risks have been markedly decreased with the introduction of colonoscopic polypectomy (51).

Recommendations

There is a difference between general population screening and case-finding in patients who enter a medical care setting. The perspective may be different for individuals in the health care system who seek check-ups to prevent lethal and morbid consequences of advanced cancer. For physicians who elect to screen asymptomatic people in their practice for occult stool-blood, one can provide certain mathematical projections based on available data. Approximately 2% of

patients will have a positive test and at least one out of four of these people will have an adenoma or cancer on further investigation. This neoplastic yield is comparable to that found in high-risk groups. Unfortunately, approximately 30% of the cancers and a majority of adenomas may be missed by one screening with standard guaiac slide tests. The anatomic area with the highest rate of misses is the rectosigmoid.

The American Cancer Society, the International Workgroup on Colorectal Cancer, and the U.S. National Cancer Institute (NCI) have recommended screening guidelines, while other groups such as the Canadian Cancer Society, the International Union against Cancer, and the U.S. Preventive Service Task Force as yet have not (1, 4, 36, 52-55). In developing its working guidelines, the NCI requested and obtained assistance from major medical organizations in the USA. Efforts were made to develop guidelines that were reasonable and practical and which would help practising physicians and patients select the most appropriate approaches for early detection of cancer. Furthermore, the NCI indicated that the weight of evidence needed for proof of benefit is different for case-finding and mass screening.

The NCI has already noted that early detection and treatment were associated with a decreasing mortality rate from colorectal cancer, in spite of an increasing incidence (52). Although the reasons for these trends are unclear this may have resulted in part from the utilization of techniques for earlier detection and a greater attention to early symptoms and familial risk factors. Physicians who utilize the best available data, concepts, technology, expert opinion, knowledge of the disease, and clinical judgement may be having an impact on the natural history of colorectal cancer with improved outcome for a greater proportion of their patients.

Studies are currently under way to test the hypothesis that a significant proportion of colorectal cancer is caused by a dominant gene with low penetrance (11, 56, 57). Classification of the genetic basis of colorectal cancer and a better means of identifying high-risk patients would allow more effective application of screening and would help reduce major problems of patients' acceptance of these preventive measures.

Recommendations for practice

1. Men and women should be encouraged to seek medical check-ups.
2. Persons with symptoms suggesting colorectal neoplasia are not candidates for screening but should be investigated for a diagnosis.
3. Asymptomatic individuals should have their risk evaluated to rule out inherited syndromes, in-

flammatory bowel disease or a past history of adenomas or colorectal cancer; they need individualized surveillance according to guidelines for high-risk people.

4. Asymptomatic men and women seeking check-ups who have no risk factors should have a digital rectal examination annually beginning at age 40, a stool occult-blood test annually beginning at age 50, and sigmoidoscopy every 3-5 years beginning at age 50.

5. A patient with a positive stool test should have a complete evaluation of the colon by double-contrast barium enema or colonoscopy. Colonoscopy is preferred. An upper gastrointestinal evaluation should be done if the results of colon studies are not significant.

6. Polyps found on sigmoidoscopy require histological evaluation; if they are adenomatous the patient needs complete evaluation of the colon for synchronous neoplastic lesions.

7. These examinations should be done as part of comprehensive primary and secondary preventive measures in individuals during their medical check-ups.

8. This approach should not be encouraged for healthy individuals in the general population who are not seeking individual health check-ups until improved mortality data become available.

9. This approach is reasonable for case-finding of asymptomatic, early stage colon cancer and large adenomatous polyps in the physician's office or surgery, medical clinics and hospitals or as part of established cancer-related check-ups. It is justified by the interim results of ongoing controlled screening studies and two decades of carefully monitored clinical application of the stool occult-blood test.

Final results from these studies confirming reduced mortality are needed before this approach can be recommended to the health authorities and governments as a separate screening procedure for the general population.

Research recommendations

1. Current trials evaluating the effect of stool-blood tests on colorectal cancer mortality should be supported until completion.
2. Additional, new tests for screening of colorectal cancer and adenomas, including those that test specifically for blood and those that test for other markers of colonic neoplasia, should be evaluated in large controlled trials.
3. New and improved collection devices need to be evaluated for the stool-blood test.
4. Factors related to patient acceptance of screening need to be studied.

5. Factors related to physician application of screening and diagnostic testing need to be studied.

6. Mathematical modelling needs to be used with new data that will be forthcoming to determine the effects of screening by itself and in conjunction with evolving methods of primary prevention.

7. Randomized trials with a mortality end-point need to be considered regarding the value of flexible sigmoidoscopy.

8. Familial risk factors need to be examined further to determine their value in helping to predict patients with a higher probability of developing adenomas or cancer.

9. The relative cost-effectiveness of flexible sigmoidoscopy with double-contrast barium enema versus primary colonoscopy in the evaluation of patients with a positive screening test needs to be examined.

10. Colonoscopy needs to be studied as a screening test in familial high-risk and average-risk individuals.

lesquels la maladie a une forte probabilité de ceux chez lesquels cette probabilité est faible.

La sigmoïdoscopie, particulièrement quand elle est effectuée avec les longs endoscopes flexibles, est capable de déceler approximativement 50% des cancers et des adénomes colorectaux. L'efficacité de la sigmoïdoscopie flexible en tant que test de dépistage n'a pas été bien étudiée dans des essais contrôlés, mais divers rapports indiquent que cet examen est bien accepté par les malades et qu'il permet une détection de la maladie à un stade plus favorable. La recherche de sang occulte dans les selles en utilisant des lames imprégnées de gaïac a été prouvée comme étant une méthode possible dans diverses études; elle permet de diagnostiquer de gros adénomes, et donc de procéder ensuite à leur ablation mais elle n'a probablement que peu de valeur en soi pour la détection des petits adénomes, plus fréquents.

Actuellement, plus de 300 000 sujets ont été inclus dans des essais cliniques contrôlés. Les données montrent un taux de positivité de 1-4% avec des lames non-hydratées, une valeur de prédiction positive pour les adénomes et les cancers d'environ 20-50%, le diagnostic plus précoce des cancers, et une amélioration de la survie. La sensibilité et la spécificité étaient de 70% et 98%, respectivement. De nouveaux tests sont en cours d'évaluation, qui peuvent augmenter la sensibilité sans perte de spécificité. Les résultats des études actuelles capables de prouver l'impact du dépistage sur la mortalité par cancer colorectal sont attendus pour que cette méthode soit considérée comme valable.

L'évaluation diagnostique complète des malades ayant un test de dépistage positif est essentielle pour confirmer l'efficacité du programme de dépistage. La colonoscopie et le lavement baryté à double contraste sont des méthodes sensibles pour poser un diagnostic précis de lésions du côlon. La colonoscopie a une sensibilité plus grande pour le diagnostic de petites lésions et a également l'avantage de permettre l'obtention de biopsies et l'ablation de polypes. L'acceptation des malades est d'une importance capitale pour la mise en œuvre de ces stratégies. Les calculs préliminaires de coût/efficacité sont favorables. Actuellement, il est raisonnable que des sujets asymptomatiques âgés de plus de 50 ans et à risque moyen aient une recherche de sang dans les selles chaque année et une sigmoïdoscopie flexible tous les 3-5 ans au titre de leurs soins médicaux normaux, et que ceux dont le test est positif aient une colonoscopie. De nouvelles données peuvent modifier ces recommandations à l'avenir. Il est vraisemblable que de

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Résumé

Dépistage des individus à risque moyen de cancer colorectal

Le cancer colorectal se prête à des méthodes de dépistage car c'est une maladie suffisamment répandue pour qu'elle soit détectée à un stade précoce avec, ainsi de meilleures perspectives de survie des malades. Un second bénéfice possible du dépistage est lié à la découverte et à l'ablation des adénomes pré-malins ayant pour conséquence une diminution de l'incidence future du cancer colorectal. Certains malades peuvent être considérés comme étant à haut risque parce qu'ils ont une colite ulcéreuse chronique sous-jacente ou des antécédents familiaux ou personnels de cancers ou d'adénomes colorectaux. Ces sujets demandent une surveillance spéciale, plus étroite. La majorité des individus sont "à moyen risque" pour la maladie s'ils sont âgés de 50 ans (et plus), âge auquel l'incidence commence à augmenter de façon significative. Il faudrait disposer d'une méthode de dépistage basée sur des tests rapides, simples, capables de bien séparer les sujets chez

nouvelles recherches génétiques apporteront des éléments permettant d'identifier le sous-groupe d'individus candidats à un dépistage plus ciblé à l'avenir. On aboutirait ainsi à des solutions d'un meilleur rapport coût/efficacité et plus acceptables.

References

1. Parkin, D.M. et al. Estimates of the worldwide frequency of sixteen major cancers in 1980. *Int. j. cancer*, **41**: 184-197 (1988).
2. Winawer, S.J. et al. Surveillance and early diagnosis of colorectal cancer. *Cancer detection and prevention*, **8**: 373-392 (1985).
3. Winawer, S.J. Screening for colorectal cancer. In: DeVita, V. et al., ed. *Cancer. Principles & practice of oncology*. 2nd edition. Philadelphia, J.B. Lippincott, 1987, pp. 1-16.
4. American Cancer Society. Guidelines for the cancer-related checkup: recommendations and rationale. *CA: a cancer journal for clinicians*, **30**: 194-240 (1980).
5. *Cancer facts & figures*. New York, American Cancer Society, 1988.
6. Hertz, R.E. et al. Value of periodic examinations in detecting cancer of the rectum and colon. *Postgrad. med. j.*, **27**: 290-294 (1960).
7. Gilbertsen, V.A. Proctosigmoidoscopy and polypectomy in reducing the incidence of rectal cancer. *Cancer*, **34**: 936-939 (1974).
8. Williams, A.R. et al. Polyps and cancer of the large bowel: a necropsy study in Liverpool. *Gut*, **23**: 835-842 (1982).
9. Winawer, S.J. et al. The national polyp study: overview of program and preliminary report of patient and polyp characteristics. In: G. Steele, Jr. et al., ed. *Basic and clinical perspectives of colorectal polyps and cancer*. New York, Alan R. Liss, 1988, p. 35-49.
10. Lipkin, M. & Winawer, S.J. Inherited colon cancer: clinical implications. *Am. j. gastroenterol.*, **72**: 448-457 (1979).
11. Burt, R.W. et al. Dominant inheritance of adenomatous colonic polyps and colorectal cancer. *New Engl. j. med.*, **312**: 1540-1544 (1985).
12. Devroede, G. & Taylor, W.F. On calculating cancer risk and survival of ulcerative colitis patients with the life table method. *Gastroenterology*, **71**: 509-509 (1976).
13. Kewenter, J. et al. Cancer risk in extensive ulcerative colitis. *Ann. surg.*, **188**: 824-827 (1978).
14. Greenstein, A.J. et al. Cancer in universal and left-sided ulcerative colitis: factors determining risk. *Gastroenterology*, **77**: 290-294 (1979).
15. Crespi, M. et al. The role of proctosigmoidoscopy in screening for colorectal neoplasia. *CA: a cancer journal for clinicians*, **34**: 158-166 (1984).
16. Zucker, G.M. et al. The advantages of the 30-cm flexible sigmoidoscope over the 60-cm flexible sigmoidoscope. *Gastrointest. endosc.*, **30**: 59-64 (1984).
17. Groveman, H.D. Training primary care physicians in flexible sigmoidoscopy: performance evaluation of 17 167 procedures. *Western j. med.*, **148**: 221-224 (1988).
18. Department of Health, Education and Welfare. *Screening and early detection of colorectal cancer* (NIH Publication No. 80-2075). Washington DC, U.S. Government Printing Office, 1979.
19. Dales, L.G. et al. Multiphasic checkup evaluation study. 3. Outpatient clinic utilization, hospitalization and mortality experience after seven years. *Preventive medicine*, **2**: 221-235 (1973).
20. Friedman, G.D. et al. Multiphasic health checkup evaluation: a 16-year follow-up. *J. chron. dis.*, **39**: 453-463 (1986).
21. Selby, J.V. et al. Sigmoidoscopy and mortality from colorectal cancer: the Kaiser Permanente Multiphasic Evaluation Study. *J. clin. epidemiol.*, **41**: 427-434 (1988).
22. Gnauck, R. et al. How to perform the fecal occult blood test. *CA: a cancer journal for clinicians*, **34**: 134-147 (1984).
23. Winawer, S.J. et al. Current status of fecal occult blood testing in screening for colorectal cancer. *CA: a cancer journal for clinicians*, **32**: 100-112 (1982).
24. Gregor, D.H. Occult blood testing for detection of asymptomatic colon cancer. *Cancer*, **28**: 131-134 (1971).
25. Macrae, F.A. et al. Optimal dietary conditions for hemoccult testing. *Gastroenterology*, **82**: 899-903 (1982).
26. Macrae, F.A. & St. John, D.J.B. Relationship between patterns of bleeding and hemoccult sensitivity in patients with colorectal cancers or adenomas. *Gastroenterology*, **82**: 891-898 (1982).
27. Stroehlein, J.R. et al. Hemoccult detection of fecal occult blood quantitated by radioassay. *Digestive diseases*, **21**: 841-844 (1976).
28. Kewenter, J. et al. Screening and rescreening for colorectal cancer: A controlled trial of fecal occult blood testing in 27 700 subjects. *Cancer*, **62**: 645-651 (1988).
29. Hammes, P.H. & Gnauck, R. [Improved "rehydration" for Hemoccult screening for intestinal cancer.] *Z. Gastroenterol.*, **23**: 676-680 (1985) (in German).
30. St. John, D.J.B. et al. Detection of colorectal neoplasia: comparison of guaiac, porphyrin and immunochemical tests for occult blood. *Gastroenterology*, **96** (5(2)): A492 (1989) (Abstract).
31. Sontag, S.J. et al. Fecal occult blood screening for colorectal cancer in a Veterans Administration Hospital. *Am. j. surg.*, **145**: 89-94 (1983).
32. Simon, J.B. Occult-blood screening for colorectal carcinoma: a clinical review. *Gastroenterology*, **88**: 820-837 (1985).
33. Winchester, D.P. et al. Risks and benefits of mass screening for colorectal neoplasia with the stool guaiac test. In: *Detecting colon and rectum cancer*. New York, American Cancer Society, Inc., 1983, pp. 5-15.
34. Schwartz, F.W. et al. Preliminary report of fecal occult blood testing in Germany. In: Winawer, S.J. et al., ed. *Colorectal cancer: prevention, epidemiology and screening*. New York, Raven Press, 1980, pp. 267-270.

35. **Flehinger, B.J. et al.** Screening for colorectal cancer with fecal occult blood test and sigmoidoscopy: preliminary report of the colon project of Memorial Sloan-Kettering Cancer Center and PMI-Strang Clinic. In: Chamberlain, J. & Miller, A.B., ed. *Screening for gastrointestinal cancer*. Toronto, Hans Huber, 1988, pp. 9–16.
36. **Chamberlain, J. et al.** Proceedings of the UICC workshop of the project on evaluation of screening programs for gastrointestinal cancer. *Int. j. cancer*, **37**: 329–334 (1986).
37. **Kronborg, O. et al.** Initial mass screening for colorectal cancer with fecal occult blood test. *Scand. j. gastroenterol.*, **22**: 677–686 (1987).
38. **Gilbertsen, V.A. et al.** The early detection of colorectal cancers: a preliminary report of the results of the occult blood study. *Cancer*, **45**: 2899–2901 (1980).
39. **Hardcastle, J.D. et al.** Randomized controlled trial of fecal occult-blood screening for colorectal cancer. The results of the first 107 349 subjects. *Lancet*, **1**: 1160–1164 (1989).
40. **Leinicke, J.L. et al.** A comparison of colonoscopy and roentgenography for detection of polypoid lesions of the colon. *Gastrointest. radio.*, **2**: 125–128 (1977).
41. **Adamsen, S. et al.** Reproducibility and diagnostic value of Hemoccult-II test: a colonoscopic evaluation in asymptomatic patients. *Scand. j. gastroenterol.*, **20**: 1073–1077 (1985).
42. **Eddy, D.M. et al.** Screening for colorectal cancer in a high-risk population: results of a mathematical model. *Gastroenterology*, **92**: 682–692 (1987).
43. **Bralow, S.P. & Kopel, J.** Hemoccult screening for colorectal cancer: an impact study on Sarasota, Florida. *J. Florida Med. Assoc.*, **66**: 915–919 (1979).
44. **Farrands, P.A. & Hardcastle, J.D.** Factors affecting compliance with screening for colorectal cancer. *Community medicine*, **6**: 12–19 (1984).
45. **Dent, O.F. et al.** Participation in fecal occult blood screening for colorectal cancer. *Soc. sci. med.*, **17**: 17–23 (1983).
46. **Snyder-Halper, M. et al.** Issues of patient compliance. In: Winawer, S.J. et al., ed. *Colorectal cancer: prevention, epidemiology and screening*. New York, Raven Press, 1980, pp. 299–310.
47. **American Cancer Society.** Cancer of the colon and rectum: a summary of a public attitude survey. *CA: a cancer journal for clinicians*, **33**: 31–37 (1983).
48. **American Cancer Society.** Survey of physicians' attitudes and practices in early cancer detection. *CA: a cancer journal for clinicians*, **35**: 197–213 (1985).
49. **Allison, J.E. & Feldman, R.** Cost benefits of Hemoccult screening for colorectal carcinoma. *Digestive diseases and sciences*, **9**: 860–865 (1985).
50. **Eddy, D.M.** Computer models and the evaluation of colon cancer screening programs. In: Winawer, S. et al., ed. *Colorectal cancer: prevention, epidemiology and screening*. New York, Raven Press, 1980, pp. 285–298.
51. **Enker, W.E.** Extent of operations for large bowel cancer. In: DeCosse, J.J., ed. *Large bowel cancer*. New York, Churchill Livingstone, 1981, pp. 78–93.
52. **National Cancer Institute. Early Detection Branch, Division of Cancer Prevention and Control.** *Working guidelines for early cancer detection*. Bethesda, MD, 1987.
53. **Selby, J.V. & Friedman, G.D.** Sigmoidoscopy in the periodic health examination of asymptomatic adults. *J. Am. Med. Assoc.*, **261**: 595–600 (1989).
54. **Knight, K.K. et al.** Occult blood screening for colorectal cancer. *J. Am. Med. Assoc.*, **261**: 587–593 (1989).
55. **Fleischer, D.E. et al.** Detection and surveillance of colorectal cancer. *J. Am. Med. Assoc.*, **261**: 580–585 (1989).
56. **Cannon-Albright, L.A. et al.** Common inheritance of susceptibility to colonic adenomatous polyps and associated colorectal cancers. *New Engl. j. med.*, **319**: 533–537 (1988).
57. **Vogelstein, B. et al.** Genetic alterations during colorectal tumor development. *New Engl. j. med.*, **319**: 525–532 (1988).