Canadian Association of Gastroenterology and the Canadian Digestive Health Foundation: Guidelines on colon cancer screening

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POSITION

The Canadian Association of Gastroenterology (CAG) and the Canadian Digestive Health Foundation (CDHF) strongly support the establishment of screening programs for colorectal cancer. The test that is used for screening should be determined by patient preference, current evidence and local resources.

BACKGROUND

The technical report by the National Committee on Colorectal Cancer Screening prepared for Health Canada contains a comprehensive review of the subject, which can be found at <www.hc-sc.gc.ca/pphb-dgspsp/publicat/ncccs-cndcc/intro_e.html>.

Colorectal cancer is the third most prevalent cancer affecting both men and women in Canada (1), with 20,000 cases annually. One-third of people afflicted with this cancer will die of the disease (2).

Many of these cancers are preventable. There is good evidence that most colorectal cancers arise from precursor adenomatous polyps (3). Removal of these polyps can prevent subsequent development of cancer. Screening may allow detection of tumours at an early stage, which would improve the prognosis (4). Ideally, therefore, a screening program for colon cancer would permit detection of precancerous polyps and allow earlier detection of established cancers.

About 5% of colon cancers are associated with genetically defined colon cancer family syndromes, and 20% to 30% of all colon cancers have a potentially definable inherited cause (5). In the absence of defined genetic syndromes, three variables affect the risk of colon cancer: age, past medical history and family history. The risk of colorectal cancer increases with age. It is estimated that the incidence of colon cancer in the next 10 years is 1 in 500 for persons 40 to 49 years of age, but increases to about 1 in 125 in the 50- to 59-year-old age group (6). Long-standing inflammatory bowel disease predisposes to colon cancer as does a previous history of polyps or colon cancer. A history of colon cancer in a first-degree relative also increases the risk, especially if more than one relative is affected or if the relative is diagnosed before age 45 years (7).

These variables form the basis for risk stratification. Higher risk is associated with age over 50 years or having at least one first-degree relative with cancer (especially with onset under age 50 years). Conversely, persons under 50 years of age without a family history of colon cancer are at lower risk.

There are several diagnostic tools that can be used for screening. Three factors determine the choice of modality: the operational characteristics of the tool, the risk of cancer in the screened population and the feasibility of applying the technique to the population to be screened. Tests that can readily be applied to the population at large may not necessarily have the best operational characteristics. For example, fecal occult blood testing (FOBT), which may be appropriate for general population screening, is not considered sufficiently sensitive for screening of high risk patients.

The provider's perspective also influences the choice of screening technique. A physician may recommend a course of action for an individual patient that could not be justified from a population health perspective.

Colon cancer screening entails more than performing a test. A screening program involves family physicians, nurses, genetic counsellors, radiologists and surgeons, as well as gastroenterologists. Education programs aimed at medical professionals and the public enhance the acceptance of screening programs and help ensure their appropriateness, efficacy and efficiency.

CURRENT ACCESS TO GASTROENTEROLOGY SPECIALIST CARE

Although it has not been studied formally, input to the CAG regional committees indicates that access to gastrointestinal

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(GI) specialty care varies across the country. Timely emergency care is generally available but wait times for elective GI consultation are three to 10 months. It is clear that, in many parts of Canada, access to specialist GI care is limited. This problem needs to be addressed, and additional human and physical resources acquired, before new cancer screening programs are initiated. In other regions, it appears that the resources are in place but are underutilized due to financial and other constraints.

CANADIAN, BRITISH AND AMERICAN GUIDELINES

We are indebted to our American and British colleagues for their work in preparing practice guidelines (8,9). The CAG-CDHF group has reached the same conclusions based on our review of the evidence. The guidelines outlined here are very similar to those of the American Gastroenterology Association (AGA) and the British Society of Gastroenterology (BSG) on screening of high risk groups. We differ only in that we recommend fecal occult blood testing every two years instead of every year, and we suggest that clinical judgement determine the type of follow-up for advanced adenomas (instead of colonoscopy after three years, as in the AGA guidelines).

STRATIFICATION OF RISK OF COLON CANCER

The majority of the population does not have an affected relative and is at average risk of developing colorectal cancer. Taking the population as a whole, it has been estimated that a 50-year-old person has a 6% lifetime risk of developing this tumour.

Certain groups are at higher than average risk. The largest such group comprises patients who have a first-degree relative with colon cancer. The risk is especially high if colon cancer or other related cancers occur in young persons in more than one generation. The family history in these cases may be indicative of an underlying genetic defect. Patients with a history of familial adenomatous polyposis (FAP) or hereditary nonpolyposis colon cancer are also at significantly increased risk (10), as are those with long-standing inflammatory bowel disease (11).

At present there is no Canadian approach to screening of high risk patients. FOBT does not have adequate sensitivity. A screening program for colon cancer must consider the resources needed for endoscopic screening of high risk patients.

Patients testing positive for occult blood should undergo colonoscopy because colon cancer will be found in about 12% (12).

SCREENING OPTIONS

Detailed information on the operating characteristics of screening tests is available at <http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/ncccs-cndcc/intro_e.html>. That review is extensively referenced. The intent of the present article is to summarize the advantages and disadvantages of each testing modality.

FOBT

The major advantage of FOBT is the relative ease of initial testing. The test can be administered by the patient or at the primary care level, and does not require technical expertise or specialist referral.

Disadvantages include poor sensitivity and specificity. Logistical difficulties arise for primary care practitioners who are responsible for scheduling the test. In addition, the test is designed to detect cancers at an early stage and not specifically to interrupt the polyp-cancer sequence. Therefore, it is more an early detection strategy rather than a truly preventive technique.

Feasibility: No Canadian clinical trial data are available, but the feasibility of FOBT has been studied in detail by Health Canada using computer modelling <http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/ncccs-cndcc/index.html>. Based on Health Canada projections we can estimate that 1 to 1.5 full-time gastroenterologists (or equivalent) would be required to screen 100,000 persons.

Colonoscopy

The advantages of this test are its high sensitivity and specificity for the detection of both polyps and carcinomas, provided that there is a complete examination of a well-prepared colon. Controlled studies of efficacy are lacking but most gastroenterologists would agree that colonoscopy is the gold standard test.

The major disadvantage of this test is that it requires considerable physical resources and skilled personnel. Expertise is required to successfully and safely pass the colonoscope to the cecum and to undertake polypectomy. Complications can result from sedation and the risk of perforation or bleeding is approximately 1:1000 to 1:2000 cases (with rare fatalities). Patient adherence may be limited by the fact that the test can be uncomfortable, even with sedation. Some lesions are missed. Moreover, in approximately 5% of cases, it is not possible to visualize the entire colon, either because of poor preparation or a technically difficult bowel.

Feasibility: There have been no studies estimating the number of colonoscopies that would be required to screen the average-risk population in Canada if this were the primary screening tool. Nor is it known what percentage of the at-risk population already undergo colonoscopy each year. Waiting lists for non-screening diagnostic colonoscopy vary considerably throughout Canada, and it is unlikely that a colonoscopic screening program could be put in place, in any part of the country, without significant further investment in human and physical resources.

It is generally accepted that colonoscopy is the appropriate screening tool for high risk individuals, but there is currently no organized program to provide screening for these individuals. The magnitude of the problem and required resources are not known.

Flexible sigmoidoscopy

The advantage of flexible sigmoidoscopy is that it is sensitive and specific for distal colonic lesions. The test can be performed by nurses or by nonspecialist physicians.

The disadvantage is that some patients have proximal tumours only, which would escape detection. The risk of perforation is minimal.

Feasibility: As with colonoscopy, the human and physical resources are not in place to institute a national flexible sigmoidoscopy-based program. The amount of resources required is not known.

Debate continues as to whether it is necessary to perform colonoscopy on every patient in whom a distal colonic

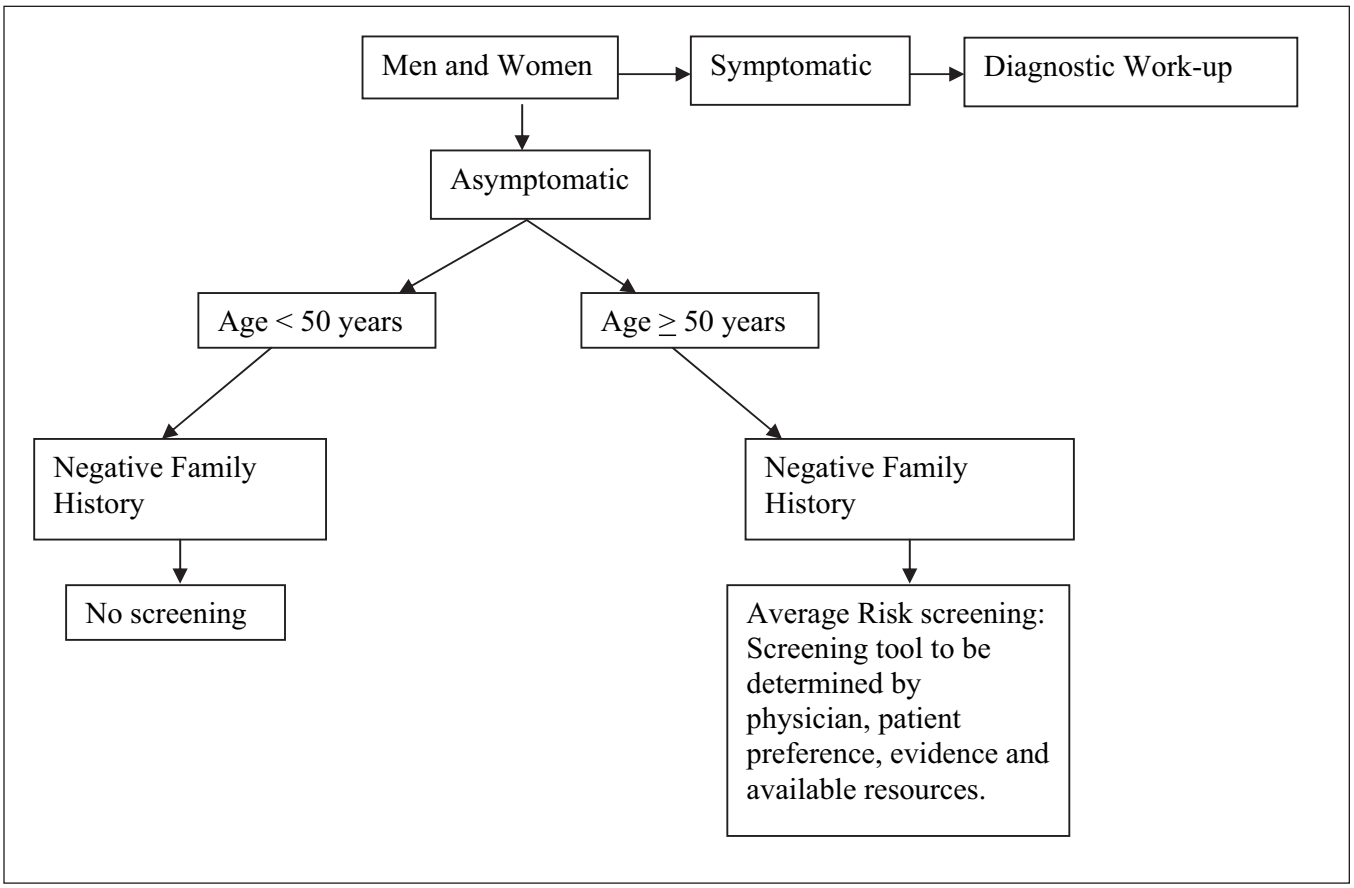

Figure 1) *Approach to average risk screening*

adenoma has been detected. The CAG-CDHF position is that colonoscopy should be offered to all such patients, but further studies are awaited.

Flexible sigmoidoscopy combined with FOBT

There are limited data on the use of combination screening. It is likely to enhance the detection rate compared with FOBT alone, but at the cost of increased workload demands. No Canadian feasibility data are available.

Double contrast barium enema

The major advantage of this test is that it can be performed by radiology technicians. Furthermore, barium x-rays permit evaluation of the entire colon.

Disadvantages include the fact that it is less sensitive and specific than colonoscopy, because of the presence of retained stool. Abnormalities need to be followed up with colonoscopy. The test involves radiation exposure, but there is no evidence that this is a significant problem.

Feasibility: This test is feasible in that an extensive radiological infrastructure already exists in most health care institutions. Therefore, a radiology-based population screening program could take place without significant additional human and infrastructure investment. On the other hand, many radiology facilities are already working at maximum capacity. The amount of resources required is not known.

RECOMMENDATIONS

Screening of individuals at average risk

Colon cancer is uncommon before the age of 50 years. The probability of developing colon cancer in the next 10 years is 1:1000 in the 30 to 39 age group, 1:125 in the 50 to 59 age group and 1:50 at age 60 to 69 years(7). Most authorities recommend that screening be offered to persons aged 50 to 65 years. This age group constitutes approximately 20% of the Canadian population.

The CAG and CDHF endorse the algorithm shown in Figure 1, which is similar, but not identical, to that in the AGA guidelines (8).

Symptomatic individuals cannot be considered as screening candidates. They need appropriate diagnostic work up. Asymptomatic individuals below the age of 50 years are unlikely to have colon cancer and screening this group is not considered helpful. The strategies outlined below each have advantages and disadvantages. We do not contend that they are equally effective nor should this idea be suggested to patients.

Individuals over the age of 50 years with a negative family history should undergo screening with one of the following strategies:

1. **FOBT every two years.** The AGA guidelines recommend screening yearly using a guaiac-based test with dietary restrictions or an immunochemical test for heme without restrictions;

Note: The Canadian Expert Panel commissioned by Health Canada recommended occult blood testing every two years. Although yearly occult blood testing does increase the detection of cancer as compared with every two years, it was not felt that this justified the resulting considerable increase in workload. In addition, testing every two years would be more achievable from a primary care perspective. The CAG-CDHF supports the position taken by the Health Canada committee and recommends that, if FOBT is used, it be performed every two years.

2. **Flexible sigmoidoscopy every five years.** The interval of five years between examinations is shorter than that recommended if colonoscopy is used, because flexible sigmoidoscopy may be less sensitive than colonoscopy even in the area examined, or;
3. **Flexible sigmoidoscopy combined with FOBT every five years.** The rationale for the interval is mentioned above, or;
4. **Double contrast barium enema every five years.** The lesser sensitivity and specificity of this test compared with colonoscopy is the rationale for the shorter screening interval compared with colonoscopy, or;
5. **Colonoscopy every 10 years.** The high sensitivity and specificity of this test means that the interval between tests can be twice as long as that of the other tests mentioned above.

Screening of individuals at higher risk

Some groups are at increased risk of colon cancer. These include patients who have first-degree relatives with the disease, a family history that suggests a definable genetic abnormality, FAP or long-standing colonic inflammatory bowel disease. Genetic counselling is an important part of the management of patients with these conditions. There should be provincial strategies to ensure timely access to all appropriate services including genetic counselling and testing.

The CAG and CDHF guidelines are similar to those of the AGA (8). These are reproduced in modified form (Figure 2).

HIGH RISK GROUPS: DEFINITIONS, CRITERIA FOR DIAGNOSIS, AND RATIONALE FOR SCREENING RECOMMENDATIONS

The timing of initial colonoscopy and repeat examinations is based on our current understanding of the natural history of colonic polyps and cancer in the populations at risk. For example, screening for patients with HNPCC begins at an earlier age than that for persons who have no first-degree relatives with colon cancer.

Colonic polyps

Both histology and the degree of dysplasia are affected by adenoma size. Larger polyps are more likely to have a villous component and are more likely to be dysplastic. Villous change is associated with a greater risk of high-grade dysplasia and cancer.

The term low grade dysplasia is now generally used to describe polyps with mild or moderate dysplasia. High-grade dysplasia denotes severe dysplastic change or carcinoma in situ. Invasive cancer means that neoplastic cells have spread through the muscularis mucosa.

Diminutive polyps, which are less than 5 mm, are common. The malignant potential of these lesions is being studied. Current recommendations are for follow-up colonoscopy at five years, but this interval might be increased in the near future.

The term advanced adenoma does not have a uniform definition in the literature (13,14). Some authors refer to invasive cancer while others do not. The AGA guidelines did not define advanced adenoma (8). We use the term for polyps larger than 1 cm in diameter or those with either a villous component or high-grade dysplasia, as defined above. Given the significant intraobserver variability when evaluating these lesions and the paucity of outcomes data (13), we recommend that follow-up intervals be based on clinical judgement. Similarly, follow-up for patients with numerous adenomas, large sessile polyps and malignancy should be determined by assessment of the overall clinical situation. Follow-up examination should be performed after a shorter interval than that for polyps with less ominous histology.

Hereditary nonpolyposis colorectal cancer

The criteria for the diagnosis of hereditary nonpolyposis colorectal cancer (HNPCC) are:

At least three relatives with an HNPCC-associated cancer (involving the colon or rectum, endometrium, small bowel, ureter or renal pelvis) (15), plus:

1. One or more relatives with colorectal cancer diagnosed under the age of 50 years;
2. Colorectal cancer involving persons in two or more successive generations;
3. One affected patient is a first-degree relative of the other two;
4. FAP is excluded; and
5. Tumours are verified by histological examination.

FAP

FAP is an autosomal dominant condition associated with the presence of hundreds, or even thousands, of colonic polyps. The polyps usually develop during the teenage years but they can occur in the first decade of life. Because the polyps are almost always found in the rectum as well as in the rest of the colon, sigmoidoscopy is an appropriate screening tool.

Attenuated FAP or attenuated adenomatous polyposis coli

Attenuated adenomatous polyposis coli is similar to classical FAP but has a somewhat different genetic basis and results in fewer polyps. Because the polyps often first appear in the right colon, sigmoidoscopy is not adequate for screening. Onset of polyposis is 10 years later than onset of classical FAP; therefore, screening is begun somewhat later.

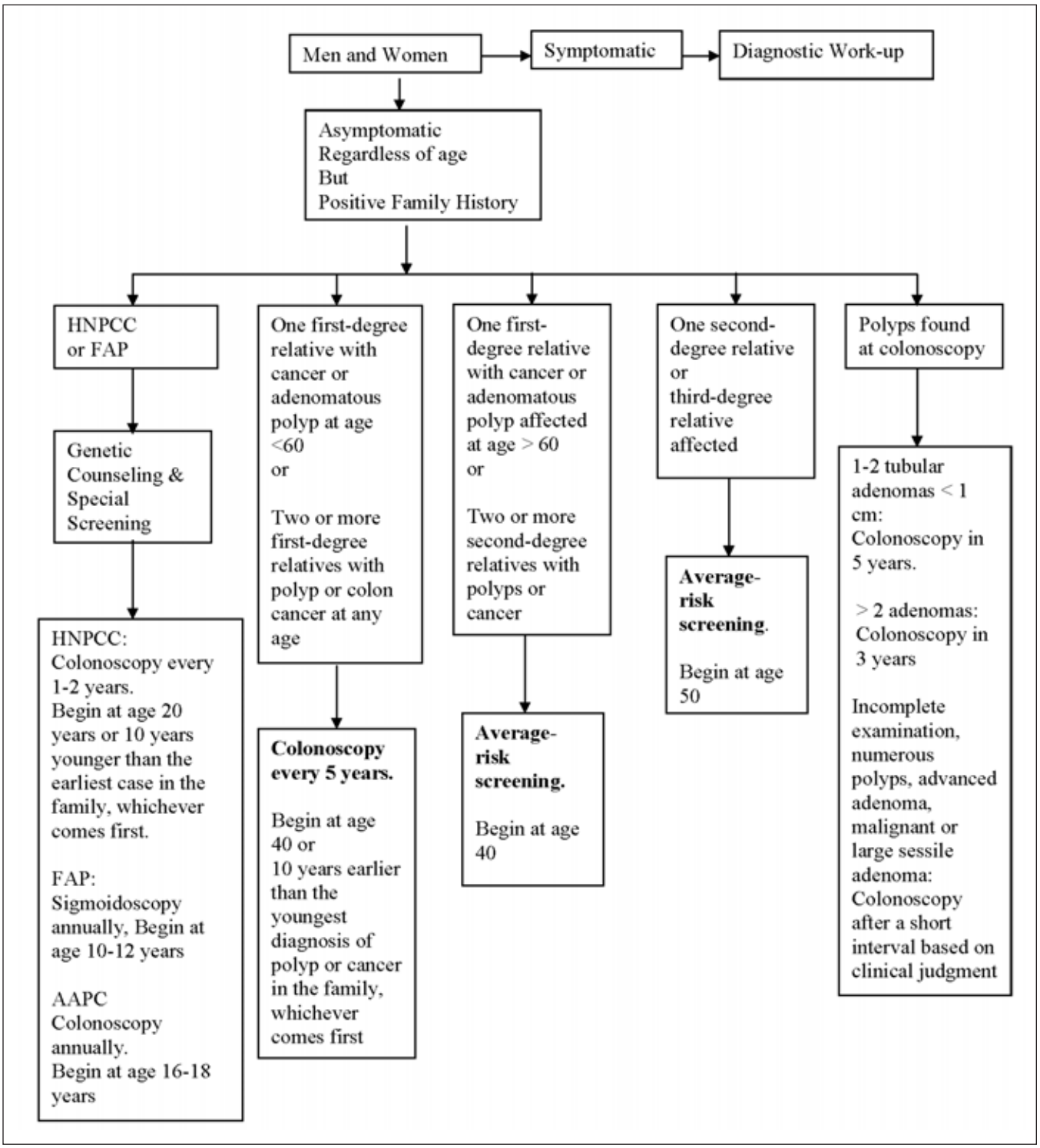

Figure 2) *Approach to higher risk screening. AAPC Attenuated adenomatous polyposis; FAP Familial adenomatous polyposis; First-degree relative Parents, siblings, children; HNPCC Hereditary nonpolyposis colorectal cancer; Second-degree Grandparent, aunt or uncle; Third-degree Great grandparent or cousin*

OTHER HIGHER RISK GROUPS

Previous history of colorectal cancer

A colonoscopy should be done preoperatively, or soon after, to exclude synchronous lesions. If this examination is normal, then the next colonoscopy can be performed three years later, and, if that is normal, five years thereafter. This recommendation is similar to that of the BSG (9).

Previous history of inflammatory bowel disease

The cancer risk is similar for Crohn's disease and ulcerative

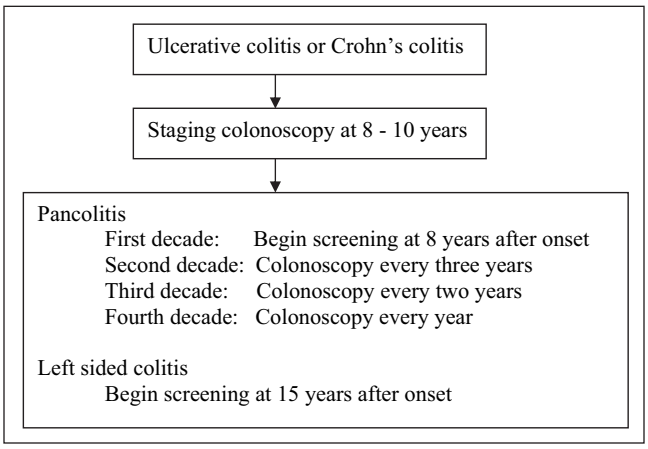

Figure 3) *British Society of Gastroenterology approach to screening and surveillance in inflammatory bowel disease*

colitis; thus, recommendations are the same for both. All patients should have a colonoscopy eight to 10 years after disease onset to help determine the extent of disease. Regular surveillance should begin after eight to 10 years for patients with pancolitis, and after 15 years for those with left-sided disease.

The screening interval should decrease with increasing duration of disease. A summary of the BSG recommendations is shown in Figure 3 (16). The CAG-CDHF position is similar in all respects.

Patients with primary sclerosing cholangitis, before or after transplantation, are at increased risk. The BSG recommends, and we concur, that these patients should undergo annual colonoscopy.

FUTURE DIRECTIONS

Carcinoma of the colon shows significant geographic variation, even in groups with similar genetic background. It is likely that factors such as diet play a significant role (17). Behavioural changes might mitigate the risk, but further research on population health, risk assessment and chemoprevention is required.

Biomarkers are cellular, biochemical, molecular and genetic markers by which normal or abnormal biological process can be recognized or monitored. They can illuminate pathological processes in asymptomatic individuals or identify individuals who are susceptible to cancer. Potential uses of biomarkers include:

1. Monitoring patients with established cancer for recurrence;
2. Early identification of asymptomatic patients;
3. Early diagnosis of symptomatic patients;
4. Surveillance of individuals known to be at high risk of cancer; and
5. Surrogate end-point markers for primary prevention strategies, such as chemoprevention.

Recent advances in molecular and cell biology have provided an excellent opportunity to develop and validate biomarkers for colorectal cancer screening and risk assessment.

Training of nonphysician endoscopists may be one option for addressing the shortage of physicians (18). Alternatives to colonoscopy for imaging the colon, such as capsule technology, may affect the screening algorithm. Virtual colonoscopy, using helical computerized tomography or magnetic resonance imaging, has been the subject of a number of recent health technology assessments, including one by the Canadian Coordinating Office for Health Technology Assessment (19). Presently, it is not felt that these techniques are suitable for mass screening, but they are certainly promising. A number of studies are underway in this area.

ADDITIONAL RECOMMENDATIONS

1. Ideally, provincial colon cancer screening policies and programs should be standardized. Recognizing that this is unlikely, we recommend that each province adopt a strategy that ensures equal access to resources.
2. The provinces should survey waiting lists for gastroenterology consultation and procedures. The availability of resources should be considered when developing screening programs.
3. Each province should develop screening programs for high risk patients. These patients should be informed of their risk and given access to appropriate screening and counselling.
4. Each province should develop screening programs for patients at average risk. If FOBT is used, provision must be made for colonoscopic follow-up of positive tests.
5. The choice of testing for average risk patients should be determined by the availability of human and infrastructure resources. Colonoscopy is the screening tool of choice for patients at high risk for colorectal cancer.
6. Education programs need to be directed to health care providers and the public. The messages need to be congruent among the provinces.
7. The development of screening programs should be linked to evaluation of their impact, as well as research on cancer prevention through dietary and other means.

ACKNOWLEDGEMENTS: We would like to acknowledge the contributions of Health Canada and the Canadian Society of Primary Care Gastroenterology.

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