Review article

SCREENING FOR COLORECTAL CANCER

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Introduction

The incidence of colorectal cancer varies throughout the world. In many countries of Western Europe however it is second only to the lung as a cause of cancer death, 60% of patients diagnosed are dead within five years. The reason for these dismal statistics is that the cancer is often at an advanced stage by the time symptoms first arise and has extended beyond curative surgical therapy in the majority of patients at the time of presentation. Although mortality could be reduced by encouraging patients to seek medical attention at an earlier stage, this would only marginally improve the outlook for most individuals. It follows that until treatment is available that is able to cure metastatic cancer, or alternatively measures can be devised to prevent the condition from arising in the first place, a significant reduction in mortality can be gained only by population screening enabling the disease to be identified at a pre-malignant or early stage.

Population screening for cancer

At first sight it would appear that screening for cancer is a desirable objective with no drawbacks. Unfortunately this is not the case. The ethics of screening must be taken into consideration. When a patient attends a doctor with symptoms or concerns relating to health the doctors duty is clear, he or she has to listen to the patient and provide the best medical advice and treatment that is available for the patient. The onus of responsibility for consultation is on the patient who brought the problem to the doctor. Screening programmes are the reverse. Health providers approach an asymptomatic individual, indicating that he or she is at risk of disease, and they, the health providers, will protect them from it in the future. The healthy population is disadvantaged firstly by being given information that will cause concern. Secondly they have to undergo medical investigations that might cause complications or death. Thirdly the procedures may provide false positive results raising more concern and more unpleasant interventions. Fourthly the intervention may not detect cancer already there and engender a false sense of security. Furthermore, if the program is expensive it will divert health care money from other programs of more immediate benefit to the population. For these reasons it is essential before setting up a screening program to ensure that it will be effective, safe, provide benefit and be cost effective.

Screening for colorectal cancer

The principles underlying an effective screening program are given in Table 1[(1)]. Colorectal cancer appears to be a suitable condition for screening according to most of these precepts. The disease is an important cause of mortality and death. Its natural history is well understood, the majority of cases arise from previously present colonic polyps. Colonoscopy is sensitive and specific. On the other hand colonoscopy is less acceptable for compliance than most screening tests and whilst giving a definitive diagnostic result which reduces mortality and morbidity it is an expensive undertaking. To date no prospective, randomised controlled trials have shown that colonoscopy is cost effective in patients at average risk of colorectal cancer. Other screening modalities such as flexible sigmoidoscopy and

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occult blood testing are less invasive and expensive, but suffer from reduced sensitivity and although a number of prospective, randomised trials have been reported they have shown only marginal benefit (18% success rate for faecal occult blood) and compliance is variable[2].

Colorectal cancer screening can be divided into two broad categories. Surveillance of individuals known to be at higher risk than normal for developing cancer and those who are at average risk. If the high risk group can be identified screening is much more likely to be effective for them than the average risk group.

Colorectal screening for patients at high risk

Table 2 and 3 sets out patients who are at greater risk than the normal population. For individuals who have known family cancer syndromes the risk of developing cancer is extremely high and affected members of the family may be offered total colectomy, others annual or biennial colonoscopy.

Other high risk groups include patients with a family history of the disease. If the patient has two first degree relatives or one who developed cancer at a relatively young age the risk of developing cancer is two to three times greater than the general population. These patients should also be offered screening, but at longer intervals.

Patients who have previously had a colorectal cancer or an adenomatous polyp in the colon are at increased risk of developing further polyps and cancer. Protocols related to these individuals are complex because small adenomatous polyps are not uncommon in the general population and the risk of developing cancer is not greatly above the norm. Table 4 divides patients with colorectal polyps into two groups, those at high risk for developing cancer and those at lower risk. In patients with polyps full colonoscopy should be undertaken with removal of all polyps present. If a polyp has been incompletely removed the colonoscopy should be repeated in three to six months, for multiple polyps (>4) it should be done again in a year. Any new polyps should be removed and the patient should be re-examined again after three years. If no further polyps have arisen then further surveillance may be unnecessary although some advise repeats at six yearly intervals. Patients with high risk polyps or those who develop further polyps should be re-colonoscoped at three yearly intervals.

The management of patients with long-standing ulcerative colitis is controversial. Patients who have had ulcerative colitis for longer than 10 years and with disease that extends beyond the splenic flexure are at increased risk of developing cancer. At 20 years the risk is roughly 15%. Many authorities advise regular annual colonoscopy with multiple biopsies. The presence of high grade dysplasia or dysplasia in association with a mass (DALM) should lead to total colectomy. Those with low grade dysplasia are encouraged to undergo more regular colonoscopic screening. There is little evidence to show that colonoscopic screening in patients with ulcerative colitis is cost effective. Analyses suggest that roughly 200-400[3] endoscopies have to be performed in order to identify one early cancer and as the mortality of cancer in ulcerative colitis is roughly 50%, only one life is saved per 600 colonoscopies. The reason for these disappointing results is that colonoscopy is a relatively crude method for identifying early colonic cancer in patients with the long-standing mucosal changes found in ulcerative colitis. There are also problems with compliance. The identification of low grade dysplasia is neither sensitive nor specific and leads to difficulties with management. In spite of these drawbacks however most clinicians consider that patients with ulcerative colitis should be colonoscoped on a regular basis. The frequency with which this is done however is not currently agreed.

Colorectal cancer for screening patients at average risk

This group is the most important because sporadic colorectal cancer represents over three quarters of colorectal cancers. Screening high risk patients, though beneficial for them as individuals, does not impact very much on the total disease load. Conversely it is in the low risk group that the ethical and cost effective criticisms of screening apply.

It is impossible to lay down general advice as to which populations should undergo colorectal screening. The decision to introduce a program will depend upon the number of individuals within the particular population who are at risk (and this varies from country to country) and also on the finance and facilities that are available for the provision of health care. Screening programs should not be introduced until randomised, prospective controlled trials have proved benefit, but in practice a number of developed countries have already acceded to public and professional pressure to put these in place.

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Even within the average risk population it is possible to sub-select those who are more likely to have cancer, for example, colorectal cancer in the West is uncommon below the age of 50, the incidence rising rapidly after 65. It is possible therefore to target those in the older age group if one wishes to increase the cost effectiveness of the policy. This, however, means that younger people who may have greater social, financial and economic responsibilities would be disadvantaged. Again this is a decision that has to be made in the light of local, economic and political factors.

Three modalities of screening are currently promoted for colorectal cancer. These are annual faecal occult blood testing, five yearly flexible sigmoidoscopy and five to ten yearly total colonoscopy.

Faecal occult blood testing (FOB)

The only prospective, randomised trials that have been undertaken so far are in this area. Several studies have shown that this policy will save roughly 18% of colorectal deaths if applied rigorously[2]. The compliance, however, long-term has been rather disappointing. Faecal occult blood testing will only detect early cancer, it will not detect polyps (they do not usually bleed until malignant transformation has occurred). One cannot therefore claim that the screening will prevent cancer. The sensitivity for faecal occult blood testing can be increased by making the test detect smaller concentrations of blood. The problem with doing this however is that the number of false positives rises steeply, meaning that many more colonoscopies have to be performed in order to check out these patients[4].

Flexible sigmoidoscopy

Flexible sigmoidoscopy screening has been strongly championed by those who point out that most colorectal cancer is in the recto-sigmoid area, that most polyps occur there and that if there are no polyps in the lower bowel the likelihood of polyps higher up is small. There appears to be better compliance in people undergoing flexible sigmoidoscopy than in those providing specimens of stool for FOB and the removal of polyps will prevent cancer rather than identify early cancer. If a "high risk" polyp is found at flexible sigmoidoscopy a total colonoscopy is subsequently undertaken in order to identify further polyps, this increases the expense and risk of the screening program. There have been no prospective, controlled trials for flexible sigmoidoscopy to date, but they are on-going.

Colonoscopy

The use of "once in a life time" colonoscopy at age 50 has been promulgated particularly in the United States[5]. It is argued that if all polyps are removed at that stage the likelihood of colon cancer will be very much reduced. Others claim that colonoscopy should be undertaken every ten years on the grounds that polyps could grow over that period and become malignant. No prospective, controlled trials have assessed the effectiveness of this approach, however, in theory it should be the most effective screening procedure. It is also the most expensive and the one most likely to lead to complications. It is probably more cost effective than any other method.

Conclusion

Colorectal cancer is a major cause of death particularly in the Western world. At present the only practical way of reducing mortality is to undertake population screening. This is cost effective in patients at high risk of developing colorectal cancer, but less so in the normal population that accounts for the vast majority of cancers. The disadvantages of screening must be taken into consideration in conjunction with local epidemiology and facilities available. At present faecal occult blood testing, flexible sigmoidoscopy at five yearly intervals and colonoscopy at ten year intervals have been put forward as suitable methods for screening if it is considered appropriate.

Table 1

Guidelines for an effective screening program
Important cause of morbidity or death
Natural history understood
Early treatment effective
Screening tests sensitive and specific
Screening tests acceptable for compliance
Definitive diagnostic tests available
Screening reduces morbidity and mortality
Reasonable cost
Audit available

from Wilson & Jugner
WHO publication 1968

Table 2

Colorectal cancer
Inherited risk factors
Family history
Adenomatous polyposis coli (APC)
HNPCC or Lynch syndromes I and II
Turcot's syndrome
Muir-Torre syndrome
Juvenile polyposis
Peutz-Jegher's syndrome
Gorlin syndrome
Cowden's disease

Table 3

Colorectal cancer
Non-inherited risk factors
Age
Previous cancer
Colorectal adenoma
Inflammatory bowel disease
Previous cholecystectomy
Previous surgery for PUD
Previous uretero colonic diversion

Table 4

Risk of cancer developing in patients found to have polyps

Low risk	**High risk**
1-2 small adenomas	> 2 adenomas
Tubular adenomas	Villous adenomas
Size < 1cm	Size > 1cm
Low grade dysplasia	High grade dysplasia
Polypoid appearance	“Depressed" appearance

References

1. Wilson JMG, Jungner G. The principles and practice of screening for disease. World Health Organization, Geneva. WHO Monographs. Public Health paper 1968;34: 1-163.
2. Towler B, Irwig L, Glasziou P, Kewenter J, Weller D, Silagy C. A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, Hemoccult. Br Med J 1998; 317: 559-565.
3. Axon ATR. Cancer surveillance in ulcerative colitis - a time for reappraisal. Gut 1994;35:5: 587-589.
4. Ahlquist DA. Fecal occult blood testing for colorectal cancer: can we afford to do this? Gastroenterol Clin North Am 1997; 26: 41-55.
5. Podolsky D. Going the distance - the case for true colorectal cancer screening. New Engi J Med 2000; 343: 207-208.

Table 1