Screening for carcinoma of the colon: current views

Colorectal cancer (CRC) is the second commonest cause of death from malignancy in the UK. Sixty per cent of patients die within 5 years of diagnosis because the cancer usually has metastasized before presentation. Increased public awareness of symptoms, the 2-week rule for patients with suspected cancer together with more specialized training for colorectal surgeons and the use of adjuvant chemotherapy and radiotherapy may improve survival rates. However, without a more radical approach, it seems unlikely that more than 50% of patients with this disease will be cured. The cause of CRC is unknown, and although dietary factors play a part in its pathogenesis and certain drugs may inhibit the polyp cancer sequence, primary prevention is not possible at present. Only population screening offers a real opportunity to impact on the mortality of this disease, which in the UK kills roughly one person in fifty.

PROBLEMS WITH SCREENING

Screening for cancer is controversial. The ethical responsibilities of a doctor are straightforward when a patient seeks advice because of symptoms. The patient has voluntarily consulted with a problem, and the doctor's duty is to do his or her best for the patient without offering any guarantee of success.

With screening, the situation is different. The health provider approaches healthy, uncomplaining people, offering the prospect of disease prevention, but unfortunately screening programmes are not without drawbacks. They raise concerns about health in large sections of the population, both in those who accept screening and in others who decline. Definitive investigation, e.g. colonoscopy, is neither free from discomfort nor devoid of risk. Primary screening modalities, e.g. faecal occult blood testing (FOBT), have limited sensitivity and specificity. False negative and positive results translate into inappropriate reassurance or unnecessary anxiety. Missed cancers cause litigation. Finally, the cost may divert resources from other areas of health care which may deserve higher priority. For these reasons, health screening programmes should be subjected to prospective randomized assessment before introduction. For cancer, mortality should be the endpoint, and an economic evaluation must be made as well.

COLORECTAL CANCER SCREENING

World Health Organization guidelines (Wilson and Jungner, 1968) suggest that CRC may be suitable for a screening programme. The natural history of the condition is understood in that most cancers arise from pre-existing colonic polyps. Treatment of polyps and of early cancer is effective, definitive diagnostic tests are available and economically it would be cost effective compared with other screening programmes.

The weakness lies in the screening tests which should be reasonably sensitive, specific, acceptable and inexpensive. FOBT can be made relatively sensitive but at the cost of being less specific. Flexible sigmoidoscopy has the disadvantage that only the distal bowel is examined. Colonoscopy carries a risk of complications, is expensive and there may be problems with compliance. All of these screening tests would increase the demand for colonoscopy, but the waiting lists for colonoscopy in most UK hospitals currently exceed 6 months, so CRC screening would place a considerable strain on gastroenterological services if it was to be introduced.

SURVEILLANCE FOR HIGH-RISK GROUPS

Certain groups are at a higher risk of CRC than the normal population. Those with hereditary colonic polyposis usually develop cancer in early adult life. Other polyposis syndromes, e.g. juvenile polyposis and Peutz–Jeghers syndrome, also carry an increased risk. Hereditary non-polyposis colonic cancer and the Lynch cancer syndromes are dominantly transmitted predispositions and carry a high risk. These conditions merit regular colonoscopic surveillance. Advances in molecular biology will, in the near future, provide a means of identifying those at risk. However, these conditions account for only 5% of the colonic cancer load in the population.

Certain acquired conditions are associated with cancer, including inflammatory bowel disease, previous cholecystectomy, previous surgery for peptic ulcer disease, uretero-colonic diversion and acromegaly. The risk in these, although higher than normal, is less than the family cancer syndromes. The decision whether to or how often to undertake surveillance colonoscopy in these patients is not yet established.

Individuals with one affected first degree relative have roughly a 1:30–40 as opposed to a 1:50 chance of developing cancer. This increases if the first degree relative is under 45 years of age or if more than one member of the family has been affected. Many doctors are therefore prepared to screen these patients. Patients at increased risk comprise only 25% of the cancers: 75% are sporadic and have no predisposing condition or family history. It is these people at average risk that must be addressed if we are to make a significant impact on CRC mortality in the UK.

SCREENING PEOPLE AT AVERAGE RISK

Symptom questionnaires are unhelpful in predicting CRC, so interest has focused on FOBT, rigid sigmoidoscopy, barium enema, flexible sigmoidoscopy and colonoscopy. Rigid sigmoidoscopy is less complete and more uncomfortable than flexible sigmoidoscopy and is no longer a serious contender. Barium enema is less sensitive for detecting colonic polyps than colonoscopy, and if identified, they cannot be removed at

the time. The cost is similar to colonoscopy, and it is just as unpleasant and carries a radiation hazard.

Newer techniques, e.g. virtual colonoscopy (Bruzzi et al, 2001), the video capsule and faecal molecular markers (Ahlquist and Shuber, 2002), may have potential but have not yet been properly evaluated. None are capable of removing polyps, and the imaging methods require full bowel preparation, identified by patients as the main unpleasantness of colonoscopy. At present, the modalities deserving consideration are FOBT, flexible sigmoidoscopy, and colonoscopy. Of these, only FOBT has been evaluated prospectively.

FAECAL OCCULT BLOOD

The principle underlying FOBT is that most cancers eventually ulcerate and bleed. If the stool is tested for blood, the cancer will be detected, and if testing is performed regularly, the cancer will be identified at a curative stage.

One difficulty is to decide how sensitive to make the test. Detecting the tiniest concentration of blood leads to a large number of false positives and many people have to be colonoscoped (up to 38% in one series), but if sensitivity is reduced, more cancers are missed. Three prospective randomized studies have been performed (Towler et al, 1998). The overall mortality rate from CRC in the cohorts invited to undergo testing was 16% lower than in the control group, and was 23% lower in subjects who accepted screening. However, when assessed for all causes of death, there was no significant difference in mortality between groups. The advantage gained by a reduction in death from CRC was compensated by an increased mortality from cardiovascular causes (Ahlquist, 1997). Another concern is that compliance was high at the start of the study but fell later, suggesting that the advantage might diminish with time.

FLEXIBLE SIGMOIDOSCOPY

Flexible sigmoidoscopy is performed on an outpatient basis. The instrument is introduced into the rectum, sigmoid and perhaps into the descending colon. The procedure can be performed by a nurse who has undergone appropriate training. Unsedated flexible sigmoidoscopy is uncomfortable and can be painful, depending upon the colonic anatomy and the experience and skill of the operator. It is less invasive and expensive than full colonoscopy, which usually requires sedation, but the whole of the bowel is not examined. Distal polyps can be removed at the time of the procedure. If large, depressed or multiple polyps are present, or if the polyp has a villous appearance or contains high grade dysplasia, full colonoscopy is required because there is a significant risk of concomitant cancer. Flexible sigmoidoscopy detects early cancers in the distal bowel (where cancers are most commonly found). Furthermore, the removal of polyps will prevent cancer, while FOBT only detects lesions which have already ulcerated.

A large UK-based prospective randomized study of flexible sigmoidoscopy has been undertaken, the results of which are awaited.

COLONOSCOPY

It is because of perceived deficiencies in FOBT and flexible sigmoidoscopy that full colonoscopy has been recommended in the USA as the most appropriate method of screening (Podolsky, 2000). As a result of media and public pressure, health-care insurance companies are prepared to reimburse screening colonoscopy. A similar arrangement exists in Italy. These measures have been taken without any direct evidence that the intervention is effective.

Computer modelling, however, suggests that this policy would be more cost effective than either flexible sigmoidoscopy or FOBT (Sonnenberg et al, 2000), and the system of health-care funding in the United States is adequate to ensure that a sufficient number of trained doctors is available to undertake the examinations. The same does not apply in the UK, where apart from the logistic problems alluded to earlier, a recent audit of colonoscopy showed that in Britain the caecal intubation rate (total colonoscopy) is only around 70%, i.e. 30% of colonoscopies are not performed to a level acceptable for colonoscopic screening.

CONCLUSION

It seems that population screening for CRC of people at average risk is unlikely to be adopted in the UK in the near future. The outcome of FOBT and its deficiencies are known and the results of flexible sigmoidoscopy are awaited. Now would seem to be an appropriate time to set up a trial of colonoscopic screening – the modality which on theoretical grounds is most likely to make a real impact on cancer mortality. There is also a responsibility on the government to increase resources for endoscopy and a professional obligation for gastroenterologists to improve the performance of colonoscopy. HM

KEY POINTS

- Colorectal cancer kills roughly 1 in 50 of the UK population.
- Screening for cancer is the only current intervention that might make an impact on mortality.
- Colonoscopic screening of people at average risk would be most effective in theory.
- A prospective trial of colonoscopy in this context is desirable.

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