Colorectal Cancer Screening For An Asymptomatic Patient - Colonoscopy or Sigmoidoscopy?

Michael McKenny

Clinical Question

The patient is a 51-year-old airline pilot with a positive family history of colorectal cancer. Although at this time he is asymptomatic, should he be advised to undergo colonoscopy or sigmoidoscopy as a screening test for colorectal cancer?

Background

The highest incidence rates of colorectal cancer are seen in developed countries. In 1998, one quarter of deaths in Ireland were due to cancer, colorectal cancer being the second and third most common causes of cancer mortality amongst males and females respectively[1,2]. Colorectal cancer is a multifactorial disease process. The accumulation of genetic lesions, both inherited and arising sporadically, is known to play a strong role; replication-signalling pathway lesions are associated with tumours proximal to the splenic flexure and a better prognosis than genetic lesions involved in the maintenance of DNA fidelity[3]. Environmental factors, primarily diet and cigarette smoking are known to be important in the pathogenesis.

What is the current approach?

At present, there is no general consensus amongst primary care physicians as to which screening tests should be used, and when. Richards *et al.*found that whether a primary care physician recommended faecal occult blood testing, sigmoidoscopy or colonoscopy for women, depended on physician speciality, physician age, perceived patient demand, physician need for additional colorectal cancer screening information, practice size and practice location[4]. Furthermore, primary care physicians in this survey recommend earlier and more aggressive screening than is suggested by current guidelines[4].

What is the current evidence?

Two studies, both published in the *New England Journal of Medicine* last year, addressed the role of colonoscopy in colorectal cancer screening. Lieberman *et al.* performed colonoscopy in 3196 asymptomatic patients enrolled in the study (mean age 62.9 years) at 13 Veteran Affairs medical centres, visualising the caecum (caecal intubation) in 97.7% of cases[5]. The purpose of the study was to determine the risk of proximal advanced neoplasia (defined for both studies as hyperplastic polyp, tubular adenoma or advanced neoplasm) in patients with and those without neoplasia in the distal colon, and the likelihood that advanced proximal neoplasia would be detected on the basis of the presence of an adenoma in the distal colon. 1637 (50%) patients, all of whom were asymptomatic, had polyps, of which 1.3% were high-grade dysplasia and 1% were invasive cancer. Importantly, of the patients with proximal advanced lesions, 52% did not have any lesion in the distal colon and would have been given a clean bill of health on sigmoidoscopy screening. Imperiale *et al.* performed colonoscopy in 1994 asymptomatic adults from the same employer, aged 50 years and older (mean age 59.8 years), achieving caecal intubation in 97% of the study group[6]. The purpose of the study was to determine the relative risk of advanced proximal neoplasia in patients with distal polyps, as compared to patients with no distal polyps. Fifty patients (2.5%) were found to have advanced proximal lesions, of which 7 had cancer. Twenty-three (46%) of these 50 patients had no lesions in the distal colon. Their results showed that if colonoscopy were used as a screening test only in those patients in whom distal polyps have been previously visualised on sigmoidoscopy, approximately half the cases of advanced proximal neoplasia would be missed.

Appraisal of the Evidence

Type of study:

Although neither study was a randomised control trial, the gold standard of clinical research, both were conducted against the following background. Colorectal carcinoma is a multistage process involving a number of morphologic steps (from normal colon to hyperproliferative epithelium and then to adenoma and on to carcinoma) and molecular steps (dysfunction of the signalling pathways controlling the cell cycle). It is also consequent on a large number of genetic and environmental risk factors. Strong evidence causally links most colorectal carcinoma to pre-existing adenomas (though conversely, not all adenomas become cancerous)[7]. Intuitively, early detection and removal of such precancerous adenomas is a desirable preventative strategy. In this setting, the studies are appropriate as they seek to determine, in asymptomatic patients, the prevalence and location of colorectal neoplasia and to establish the relative utility of colonoscopy and sigmoidoscopy as screening procedures.

The Lieberman *et al.* study population contained both a disproportionately large number of males (96.8%) and a disproportionately large number of patients with a positive family history of colorectal cancer (13.9%)[5]. This is important for two reasons: firstly, males have a higher incidence of colorectal cancer than females; secondly, it is possible that some of the patients come from families with hereditary nonpolyposis colorectal cancer, where proximal colonic lesions are much more com-

mon than in the general population, thus making it more likely that the final result would favour colonoscopy over sigmoidoscopy as a screening test. However, the Imperiale *et al.* study had similar results, in the absence of this apparently biasing factor[6]. This latter study population was on average several years younger, and both studies excluded patients who were symptomatic in any way (bleeding per rectum, any recent change in bowel habit or lower abdominal pain, previous cancer, polyps or inflammatory bowel disease). The results are applicable to the patient in question. He is asymptomatic and though younger than the populations studied, age does not become an independent risk factor for advanced proximal neoplasia until 65 years old[8]. The patient has a positive family history of colorectal cancer. Such patients are over-represented in the Lieberman *et al.* study population, and though it doesn't appear to have biased the result significantly, if anything, it would make these results more strongly applicable to the clinical question[5].

Does efficacious treatment exist?

Efficacious treatments exist in the form of polypectomy, surgical bowel resection, chemotherapy and radiotherapy. But the long-term survival rate is only meaningful if colorectal cancer in genesis is detected and removed by polypectomy during the adenoma phase.

Does the current burden of suffering warrant screening?

The current burden of disease in Ireland is as follows: 1762 cases of colorectal cancer (1069 male) which resulted in 964 deaths (524 male) and a five-year survival of 54% for males and 58% for females (1997 statistics)[2]. Ireland is first in the European league of cumulative colorectal cancer incidence[2].

Does the screening test have a high degree of specificity and sensitivity?

Colonoscopy as a screening test has a high degree of specificity and sensitivity, but only when carried out by highly trained and practiced operators who will visualize the entire colon and collect appropriate biopsy samples. This must be performed in conjunction with subsequent high quality histopathology. Biopsies are taken from the rectal, sigmoidal and caecal walls, with particular attention to suspect lesions.

Can the health system cope with a screening program and will people participate?

At present, the health system cannot cope with a screening programme based on colonoscopy; there are presently insufficient numbers of highly skilled operators to perform colonoscopies on symptomatic patients[9]. It is possible that positive screenees are more likely to come from lower socio-economic groups where compliance and follow-up are normally more problematic. Additionally, screening procedures are unpleasant, and effective communication of the reasons for screening are therefore of great importance.

What are the other screening tests available for colorectal cancer?

Faecal occult blood testing, which has a low positive predictive value of 50%, has only conclusively demonstrated a reduction in mortality when used as a screening procedure in one large randomised study. In this study the 13-year cumulative mortality rate was decreased by 33%[10]. The limitations of sigmoidoscopy with regard to the detection of proximal lesions have been described above; there is no definitive sentinel lesion in the rectosigmoid and the presence or absence of polyps in the distal colon does not accurately predict the presence of high-risk adenomas more proximally[11]. Should a suspect lesion be detected on barium enema, which is difficult in any event due to the confounding presence of diverticular disease in about 40% of a screened population, a full colonoscopy is needed regardless, the latter not exposing patient and staff to radiation[3,12]. The value of hydrocolonic sonography, where trans-abdominal ultrasound is used to visualise a fluid-filled colon, as a screening test, is limited. In one 52 patient study it detected no cancers and only 2 polyps, when in fact 4 patients had cancer and 29 had polyps[13].

Conclusion

Lieberman *et al.* and Imperiale *et al* do not state that life expectancy is increased by performing colonoscopic screening of asymptomatic persons aged 50 years or older[5,6]. However, it seems unlikely, given the pathogenesis of the disease process, the morphological changes and time-scale involved, that such would not be the outcome of a properly implemented screening program. Brown suggests that cost effectiveness has been established for colorectal cancer screening which includes annual faecal occult blood testing and a single colonoscopy to stratify patients according to risk[14]. This procedure compares favourably with screening mammography in women over 50 years in terms of the cost per life year saved[14]. Inadomi *et al.* state on the basis of their meta-analysis that, depending on the screening regimen used, between 2.9 and 6 screening colonoscopies are needed for every year of expected life saved, but it should be kept in mind that direct complications cause the death of one of every ten thousand patients who undergo colonoscopy[12,15]. Whilst no consensus exists at present, recent evidence suggests that the use of colonoscopy screening in males over 50, may be used in conjunction with family history and other risk factors, to stratify patients into risk categories. Unless a full colonoscopy is performed, rather than sigmoidoscopy, approximately half of the cases of advanced proximal neoplasia will be missed. This risk assessment will in future involve reliable molecular markers and perhaps eventually it will even become guided by the use of an algorithm, similar to that suggested for the risk assessment of hypertension by the Third Report of the British Hypertension Society[16,17]. In conclusion, our asymptomatic, 51-year-old airline pilot, with a positive family history of colorectal cancer should have a full colonoscopy, after a thorough history and examination. In the future, virtual colonoscopy with MRI is likely to be the investigation of choice[12].

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