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EDITORIAL

Colorectal cancer screening

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Abstract

Colorectal cancer is a major public health burden worldwide. There is clear-cut evidence that screening will reduce colorectal cancer mortality and the only contentious issue is which screening tool to use. Most evidence points towards screening with fecal occult blood testing. The immunochemical fecal occult blood tests have a higher sensitivity than the guaiac-based tests. In addition, their automation and haemoglobin quantification allows a threshold for colonoscopy to be selected that can be accommodated within individual health care systems.

Key words: Screening; Colorectal cancer; Fecal occult blood testing; Colonoscopy

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INTRODUCTION

Colorectal cancer is a major public health burden. It is the fourth most common form of cancer worldwide and the most frequent in North America, Australia, New Zealand, Argentina, and parts of Europe[1]. When colorectal cancer is detected at an early stage, the prognosis is excellent with a five year survival in excess of 97%[2]. The risk of nodal metastases and thus poorer prognosis increases as colorectal cancer develops with a risk of 2%-3% when confined to the submucosa compared with 8%-12% when confined to the muscularis propria[3,4]. The evidence that screening for colorectal cancer leads to earlier detection and improved survival is now incontrovertible and has led to a consensus that colorectal cancer screening will reduce mortality; however there is no consensus as to the best screening tool[5-11]. The four possible screening options currently cited are barium enema, fecal occult blood testing or fecal occult blood testing (FOBT), sigmoidoscopy, colonoscopy, or a combination thereof. Cost-effective analyses do not help distinguish between the strategies with the median incremental cost-effectiveness ratios being €9950/life-year saved, €13 200/life-year saved, and €10 000/life-year saved, for FOBT, sigmoidoscopy, and colonoscopy respectively compared with no screening[12].

Inadequate screening capacity is an important barrier to consider in colorectal cancer screening. Colonoscopy is the final pathway of all colorectal cancer screening. Depending on which fecal test is used, 2%-15% of participants will need a colonoscopy[13]. Between 5%-10% of participants undergoing screening flexible sigmoidoscopy screening will need a colonoscopy[14]. If colonoscopy is used as the screening option then potential annual demand for screening colonoscopy can be calculated at 45%-50% of those aged 50-70 years[15]. The endoscopy capacity of a health care system carries significant weight when deciding the best screening tool.

BARIUM ENEMA

There are drawbacks to each of the screening options. Although double contrast barium enema is recommended for screening no published studies of its efficacy in this role exist. The sensitivity of barium enema for polyps > 1 cm is 48% and for colorectal cancer 82.9%[16,17]. Despite the presence of barium enema in screening guidelines, its place lies for those individuals who have had a failed colonoscopy rather than as a screening tool.

SIGMOIDOSCOPY

Sigmoidoscopy is an attractive option as it takes only five minutes, requires no sedation and only a self-administered enema to clear the bowel. In a pivotal retrospective case controlled study those with colorectal cancer were less likely to have had a prior sigmoidoscopy than the control group with an odds ratio of 0.3[8]. Four flexible sigmoidoscopy trials were carried out on the strength of retrospective studies[10,18-20]. Long-term follow up was available from only one of these studies with a reduction in colorectal cancer incidence and mortality of 80% and 50% respectively over 13 years[10]. Much controversy has surrounded the question of right-sided colonic lesions missed by sigmoidoscopy. In men sigmoidoscopy failed to identify 29.7% of advanced colonic lesions and in women 65.3%[21,22]. As a consequence, a very persuasive argument against sigmoidoscopy has been the claim that screening flexible sigmoidoscopy is as illogical as screen-

ing only one breast during mammography[23]. In reality, just 2%-5% of asymptomatic individuals are believed to have isolated advanced proximal neoplasia[24]. The real concern surrounding sigmoidoscopy is its acceptance rate and its invasiveness as a screening test in asymptomatic individuals. In studies, which represent the ideal clinical situation, the acceptance rate varies from 33%-80%[10,18,19]. Screening sigmoidoscopy is an invasive procedure and is associated with risks which may not be acceptable in asymptomatic individuals: a perforation rate of 1 in 25 000, bleeding in 3.2%, and pain in 14%[25,26].

COLONOSCOPY

Evidence-based guidelines place greatest weight on large-scale randomized trials, but the corroboration for colonoscopy comes from indirect evidence or small case-control studies. The US National Polyp Study and the Italian multi-center study showed a reduction in colorectal cancer incidence of 75%-90% over a follow-up period of 5.9 and 10.5 years respectively[9,27]. However, the primary aim of both studies was to determine the effects of resecting colorectal polyps on colorectal cancer incidence. Case-control studies have evaluated the feasibility of colonoscopy in colorectal cancer screening with advanced lesions detected in 10.5%-12.5% of asymptomatic individuals[28,29]. It should be born in mind that both studies enrolled individuals who wished to participate in colorectal cancer screening, and population-based studies reveal that the acceptance rate for colonoscopy is less than 20%[30,31]. For any screening test to be effective the acceptance rate must be over 60% and the acceptability of colonoscopy to the population may limit its usefulness as a screening tool. In addition, in clinical practice the yield from screening colonoscopy in average-risk individuals has been lower than case control studies with only 5.1% having a polyp > 9 mm[32]. The sensitivity of colonoscopy for colorectal cancer and polyps may have been over-estimated. In retrospective studies and prospective FOBT screening trials the sensitivity of colonoscopy for colorectal cancer is over 95%[17,33]. Back-to-back colonoscopy studies reveal that the miss rates for polyps > 1 cm is 0%-6%[34,35]. Virtual colonoscopy followed by colonoscopy reveals a miss rate of 12% for polyps > 1 cm[36]. Colonoscopy technique is of crucial importance in detection rates. In particular, the quality of bowel preparation and colonoscopy withdrawal times have been identified as factors impacting on colonoscopy detection rates[37-39]. Indeed, improving the quality of colonoscopy techniques is estimated to reduce interval cancers by up to 50%[40]. Finally as with sigmoidoscopy, colonoscopy is an invasive procedure and may not be acceptable as a screening tool in asymptomatic individuals. Although the risk associated with a single colonoscopy is small with a 0.2%-0.3% risk of serious complication and a 0.1% risk of death, the cumulative risk of repeat screening colonoscopy may outweigh the benefit obtained from screening colonoscopy[41].

FECAL OCCULT BLOOD TESTING

The most robust evidence for the effectiveness of colorectal cancer screening lies with FOBT. Long-term follow up available in four randomized controlled trials of over 330 000 individuals and three non-randomized trials of just over 200 000 individuals reveals a reduction in colorectal cancer mortality of 12%-33%. Adjusting for compliance gives a 23% reduction in colorectal mortality with guaiac-based FOBT[5-7,42-44]. It is sometimes claimed that the mortality reduction in the American study is attributable to the high colonoscopy rate of 28%-38%[6]. However only 4% of individuals in the European studies, and just over 6% of individuals in the Chinese study underwent endoscopy[5,7,43].

The sensitivity of FOBT is often seen as a liability, and it is true that the once-off sensitivity of FOBT for colorectal cancer ranges from 26%-69%, and for adenomas ranges from 9%-36%[13,21,45]. Yet FOBT screening involves repeated testing at 1-2 yearly intervals and within this context the programme sensitivity of FOBT for detecting cancer is as high as 90%[6]. From an acceptability point of view FOBT is non-invasive, can be carried out at home, and does not necessitate any bowel preparation or taking time off work.

Guaiac-based FOBT depends on fecal blood to catalyze the phenolic oxidation of guaiac in the presence of hydrogen peroxide to produce a blue chromogen. Immunochemical FOBTs use antibodies specific for human haemoglobin and have a higher sensitivity of 66%-90% and a specificity > 90%[46,47]. Immunochemical FOBTs have evolved further with the development of quantitative results, thus allowing the positivity threshold to be varied and achieve an increased sensitivity with lowered specificity or a decreased sensitivity with an increased specificity[48,49].

ALTERNATIVE SCREENING TOOLS

Virtual colonoscopy, despite improvements in technology, continues to show widely varying results with sensitivities for detecting polyps ⩾ 10 mm ranging from 55% to 92%[36,50]. As such it is still not ready for population screening. Fecal calprotectin failed to live up to its initial promise in subsequent studies[51]. Fecal DNA tests are affected by the relatively low frequency of single marker alterations in colorectal cancer. Even the use of a broad panel of markers in fecal DNA still fails to be convincing for population screening[52].

CONCLUSION

Screening will reduce the mortality from colorectal cancer and should be implemented now. For those at average risk of developing colorectal cancer most evidence points towards screening with FOBT. Depending on which FOBT is used, between 2%-15% of individuals screened will need colonoscopy, a figure that can be accommodated without too much difficulty.

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