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Colorectal cancer screening with the addition of flexible sigmoidoscopy to guaiac-based faecal occult blood testing: A French population-based controlled study (Wintzenheim trial)

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ABSTRACT

Objective: To assess the feasibility, participation and neoplasia yield of adding a flexible sigmoidoscopy (FS) once in a lifetime to a colorectal cancer screening programme with guaiac-based faecal occult blood test (gFOBT).

Methods: A total of 4771 average risk residents aged 50–74 of a canton of the Haut-Rhin, a French administrative area, were invited every other year to participate in an organised screening programme with gFOBT. Of them, those aged 55–64 (1824 people) were, in addition, invited once by mail to visit their general practitioner (GP) for a screening with FS performed by a gastroenterologist.

Results: In all, 2717 people (56.9%) (95% confidence interval (CI) 55.5–58.4) were screened with one or other of the two tests or with both tests. Compliance was 56.7% (55.3–58.1) with gFOBT and 20.9% (19.1–22.8) with FS. Both tests were performed by 20.2% (18.4–22.1) of people. Compliance with FS was 1.9% in people who had not complied with gFOBT and 31.9% in people who complied. The latter was $\geqslant$50% in patients of 26 motivated GPs. The detection rate for advanced neoplasia was 17.7 per 1000 people screened (12.7–22.6) with the combined procedure, more than three times higher than that with gFOBT alone.

Conclusion: A population-based screening programme with the addition of FS to gFOBT is feasible and safe through an organisation involving GPs. The performances of the two screening tools are complementary: high compliance – low yield for gFOBT and vice versa for FS. The addition of a single FS screening in people aged 55–64 to an organised programme with biennial gFOBT in people aged 50–74 is a colorectal cancer screening option that deserves further exploration.

1. Introduction

Colorectal cancer (CRC) is the second most common cause of death from malignant disease in France and resulted in 16,865 deaths in 2005.[1] Data from cancer registries and EUROCARE-3 and -4 indicate that from the mid 1990s to early 2000 the incidence of CRC increased slightly for both sexes in France whereas mortality from CRC decreased and

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5-year relative survival improved.[1,2] In 2002, France initiated an organised population-based CRC screening programme with a biennial guaiac-based faecal occult blood test (gFOBT). The results of the first round in the administrative district of the Haut-Rhin in eastern France have been published.[3] gFOBT is simple, easy to perform, inexpensive and the only screening tool with high quality evidence obtained from randomised controlled trials (RCTs) demonstrating its efficacy to reduce CRC mortality.[4–7] However, gFOBT is not perfect. The main disadvantages are its low sensitivity[8,9] and the requirement for frequent testing, which may limit compliance and thereby effectiveness.

Indirect evidence suggests that endoscopic screening may be far more effective than FOBT screening, but results from RCTs are still awaited.[10–13] Moreover, the benefit of flexible sigmoidoscopy (FS) screening is long lasting, persisting for up to 10 years[14] or even 16 years.[15]

In theory, the combination of FOBT and FS should be more effective than either test alone since the two tests are complementary. Two thirds of interval cancers missed by screening with gFOBT in the British and Danish trials were situated within the reach of FS.[5,6] Three RCTs showed that the yield for advanced neoplasia was significantly higher (4–5-fold) with the combination than with FOBT alone.[16–18] They all assessed a once only screening with FOBT and not a programme with repeat FOBT testing. The effectiveness of the combined strategy in reducing CRC mortality has never been directly studied in a RCT, and in France, screening neither with FS alone nor with the FOBT – FS combination has been assessed.

The aim of this study was to assess the feasibility, participation rate and neoplasia yield of adding an FS once in a lifetime for people aged 55-64 years to an organised CRC screening programme with biennial gFOBT.

2. Methods

2.1. Study population

This trial was performed in the canton of Wintzenheim (18,620 inhabitants), an administrative district in the Haut-Rhin (710,000 inhabitants). All residents of this canton aged 50–74 were invited, as were all residents of Haut-Rhin, to participate in a biennial gFOBT screening programme.[3] In addition, an FS was proposed to all those aged 55–64 who had a negative gFOBT or who had not complied with gFOBT.

2.2. gFOBT screening

The design of the gFOBT screening programme has been previously described.[3] Briefly, residents aged 50–74 were invited by mail every other year to participate. A first letter invited them to visit their general practitioner (GP) for CRC screening. Three recall letters were mailed to all those who had not complied. The second recall letter was mailed along with the gFOBT itself. People with serious illness, recent CRC screening or high CRC risk were excluded. The gFOBT (Haemoccult II) was used without dietary restriction and was processed without rehydration. The test was defined as positive as soon as one slide was positive. People with a positive gFOBT were referred for colonoscopy.

2.3. FS screening invitation

A first letter was mailed at the beginning of the study to all residents aged 55–64 of the canton informing them about the trial. Then, all of them who had a negative gFOBT or had not complied with gFOBT were invited once by mail to visit their GP for FS screening. There was no recall letter. A leaflet explaining the FS procedure and the advantages and risks of adding FS to gFOBT accompanied the invitation letter. The gFOBT screening was to be performed before the FS screening. GPs were instructed to exclude from screening with FS any person with a positive gFOBT, recent digestive symptoms, recent (<5 years) colonoscopy or FS procedure, high CRC risk or serious illness. GPs were asked to try to convince eligible people to participate and to complete a questionnaire about socio-demographic characteristics and family history of CRC. The FS appointment was obtained by phone either by the GP or by the enrolled person. Written informed consent was obtained from each subject by the GP. In all, 110 GPs were involved in the study. This study was approved by the ethics committee of the University of Strasbourg.

2.4. FS procedure

Bowel preparation was limited to a single 130 ml sodium phosphate enema (Normacol®) administered by a nurse in the endoscopy suite immediately before the FS procedure. Before the examination, participants were asked to complete a questionnaire administered by a nurse asking about their knowledge about the FS procedure, its reputation and their possible fear of the examination. FS procedures were performed without sedation in a single hospital endoscopy unit by 10 senior gastroenterologists practicing in the area. The FS was undertaken with an Olympus 100 cm upper videoendoscope (GIFQ 160). The aim was to advance the endoscope to the extent that it could be achieved without causing undue pain. If the bowel preparation was inadequate, a second enema was administered in the endoscopy suite and a second examination was performed immediately thereafter. Polyps <10 mm detected during the FS were either removed or biopsied without removal at the discretion of the endoscopist. Polyps and specimens were sent for histological examination. As a screening test, FS was called positive when referral to colonoscopy was indicated, i.e. for people with polyps $\geqslant$10 mm or any neoplasia at FS and people who had a polyp that could not be biopsied or a polyp and inadequate bowel preparation. The result of each endoscopic procedure, either FS or colonoscopy, was classified according to the lesion with the worst prognosis.

The endoscopist recorded on a standard form information about adequacy of bowel preparation (rated on a 10 point scale), reach of the scope, technical adequacy and duration of the examination, characteristics of detected lesions and occurrence of immediate adverse effects. FS examination was considered technically inadequate if the depth of insertion was <40 cm or the visual inspection limited to <90% of the mucosal surface due to inadequate bowel preparation with no detection of a polyp or mass. Immediately after the examination participants were asked to answer a questionnaire administrated by a nurse asking about their discomfort