Rate of Detection of Advanced Neoplasms in Proximal Colon by Simulated Sigmoidoscopy vs Fecal Immunochemical Tests

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BACKGROUND & AIMS: **We compared the ability of biennial fecal immunochemical testing (FIT) and one-time sigmoidoscopy to detect colon side-specific advanced neoplasms in a population-based, multicenter, nationwide, randomized controlled trial.**

METHODS: **We identified asymptomatic men and women, 50–69 years old, through community health registries and randomly assigned them to groups that received a single colonoscopy**

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Abbreviations used in this paper: APN, advanced proximal neoplasm; CI, confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical testing; FOBT, fecal occult blood test; OR, odds ratio; RR, relative risk.

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examination or biennial FIT. Sigmoidoscopy yield was simulated from results obtained from the colonoscopy group, according to the criteria proposed in the UK Flexible Sigmoidoscopy Trial for colonoscopy referral. Patients who underwent FIT and were found to have ≥75 ng hemoglobin/mL were referred for colonoscopy. Data were analyzed from 5059 subjects in the colonoscopy group and 10,507 in the FIT group. The main outcome was rate of detection of any advanced neoplasm proximal to the splenic flexure.

RESULTS: **Advanced neoplasms were detected in 317 subjects (6.3%) in the sigmoidoscopy simulation group compared with 288 (2.7%) in the FIT group (odds ratio for sigmoidoscopy, 2.29; 95% confidence interval, 1.93–2.70; $P = .0001$). Sigmoidoscopy also detected advanced distal neoplasia in a higher percentage of patients than FIT (odds ratio, 2.61; 95% confidence interval, 2.20–3.10; $P = .0001$). The methods did not differ significantly in identifying patients with advanced proximal neoplasms (odds ratio, 1.17; 95% confidence interval, 0.78–1.76; $P = .44$). This was probably due to the lower performance of both strategies in detecting patients with proximal lesions (sigmoidoscopy detected these in 19.1% of patients and FIT in 14.9% of patients) vs distal ones (sigmoidoscopy detected these in 86.8% of patients and FIT in 33.5% of patients). Sigmoidoscopy, but not FIT, detected proximal lesions in lower percentages of women (especially those 50–59 years old) than men.**

CONCLUSIONS: **Sigmoidoscopy and FIT have similar limitations in detecting advanced proximal neoplasms, which depend on patients' characteristics; sigmoidoscopy underperforms for women 50–59 years old. Screening strategies should be designed on the basis of target population to increase effectiveness and cost-effectiveness. ClinicalTrials.gov number: NCT00906997**

Keywords: Colorectal Cancer; Prevention; Screening; Fecal Occult Blood Testing; Endoscopy.

Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of cancer-related death.[1] Evidence from several studies has shown that screening is effective[2,3] and cost-effective[4,5] for CRC prevention in average-risk population. Indeed, both flexible sigmoidoscopy and fecal occult blood testing (FOBT) have demonstrated to reduce CRC-specific mortality[6–10] and incidence[9–12] in randomized controlled trials. Accordingly, these 2 strategies, along with colonoscopy, have been universally accepted and recommended for CRC screening.[2,13]

Colonoscopy has a dual critical role in CRC screening because it constitutes a primary strategy and also represents the mandatory work-up examination to evaluate those individuals with a positive result in either FOBT-based or sigmoidoscopy-based strategies.[2,13] Indeed, whereas presence of blood in feces should be considered as a biomarker of colorectal neoplasm,[14,15] effectiveness of sigmoidoscopy relies on its capacity to detect neoplastic lesions in the distal colon as well as on the fact that these distal findings predict the risk of advanced proximal neoplasia.[16–19]

Despite the evidence on the efficacy of sigmoidoscopy and FOBT in CRC screening, both strategies have largely been criticized because of their potential limitation for detecting proximal lesions. However, there is very limited information on their comparative effectiveness with respect to this relevant aspect. In fact, analyses mainly encompass indirect comparisons of results obtained in each specific strategy,[20] with 2 remarkable exceptions.[21,22] In a first randomized trial, Segnan et al[21] compared biennial FOBT by using a low-sensitivity fecal immunochemical test (FIT), one-time sigmoidoscopy, and one-time colonoscopy and demonstrated a lower detection rate of advanced neoplasia in the first 2 strategies with respect to the latter, which, in turn, was associated with lower participation. In a second randomized trial, Hol et al[22] compared guaiac-based FOBT, FIT, and sigmoidoscopy, and they demonstrated that FIT outperformed guaiac-based screening in participation and detection rate, but sigmoidoscopy was associated with a higher diagnostic yield than both fecal tests. It is important to mention, however, that comparisons of screening approaches have been performed according to overall outcomes, with no differentiation between proximal and distal findings and without stratifying participants according to age and gender, a critical issue because of the well-recognized differences on both overall and right-sided colorectal neoplasm prevalence regarding these characteristics.

The ColonPrev study, a population-based, multicenter, nationwide, randomized controlled trial designed to assess the efficacy of one-time colonoscopy and biennial FIT for reducing CRC mortality at 10 years, has recently reported the results obtained at the baseline screening exam.[14] This study constitutes a unique opportunity to estimate the yield of sigmoidoscopy-based CRC screening in average-risk population[23] and to compare the performance of this strategy with the results obtained in the FIT-based approach. For this purpose, sigmoidoscopy yield was simulated from the colonoscopy data according to the criteria proposed by the UK Flexible Sigmoidoscopy trial[9] to refer individuals