Diagnostic Accuracy of a Qualitative Fecal Immunochemical Test Varies With Location of Neoplasia But Not Number of Specimens

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BACKGROUND & AIMS: We compared the accuracy of a qualitative fecal immunochemical test (FIT) in identifying patients with proximal vs distal advanced neoplasia and evaluated whether analysis of 2 specimens performed better than analysis of 1 specimen. Distal advanced neoplasia was defined as colorectal cancer (CRC), any colorectal adenoma ≥10 mm in diameter, high-grade dysplasia, or a lesion with villous or tubulovillous histologic characteristics in a location distal to the splenic flexure, including the descending colon, the rectosigmoid, and the rectum.

METHODS: We collected data from 5343 subjects (50−70 years old) who received 2 FITs (Hemosure; cutoff value, 10 μg hemoglobin/g feces) before colonoscopy in an invitational CRC screening program in Hong Kong from 2008 through 2012. We calculated the FIT's sensitivity, specificity, positive predictive value (PPV), and negative predictive value in detecting colorectal neoplasia.

RESULTS: Of the participants, 13.6%, 12.2%, and 6.0% had distal, proximal, and synchronous distal or proximal neoplasia, respectively. Advanced neoplasia was detected in 291 subjects (5.4%); 22 (0.4%) had CRC. FIT detected distal advanced adenoma with 39.7% sensitivity (95% confidence interval [CI], 32.0%−48.0%) vs proximal advanced adenoma with 25.0% sensitivity (95% CI, 17.3%−34.6%; $P = .014$), distal advanced neoplasia with 40.0% sensitivity (95% CI, 32.5%−47.9%) vs proximal advanced neoplasia with 27.9% sensitivity (95% CI, 20.0%−37.4%; $P = .039$), and any distal adenoma ≥10 mm, irrespective of other lesion characteristics, with 39.5% sensitivity (95% CI, 31.0%−48.7%) vs proximal adenoma with 25.3% sensitivity (95% CI, 16.5%−36.6%; $P = .038$). The specificity of FIT in detecting CRC was similar between the proximal and distal colon. FIT detected distal lesions with higher PPV than proximal lesions. One FIT detected advanced neoplasia with 31.8% sensitivity (95% CI, 25.9%−38.4%) and 92.4% specificity (95% CI, 91.6%−93.2%), whereas 2 FITs detected advanced neoplasia with 34.1% sensitivity (95% CI, 28.0%−40.8%; $P = .617$) and 91.9% specificity (95% CI, 91.0%−92.7%; $P = .327$). FIT detected distal advanced neoplasia with greater sensitivity and higher PPV than proximal advanced neoplasia.

CONCLUSIONS: In an analysis of data from subjects who underwent CRC screening in Hong Kong, FIT detected distal advanced neoplasia with higher sensitivity than proximal advanced neoplasia. Analysis of 1 vs 2 specimens by FIT identified advanced neoplasia with similar test characteristics.

Keywords: Colorectal Cancer Screening; Sensitivity; Specificity; Specimen Number.

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Colorectal cancer (CRC) is the second most common cancer worldwide.[1] International guidelines recommend CRC screening for average-risk subjects aged older than 50 years.[2–4] The use of fecal immunochemical tests (FITs) has been endorsed as one of the primary

Abbreviations used in this paper: AN, advanced neoplasia; CRC, colorectal cancer; FIT, fecal immunochemical test; LR–, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

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screening tools by several U.S. professional societies.[5,6] FIT precludes dietary restrictions and is gaining popularity in many European and Asian countries.[7,8] Some countries still use guaiac-based fecal test as the initial screening test, but all are planning to adopt FIT in the future.[9]

However, there still exist 2 controversies with respect to the accuracy of FIT in different circumstances. The first regards the diagnostic performance of FIT in the detection of proximal vs distal neoplasia. Whereas some studies showed that FIT had similar performance characteristics in detecting proximal and distal lesions,[10,11] a recent screening pilot showed no difference in diagnostic accuracy when distal or proximal neoplasia was present.[12,13] This knowledge gap is important because the prevalence and distribution of colorectal neoplasia are different according to ethnicity and races.[14,15]

Second, it is currently unknown whether a CRC screening program might benefit by using a 2-specimen instead of a 1-specimen screening strategy. Several studies have compared the diagnostic accuracy of these 2 strategies, with inconclusive findings.[16–18] The screening program in the United States uses annual FIT, and the number of specimens ranges from 1 to 3. The national screening programs in the Asia Pacific countries adopt either 1-specimen or 2-specimen strategies.

This study aims to test 2 a priori hypotheses, namely the diagnostic performance of FIT differs (1) in detecting distal neoplasia vs proximal neoplasia and (2) with the use of 1 specimen vs 2 specimens. For the latter objective, we examined the concordance rate for 2 FIT specimens.

Materials and Methods

The study setting has been described elsewhere.[19,20] All eligible Hong Kong residents were invited for free CRC screening via several territory-wide media invitations (2008–2012). This study was approved by the Clinical Research and Ethics Committee of the Chinese University of Hong Kong (protocol CRE-2008.404). The STARD checklist was used (Supplementary File 1).[21]

Study Participants

Eligible residents could register for the program by telephone, e-mail, fax, online enrollment, or walk-in. The eligibility criteria included (1) age between 50 and 70 years; (2) the absence of any symptoms suggestive of CRC such as per rectal bleeding, tarry stool, loss of appetite, or a change in bowel habit in the past 4 weeks or a weight loss of greater than 5 kg in the past 6 months; and (3) not having undergone any CRC screening tests within the past 5 years. Subjects were excluded if they had a history of any colorectal adenoma, CRC, diverticular disease, inflammatory bowel disease, prosthetic heart valve or vascular graft surgery, or if they had medical conditions that were contraindications for colonoscopy such as cardiopulmonary insufficiency and the use of double antiplatelets. Each eligible participant completed a self-administered survey that consists of sociodemographic and clinical information. We included all screening participants who completed 2-specimen FIT and 1 direct colonoscopy.

Procedures of Fecal Immunochemical Test

We used a qualitative FIT (Hemosure; W. H. P. M., Inc, El Monte, CA) from a single manufacturing lot. The device collected 20 mg feces with a serrated probe attached to the cap into 2 mL buffer. Participants were instructed to poke the spiral applicator 6 times at random into the freshly passed whole feces and then reinsert the probe into the collection tube. The screenees were instructed to collect 2 distinct specimens from 2 consecutive bowel movements on different days. Participants were reminded to store the specimens at room temperature and return their collection tubes containing fecal specimens to the center in person 6 days within the fecal collection (median, 3 days; range, 1–6 days). The date of specimen collection was written on the device label before returning to the center. Specimens that were received more than 10 days from date of collection were termed expired and not tested further (none in this study). Specimens were tested once on the day of receipt in the center by squeezing each tube to dispense 3 drops into the sample well, and the results were interpreted at 5 minutes. A cutoff concentration of 10 μg hemoglobin/g feces was used according to the manufacturer, whereas most qualitative FITs in the United States have a cutoff concentration of 20 μg hemoglobin/g feces.[22] Two independent laboratory technicians trained for accurate interpretation of at least 100 FIT specimens interpreted the FITs and recorded the results manually. The analysts were blinded to the clinical information of the participants. A positive test was recorded when at least 1 of the FITs was positive.

Colonoscopy Procedure

Before the scheduled colonoscopy appointment, the detailed procedure of colonoscopy was explained to each study participant. Polyethylene glycol (Klean-Prep; Helsinn Birex Pharmaceuticals Ltd, Dublin, Ireland) was used as the standardized bowel preparation regimen for each participant in split dosing. All colonoscopies were performed by experienced colonoscopists in endoscopy centers that were affiliated with 2 major hospitals. They were blinded to the FIT results. The sedation regimen consisted of midazolam 2.5 mg (Groupe Panpharma, Luitre, France), and meperidine 25 mg (Martindale Pharmaceuticals, Romford, United Kingdom) was administered intravenously. Depending on the participants' comfort level, additional doses of midazolam and