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Noncathartic CT Colonography: Image Quality Assessment and Performance and in a Screening Cohort

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Abstract

OBJECTIVE—Cathartic bowel preparation is a major barrier for colorectal cancer screening. We examined noncathartic CT colonography (CTC) quality and performance using four similar bowel-tagging regimens in an asymptomatic screening cohort.

SUBJECTS AND METHODS—This prospective study included 564 asymptomatic subjects who underwent noncathartic CTC without dietary modification but with 21 g of barium with or without iodinated oral contrast material (four regimens). The quality of tagging with oral agents was evaluated. A gastrointestinal radiologist evaluated examinations using primary 2D search supplemented by electronic cleansing (EC) and 3D problem solving. Results were compared with complete colonoscopy findings after bowel purgation and with retrospective unblinded evaluation in 556 of the 564 (99%) subjects.

RESULTS—Of the 556 subjects, 7% (37/556) and 3% (16/556) of patients had 52 and 20 adenomatous polyps ≥ 6 and ≥ 10 mm, respectively. The addition of iodine significantly improved the percentage of labeled stool ($p = 0.0002$) and specificity (80% vs 89–93%, respectively; $p = 0.046$). The overall sensitivity of noncathartic CTC for adenomatous polyps ≥ 6 mm was 76% (28/37; 95% CI, 59–88%), which is similar to the sensitivity of the iodinated regimens with most patients (sensitivity: 231 patients, 74% [14/19; 95% CI, 49–91%]; 229 patients, 80% [12/15; 95% CI, 52–96%]). The negative predictive value was 98% (481/490), and the lone cancer was detected (0.2%, 1/556). EC was thought to improve conspicuity of 10 of 21 visible polyps ≥ 10 mm.

CONCLUSION—In this prospective study of asymptomatic subjects, the per-patient sensitivity of noncathartic CTC for detecting adenomas ≥ 6 mm was approximately 76%. Inclusion of oral iodine contrast material improves examination specificity and the percentage of labeled stool. EC may improve polyp conspicuity.

Keywords

bowel preparation; colon cancer screening; CT colonography; patient compliance

Approximately 40% of the U.S. population older than 50 years currently does not undergo colorectal cancer screening, with patients having disparate and individualized reasons for not undergoing cancer screening [1]. Purgation bowel cleansing is a major disincentive to colorectal cancer screening at colonoscopy [2]. CT colonography (CTC) has been endorsed as an accepted method of full structural colorectal cancer screening [3] and may improve colorectal cancer screening rates [4-6] but currently requires a cathartic bowel preparation.

Noncathartic CTC is a promising technique for detecting colorectal neoplasia. We recently performed a multireader study in a polypenriched cohort in which noncathartic CTC showed a sensitivity of more than 90% for large adenomatous polyps [7]. Liedenbaum et al. [8-10] studied minimal cathartic colonography with dietary modification in 302 patients who had positive fecal occult blood test (FOBT) results. In that study in which iodinated tagging and a low-fiber diet were used, the sensitivity using double-read CTC examinations was 82% for polyps ≥ 1 cm, with improved performance if only adenomatous polyps and cancers were considered. Zalis et al. [11] recently evaluated 605 asymptomatic patients with an average to moderate risk for colon cancer with a laxative-free, low-fiber regimen before CTC; their results showed a sensitivity of 91% for patients with adenomatous lesions and cancer ≥ 10 mm and 57% for patients with adenomatous lesions ≥ 6 mm [11].

The purpose of our study was to examine image quality and performance of noncathartic CTC with four similar bowel-tagging regimens using standard noncathartic CTC visualization techniques in an asymptomatic screening cohort.

Subjects and Methods

This prospective HIPAA-compliant study was approved by our institutional review board (IRB); 564 subjects were recruited from patients who had been referred for colonoscopy. Figure 1 summarizes patient recruitment and index and reference tests. The inclusion criteria were a lack of symptoms and being prescheduled for optical colonoscopy. The exclusion criteria were melena, hematochezia, inflammatory bowel disease, familial polyposis, pregnancy, and recent bowel resection for reasons other than colorectal polyp or malignancy in the past 2 months.

There were no dietary modifications before noncathartic CTC other than the ingestion of tagging agents. We used barium sulfate (95% w/v [percentage weight/volume] barium sulfate USP in this study. All subjects ingested 21 g of barium sulfate administered over 2 days before the examination (as shown in Table 1) and an additional 250 mL of 4% barium suspension (Scan C, Mallinckrodt) given the morning of the noncathartic CTC procedure. Based on radiologist feedback regarding the suboptimal quality of stool tagging using barium tagging only, sorbitol was initially added in an attempt to improve the homogeneity of tagged stool. After suboptimal tagging using oral barium and sorbitol in the first 46 subjects, additional agents (diatrizoate meglumine and diatrizoate sodium solution [Gastroview, Mallinckrodt Pharmaceuticals] or iohexol 240 [Omnipaque 240, GE Healthcare]) were added to the oral barium as shown in Table 1, which were also approved by our IRB. The amounts—60 mL of Gastroview and 100 mL of Omnipaque—were chosen so that the same number of grams of iodine was delivered using these two regimens; however, Omnipaque is a low-osmolal iodinated contrast agent that tags fluid and stool in a manner similar to the other agent but has less osmotic pull [12]. The addition of 60 mL of Gastroview resulted in complaints of diarrhea by some subjects, so oral iodine supplementation was switched to Omnipaque.

Noncathartic CTC was performed using an automatic insufflator (PROTOCO₂L, Bracco Diagnostics). CT was performed with the patient in the supine and prone positions on either

a 16-MDCT system (LightSpeed 16, GE Healthcare) or a 64-MDCT system (Sensation 64, Siemens Healthcare) using similar slice thicknesses (1.25 and 1.0 mm, respectively) and analogous parameters to yield similar spatial resolution and scanner radiation output (i.e., volume CT dose index [CTDI_{vol}] per acquisition of 6–7 mGy). Specifically, the 16-MDCT acquisition protocol used a rotation time of 0.5 second, a detector configuration of 16 × 0.625, a pitch of 1.375, 120 kV, and 170 mA. Images were recon reconstructed using a standard reconstruction kernel at a 1.25-mm slice thickness with a reconstruction interval of 0.8 mm. The 64-slice protocol used analogous parameters: a 0.5-second tube rotation time, 32 × 0.6 mm detector configuration with a z-flying focal spot, pitch of 1.4, 120 kV, 100 quality reference mAs, and automatic exposure control (CareDose4D, Siemens Healthcare). Images were reconstructed using a B30 reconstruction kernel, 1-mm slice thickness, and 0.8-mm reconstruction interval.

Electronic cleansing (EC)—that is, stool subtraction algorithms—developed for the diagnostic challenges of noncathartic CTC [13] was performed using an offline computer workstation before radiologist review because a commercial stool subtraction algorithm with the patient in the supine and prone positions for noncathartic CTC does not exist. We used an EC algorithm that is based on quadratic regression of the intensity and gradient values of the pixels and their neighbors and that was implemented with full 3D processing [7]. The EC algorithm classifies partial volume pixels as tissue-air interface, air-stool interface, stool, and tissue [14, 15] and permits locally adaptive regional variations in tagging quality that are seen in noncathartic CTC. EC parameters were not varied over the course of the study. We have previously tested this EC software in a polyp-enriched cohort of 114 patients and 156 adenomatous lesions using three readers [7]. Our results showed that EC improved the sensitivity for detecting adenomas 6–9 mm by 3–28%, with 0–9% improvement for larger polyps, and readers reported moderate-to-severe polyp distortion artifacts in 14% [7].

Optical colonoscopy served as the reference standard for the presence or absence of polyps and was performed within 30 days of noncathartic CTC by staff gastroenterologists (in some cases with trainee involvement) according to a standard clinical protocol including preprocedure bowel purgation cleansing with 4 L of polyethylene glycol–electrolyte solution. Polyp findings were retrospectively obtained from the colonoscopy report (location, number, size) and pathology report (size, histologic subtype). Gastroenterologists performed optical colonoscopy for clinical purposes and were not aware of noncathartic CTC findings. A number of different colonoscopes were available for the study period. Polyp size was estimated by endoscopic comparison of polyp size with open biopsy forceps. Endoscopy withdrawal times were not recorded, and segmental unblinding was not performed.

Assessment of Oral Tagging Image Quality

We performed an assessment of oral tagging image quality because image quality has been found to be associated with false-negative examinations at noncathartic CTC [11]. For image quality assessment of noncathartic CTC regimens, the colorectum was divided into four segments: cecum and ascending colon, transverse colon, descending colon and sigmoid colon, and rectum. For each segment, the percentage of labeled stool was visually estimated. Additionally, residual fluid, the size of the residual stool particles, and colonic distention (i.e., percentage of distention compared with estimated maximal distention: > 90%, 76–90%, 50–75%, < 50%) were examined and compared with a visual chart (Fig. 2). Quality assessment was performed by a radiologic technologist at our institution who double-reads CTC examinations and had completed image quality evaluation training with 50 cases conducted by the unblinded radiologist.

Prospective Image Interpretation

Image interpretation was performed by one of two gastrointestinal radiologists with extensive experience with cathartic CTC (> 500 and > 150 endoscopically confirmed cases, respectively) using commercial colonography software (Advantage Windows 4.2, GE Healthcare). Each case was assigned to one of the radiologists for interpretation on the basis of a randomization scheme provided by the study statisticians. The previously described EC algorithm removed tagged stool and fluid [14, 15], and the subtracted images were imported into the commercial workstation. Each radiologist performed a primary 2D search of the colorectum for suspicious abnormalities and used 3D images for problem solving. The workstation had two monitors: Readers evaluated axial images with EC and without EC on each monitor for each position. The location of each suspicious polyp was recorded (slice number and colon segment) for reference standard correlation. Radiologists were asked to rate their confidence on a scale of 0–5 (0 = not present, 5 = definite) [16]. Radiologists did not record prospectively if polyps were detected on subtracted or unsubtracted images.

Reference Standard Assessment

A third gastrointestinal radiologist (with 15 years of experience with CTC and > 2000 cases) not participating in the prospective blinded interpretations matched the prospective noncathartic CTC detections with reference standard colonoscopy using standard matching rules (i.e., within one colonic segment and 50% estimation of size) [16, 17] and the clinical colonoscopy and histopathology reports.

If a polyp was removed in one piece and placed in a single bottle, the pathology size served as the reference size. If a polyp was removed in pieces or multiple polyps were placed in a single bottle, the size recorded by the endoscopist served as the reference size. For histologic categorization, the pathology report served as the reference. In the unexpected circumstance that multiple polyps were placed in the same bottle and histologic reports stated that adenomatous and hyperplastic fragments were present, all polyps in that bottle were rated as being “mixed adenomatous and hyperplastic.”

The unblinded gastrointestinal radiologist also evaluated noncathartic CTC images of all colonic segments and adjacent neighboring segments in which polyps were identified by reference standard colonoscopy but not the prospective noncathartic CTC interpretation (i.e., false-negative examinations). If the unblinded reader identified a polyp with a high degree of confidence corresponding in location and size to that seen at colonoscopy, the false-negative examination was classified as a perceptual error. The classification of perceptual errors missed by the prospective readers but present on CTC images was based on the 2D and 3D morphology of the polyp, its appearance in supine and prone images, and the unblinded reader’s extensive clinical experience [18, 19]. Otherwise the unidentified polyp was classified as radiographically occult [19]. For eight cases of incomplete colonoscopy, endoscopically assessed segments of the colon were matched to noncathartic CTC findings, but no assessment was performed in colonic segments without endoscopic correlation.

Our study design did not test polyp detection using EC alone. To estimate the potential contribution of EC or artifacts from EC, the unblinded gastrointestinal radiologist who evaluated the appearance of every polyp on 2D images with and without EC used a relative polyp conspicuity score. It is known that artifacts such as incomplete subtraction at air–tagging-agent and air–soft-tissue interfaces can cause luminal artifacts and that erroneous segmentation near mucosal structures can result in polyp and fold erosion [13, 20]. For every endoscopically confirmed polyp identified on noncathartic CTC images, the potential benefit of stool-subtracted images was rated on a 5-point scale to estimate the benefit and artifact resulting from EC (3 = markedly improves conspicuity, potential miss without

subtraction; 2 = polyp visible on unsubtracted images, but conspicuity definitely improves with subtraction; 1 = subtraction images potentially helpful, slightly improved conspicuity on subtracted images; 0 = polyp conspicuity equivalent with or without EC; -1 = polyp conspicuity degraded on subtracted images because of artifact or erosion of edges).

Statistical Analysis

Predefined endpoints for noncathartic CTC performance included adenomatous polyps and cancers ≥ 6 and ≥ 10 mm. Receiver operating characteristic (ROC) curve analysis was used to determine whether there was a difference in performance between readers. Analysis was subsequently performed with pooling of results from both readers on a per-patient basis and areas under the curve (AUCs) were calculated using ROC curve analysis for the entire cohort. We additionally evaluated performance characteristics using a substratified analysis by tagging regimen to compare false-positive rates (i.e., the percentage of false-positive examinations).

For image quality evaluation, descriptive statistics are used. Comparisons of noncathartic CTC image quality were performed using the Kruskal-Wallis test for each colonic segment between oral contrast agents. A p value of less than 0.05 was considered statistically significant. Given the sample sizes, we had sufficient power ($\geq 80\%$) for only very large differences in sensitivities (i.e., $\geq 50\%$). Thus, for sensitivities, we reported estimates and 95% CIs. For specificities, there was 80% power to detect a difference of 8.5% between the regimens based on the current sample size. Statistical analysis was performed using statistics software (SAS, version 9.2, SAS Institute).

Results

Asymptomatic Study Cohort

The study cohort was composed of 564 patients who underwent noncathartic CTC for colorectal cancer screening: 93% (525/564) were patients with an average risk of colorectal cancer, 7% (38/564) had a family history of colorectal neoplasia, and 0.2% (1/564) had a personal history of polyps. There were 235 men (42%) and 329 women (58%), with a median age of 56 years (range, 40–84 years). Most patients were white (91%, 514/564; Asian, 4%, 25/564; African American, 2%, 13/564; Hispanic, 2%, 13/564; Native American, 0.2%, 1/564). Procedure indications for colonoscopy included average-risk screening in most patients ($n = 525$, 93%), a family history of colorectal neoplasia ($n = 38$, 7%), and a personal history of polyps ($n = 1$, 0.2%). Most patients ingested barium capsules plus 30 mL of Gastroview (41%, 231/564) or 100 mL of Omnipaque (41%, 229/564) before noncathartic CTC. A smaller number of patients received barium capsules plus 60 mL of Gastroview (10%, 58/564) or barium capsules with sorbitol (8%, 46/564).

Fifty-four patients (9.7%, 54/564) had at least one polyp ≥ 6 mm and slightly less than 7% (6.7%, 37/564) had an adenoma or cancer ≥ 6 mm. There were one cancer (Fig. 3), eight tubulovillous adenomas, two serrated adenomas, 34 tubular adenomas with low-grade dysplasia, seven mixed adenomas and hyperplastic polyps, and zero tubular adenomas with high-grade dysplasia. There were 27 polyps ≥ 10 mm in 21 patients: 74% were adenomas (20/27) and 26% were nonadenomas (7/27). Sixteen (2.9%) of the patients had either an adenoma ≥ 10 cm or more than two adenomas ≥ 6 mm. There were no complications from noncathartic CTC or reference standard colonoscopy.

Oral Tagging Quality

Figure 4 summarizes the oral tagging quality of the noncathartic CTC examinations. The percentage of labeled stool differed across tagging preparations ($p < 0.001$) and was greater

for oral regimens containing iodine than for those without iodine (93–99% vs 75–84%, respectively; $p = 0.0002$). For residual fluid, sorbitol alone resulted in less fluid compared with 60 mL of Gastroview or 100 mL of Omnipaque ($p < 0.05$ for all comparisons). The use of 60 mL of Gastroview resulted in smaller solid stool particles ($p < 0.02$), likely because of the increased osmotic pull of Gastroview. There were no significant differences in colonic distention between oral tagging regimens.

Noncathartic CTC Performance Estimates

By use of a confidence score of 1 or greater for polyp identification, the per-patient sensitivity for adenomatous polyps or cancer ≥ 6 mm was 76% (28/37; 95% CI, 59–88%). The specificity was 92% (486/527; 95% CI, 90–94%), and the negative predictive value was 98% (481/490; 95% CI, 96–99%). The positive predictive value was 38% (28/74; 95% CI, 27–49%). The AUC for patients with adenomatous polyps ≥ 6 mm was 0.86 ± 0.04 (mean $\pm$ standard error [SE]). The per-polyp sensitivity for adenomas ≥ 6 mm was 60% (31/52; 95% CI, 45–73%).

There were 20 adenomas ≥ 10 mm in 16 patients. All prospectively identified large polyps were assigned a confidence score of 3 or greater. The per-patient sensitivity for the detection of any adenoma ≥ 10 mm was 69% (11/16; 95% CI, 41–89%). The specificity was 97% (533/548; 95% CI, 96–98%), and the negative predictive value was 99% (533/538; 95% CI, 98–99.7%); the AUC was 0.83 ± 0.06 . The per-polyp sensitivity for adenomatous polyps ≥ 10 mm was 65% (13/20; 95% CI, 41–85%). The single cancer was detected (sensitivity, 100%, 1/1; 95% CI, 3–100%).

All eight tubulovillous adenomas were detected by noncathartic CTC: Four polyps were ≥ 10 mm, and four polyps were 6–9 mm. Two small serrated adenomas (6 and 9 mm) were not detected. Consequently, the sensitivity for advanced colorectal neoplasia (i.e., adenoma ≥ 10 mm, villous histology, high-grade dysplasia or cancer) was 65% (17/26; 95% CI, 44–83%).

Stratified assessments of observer performance were also performed for the different oral tagging regimens (Table 2). The specificity of noncathartic CTC for patients without adenomatous polyps was compared between tagging regimens and differed significantly ($p = 0.046$), with the specificity for patients without polyps improving with iodine supplementation (supplemental dose of 30 mL of Gastroview vs barium capsules and sorbitol only, $p = 0.03$; supplemental Omnipaque vs barium capsules and sorbitol only, $p < 0.01$). Our data do not have sufficient power to allow comparison of sensitivities between oral contrast regimens, but the 95% CIs are reported and overlap widely.

There was no significant difference in the AUCs between the two radiologist readers for the detection of adenomatous polyps ≥ 6 mm ($p = 0.28$), 6–9 mm ($p = 0.50$), or ≥ 10 mm ($p = 0.67$) or for the detection of patients with adenomas ≥ 6 or ≥ 10 mm.

Of seven false-negative examinations for adenomatous polyps ≥ 10 cm, four false-negative polyps were perceptual errors and three polyps were radiographically occult. Overall, therefore, 85% (17/20) of the adenomas ≥ 10 mm could be viewed on the noncathartic CTC datasets. Of the adenomas 6–9 mm, 11 of 14 polyps missed at noncathartic CTC were radiographically occult.

Estimated Benefit of Electronic Cleansing

Because our study design tested observer performance with combined review of noncathartic CTC with EC and without EC, a gastrointestinal radiologist retrospectively evaluated the potential effect of EC in the 21 visible polyps ≥ 10 cm (irrespective of histopathology); six polyps of this size were radiographically occult. In nine patients, the

subtraction images were neither beneficial nor harmful because the polyps were seen equally with EC and without EC. EC images were thought to be beneficial in assessing approximately half (10/21) of the visualized polyps (i.e., benefit = 1, $n = 6$; benefit = 2, $n = 3$; benefit = 3, $n = 1$; Fig. 5). In only two patients (10%, 2/21), there was significant erosion of the edges of the polyp that degraded polyp conspicuity. Of the 47 polyps 6–9 mm, 21 were identified prospectively and an additional six were identified on unblinded review. Of these 27 polyps, EC was helpful in seven (26%) and there were detrimental artifacts in three (11%).

Discussion

Noncathartic CTC without dietary modification showed a moderate ability to detect adenomatous polyps ≥ 6 mm, with an AUC of 0.86 ± 0.04 (mean $\pm$ SE) and a per-patient sensitivity and specificity of 76% (95% CI, 59–88%) and 92% (95% CI, 90–94%), respectively, and showed similar performance for detecting adenomatous polyps ≥ 10 mm. The solitary cancer was identified. We found that additional iodine supplementation significantly improves both the percentage of labeled stool at image quality assessment and reader specificity in identifying colorectal polyps at noncathartic CTC.

Our study differs from other studies of noncathartic CTC [8–10] in several respects. Our study was performed in an asymptomatic screening cohort with predominantly average risk and a prevalence of adenomas ≥ 6 mm and cancers of only 7% and 0.18%, respectively, similar to prior screening studies [21]. In contrast, the prevalence of adenomatous polyps and cancer in the FOBT-positive cohort used for a study by Liedenbaum et al. [10] was nearly 10 times higher (7% with a cancer and 45% with a large adenoma). Jensch et al. [22] examined a cohort with a prevalence of 33% for subjects with adenomas ≥ 6 mm, and Johnson et al. [7] examined a polyp-enriched cohort. Zalis et al. [11] also examined an asymptomatic screening cohort as we did, but the prevalence of adenomas ≥ 6 mm was nearly twice as high in their study (12%), potentially because of a larger number of moderate-risk subjects. Nonetheless, our results are similar to those of Zalis et al. [11] for the detection of patients with adenomatous lesions ≥ 6 mm (AUC, 0.86 ± 0.04 vs 0.80 ± 0.03 , respectively) but are slightly less for patients with larger lesions (AUC, 0.83 ± 0.06 vs 0.94 ± 0.02). Observer performance may fall in a screening cohort with a low prevalence of disease, potentially because of a loss of reader vigilance [23, 24]. Additionally, Liedenbaum et al. [10] performed double-readings of noncathartic CTC examinations in contradistinction to our single read. We have shown previously that doublereading improves performance for noncathartic CTC interpretation [16, 24]. Finally, unlike these other noncathartic CTC studies, we did not use a low-fiber diet in combination with fecal tagging because of our preliminary assessment of test performance and the potential advantage in terms of patient acceptance [2, 7, 25].

Noncathartic CTC images are complex and present interpretive challenges owing to the greater number of air-stool interfaces and increased partial volume averaging [20]. We found electronic stool subtraction helpful in increasing the conspicuity of nearly half of the visualized polyps ≥ 10 mm, but we also found that EC caused artifacts in a minority of patients that precluded reliance on EC images alone. These findings are similar to those observed by Johnson et al. [7] and reported by Cai et al. [20, 26]. When polyps are not juxtaposed next to tagged stool or fluid, little benefit from using EC is expected. Another approach to this interpretive difficulty is to identify potential polyp candidates for visual assessment using computer-assisted detection (CAD) modified for the noncathartic colorectum [27]. Because more small polyps were radiographically occult at noncathartic CTC, double-reading, electronic stool subtraction, and noncathartic CTC CAD would likely preferentially improve the performance of noncathartic CTC for large polyps. These aids

may be beneficial in identifying approximately half of the missed large polyps that could be detected in retrospect on noncathartic CTC images.

Noncathartic CTC likely has a potential role in colorectal cancer detection. Our results and those of Zalis et al. [11] show that the anticipated upper limit of performance for that technique is similar to that of bowel purgation CTC [17, 28]. Although our study does not directly address who would benefit from noncathartic CTC, others have suggested that it may be an important option for polyp detection in higher-risk patients who are frail or in those unwilling to undergo an alternative full structural evaluation of the colorectum. The selection of older patients is reinforced by the improved radiologic conspicuity of the large (over small) polyps in our cohort. Iafrate et al. [29] implemented noncathartic CTC after incomplete colonoscopy in patients older than 70 years old and found noncathartic CTC to be a safe and technically successful procedure. Keeling et al. [30] evaluated noncathartic CTC with a low-fiber diet in frail elderly patients with diminished performance status and reached similar conclusions. When noncathartic CTC is performed in these settings, iodine tagging, likely supplemented by dietary restriction to a low-fiber diet, should be used and double-reading by two experienced CTC readers appears to be warranted. The addition of sorbitol and oral iodine to oral barium may cause loose stools in some patients, and this potential should be explained to patients before the procedure. In a large populationbased randomized cohort trial evaluating the diagnostic yield of laxative-free CTC versus colonoscopy, participation in screening using noncathartic CTC was significantly better than participation in screening using colonoscopy and the diagnostic yield of identifying advanced neoplasia was similar [6].

Our study has several limitations. The most important one is that we varied the oral tagging regimen over the course of the study because of radiologists' complaints of untagged residual stool (barium and sorbitol preparation) and patient complaints of loose bowel movements (barium and 60 mL of Gastroview preparation). These changes were necessary because preliminary observations of image quality in a polyp-enriched cohort [7] did not hold in our asymptomatic cohort. Zalis et al. [11] also found that nearly three quarters of false-negative examinations occurred in patients with suboptimal oral tagging image quality. Nevertheless, a substratified analysis showed there was no difference in polyp detection between the techniques. Additionally, two of the four tagging regimens (i.e., barium with 30 mL of Gastroview or barium with 100 mL of Omnipaque) were used in more than 200 asymptomatic subjects (Table 2), showed similar test performance, and would have been substantial studies in their own right. Third, because subjects were recruited at three sites and studies were interpreted by one of two readers (potentially in different cities) by randomized assignment, noncathartic CTC interpretation could not be performed before reference colonoscopy, precluding segmental unblinding [17]. Although different CT systems were used for noncathartic CTC examinations, the resulting spatial resolution of the examinations was similar and is in line with the specifications of the National Colonography Study and American College of Radiology's white paper on colonography [31]. A double-reading using a consensus paradigm would likely have improved performance [10] but was not practical because of cost constraints; we had experienced readers with excellent track records at bowel-cleansed CTC and promising data using noncathartic CTC in enriched cohorts.

Additionally, there are inherent difficulties comparing polyp sizes and histologies between colonoscopic findings and CTC [32]. Our size-matching rules and assignment of "mixed hyperplastic and adenomatous" histology when an adenomatous polyp fragment was identified in the exceptional circumstance when multiple polyps were placed in the same bottle may have influenced our results. Most polyps were placed in single bottles for histologic analysis. Four patients had six "mixed adenomatous or hyperplastic" polyps (two

polyps 10 cm; four polyps, 6–9 mm), with two subcentimeter polyps (7 and 8 mm) in this histologic category being identified by the prospective readers (and the other polyps being missed). The effect of treating polyps placed in the same bottle is consequently believed to be small and to not alter study conclusions. Our study design did not test the contribution of EC separately from the unsubtracted tagged images alone. Other stool subtraction methods for noncathartic colonography have been described [20], but we cannot compare those methods to the locally adaptive approach we used.

In conclusion, noncathartic CTC in an asymptomatic screening population performed with an estimated sensitivity for neoplasia that was slightly less than previously reported in symptomatic populations with a higher prevalence of disease and was not as high as CTC after bowel purgation cleansing in similar populations. Including iodine tagging agents substantially improves tagging of particulate stool and examination specificity. Additional improvements in performance might be realized by further refinements in electronic stool subtraction, double-reading, dietary restriction to low-fiber foods before examination, and development of CAD for the minimally prepared colorectum. Noncathartic CTC may be a useful tool for the detection of colorectal cancer and polyps in a limited role, particularly in frail patients in whom bowel purgation cleansing is extremely difficult or in those unwilling to undergo or intolerant of bowel preparation.

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Fig. 1.

Flowchart shows summary of study recruitment and index and reference standard tests. CTC = CT colonography, IBD = inflammatory bowel disease.

Residual Fluid		Residual Stool		Distention	
0 = No fluid		0 = No stool		1 = > 90%
1 = Mild < 1/3 of lumen		1 = Mild Could miss polyp < 5 mm		2 = > 75–90%
2 = Moderate 1/3 lumen Both prone and supine		2 = Moderate Could miss polyp 5.9 mm		3 = 50–75%
3 = Nondiagnostic: > 1/3 lumen Both prone and supine		3 = Nondiagnostic Could miss polyps ≥ 10 mm		4 = < 50%

Fig. 2.

Chart used to assess oral tagging image quality rank according to amount of residual fluid, size of residual stool particles, and colonic distention.

Fig. 3.
54-year-old woman.
A–D, Supine (**A** and **B**) and prone (**C** and **D**) CT colonography (CTC) images show 1.1-cm sigmoid adenocarcinoma arising in tubular adenoma (*arrows*) that was prospectively identified at noncathartic CTC before endoscopy. **B** and **D** show results after electronic stool subtraction.

Fig. 4.

Noncathartic CT colonography (CTC) image quality. (Gastroview [diatrizoate meglumine and diatrizoate sodium solution] is manufactured by Mallinckrodt Pharmaceuticals and Omnipaque, [iohexol] is manufactured by GE Healthcare).

A, Bar graph shows mean percentage of labeled stool by colonic segment for each noncathartic CTC oral tagging regimen. Percentage of labeled stool differed across tagging preparations ($p < 0.001$) and was greater for oral regimens containing iodine than for those without iodine (93–99% vs 75–84%, respectively; $p = 0.0002$).

B, Bar graph shows mean colonic distention, amount of residual colonic fluid, and size of residual particulate stool by colonic segment for each noncathartic CTC oral tagging regimen. Image quality ranks are provided in Figure 2. For residual fluid, sorbitol alone resulted in less fluid compared with 60 mL of Gastroview or 100 mL of Omnipaque ($p < 0.05$ for all comparisons). Use of 60 mL of Gastroview resulted in smaller solid stool particles ($p < 0.02$), likely because of increased osmotic pull of Gastroview. There were no significant differences in patterns of residual stool or colonic distention between oral tagging regimens.

Fig. 5.
57-year-old woman.
A–D, Coronal supine (**A** and **B**) and prone (**C** and **D**) noncathartic CT colonography (CTC) images without (**A** and **C**) and with (**B** and **D**) electronic stool subtraction show prospectively identified 2.6-cm sessile tubular adenoma (*arrows*) straddling haustral fold in ascending colon. Electronic stool subtraction (**B** and **D**) was thought to be potentially helpful.

TABLE 1

Tagging Regimens Used for Noncathartic CT Colonography (CTC)

Tagging Regimen	2 Days Before CTC	1 Day Before CTC	Day of CTC
Barium and sorbitol (<i>n</i> = 46)	2.28 g of BaSO ₄ and 30 mL of 70% sorbitol at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 30 mL of 70% sorbitol at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 250 mL of 2.1% BaSO ₄ suspension in the morning
Barium and 30 mL of Gastroview ^a (<i>n</i> = 231)	2.28 g of BaSO ₄ at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 10 mL of Gastroview at breakfast, lunch, dinner; 2.28 g of BaSO ₄ at bedtime	2.28 g of BaSO ₄ and 250 mL of 2.1% BaSO ₄ suspension in the morning
Barium and 60 mL of Gastroview ^a (<i>n</i> = 58)	2.28 g of BaSO ₄ at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 20 mL of Gastroview at breakfast, lunch, dinner; 2.28 g of BaSO ₄ at bedtime	2.28 g of BaSO ₄ and 250 mL of 2.1% BaSO ₄ suspension in the morning
Barium and Omnipaque 240 ^b (<i>n</i> = 229)	2.28 g of BaSO ₄ at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 25 mL of 240 Omnipaque at breakfast, lunch, dinner, and bedtime	2.28 g of BaSO ₄ and 250 mL of 2.1% BaSO ₄ suspension in the morning

Note—Patients had no dietary modification. Boldface shows agents that are unique to one specific regimen.

^a Diatrizoate meglumine and diatrizoate sodium. Gastroview is manufactured by Mallinckrodt Pharmaceuticals.

^b Iohexol 240 mg I/mL. Omnipaque 240 is manufactured by GE Healthcare.

TABLE 2
Noncathartic CT Colonography (CTC) Performance for Detecting Patients With Adenomatous Polyps 6 mm by Fecal Tagging Regimen

Tagging Regimen	Sensitivity		Specificity ^a		Positive Predictive Value		Negative Predictive Value	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Barium and sorbitol (<i>n</i> = 46)	100 (1/1)	3–100	80 (36/45)	65–90	10 (1/10)	3–45	100 (36/36)	90–100
Barium and 30 mL of Gastroview ^b (<i>n</i> = 231)	74 (14/19)	49–91	92 (195/212)	87–95	45 (14/31)	27–64	98 (195/200)	94–99
Barium and 60 mL of Gastroview ^b (<i>n</i> = 58)	50 (1/2)	1–99	89 (50/56)	78–96	14 (1/7)	4–58	98 (50/51)	90–100
Barium and 100 mL of Omnipaque 240 ^c (<i>n</i> = 229)	80 (12/15)	52–96	93 (200/214)	89–96	46 (12/26)	27–67	99 (200/203)	96–100

Note—Raw data are shown in parentheses.

^aThe overall test for differences in estimates among the four fecal tagging regimens was significant (*p* = 0.046). Significant pairwise comparisons included barium capsules and sorbitol versus barium capsules and 30 mL of Gastroview (*p* = 0.03) and barium capsules and sorbitol versus barium capsules and 100 mL of Omnipaque 240 (*p* < 0.01).

^bDiatrizoate meglumine and diatrizoate sodium. Gastroview is manufactured by Mallinckrodt Pharmaceuticals.

^cIohexol 240 mg I/mL. Omnipaque 240 is manufactured by GE Healthcare.