Computed Tomographic Colonography Compared With Colonoscopy in Patients at Increased Risk for Colorectal Cancer

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Background & Aims: To date, computed tomographic (CT) colonography has been compared with an imperfect test, colonoscopy, and has been mainly assessed in patients with positive screening test results or symptoms. Therefore, the available data may not apply to screening of patients with a personal or family history of colorectal polyps or cancer (increased risk). We prospectively investigated the ability of CT colonography to identify individuals with large (≥10 mm) colorectal polyps in consecutive patients at increased risk for colorectal cancer. *Methods:* A total of 249 consecutive patients at increased risk for colorectal cancer underwent CT colonography before colonoscopy. Two reviewers interpreted CT colonography examinations independently. Sensitivity, specificity, and predictive values were determined after meticulous matching of CT colonography with colonoscopy. Unexplained large false-positive findings were verified with a second-look colonoscopy. *Results:* In total, 31 patients (12%) had 48 large polyps at colonoscopy. This included 8 patients with 8 large polyps that were overlooked initially and detected at the second-look colonoscopy. In 6 of 8 patients, the missed polyp was the only large lesion. With CT colonography, 84% of patients (26/31) with large polyp(s) were identified, paired for a specificity of 92% (200–201/218). Positive and negative predictive values were 59%–60% (26/43–44) and 98% (200–201/205–206), respectively. CT colonography detected 75%–77% (36–37/48) of large polyps, with 9 of the missed lesions being flat. *Conclusions:* CT colonography and colonoscopy have a similar ability to identify individuals with large polyps in patients at increased risk for colorectal cancer. The large proportion of missed flat lesions warrants further study.

Colorectal cancer is the second leading cause of cancer-related mortality in the United States, with an estimated 56,600 deaths in 2002.[1] There is compelling evidence that early diagnosis and treatment of colorectal adenomas and cancer reduces the disease-specific mortal-ity.[2] Patients with a personal or family history of colorectal adenomas or cancer are well known to be at increased risk for colorectal cancer, and many organizations recommend colonoscopic screening of these patients[3]; however, even in these groups, use of colorectal screening varies widely.[4–6]

Colonoscopy is the preferred investigation for patients with a personal or family history of colorectal polyps or cancer. The disadvantages of colonoscopy are the attendant discomfort, a reason that is frequently mentioned to decline screening,[7] and the small but definite risk for complications.[8] Ideally, its use should be targeted at patients with polyps who are preselected by means of a less invasive test.

Early studies have shown that computed tomographic (CT) colonography accurately detects colorectal polyps ≥10 mm.[9–12] However, the existing data may not apply to practice for 2 reasons. First, these studies compared CT colonography with an imperfect gold standard, colonoscopy.[9–11] Because this test is known to occasionally miss large polyps,[13,14] the existing reports may underestimate the accuracy of CT colonography. Second, because previous studies partly comprised patients with positive screening test results and patients who were primarily examined for evaluation of symptoms,[9–12] these results may not apply to patients who are screened because of a personal or family history of colorectal polyps or cancer.

To gain insight into the potential of CT colonography to serve for screening of patients with a personal or family history of colorectal polyps or cancer (increased risk), we assessed the ability to identify patients with large polyps (≥10 mm) and performed a second-look

colonoscopy to verify large unexplained false-positive findings. Our secondary aims were to investigate the accuracy to detect individual polyps and to determine interobserver agreement.

Materials and Methods

Patients and Setting

Patients who were scheduled to undergo a colonoscopy because of a personal or family history of colorectal polyps or cancer (increased risk) at the endoscopy departments of the Academic Medical Center and Slotervaart Hospital were included between October 29, 2000, and September 25, 2002. Exclusion criteria were as follows: age younger than 18 years, impossibility to understand patient information/informed consent or refusal to sign the latter, colorectal polyps or cancer diagnosed during recent examination of the colon, or colostomy after colorectal surgery. The medical ethics committees of the Academic Medical Center and Slotervaart Hospital approved the study, and all patients provided written informed consent.

Diagnostic Procedures

Patients underwent CT colonography and, approximately 1 hour later, colonoscopy.

Bowel preparation. Patients ingested 4–6 L of polyethylene glycol electrolyte solution (KleanPrep; Helsinn Birex Pharmaceuticals, Dublin, Ireland) for bowel preparation on the day before and/or the day of the examinations.

CT colonography. A balloon-tipped rectal enema tube was inserted, and subsequently the balloon was filled with approximately 50 mL of water. A total of 20 mg butyl scopolamine bromide (Buscopan, Ingelheim, Germany) or 1 mg glucagon hydrochloride (Glucagen; Novo-Nordisk A/S, Bagsvaerd, Denmark) was administered intravenously. To distend the colon, approximately 2 L of air (13.4 volume % carbon dioxide) was insufflated manually. To prevent air leakage from the anus, the balloon-tipped rectal enema tube was left in situ during scanning. Before a patient was scanned, a preview image was obtained to estimate the distention; if necessary, additional air was insufflated. CT scans were performed with patients in the supine and prone positions, each during a breath hold of approximately 22 seconds. The scans were performed with an Mx8000 multislice CT scanner (Philips Medical Systems, Best, The Netherlands) with the following scan parameters: 120 kV; collimation, 4 × 2.5 mm; rotation time, 0.75 seconds; pitch, 1.25; slice thickness, 3.2 mm; reconstruction interval, 1.6 mm; and reconstruction filter C. The first 30 patients were scanned with an effective mAs value of 100 mAs; however, during the course of the study, reports showed that a substantial reduction in the dose of radiation did not impair sensitivity and specificity,[15] so we reduced the effective mAs. Because the image noise is related to the dimensions of the patient, we adjusted the effective mAs to the circumference of the patient, as measured midway between the lowest rib and the iliac crest. Thin patients

(≤87.5 cm) were scanned with 25 mAs, medium-sized patients (>87.5 cm and ≤102.5 cm) with 40 mAs, and large patients (>102.5 cm) with 70 mAs. CT colonography was performed by a research fellow or a specially trained technician, both with extensive experience with the procedure.

Evaluation of CT colonography data. One experienced abdominal radiologist (reviewer 1, CYN) and 1 research fellow (reviewer 2, JF), who both had evaluated more than 50 cases before the start of the study, scored all CT colonography data blinded for the colonoscopy results. Analysis was performed by using a 3-dimensional display mode, and additional 2-dimensional displays were used for further inspection of suspected lesions. The 3-dimensional display method that is used is described in detail elsewhere.[16]

Lesions were measured, and a certainty was assigned (0%, no polyp; 25%, probably no polyp; 50%, possibly a polyp; 75%, probably a polyp; 100%, certainly a polyp). Interpretation time was recorded with a stopwatch.

Colonoscopy. Patients underwent colonoscopy with a standard colonoscope (CF-140L; Olympus, Tokyo, Japan) at the Endoscopy Departments of the Academic Medical Center or Slotervaart Hospital. During this procedure, patients received sedatives (midazolam; Roche, Basel, Switzerland) and analgesics (fentanyl; Janssen Pharmaceuticals, Beerse, Belgium) on request. Colonoscopy was performed by an experienced staff member alone (gastroenterologist or gastrointestinal surgeon) in 47% of cases and by a gastroenterology fellow under direct supervision of the attending gastroenterologist in 53% of cases. A research fellow recorded the examination on videotape. During the colonoscopy, the endoscopist scored polyps, if present, with respect to size, morphology (pedunculated, sessile, flat), and the segment (cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum) in which they were located. The estimation of polyp size was based on a comparison of the polyp with an open biopsy forceps of known size (8 mm). The morphology of polyps was classified as pedunculated when a stalk was present. A polyp was considered flat if its height was less than one half the diameter of the lesion.[17] In our data, these flat lesions were generally <4 mm. The remainder of polyps was classified as sessile.

The information regarding size, morphology, and segmental location of polyps was filled out on a case record form by the endoscopist who performed the examination and the research fellow who attended the colonoscopy.

Determination of lesion status. The research fellow (RVG) matched CT colonographic and colonoscopic findings (reference standard). For this purpose, we used a face-to-face comparison of the videotaped colonoscopy with the CT colonography images and used the aforementioned case record form. A polyp detected at CT colonography was labeled as a true positive based on 3 criteria: (1) the segmental location of the CT colonographic finding corresponded with the segmental location as indicated on the case record form or the adjacent segment, (2) the polyp size as estimated by the endoscopist corresponded with the CT colonography measurement, and (3)

its appearance closely resembled that of the corresponding polyp at the videotaped colonoscopy.

Because the estimation of polyp size at colonoscopy is prone to error, we accepted a margin of error of 3 mm for polyps <6 mm and 5 mm for polyps ≥6 mm. Only CT colonography lesions that were scored with a certainty of 50% or more were considered for analysis.

False-positive findings ≥10 mm. After all CT colonography examinations had been reviewed and matched, the research fellow (R.E.V.) and a senior gastroenterologist (J.F.B.) scrutinized the nature of false-positive findings ≥10 mm, as measured by at least 1 of the reviewers. This was done by means of review of the videotaped colonoscopy and the CT scan. If the cause of the false-positive finding could not be attributed to residual stool, haustral folds, impression of organs, or normal variations of the ileocecal valve, the patient was scheduled for a second-look colonoscopy based on detailed information of CT colonography. If the surmised polyp was present at the second-look colonoscopy, this finding was added to the colonoscopic results and taken into account for the determination of the diagnostic value of CT colonography.

Detection parameters. The potential future role of CT colonography is to preselect patients with polyps who might benefit from further endoscopic diagnostic and therapeutic procedures. Therefore, our main outcome parameter was patient sensitivity, indicating the ability of CT colonography to identify patients with at least one clinically relevant polyp.

Although some advocate the removal of polyps ≥10 mm only,[18] clinicians and patients are unlikely to accept that lesions between 6 and 9 mm remain undetected.[19] Therefore, we used the 6-mm cutoff value in addition to the 10-mm threshold. The endoscopist's measurements of polyp size were used for subdivision of polyps according to size thresholds and categories.

Patient sensitivity was defined as the proportion of patients with at least one true-positive lesion out of all patients with polyps at colonoscopy. For the 6-mm and 10-mm thresholds, findings were considered to be true positive if at least one polyp in the respective size range was detected and false negative when no true-positive polyps or only those of a lower size category were detected.

Patient specificity was defined as the proportion of patients without false-positive findings out of all patients without polyps at colonoscopy. For the 6-mm and 10-mm thresholds, findings were considered true negative if patients without polyps ≥6 mm or ≥10 mm had no false-positive findings ≥6 mm and ≥10 mm, respectively.

Polyp sensitivity was defined as the proportion of true-positive polyps out of all polyps detected during colonoscopy. Polyp sensitivity was analyzed according to polyp size categories (<6 mm, small; 6–9 mm, medium; ≥10 mm, large) and morphology (pedunculated, sessile, flat). Additionally, adenoma sensitivity was determined based on the pathology reports.

Predictive values. The positive predictive value was defined as the proportion of patients with a true-positive finding out of all patients with findings at CT colonography. The negative predictive value was defined as the proportion of patients with a true-negative finding out of all patients without findings at CT colonography. Also, the positive predictive value was determined per polyp, which was defined as the proportion of true-positive polyps out of all findings at CT colonography. These outcome parameters were analyzed according to the aforementioned size categories.

Interobserver agreement. Interobserver agreement analysis was performed by segment. Reviewers were considered to agree if they both recorded one or more lesions in the same segment or if both recorded no findings. κ statistics with 95% confidence intervals were calculated. The κ values were interpreted as follows: κ < 0.20, poor agreement; κ = 0.21–0.40, fair; κ = 0.41–0.60, moderate; κ = 0.61–0.80, good; κ = 0.81–1.00, very good.

Results

Baseline Characteristics of the Subjects

A total of 288 patients participated in this study. Bowel preparation was insufficient in 12 patients (4%), preventing CT colonographic and colonoscopic evaluation. In 20 patients (7%), CT colonography was inadequate because of unsatisfactory bowel insufflation (8 [3%]), severe breathing artifacts (3 [1%]), artifacts due to spondylodesis (2 [1%]), and technical problems during scanning (7 [2%]). Colonoscopy failed to reach the cecum in 5 patients (2%). Three other patients (1%) did not show up. The data from patients with failed bowel preparation or examinations or who did not show up (39 [14%]) were not analyzed, leaving 249 patients. Because both bowel preparation and CT colonography were not adequate in 1 patient, data from 39 instead of 40 patients were not analyzed.

Of these 249 patients, 20 (8%) had a history of mild abdominal symptoms: 8 had mild abdominal pain, 2 had hematochezia, and 10 had altered bowel habits.

A total of 103 (41%) of the 249 patients were women. The mean age was 56 years (SD, 13). Ninety-one patients (36%) underwent colonoscopy for screening because of a family history of colorectal polyps or cancer and 158 patients (64%) for surveillance because of a history of colorectal polyps or cancer. For the patients who were examined because of a history of colorectal polyps or cancer, a median interval of 25 months (interquartile range, 14–37 months) had elapsed since their previous surveillance colonoscopy.

Colonoscopic Results

The median colonoscopy examination time, consisting of insertion and inspection, was 30 minutes 0

Table 1. Patient Sensitivity and Specificity of CT Colonography

	Colonoscopy (n)	Reviewer 1 n (%)	95% Confidence interval (%)	Reviewer 2 n (%)	95% Confidence interval (%)
Sensitivity					
Patients with polyps					
Of any size	141	87 (62)	54–69	88 (62)	54–70
≥6 mm	45	34 (76)	61–86	36 (80)	66–89
≥10 mm	31 (25 + 6)[a]	26 (84)	67–93	26 (84)	67–93
Specificity					
Patients without polyps					
Of any size	108	34 (32)	24–41	32 (30)	22–39
≥6 mm	204	144 (71)	64–76	140 (69)	61–74
≥10 mm	218 (224 − 6)[b]	200 (92)	87–95	201 (92)	88–95

NOTE. The displayed data of colonoscopy are combined findings of initial and second-look colonoscopy. For patients with and without large polyps, the results of the initial and second-look colonoscopy are specified in parentheses.
[a]Twenty-five patients were identified at the initial colonoscopy and 6 at the second-look colonoscopy.
[b]After the second-look colonoscopy, the number of patients without polyps ≥10 mm decreased by 6.

seconds (interquartile range, 21 minutes 0 seconds to 49 minutes 30 seconds).

For the initial and second-look colonoscopy combined, 141 of 249 patients (57%) had 489 polyps, 45 patients (18%) had 84 polyps ≥6 mm, and 31 patients (12%) had 48 polyps ≥10 mm. Included in these data are 8 large polyps that were found in 8 patients during second-look colonoscopies to verify a large false-positive finding at CT colonography. In 6 of these 8 patients, no large polyp was seen at the initial colonoscopy. The other 2 patients also had another large polyp. Another second-look colonoscopy was performed to verify a large false-positive finding at CT colonography, which appeared to be an ileocecal valve. The mean interval between the initial and second-look colonoscopy was 13 months (SD, 7).

Histopathology specimens were obtained in 270 (66%) of 407 small polyps, 33 (92%) of 36 medium polyps, and 40 (83%) of 48 large polyps. Of all small polyps, 96 (24%) were adenomatous. Of all medium polyps, 15 (42%) were adenomatous and none were malignant. Of all large lesions, 23 (48%) were adenomatous and 4 (8%) were cancers. These 4 cancers were diagnosed in 4 patients (1.6%). The histopathologic diagnoses of the polyps that were overlooked by initial colonoscopy were lipoma in 1, hyperplasia in 1, adenoma in 3, and cancer in 1. One polyp with an adenomatous appearance was lost after polypectomy, and one polyp with a pale hyperplastic appearance could not be removed due to its difficult location (behind the ileocecal valve).

CT Colonography

The median examination room time was 21 minutes 30 seconds (interquartile range, 18 minutes 40 seconds to 26 minutes 58 seconds), and the median

evaluation time was 14 minutes 12 seconds (interquartile range, 10 minutes 58 seconds to 17 minutes 26 seconds) for reviewer 1 and 13 minutes 26 seconds (interquartile range, 11 minutes 6 seconds to 16 minutes 24 seconds) for reviewer 2.

Patient sensitivity and specificity. Table 1 shows the sensitivity and specificity per patient for both reviewers. The mean sensitivity for patients with at least 1 large polyp was 84%. For patients with at least 1 polyp ≥6 mm or with a polyp of any size, these mean values were 78% and 62%, respectively.

The mean specificity for the identification of patients without large polyps was 92%. The mean specificity for patients without polyps ≥6 mm and without any polyp was 70% and 31%, respectively.

Polyp sensitivity. Table 2 shows the polyp sensitivity for both reviewers. The mean polyp sensitivity for large polyps was 76%. For medium and small polyps, these values were 70% and 35%, respectively. Stratified according to lesion morphology, the mean sensitivity was only 33% and 14% for large and medium flat polyps, respectively. However, the mean sensitivity was 95% and 81% for large and medium sessile polyps and 92% and 92% for large and medium pedunculated polyps, respectively. For large and medium adenomas, the mean sensitivity was 78% and 77%, respectively (Table 3).

Predictive values. Tables 4 and 5 show the number of true-positive and false-positive findings, the true-negative and false-negative findings, and the resulting predictive values. As a result of the large number of false-positive findings, the mean positive predictive values for the identification of patients with polyps ≥10 mm and ≥6 mm were low (60% and 36%, respectively). Mean positive predictive values per polyp were 61% and 17% for large and medium-sized polyps, respectively.

Table 2. Polyp Sensitivity According to Morphology

Morphology	Polyp size (*mm*)	Colonoscopy (n)	Reviewer 1 n (%)	95% Confidence interval (%)	Reviewer 2 n (%)	95% Confidence interval (%)
All	<6	405	149 (37)	32–42	132 (33)	28–37
	6–9	36	23 (64)	48–78	27 (75)	59–86
	≥10	48 (40 + 8)[a]	36 (75)	61–85	37 (77)	64–87
Sessile	<6	306	126 (41)	36–47	110 (36)	31–42
	6–9	23	17 (74)	54–88	20 (87)	68–96
	≥10	21 (17 + 4)[a]	20 (95)	77–99	20 (95)	77–99
Pedunculated	<6	11	5 (45)	21–72	8 (73)	43–90
	6–9	6	5 (83)	54–88	6 (100)	61–100
	≥10	13 (12 + 1)[a]	12 (92)	67–99	12 (92)	67–99
Flat	<6	88	18 (20)	13–30	14 (16)	10–25
	6–9	7	1 (14)	3–51	1 (14)	3–51
	≥10	14 (11 + 3)[a]	4 (29)	12–55	5 (36)	16–61

[a]Polyps detected at initial colonoscopy + polyps detected at second-look colonoscopy.

Mean negative predictive values for patients without polyps ≥10 mm and ≥6 mm were 98% and 94%, respectively.

Analysis of false-positive findings. Reviewers 1 and 2 had 25 and 22 large false-positive findings, respectively. Based on the videotaped colonoscopy and review of the CT scans, we concluded that 22 and 10 of these false-positive findings were caused by residual stool for reviewers 1 and 2, respectively. One and 5 large false-positive findings were caused by protruding folds in suboptimally distended segments for reviewers 1 and 2, respectively. Two colonic varices caused 2 false-positive results for reviewer 1. Reviewer 2 erroneously interpreted the ileocecal valve to be abnormal in 5 cases. A splenic impression in the proximal descending colon caused another false-positive finding for reviewer 2. One false-positive finding by reviewer 2 could not be explained but, because the patient died of lung cancer during the course of the study, a second-look colonoscopy could not be performed. Nevertheless, retrospective evaluation of the videotaped colonoscopy raised the suspicion that it concerned a colonoscopically missed flat lesion.

Interobserver analysis. Interobserver agreement with regard to the correspondence of segment judgments was good (κ = 0.70; 95% confidence interval, 0.66–0.74).

Discussion

Although colonoscopy is highly effective in the diagnosis and treatment of colorectal polyps, it is asso-

ciated with a small but definite risk for complications due to its invasive nature. Hence, colonoscopy may preferably be targeted at preselected patients with polyps. For CT colonography to be valuable in this respect, its accuracy must be similar to colonoscopy. The present study indicates that CT colonography and colonoscopy have a similar ability to identify patients with large polyps in a population with a personal or family history of colorectal polyps or cancer. If patients with large polyps were to be selected for colonoscopy based on CT colonography, 82%–83% (205–206/249) of patients would not have to undergo colonoscopy, whereas 5 (16%) of 31 patients with large polyps were overlooked. By comparison, 6 patients (19%) with large polyps were initially overlooked by colonoscopy in the present study.

We compared CT colonography with colonoscopy, the present gold standard for the detection of colorectal polyps. Studies of back-to-back colonoscopy vary with regard to the proportion of missed large polyps (0–6%).[13,14] In the present study, 8 (17%) of 48 large polyps were overlooked with colonoscopy, which is rather high compared with these previous reports. Actually, the miss rate of colonoscopy may be higher than previously reported, because the reference test (a second colonoscopy) had the same limitations (e.g., haustral folds, flexures) as the index test. This assumption is supported by a recent study on CT colonography by Pickhardt et al.,[20] in which colonoscopic miss rates for large polyps were also generally higher (11.8%) than previously observed.

Table 3. Sensitivity for Adenomatous Polyps

Adenomatous lesions according to size (*mm*)	Colonoscopy (*n*)	Reviewer 1 n (%)	95% Confidence interval (%)	Reviewer 2 n (%)	95% Confidence interval (%)
<6	96	40 (42)	32–52	38 (40)	30–50
6–9	15	11 (73)	48–89	12 (80)	55–93
≥10	27 (23 + 4)[a]	21 (78)	59–89	21 (78)	59–89

[a]Polyps detected at initial colonoscopy + polyps detected at second-look colonoscopy.

Table 4. Positive Predictive Values

Findings according to size	Reviewer 1				Reviewer 2			
	TP	FP	PPV %	95% CI	TP	FP	PPV %	95% CI
Per patient								
All	87	74	54	46–62	88	76	54	46–61
≥6 mm	34	60	36	27–46	36	64	36	27–46
≥10 mm	26	18	59	44–72	26	17	61	46–74
Per polyp (mm)								
<6	149	411	27	23–30	132	490	21	18–25
6–9	23	129	15	10–22	27	114	19	14–26
≥10	36	25	59	47–71	37	22	63	50–74

TP, true positives; FP, false positives; PPV, positive predictive value; CI, confidence interval.

As in common academic practice, gastroenterology fellows were involved in almost one half of the colonoscopies, which may have contributed to the relatively high miss rate. Because the technical success of colonoscopy in our study was excellent (98% cecal intubation) and colonoscopic inspection was performed by both the gastroenterology fellow and the gastroenterologist, it is unlikely that our colonoscopy sensitivity is lower than in routine clinical practice. Although 7 of 8 colonoscopies during which a large polyp was missed were performed by a gastroenterology fellow under direct supervision of the attending gastroenterologist, 3 of 7 fellows were experienced (≥500 colorectal endoscopic procedures).

Almost all sessile and pedunculated polyps ≥6 mm were detected with CT colonography in the present study. However, flat lesions were an important source of false negative results with CT colonography, which is in line with data from a previous study.[21] Of the 10 flat lesions that were missed with CT colonography, 3 were adenomas and one was a cancer. In retrospect, 5 of 10 missed flat lesions could be identified in the CT colonography images, among which were one adenomatous polyp and the cancer.

Large flat lesions are more likely to contain early malignant disease than polypoid lesions.[17] Therefore, detection of flat lesions with CT colonography must be improved. There are several ways to achieve this. First, increasing the spatial resolution through scanning with thinner slices improves visualization of flat lesions.[22] Second, an additional primary 2-dimensional review is believed to be preferable for visualization of flat lesions[21] and additional 2-dimensional review may improve the detection of these lesions. Third, because 5 of 10 large flat lesions could be detected retrospectively, further training of radiologists in recognizing such lesions may improve sensitivity.

In the present study, we used a balloon-tipped rectal enema tube to insufflate the colon, which was left in situ during the examination. This device obscured the distal 2 cm of the rectum and the anorectal transition; consequently, 1 large villous lesion that was situated in this area was missed with CT colonography. Because it has recently been shown that the use of a thin flexible rectal tube without a balloon still results in clinically acceptable distention of the colon,[23] the use of these thin tubes will improve the visualization of this area.

Although it is generally agreed that patients with polyps ≥10 mm require colonoscopic polypectomy, patients with polyps 6–9 mm may require more frequent follow-up than patients without or with only diminutive polyps. In the present study, many CT colonographic findings in these size ranges were false positive. If large CT colonographic findings had triggered colonoscopy, 41% of patients (17–18/43–44) with such findings would have undergone colonoscopy unnecessarily. If CT colonographic findings of 6 mm or larger would have triggered colonoscopy or frequent follow-up with CT colonography, an even higher proportion of patients (64%) would have undergone these examinations unnecessarily (60–64/94–100). This relatively high proportion of unnecessary examinations reduces the potential benefit of preselection.

Our high number of false-positive findings is in contrast to previous reports. This may be caused in part by our primary 3-dimensional review method. Although this approach may result in improved polyp visualization,[24] this may be at the expense of an increased number of false-positive findings. Residual stool was an important cause of false-positive findings in our study. In future studies, 2 measures can be applied to reduce the misinterpretation of residual stool. First, contrast agents can be added to tag residual stool.[25] Second, scanning with thinner slices is known to improve the visibility of air inside CT lesions,[26] a strong indicator of fecal matter. It can be expected that both measures will reduce the number of false-positive findings without affecting the number of true positives.

The accuracy of CT colonography has been repeatedly reported in the past 7 years. Except for 2 studies that were hampered by suboptimal technique and learning curves,[27,28] many early reports were enthusiastic; the

Table 5. Negative Predictive Values

Findings per patient	Reviewer 1				Reviewer 2			
	TN	FN	NPV %	95% CI	TN	FN	NPV %	95% CI
All	34	54	39	29–49	32	53	38	28–48
≥6 mm	144	11	93	88–96	140	9	94	89–97
≥10 mm	200	5	98	94–99	201	5	98	94–99

TN, true negative; FN, false negative; NPV, negative predictive value; CI, confidence interval.

sensitivities and specificities for patients with large polyps ranged from 75% to 100% and 73% to 96%, respectively.[9–12] These results were predominantly obtained in patient groups that partly comprised subjects with positive screening test results and subjects who were primarily evaluated for symptoms. Because this may result in different disease spectra and prevalences, these data do not apply to patients who are screened for a personal or family history of colorectal polyps or cancer.

A study by Johnson et al.[29] previously reported the sensitivity and specificity of CT colonography in increased-risk patients. In this study of 703 patients, the sensitivity after double reading was lower (64%) than previously reported, with an acceptable specificity (95%).[29] The investigators, who used a primary 2-dimensional display mode to evaluate the data, found that a large proportion of missed polyps ≥10 mm (34%; 20 of 59) were perceptual errors. Although there are only a few comparisons of primary 2-dimensional and 3-dimensional display modes, the available data suggest that primary 3-dimensional display modes improve polyp visualization.[24]

Although the same investigators verified false-positive findings with videotaped colonoscopy, no second-look colonoscopy was performed. In our experience, none of the 8 large polyps that were overlooked at colonoscopy could be retrospectively confirmed by reviewing the videotaped colonoscopy. Consequently, if we had not performed a second-look colonoscopy, our sensitivity for patients with large polyps would have been 80% (20 of 25) instead of 84% (26 of 31). Thus, both our 3-dimensional approach and verification procedure may have contributed to our higher sensitivity.

A recent study in 1233 asymptomatic individuals compared CT colonography and colonoscopy, also with 3-dimensional display, and reported a comparable sensitivity for both modalities as in our study. However, the investigators used a different verification procedure. After the endoscopist completed the evaluation of a given segment of the colon, a study coordinator revealed the results of CT colonography for the previously examined segment. If findings ≥5 mm were present at CT colonography but not at colonoscopy, these lesions were directly verified based on detailed information of CT colonography.[20] This procedure, known as "segmental unblinding," enables verification of lesions of any size.[30]

A number of limitations of our study must be considered. We performed a second-look colonoscopy in patients with large unexplained false-positive findings, and the causes of many medium and small false-positive findings remain unknown. As with colonoscopy, medium-sized polyps are missed more frequently than large ones,[13,14] the proportion of medium-sized false-positive findings that in fact represent endoscopically missed polyps may have been even higher than observed in the present study for large lesions. To further elucidate this issue, future research on the accuracy of CT colonography should preferably comprise segmental unblinding to enable direct verification of false-positive lesions of any size.[30] Segmental unblinding is clearly preferable for the determination of the diagnostic accuracy of CT colonography per se. However, it may hamper a comparison of the diagnostic value between CT colonography and colonoscopy because of a "learning effect"; if the endoscopist misses a lesion in a particular segment, he or she may unintentionally adjust the examination style during the examination of the remaining segments.

As a result of our verification procedure, there was a considerable delay (mean, 13 months) between the initial and second-look colonoscopies, during which polyps might have grown. Theoretically these missed polyps might have been smaller than 10 mm at the time of the initial colonoscopy; however, because these lesions were at least 10 mm as measured at CT colonography, we consider it unlikely that the sizes of lesions were misclassified.

Because both observers had many false-positive findings, theoretically the chance increases that a lesion detected at CT colonography is labeled as a true-positive finding. To reduce this effect, our matching procedure comprised a face-to-face comparison of the videotaped colonoscopy and the CT colonography images and strict criterions with regard to location and size (case record form). In our experience, this procedure left little room for alternative interpretations; therefore, we deem it unlikely that this effect considerably influenced our results.

Because CT colonography, as performed according to current standards, is preferred to colonoscopy by patients,[20] it is expected to improve attendance rates. Bowel preparation, a major obstacle to participation in colonoscopic screening,[7] will not be required for CT colonography in the near future.[25] Most importantly, however, CT colonography must prove to have an ability similar to colonoscopy to identify patients with large colorectal polyps. The present results are encouraging, but more data are required to confirm our observations.

In conclusion, our data indicate that CT colonography and colonoscopy have a similar ability to identify large colorectal polyps in patients with a personal or family history of colorectal polyps or cancer. However, the majority of flat lesions were overlooked, a finding that requires further study.

References

1. Cancer facts and figures 2002. Atlanta, GA: American Cancer Society, 2002.
2. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:132–141.
3. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, Ganiats T, Levin T, Woolf S, Johnson D, Kirk L, Litin S, Simmang C. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. Gastroenterology 2003;124:544–560.
4. Pariente A, Milan C, Lafon J, Faivre J. Colonoscopic screening in first-degree relatives of patients with "sporadic" colorectal cancer: a case-control study. The Association Nationale des Gastro-enterologues des Hopitaux and Registre Bourguignon des Cancers Digestifs (INSERM CRI 9505). Gastroenterology 1998;115:7–12.
5. Cooper GS, Yuan Z, Chak A, Rimm AA. Patterns of endoscopic follow-up after surgery for nonmetastatic colorectal cancer. Gastrointest Endosc 2000;52:33–38.
6. Hackelsberger A, Fruhmorgen P, Weiler H, Heller T, Seeliger H, Junghanns K. Endoscopic polypectomy and management of colorectal adenomas with invasive carcinoma. Endoscopy 1995;27:153–158.
7. Harewood GC, Wiersema MJ, Melton LJ III. A prospective, controlled assessment of factors influencing acceptance of screening colonoscopy. Am J Gastroenterol 2002;97:3186–3194.
8. Dominitz JA, Eisen GM, Baron TH, Goldstein JL, Hirota WK, Jacobson BC, Johanson JF, Leighton JA, Mallery JS, Raddawi HM, Vargo JJ, Waring JP, Fanelli RD, Wheeler-Harbough J, Faigel DO. Complications of colonoscopy. Gastrointest Endosc 2003;57:441–445.
9. Yee J, Akerkar GA, Hung RK, Steinauer-Gebauer AM, Wall SD, McQuaid KR. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. Radiology 2001;219:685–692.
10. Fenlon HM, Nunes DP, Schroy PC III, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med 1999;341:1496–1503.
11. Johnson CD, Toledano AY, Herman BA, Dachman AH, McFarland EG, Barish MA, Brink JA, Ernst RD, Fletcher JG, Halvorsen RA Jr, Hara AK, Hopper KD, Koehler RE, Lu DS, Macari M, MacCarty RL, Miller FH, Morrin M, Paulson EK, Yee J, Zalis M. Computerized tomographic colonography: performance evaluation in a retrospective multicenter setting. Gastroenterology 2003;125:688–695.
12. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, Mikulaninec C, Vining DJ. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. Gastroenterology 2003;125:304–310.
13. Rex DK, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ, Lehman GA, Mark DG. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology 1997;112:24–28.
14. Hixson LJ, Fennerty MB, Sampliner RE, McGee D, Garewal H. Prospective study of the frequency and size distribution of polyps missed by colonoscopy. J Natl Cancer Inst 1990;82:1769–1772.
15. van Gelder RE, Venema HW, Serlie IW, Nio CY, Determann RM, Tipker CA, Vos FM, Glas AS, Bartelsman JF, Bossuyt PM, Lameris JS, Stoker J. CT colonography at different radiation dose levels: feasibility of dose reduction. Radiology 2002;224:25–33.
16. Vos FM, van Gelder RE, Serlie IW, Florie J, Nio CY, Glas AS, Post FH, Truyen R, Gerritsen FA, Stoker J. Three-dimensional display modes for CT colonography: conventional 3D virtual colonoscopy versus unfolded cube projection. Radiology 2003;228:878–885.
17. Rembacken BJ, Fujii T, Cairns A, Dixon MF, Yoshida S, Chalmers DM, Axon AT. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. Lancet 2000;355:1211–1214.
18. Bond JH. Colon polyps and cancer. Endoscopy 2001;33:46–54.
19. Rex DK. Barium studies/virtual colonoscopy: the gastroenterologist's perspective. Gastrointest Endosc 2002;55:S33–S36.
20. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, Wong RK, Nugent PA, Mysliwiec PA, Schindler WR. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003;349:2191–2200.
21. Fidler JL, Johnson CD, MacCarty RL, Welch TJ, Hara AK, Harmsen WS. Detection of flat lesions in the colon with CT colonography. Abdom Imaging 2002;27:292–300.
22. Laghi A, Iannaccone R, Mangiapane F, Piacentini F, Iori S, Passariello R. Experimental colonic phantom for the evaluation of the optimal scanning technique for CT colonography using a multidetector spiral CT equipment. Eur Radiol 2003;13:459–466.
23. Taylor SA, Halligan S, Goh V, Morley S, Bassett P, Atkin W, Bartram CI. Optimizing colonic distention for multi-detector row CT colonography: effect of hyoscine butylbromide and rectal balloon catheter. Radiology 2003;229:99–108.
24. McFarland E, Brink J, Pilgram T, Heiken J, Balfe D, Hirselj D, Weinstock L, Littenberg B. Spiral CT colonography: reader agreement and diagnostic performance with two- and three-dimensional image-display techniques. Radiology 2001;218:375–383.
25. Lefere PA, Gryspeerdt SS, Dewyspelaere J, Baekelandt M, Van Holsbeeck BG. Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. Radiology 2002;224:393–403.
26. Lui YW, Macari M, Israel G, Bini EJ, Wang H, Babb J. CT Colonography data interpretation: effect of different section thicknesses—preliminary observations. Radiology 2003;229:791–797.
27. Pescatore P, Glucker T, Delarive J, Meuli R, Pantoflickova D, Duvoisin B, Schnyder P, Blum AL, Dorta G. Diagnostic accuracy and interobserver agreement of CT colonography (virtual colonoscopy). Gut 2000;47:126–130.
28. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). Gastrointest Endosc 1999;50:309–313.
29. Johnson CD, Harmsen WS, Wilson LA, MacCarty RL, Welch TJ, Ilstrup DM, Ahlquist DA. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. Gastroenterology 2003;125:311–319.
30. Pineau BC, Paskett ED, Chen GJ, Durkalski VL, Espeland MA, Vining DJ. Validation of virtual colonoscopy in the detection of colorectal polyps and masses: rationale for proper study design. Int J Gastrointest Cancer 2001;30:133–140.