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Accuracy of CT Colonography for Detection of Large Adenomas and Cancers

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ABSTRACT

BACKGROUND

Computed tomographic (CT) colonography is a noninvasive option in screening for colorectal cancer. However, its accuracy as a screening tool in asymptomatic adults has not been well defined.

METHODS

We recruited 2600 asymptomatic study participants, 50 years of age or older, at 15 study centers. CT colonographic images were acquired with the use of standard bowel preparation, stool and fluid tagging, mechanical insufflation, and multidetector-row CT scanners (with 16 or more rows). Radiologists trained in CT colonography reported all lesions measuring 5 mm or more in diameter. Optical colonoscopy and histologic review were performed according to established clinical protocols at each center and served as the reference standard. The primary end point was detection by CT colonography of histologically confirmed large adenomas and adenocarcinomas (10 mm in diameter or larger) that had been detected by colonoscopy; detection of smaller colorectal lesions (6 to 9 mm in diameter) was also evaluated.

RESULTS

Complete data were available for 2531 participants (97%). For large adenomas and cancers, the mean (±SE) per-patient estimates of the sensitivity, specificity, positive and negative predictive values, and area under the receiver-operating-characteristic curve for CT colonography were 0.90±0.03, 0.86±0.02, 0.23±0.02, 0.99±<0.01, and 0.89±0.02, respectively. The sensitivity of 0.90 (i.e., 90%) indicates that CT colonography failed to detect a lesion measuring 10 mm or more in diameter in 10% of patients. The per-polyp sensitivity for large adenomas or cancers was 0.84±0.04. The per-patient sensitivity for detecting adenomas that were 6 mm or more in diameter was 0.78.

CONCLUSIONS

In this study of asymptomatic adults, CT colonographic screening identified 90% of subjects with adenomas or cancers measuring 10 mm or more in diameter. These findings augment published data on the role of CT colonography in screening patients with an average risk of colorectal cancer. (ClinicalTrials.gov number, NCT00084929; American College of Radiology Imaging Network [ACRIN] number, 6664.)

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Colorectal cancer is the third most common cancer and the second leading cause of death from cancer in the United States, with an estimated 154,000 new cases and 52,000 deaths in 2007.[1] There is an enormous opportunity to save lives with broadly applied, widely accepted early-detection programs, since the natural history of colorectal cancer permits the recognition and curative treatment of both precursor adenomas and localized cancers. According to data from multiple sources, mortality from colorectal cancer is reduced with regular screening.[1-3] Despite its effectiveness, colorectal-cancer screening remains underused for many reasons, including drawbacks in terms of the performance, comfort, availability, and expense of currently endorsed test options.

Computed tomographic (CT) colonography uses advanced visualization technology that permits a minimally invasive, structural evaluation of the entire colorectum. It has several potential advantages over other screening tests for colorectal cancer, including rapid imaging of the entire colorectum; a relatively noninvasive technique, with no need for sedation; and a low risk of procedure-related complications.[4,5]

The degree to which CT colonography is effective in detecting asymptomatic colorectal lesions remains a controversial topic, perhaps in part because of differences in patient populations, imaging protocols, and radiologists' qualifications in prior studies. The National CT Colonography Trial of the American College of Radiology Imaging Network was designed to assess the accuracy of CT colonography in detecting histologically confirmed, large colorectal adenomas and cancers (≥10 mm in diameter), with optical colonoscopy (the current clinical standard for colorectal cancer screening) and histologic review used as the reference standard.

METHODS

A total of 15 clinical sites participated in the study, which complied with the provisions of the Health Insurance Portability and Accountability Act, and approval was obtained from the institutional review board at each site. Participants were recruited from among all asymptomatic patients 50 years of age or older who were scheduled to undergo routine colonoscopy at the participating sites between February 2005 and December 2006. Patients were excluded from the study if they had had melena or hematochezia on more than one occasion in the previous 6 months; if they had lower abdominal pain, inflammatory bowel disease or familial polyposis syndrome, or a serious medical condition associated with an increased risk of complications from colonoscopy; if they had undergone colonoscopy in the preceding 5 years; or if they had anemia (a hemoglobin level of less than 10 g per deciliter) or a positive result on a fecal occult-blood test. Each study participant provided written informed consent before enrollment.

RADIOLOGIST TRAINING

Each participating radiologist was required to submit confirmation of having interpreted at least 500 CT colonographic examinations or having participated in a specialized 1.5-day training session on CT colonography. In addition, all participating radiologists were required to complete a qualifying examination in which they achieved a detection rate of 90% or more for polyps measuring 10 mm or more in diameter in a reference image set. Of 20 radiologists who met the initial entry criteria, the 15 with the highest scores on the qualifying examination were subsequently invited to participate in the study. Details regarding the credentialing process have been reported previously.[6]

CT COLONOGRAPHY

The preparation for CT colonography included stool tagging, laxative purgation, and fluid tagging (see the Supplementary Appendix, available with the full text of this article at www.nejm.org). Colonic insufflation was obtained with an automated carbon dioxide insufflator (PROTOC0$_2$L, E-Z-EM). Manual insufflation with room air was used if adequate colon distention could not be obtained with the mechanical insufflator. One milligram of subcutaneous glucagon was administered 7 to 15 minutes before the examination unless contraindicated or declined by the study participant.

Data were obtained with patients in the supine and prone positions. All examinations were performed with multidetector-row CT scanners that had a minimum of 16 rows. Images were acquired with the following specifications: collimation, 0.5 to 1.0 mm; pitch, 0.98 to 1.5; matrix, 512 by 512; field of view to fit the patient, 50 effective mAs; and peak voltage, 120 kV. A standard reconstruction algorithm was used. Images obtained with patients in the prone and supine positions

were reconstructed to slice thicknesses of 1.0 to 1.25 mm, with a reconstruction interval of 0.8 mm.[7]

The study data were randomly assigned to be read independently with the use of either a primary two-dimensional search method (conventional two-dimensional image display with three-dimensional endoluminal problem solving) or a primary three-dimensional search method (including the capability of displaying multiplanar two-dimensional images). For each abnormality, the location and size were noted, as well as the radiologist's degree of confidence that the lesion was a polyp. The determination of size was based on two-dimensional images and use of the greatest diameter. The radiologist's confidence that each finding was a polyp was rated on a scale of 0 (not a lesion) to 5 (high confidence). The radiologists made their interpretations without knowledge of the colonoscopic results and were instructed to record only lesions measuring 5 mm or more in diameter.

COLONOSCOPY

After the CT colonographic examination, index colonoscopy was performed according to the standard clinical protocol at each participating site. Same-day CT colonographic and colonoscopic examinations were performed for 2512 of 2531 (99%) participants. Identified lesions were photographed during the withdrawal phase. Withdrawal times were not included, since these data were not routinely available from colonoscopic reports. All index colonoscopic examinations were performed or directly supervised by an experienced endoscopist (staff gastroenterologist or surgeon) without prior knowledge of the CT colonographic results. For cases in which lesions that were 10 mm or more in diameter were detected on CT colonography but not on colonoscopy, patients were advised to undergo an additional colonoscopic examination within 90 days; endoscopists were provided with the CT colonographic results before the colonoscopy was repeated.

HISTOLOGIC REVIEW AND LESION MATCHING

Tissue samples from all lesions measuring 5 mm or more were centrally reviewed by one of the authors, an experienced gastrointestinal pathologist, and these data were used for all analyses of histologic findings. Adenomas were defined as polyps with cytologic dysplasia involving the epithelium at the luminal surface and extending to any crypt depth or as polyps that met the criterion of aberrant proliferation (sessile serrated adenomas, as defined by Li and Burgart[8] and by Torlakovic et al.[9]). Hyperplastic polyps were defined as polyps having a serrated architecture, with no superficial epithelial hyperchromasia and without the proliferative, full-thickness mucosal changes that characterize sessile serrated adenoma.

In accordance with prior studies,[10,11] lesion size was determined from the pathology report, unless the lesion was resected piecemeal, fulgurated, or not removed, in which case colonoscopy-derived estimates of size were used. Two of the authors, both experienced radiologists who had not been involved in initial lesion detection, matched the lesions found on CT colonography and colonoscopy on the basis of an established algorithm that incorporated the location of the lesion (within one colonic segment) and its size (within 50% of its reference standard measure).[10,12,13] Lesion matching was also evaluated electronically with the use of the same algorithm. Discrepancies in the results of the lesion-matching analyses were adjudicated by these radiologists. If they could not reach a consensus, the case in question was reviewed by one of the authors, an experienced gastroenterologist, for final determination of match status.

STATISTICAL ANALYSIS

The results of colonoscopy (including a second colonoscopy, when performed) and pathological examination of tissue specimens were the reference standard for determining lesion size, location, and histologic type. A positive result on CT colonography was defined as identification of a lesion measuring 5 mm or more in diameter. If the result of CT colonography was positive and one or more lesions that met the criteria for size (i.e. ≥10 mm or 6 to 9 mm) were identified with the use of the reference standard, the CT colonographic result was considered to be a true positive result for a lesion in that size range. If the result of CT colonography was positive but no lesions of the appropriate size were found on the reference standard, the colonography result was considered a false positive result for lesions in that size range. The usefulness of CT colonography as a screening tool was assessed in accordance with per-patient accuracy.

To reflect community practice, we averaged the results among radiologists.[10,13-15] The per-patient

sensitivity, specificity, positive predictive value, and negative predictive value were first estimated for each radiologist, and then the average values among the radiologists were calculated.[16]

Sensitivity, for each radiologist, was calculated as the proportion of patients with lesions that were larger than or equal to the prespecified threshold and that were detected on both colonoscopy and CT colonography. One minus the sensitivity is equal to the false negative rate for CT colonography and estimates the proportion of patients with lesions detected on optical colonoscopy that were missed on CT colonography for each radiologist. Specificity, for each radiologist, was calculated as the proportion of patients who did not have lesions larger than the prespecified threshold on colonoscopy as well as CT colonography. One minus the specificity is equal to the false positive rate for CT colonography and estimates the proportion of patients whose test results were negative on optical colonoscopy but positive on CT colonography for each radiologist. The positive predictive value was calculated as the proportion of patients with CT colonographic findings that were also seen on colonoscopy, and the negative predictive value was calculated as the proportion of patients with no CT colonographic findings larger than the prespecified threshold that were not detected on colonoscopy.

Exact 95% confidence intervals were calculated for each radiologist, and large-sample 95% confidence intervals were calculated for overall estimates, with the use of standard errors that allowed for estimation of variation among radiologists. The sample size was calculated to provide a sufficient number of patients with at least one histologically confirmed adenoma or cancer measuring 10 mm or more in diameter on colonoscopy to ensure that for anticipated values of sensitivity, the standard error of the average sensitivity among radiologists was less than 0.05 when that standard error allowed for anticipated variation in sensitivity among radiologists. Receiver-operating-characteristic (ROC) curves were estimated with the use of data pooled from the radiologists because of the small number of positive cases reviewed by each radiologist. Similar analyses were also performed for per-polyp sensitivities and for the identification of patients with any abnormal lesions measuring 10 mm or more — that is, analyses were not limited to adenomatous lesions. Per-polyp sensitivity was calculated as the percentage of lesions greater than or equal to the prespecified threshold size that were detected on colonoscopy and that matched the findings on CT colonography with the use of the algorithm described above.

Estimates of sensitivity, specificity, negative predictive value, and positive predictive value were obtained for patients at increased risk for colorectal cancer because of familial or personal history as well as for patients at average risk. In addition, sensitivities were calculated for two-dimensional and three-dimensional search methods, for different types of bowel preparation, and for differences in the overall quality of preparation. Because of the small number of positive cases each radiologist reviewed for these subgroup analyses, only pooled estimates for sensitivity were calculated, and uncertainty in estimates was quantified with the use of exact 95% confidence intervals.

RESULTS

The total number of participants enrolled was 2600 (2617 registrations and 17 duplicates). Complete CT colonographic and colonoscopic results were available for 2531 participants (97%), which constituted the study data set (see the Supplementary Appendix). Demographic data are provided in Table 1. The majority of the participants (89%) had no known risk factors for colorectal cancer other than age. There were 235 participants (9%) who had a first-degree relative with a history of colorectal polyps or cancer, 34 (1%) who had a personal history of polyps or cancer, and 13 (<1%) who had both. All others were considered to be at average risk for colorectal cancer. The baseline demographic characteristics of the final cohort were similar to those of all eligible participants.

PER-PATIENT ASSESSMENT

The overall diagnostic performance of CT colonography in detecting at least one lesion (adenoma or cancer) measuring 5 mm or more in diameter is shown in Table 2. The mean (±SD) sensitivity, specificity, positive predictive value, negative predictive value, and area under the ROC curve (AUC) for lesions measuring 10 mm or more were 0.90±0.031, 0.86±0.022, 0.23±0.020, 0.99±0.002, and 0.89±0.020, respectively. Our estimate of a sensitivity of 0.90 for identifying patients with large lesions was based on the following calcula-

Table 1. Characteristics of the Study Participants Overall and According to the Size of Reported Colorectal Neoplasms.*

Characteristic	No Cancer or Adenoma ≥5 mm (N=2249)	Cancer or Adenoma ≥5 mm and <10 mm (N=173)	Cancer or Adenoma ≥10 mm (N=109)	Total (N=2531)
Age at enrollment — yr				
Mean	58.0	59.6	60.8	58.3
Interquartile range	52–62	53–65	54–66	52–62
Sex — no. (%)				
Male	1036 (46)	108 (62)	61 (56)	1205 (48)
Female	1213 (54)	65 (38)	48 (44)	1326 (52)
Race or ethnic group — no.†				
American Indian or Alaskan Native	18	2	3	23
Asian	55	4	0	59
Black	295	24	14	333
Native Hawaiian or other Pacific Islander	7	0	0	7
White	1856	142	93	2091
Unknown or missing	42	2	2	46
Hispanic or Latino ethnicity — no. (%)				
No	2156 (96)	170 (98)	104 (95)	2430 (96)
Yes	89 (4)	3 (2)	5 (5)	97 (4)
Unknown	4 (<1)	0	0	4 (<1)
Medical history of polyps or colon cancer — no. (%)				
Family history	213 (9)	12 (7)	10 (9)	235 (9)
Personal history	30 (1)	1 (<1)	3 (3)	34 (1)
Both family and personal history	13 (<1)	0	0	13 (<1)

* Percentages may not sum to 100 because of rounding.
† Race or ethnic group was self-reported; more than one race or ethnic group may have been reported by a single participant.

tion: of the 1 to 13 patients who were seen by each radiologist and who had one or more large lesions that were detected on optical colonoscopy, CT colonography detected large lesions in 90% of patients on average; this indicates that for 10% of patients with one or more large lesions detected by colonoscopy, CT colonography did not detect a large lesion. The sensitivity for the detection of adenomas or cancers greater than or equal to 5 mm, 6 mm, 7 mm, 8 mm, and 9 mm was 0.65, 0.78, 0.84, 0.87, and 0.90, respectively, with specificity ranging from 0.86 to 0.89. The sensitivity, specificity, positive predictive value, and negative predictive value were similar for participants at increased risk for colorectal cancer and for those at average risk. Estimates of the sensitivity for individual radiologists are shown in Figure 1. Sensitivity ranged from 0.67 to 1.00, with 7 of 15 radiologists (47%) identifying all the patients with large lesions. For identification of patients with lesions regardless of histologic type, the estimates of sensitivity, specificity, positive predictive value, negative predictive value, and AUC were 0.87±0.035, 0.86±0.022, 0.28±0.026, 0.99±0.002, and 0.88±0.019, respectively.

The distribution, histologic type, and size of the lesions found on colonoscopy are listed in Table 3. There were 128 large adenomas or carcinomas in 109 of the 2531 patients (4%). Seven adenocarcinomas in seven patients were 10 mm or

Table 2. Estimated Per-Patient Accuracy in Detecting Adenomas or Cancers on CT Colonography.*

Performance Measure	Size of Adenoma or Cancer Detected on Optical Colonoscopy					
	≥5 mm	≥6 mm	≥7 mm	≥8 mm	≥9 mm	≥10 mm
Sensitivity						
Value (95% CI)	0.65 (0.58–0.73)	0.78 (0.71– 0.85)	0.84 (0.78–0.91)	0.87 (0.80–0.93)	0.90 (0.83–0.96)	0.90 (0.84–0.96)
No. of patients	282	210	174	154	120	109
Specificity						
Value (95% CI)	0.89 (0.851–0.923)	0.88 (0.840–0.920)	0.87 (0.831–0.914)	0.87 (0.825–0.909)	0.86 (0.817–0.902)	0.86 (0.813–0.900)
No. of patients	2249	2321	2357	2377	2411	2422
Positive predictive value						
Value (95% CI)	0.45 (0.389–0.513)	0.40 (0.335–0.463)	0.35 (0.299–0.397)	0.31 (0.256–0.355)	0.25 (0.209–0.292)	0.23 (0.194–0.273)
No. of patients	423	423	423	423	423	423
Negative predictive value						
Value (95% CI)	0.95 (0.941–0.965)	0.98 (0.971–0.984)	0.99 (0.980–0.992)	0.99 (0.984–0.994)	0.99 (0.990–0.998)	0.99 (0.991–0.998)
No. of patients	2108	2108	2108	2108	2108	2108
Area under ROC curve						
Value (95% CI)	0.80 (0.763–0.828)	0.84 (0.810–0.878)	0.87 (0.833–0.902)	0.88 (0.842–0.913)	0.89 (0.853–0.930)	0.89 (0.854–0.933)
No. of patients	2531	2531	2531	2531	2531	2531

* Values for detection of lesions on CT colonography were averaged among radiologists. Sensitivity indicates the proportion of patients who had lesions (of the specified size) detected on optical colonoscopy that were also detected on CT colonography. Specificity indicates the proportion of patients who had no lesions detected on optical colonoscopy or on CT colonography. Positive predictive value indicates the proportion of patients with CT colonographic findings (of the specified size) that were also detected on optical colonoscopy. Negative predictive value indicates the proportion of patients with no lesions of the specified size detected on CT colonography who also had no lesions detected on optical colonoscopy. The receiver-operating-characteristic (ROC) curve plots sensitivity versus the false positive rate, and the area under the ROC curve represents the accuracy of CT colonography.

more in diameter. A total of 547 lesions measuring 5 mm or more in diameter were detected. Nonadenomatous lesions included 136 hyperplastic polyps (25%), 7 lipomas (1%), and 30 lesions with other histologic features (5%).

PER-POLYP ASSESSMENT

The sensitivity of CT colonography for the detection of lesions of various sizes is shown in Table 4 for the overall study population. The overall sensitivity estimate for the detection of large lesions was 0.84±0.043.

ASSESSMENT OF MISSED LESIONS

The median size of neoplasms (≥5 mm in diameter by study design) that were detected and those that were missed on CT colonography was 10 mm and 6 mm, respectively. There was no association between undetected polyps and their location or histologic type. A single 10-mm cancer in the low rectum was missed on CT colonography. This lesion was not visible on a second review.

A total of 30 lesions measuring 10 mm or more were detected in 27 participants on CT colonography but were not detected on the initial colonoscopy. Fifteen of these 27 participants, with 18 reported lesions, returned for a second colonoscopy, as called for by the protocol. Five of 18 lesions were confirmed on the second colonoscopy (considered to be true positive CT colonographic findings). The diameters of these five lesions were 9 mm (inflammatory polyp), 10 mm (tubular adenoma), 11 mm (tubular adenoma), 14 mm (inflammatory polyp), and 35 mm (tubulovillous adenoma with dysplasia); they were polypoid and located in five different segments. Confirmatory colonoscopy was not performed for the remaining 12 patients. Three patients had findings that did not warrant the recall (one surgical hemicolectomy, one benign stricture, and one instance in which the CT colonographic finding was discounted by the colonoscopist), three patients declined to return, and six patients did not return because the referring physician determined that the recall was not warranted.

COLON PREPARATION

Polyethylene glycol solution was used for colon preparation in 1020 of the 2531 participants (40%), sodium phosphate solution in 1403 (55%), magnesium citrate in 102 (4%), and other substances in 6 (<1%). Barium sulfate for fecal tagging and iodinated contrast material for fluid tagging were taken as directed by 2482 (98%) and 2390 (94%) of the participants, respectively. Glucagon was administered in 2328 (92%) participants. Glucagon was not given to 78 participants with brittle diabetes, 1 participant with a borderline glucose level, 2 with pheochromocytoma, 69 who declined, 47 for whom the drug was unavailable, and 6 for whom a physician was not available during administration.

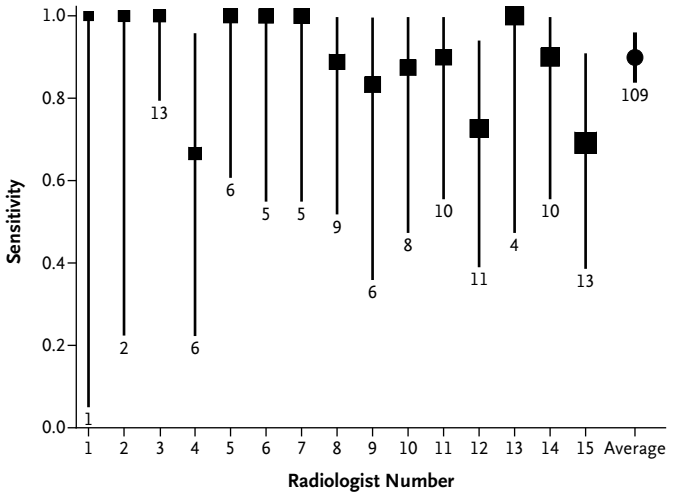

Figure 1. Individual Estimates of the Sensitivity of CT Colonography for the Detection of Adenomas or Cancers.

Sensitivity estimates, shown for each of the 15 radiologists, are for the detection of adenomas or cancers measuring 10 mm or more in diameter and are based on the identification of all lesions measuring 5 mm or more. The 15 radiologists are ordered according to the total number of cases read (i.e., Radiologist 1 read the smallest number of cases, and Radiologist 15 read the largest number); the size of each square (point estimate) is proportional to the square root of the total number of cases read. The number of positive cases (at least one adenoma or cancer ≥10 mm) is shown below each confidence interval.

IMAGING

CT colonographic examinations were performed on 16-slice scanners in 1140 patients (45%), 40-slice scanners in 83 patients (3%), and 64-slice scanners in 1308 patients (52%). Radiologists made 1280 interpretations using primary two-dimensional interpretation with three-dimensional problem solving and 1251 interpretations using primary three-dimensional endoluminal fly-through with two-dimensional problem solving. The CT colonographic software used for interpretation included Vital Images (Innerview GI), General Elec-

Table 3. Distribution of Lesions Detected on Optical Colonoscopy According to Location, Histologic Type, and Size.*

Segment and Histologic Type	No. of Lesions Detected†		
	5–9 mm	≥10 mm	Total
Rectum			
Adenoma or carcinoma	25	25	50
Nonadenomatous lesion	33	7	40
Sigmoid			
Adenoma or carcinoma	62	32	94
Nonadenomatous lesion	49	4	53
Descending			
Adenoma or carcinoma	32	8	40
Nonadenomatous lesion	16	2	18
Transverse			
Adenoma or carcinoma	52	17	69
Nonadenomatous lesion	22	4	26
Ascending			
Adenoma or carcinoma	47	27	74
Nonadenomatous lesion	16	7	23
Cecum			
Adenoma or carcinoma	28	19	47
Nonadenomatous lesion	10	3	13
Total			
Adenoma or carcinoma	246	128	374
Nonadenomatous lesion	146	27	173

* A total of seven lesions measuring 5 mm or more in diameter were malignant (two were 10 mm, one was 15 mm, two were 25 mm, one was 55 mm, and one was 100 mm); there were three in the rectum and one each in the sigmoid, descending, and transverse colon and the cecum. One malignant lesion measuring 10 mm was not seen on CT colonography. Thirteen adenomas, all measuring ≥10 mm (nine were 10 mm, one was 11 mm, two were 16 mm, and one was 25 mm), were not seen on CT colonography.

† A total of 1629 of the 2531 participants had no polyps of any size; 2141 had no polyps that were 5 mm or more in diameter; 512 had at least one polyp, with the largest being <5 mm. Data in the table represent the 258 participants with polyps measuring 5 to 9 mm and the 132 with polyps ≥10 mm. The mean (±SD) diameter of polyps measuring at least 5 mm was 8.9±7.2 mm. Size measurements from colonoscopy were used for 333 (61%) of 547 polyps because the polyps were removed in pieces.

tric (Advantage CTC), Siemens (Syngo Colonography), Viatronix (V3D:), and TeraRecon (Aquarius Workstation).

The pooled sensitivities for detecting large lesions with the use of primary two-dimensional conventional software and primary three-dimensional endoluminal fly-through software were similar: 0.87 (95% confidence interval [CI], 0.75 to 0.95) and 0.88 (95% CI, 0.76 to 0.95), respectively. The difference between the two types of viewing software was not significant. The mean time was 19.4 minutes for the primary two-dimensional interpretation, as compared with 25.3 minutes for the primary three-dimensional interpretation. There was no correlation between the number of cases interpreted and the radiologist's performance (Fig. 1).

ADVERSE EVENTS

Adverse events (grade 3 or higher) were reported in three participants (severe nausea and vomiting for less than 24 hours after CT colonography in one participant; hematochezia after snare polypectomy, requiring 2 days of hospitalization, in one; and hospitalization for *Escherichia coli* bacteremia 24 hours after both procedures in one).

Table 4. Per-Polyp Analysis of the Sensitivity of CT Colonography for the Detection of Adenomas and Cancers.*

Sensitivity	Size of Adenoma or Cancer					
	≥5 mm	≥6 mm	≥7 mm	≥8 mm	≥9 mm	≥10 mm
Value	0.59±0.045	0.70±0.046	0.75±0.042	0.80±0.041	0.82±0.042	0.84±0.043
No. of lesions	374	270	220	187	143	128

* Plus–minus values are means ±SE. Values for detection of lesions on CT colonography were averaged among radiologists. The sensitivity is the proportion of lesions (of the specified size) detected on optical colonoscopy that were matched through a lesion-matching algorithm on CT colonography. Lesion sizes were determined by the reference standard (pathological examination of tissue specimens or colonoscopic estimate).

EXTRACOLONIC FINDINGS

Extracolonic findings were observed in 66% of the participants; however, only 16% were deemed to require either additional evaluation or urgent care. These findings were located in the chest (27%), gastrointestinal tract (18%), genitourinary tract (45%), vascular system (6%), and musculoskeletal system (3%).

DISCUSSION

In our study, CT colonography identified 90% of patients with asymptomatic large colorectal adenomas or cancers (≥10 mm in diameter) that were detected by optical colonoscopy, with an AUC of 0.89. Secondary analyses showed that CT colonography had a lower sensitivity for smaller colorectal lesions (6 to 9 mm).

Our estimates of the sensitivity of CT colonography for detecting lesions found on colonoscopy are higher than estimates in some other studies.[10,13,14] Pickhardt et al. reported results similar to ours.[12] Although the higher accuracy in the study by Pickhardt et al. than in other studies has been attributed by some to use of a primary three-dimensional endoluminal reading technique, our study showed similar performance with the two image-display methods and all software brands used, with the primary three-dimensional technique requiring nearly 6 additional minutes (a 23% increase in time) for interpretation as compared with the primary two-dimensional technique.

The main objective of this prospective trial was to evaluate the screening-performance characteristics of CT colonography with the use of optimized, yet reproducible, image acquisition and interpretation methods in a diverse, multicenter setting and to compare these observations with findings on screening colonoscopy and histologic review, the reference standard. To maximize the likelihood that the colonoscopic data reflected usual clinical practice, we intentionally avoided incorporating advanced endoscopist training (beyond usual credentialing requirements) and nonstandard examination techniques (e.g., segmental unblinding) into our study design. Since undetected-adenoma rates of 2% and 13% for polyps 10 mm or larger and polyps 5 mm or larger, respectively, have been reported in tandem colonoscopic studies,[17] the CT colonographic performance characteristics reported in our trial may actually be underestimated. The specificity estimate for large lesions in our study was lower than that in other multi-institutional studies.[12-14] This may be due to the training sessions, which emphasized polyp detection (maximizing sensitivity), and may be a potential weakness of the training process. This trial required all radiologists to be trained on at least 50 CT colonographic cases before demonstrating the minimal level of competence. Most of the radiologists in our trial were required to obtain training beyond the initial 50 cases to recognize lesions that are difficult to detect.

Like other recent prospective CT colonographic screening studies,[10,12-14] our study focused on lesions measuring 5 mm or more, since the prevalence of advanced histologic features in small polyps (i.e., <5 mm) is reportedly below 2%.[18] Specificity estimates can be improved if the minimum size threshold for a radiologic finding is increased. According to the reference standard, the overall prevalence of large adenomas and cancers in this population was 4%. If all patients with a lesion measuring 5 mm or more on CT colonography were to be referred for colonoscopy, the colonoscopy-referral rate, based on our results, would be 17%. If a 6-mm threshold were used instead, the referral rate would drop to 12%. With an increase in the size threshold for radiologic

findings to 6 mm, specificity would increase to 0.91, with little decrease in sensitivity (to 0.88) for large adenomas.

Extracolonic abnormalities identified in this study were similar to those reported in previous studies.[19-24] Further definition of interdisciplinary management algorithms for these findings is needed to optimize the public health benefit from CT colonographic screening.

Despite the consensus opinion that colorectal cancer screening is effective,[2,3] adherence to current guidelines remains low among adults eligible for screening.[25] Guidelines for colorectal-cancer screening support multiple test options so that patients and providers can work together to determine their preferred method of examination. The less invasive nature of CT colonography and the low risk of procedure-related complications, as compared with colonoscopy, may be attractive to patients and may improve screening-adherence rates by addressing certain concerns of both patients and providers.

In summary, this large, multicenter study of asymptomatic adults showed that CT colonographic screening identified 90% of patients with adenomas and cancers measuring 10 mm or more in diameter. These findings support and extend previously published data regarding the role of CT colonography in screening patients with an average risk of colorectal cancer.

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