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Comparison of extracolonic findings and clinical outcomes in a screening and diagnostic CT colonography population

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Abstract

Purpose: To compare the distribution of extracolonic findings and clinical outcomes between screening and diagnostic CT colonography (CTC) populations.
Methods: 388 consecutive patients (369 men, 19 women; mean ± SD age 67.8 ± 10 years) who underwent first-time CTC (4/2011–4/2017) at a Veteran's Affairs Medical Center were divided into screening (asymptomatic) or diagnostic (symptomatic) cohorts based on CTC indication. CTC reporting and data system E-scores for extracolonic findings were retrospectively assigned based on prospective CTC radiologic reports. Multinomial logistic regression was used to examine the association between E-scores and CTC indication. Electronic medical records of all patients with E3 or E4 scores were reviewed (median follow-up 2.8 years) to determine clinical outcomes.
Results: 68% (262/388) underwent screening and 32% (126/388) diagnostic CTC. 7.2% (28/388) had extracolonic findings considered potentially significant (E4), 4.4% (17/388) had indeterminate but likely unimportant findings (E3), and 88.4% (347/388) had normal or unimportant findings (E1 or E2). E-scores were not significantly different between screening and diagnostic CTC when adjusted for age, gender, and prior imaging ($p = 0.44$). 4.6% (12/262) of patients with E3/E4 findings in the screening cohort demonstrated clinically significant outcomes, compared with 4.0% (5/126) in the diagnostic cohort, including a total of three extracolonic malignancies (0.8%) and three abdominal aortic aneurysms (0.8%). 4.6% (18/388) underwent follow-up imaging studies to confirm a benign outcome after detection of a category E3/E4 finding.
Conclusions: The distribution of extracolonic findings and clinical outcomes were not statistically significantly different between screening and diagnostic CTC populations.

Key words: CT colonography—Extracolonic findings—C-RADS—Screening

CT colonography (CTC) presents a unique challenge to colorectal cancer screening because it has the inherent ability to detect extracolonic disease. The physician interpreting CTC not only screens the colon but carefully inspects the low-dose CT scan of the abdomen and pelvis for extracolonic pathology that could affect the patient's health. Controversy exists in the literature as to whether identification of extracolonic findings on CTC is beneficial to patient care or harmful, leading to unnecessary testing, overtreatment, and increased cost.

The CT colonography reporting and data system (C-RADS) extracolonic findings E-score was designed to standardize reporting of extracolonic findings with intent to avoid unnecessary work-up of clinically unimportant findings, carefully guide potential work-up of indeterminate and likely unimportant findings, and optimally communicate potentially important findings to benefit patient outcome [1]. E1 and E2 scores indicate clinically benign or insignificant findings, do not require specific treatment or follow-up, and should raise no alarms on a CTC report. E3 (indeterminate findings) and E4 (po-

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tentially important findings) scores are of possible clinical relevance as their identification may lead to further work-up, surveillance, or management.

In 2016, the United States Preventive Services Task Force raised concerns about extracolonic findings found on CTC, citing highly variable reported prevalences of extracolonic findings and questioned whether they led to unnecessary diagnostic testing and treatment of diseases that would never impact patient health had they not been found incidentally [2]. They cited that extracolonic findings occur in "about 40% to 70% of screening tests," although this is an overestimation of clinically significant ECFs encompassing more than just E3 and E4 findings [2, 3]. Thus, although ECFs are commonly identified on CTC, by far the majority are benign lesions that do not require any additional follow-up testing. In the most comprehensive study to date, the extracolonic findings and clinical outcomes of a large screening CTC cohort found approximately 12% of patients had either E3 or E4 findings, with almost 70% of E4 and 10% of E3 findings resulting in a diagnosis of clinically significant extracolonic disease as a result of initial CTC and subsequent testing [3–5]. While this strongly validates the utility of the E-score in a screening CTC population, its utility in direct comparison to a diagnostic CTC population is not known. The objective of this study is to investigate whether screening and diagnostic CTC populations differ in their distribution of extracolonic findings and subsequent clinical outcomes.

Materials and methods

This study was HIPAA compliant and approved by our institutional review board. The requirement for informed consent was waived.

Study group

Between April 2011 and April 2017, 388 consecutive patients (369 men, 19 women, mean ± SD age 67.8 ± 10.0 years) underwent CTC at a university-affiliated Veterans Affairs Medical Center. 262 (68%) patients were referred for screening CTC, all of whom were asymptomatic and inclusive of those undergoing surveillance after negative colorectal cancer screening tests. 126 (32%) patients were referred for diagnostic CTC with one or more of the following symptoms: abdominal pain, hematochezia, heme-positive stools, iron deficiency anemia, or weight loss. Patients with incomplete optical colonoscopy who were referred for CTC were included in our study in their respective screening or diagnostic group. Patients who had prior CTC (n = 9) were excluded. All CTCs were prospectively interpreted by one of four abdominal radiologists with expertise in CTC, ranging in experience from 7 to 20 years.

CT colonography protocol

The CTC technique used in our study group has been previously published [6]. All patients underwent bowel preparation with magnesium citrate or polyethylene glycol one day prior to CTC. Fluid and fecal tagging was achieved with gastrografin and Tagitol V (Bracco, Monroe Township, NJ). Only two patients received intravenous contrast because fecal tagging was not performed. Colonic insufflation was achieved with automated continuous carbon dioxide delivery via rectal tube to maximum patent tolerance. Patients were scanned in both supine and either prone or decubitus position. Images were acquired with a GE 750 HD 64-slice scanner with the following protocol: 0.625-mm collimation, 1.25-mm reconstruction interval, 120 kVp, and 50 mAs with 40% adaptive statistical iterative reconstruction (ASIR) for the supine scan and 25 mAs with 40% ASIR for the prone or decubitus scan. Colonic review was performed on an independent workstation (Vitrea [VitalImages, Minnetonka, MN]) with primary inspection of 2D axial images and use of 3D endoluminal images for problem solving. Extracolonic review was performed on a PACS workstation (iSite [Phillips, Foster City, CA]) with routine inspection of supine axial 5-mm slices reconstructed at 3-mm intervals with selective review of thin (1.25 mm) slices, prone or decubitus series, and sagittal and coronal reconstructions as needed for problem solving. Comparison to prior imaging was performed for all patients when available.

C-RADS E-score classification

Categorization of extracolonic findings was established by the Working Group for Virtual Colonoscopy in 2005 as part of C-RADS. Category E1 denotes a normal examination or anatomic variant. Category E2 denotes a clinically unimportant finding that requires no further diagnostic work-up (i.e., simple renal cyst, cholelithiasis, nephrolithiasis, or hiatal hernia). Category E3 denotes a likely unimportant finding not completely characterized that requires further non-urgent diagnostic work-up (i.e., complex renal cyst, adnexal cyst, or small pulmonary nodule). E4 denotes a clinically significant finding that may adversely affect patient health and requires expedient work-up [1].

Because the E-score classification system was not routinely utilized for CTC examinations during the study period, prospective E-score was largely unavailable for analysis. Therefore, all 388 CTC imaging reports were retrospectively assigned a C-RADS E-score by a single rater (M.T.) blinded to clinical outcomes. E-score classification was guided by the C-RADS consensus proposal based on the most significant findings reported by the interpreting radiologist [1]. To maintain consistency with the C-RADS proposal and minimize discrepancies

in interpretation between the prospective reporting radiologist and the retrospective rater, the strength of recommendations made in the imaging report was first considered for classification of findings. Clinically significant findings reported by the radiologist with documented communication with the referring provider were classified as E4, whereas softer recommendations with consideration for additional work-up were classified as E3. In the absence of recommendations made by the radiologist and for findings of borderline significance, rater discretion guided by prior studies reporting rule-based retrospective classification schemes was used [7–10]. All extracolonic findings stable from previous imaging were classified as E2 unless they exhibited change that warranted further clinical or diagnostic work-up recommended by the radiologist. For example, known pulmonary nodules which demonstrated significant growth on CTC were classified as category E4. Lung nodule sizes ≥ 5 mm were considered for category E3 and above in keeping with 2005 Fleischner Society guidelines [11]. 27 (7%) cases with ambiguous reported extracolonic findings were re-examined by a second blinded rater (J.Y.) who determined the ultimate E-score.

Follow-up and outcome ascertainment

Review of electronic medical records of all patients with E3 or E4 scores was undertaken to assess the clinical, imaging, and interventional follow-up that was performed. Clinical provider notes and consults, imaging studies, surgical notes, and pathology reports were reviewed. The median follow-up period from date of CTC exam to date of latest clinical encounter was 2.8 years (IQR 1.3–4.2). Outcomes were divided into benign, clinically significant, and lost to follow-up or deferred. Benign outcomes were findings deemed clinically irrelevant or insignificant upon follow-up imaging. All follow-up imaging studies obtained until the final diagnosis was made or the surveillance period ended were recorded. Clinically significant outcomes were findings requiring treatment or active imaging surveillance.

Statistical analysis

Statistical analysis was performed using STATA (14.2, StataCorp, College Station, TX). Student's t test and Pearson's Chi-square test were used. A multinomial logistic regression model predicting C-RADS E-score was built to investigate its association with screening vs. diagnostic CTC type with adjustment for age, gender, and prior imaging. C-score was not included due to thin cells and separation. Assumption of independence of irrelevant alternatives was tested with the Hausman–McFadden test. All statistical tests were two-tailed with an alpha of 0.05.

Results

The screening CTC cohort (65.4 ± 8.3 years) was significantly younger than the diagnostic CTC cohort (72.8 ± 11.3 years, $p < 0.0001$). Of 388 CTCs, 28 (7%) had E4 scores, 17 (4%) had E3 scores, and 347 (89%) had E1 and/or E2 (Table 1). E-scores were not significantly different in the screening and diagnostic cohorts ($p = 0.07$) although E1 scores were more common in the screening cohort (16% vs. 7%, $p = 0.02$). Based on multinomial logistic regression analysis (Table 2), CTC indication (diagnostic vs. screening) was not an independent predictor of E-score when adjusted for age, gender, and prior imaging ($p = 0.44$).

When compared to screening CTC, diagnostic CTC was associated with 2.5 times increased odds of an E3 score (relative risk ratio [RRR] 2.55; 95% CI 0.70–9.25) and 1.4 times increased odds of an E4 score (RRR 1.43;

Table 1. Demographic data and CT colonography reporting and data system (C-RADS) scores of screening and diagnostic study cohorts

	Total CTC ($n = 388$)	Screening CTC ($n = 262$)	Diagnostic CTC ($n = 126$)	p[a]
Age, mean ± SD	67.8 ± 10.0	65.4 ± 8.3	72.8 ± 11.3	< 0.0001
Male, no. (%)	369 (95)	248 (95)	121 (96)	0.56
C-RADS E-score				0.07
E1	50 (13)	41 (16)	9 (7)	
E2	293 (76)	192 (73)	101 (80)	
E3	17 (4)	9 (3)	8 (6)	
E4	28 (7)	20 (8)	8 (6)	
C-RADS C-score				< 0.001
C0	46 (12)	30 (11)	16 (13)	
C1	250 (64)	180 (69)	70 (56)	
C2	40 (10)	27 (10)	13 (10)	
C3	44 (11)	25 (10)	19 (15)	
C4	8 (2)	0 (0)	8 (6)	
Prior imaging[b]	180 (46)	113 (43)	67 (53)	0.06

[a]Based on t test or Pearson's Chi-square test comparing screening to diagnostic
[b]Excluding prior CTC
CTC, CT colonography; C-score, colonic findings; E-score, extracolonic findings

Table 2. Multinomial logistic regression model predicting C-RADS E-score category

Predictor[a]	RRR (95% CI)	p[b]
Diagnostic vs. screening CTC		Overall 0.44
Category E2 (vs. E1 outcome)	1.76 (0.78–3.94)	0.17
Category E3 (vs. E1 outcome)	2.55 (0.70–9.25)	0.16
Category E4 (vs. E1 outcome)	1.43 (0.45–4.52)	0.61
Age (1 year)		Overall 0.11
Category E2	1.04 (1.005–1.08)	0.03
Category E3	1.06 (0.998–1.13)	0.06
Category E4	1.04 (0.988–1.10)	0.13
Sex (female vs. male)		Overall 0.30
Category E2	1.95 (0.40–9.52)	0.41
Category E3	–	–
Category E4	4.13 (0.62–27.6)	0.14
Prior referenced imaging (1 = yes)		Overall < 0.001
Category E2	8.43 (3.21–22.1)	< 0.001
Category E3	9.37 (2.39–36.7)	0.001
Category E4	4.39 (1.29–14.9)	0.02
Constant		
Category E2	0.16 (0.01–1.78)	
Category E3	0.002 (0.00003–0.15)	
Category E4	0.024 (0.0007–0.74)	
Overall model evaluation	N = 388, df = 12	< 0.001

[a]Four independent predictor variables (diagnostic vs. screening, age, sex, prior imaging) each with three parameters specified for all possible outcome comparisons (category E2 vs. E1, E3 vs. E1, E4 vs. E1) for a total of 12 model parameters in addition to constants. Parameter for sex comparing category E3 to E1 unspecified as 0 females in category E3
[b]Overall p value based on likelihood ratio test for each of 4 independent variables and whole model. Wald test p value reported for each parameter comparison of outcomes
C-RADS, CT colonography reporting and data system; CTC, CT colonography; RRR, relative risk ratio; CI, confidence interval

95% CI 0.45–4.52) than E1 when adjusted for age, gender, and prior imaging, although none of these comparisons were statistically significant. Only the presence of "prior imaging" was a statistically significant independent predictor of E-score ($p < 0.001$), which had increased odds of an E4 score (RRR 4.39; 95% CI 1.29–14.9; $p = 0.02$) and E3 score (RRR 9.37; 95% CI 2.39–36.7; $p = 0.001$) compared to E1 when adjusted for age, gender, and CTC type. Age was overall not a significant independent predictor of E-score ($p = 0.11$).

Screening CTC extracolonic findings and clinical outcomes

E3 and E4 extracolonic findings in each cohort are shown in Table 3 and the distribution of E-scores and clinical outcomes in Fig. 1. Of the 45/388 total patients with E3 and E4 findings, 35 (9%) underwent follow-up imaging studies: 24/262 (9%) in the screening and 11/126 (9%) in the diagnostic CTC cohort.

Screening CTC cohort

Nine patients had E3 scores on screening CTC (Table 3): three were deferred or lost to follow-up and six had follow-up imaging culminating in benign diagnoses (Table 4). In this screening CTC population, the positive predictive value (PPV) of a clinically significant diagnosis given an initial E3 score was 0/6 (0%). Twenty patients had E4 scores on screening CTC (Table 3): two were deferred or lost to follow-up and 18 underwent further work-up. Of the 18 patients needing work-up, 12 had a clinically significant outcome requiring treatment or active surveillance and six had benign diagnoses (Table 4). In this screening CTC population, the PPV of a clinically significant outcome given an initial E4 score was 12/18 (67%). The 12 patients with E3 and E4 scores receiving a benign diagnosis experienced the following additional imaging studies after their initial CTC: 15 CT chest, 3 CT abdomen/pelvis, 1 PET/CT, 1 trans-thoracic echocardiogram, and 1 renal ultrasound. No patients with either E3 or E4 scores in this screening CTC cohort required an invasive procedure for diagnosis of a benign condition (Fig. 2).

Diagnostic CTC cohort

8 patients had E3 scores (yielding 9 findings) on diagnostic CTC (Table 3), leading to one clinically significant outcome, three benign outcomes, and four follow-up deferrals. The positive predictive value of a significant outcome given an initial E3 score was 1/8 (13%). Eight patients had E4 scores on diagnostic CTC, leading to four clinically significant outcomes, three benign out-

Table 3. C-RADS category E3 and E4 extracolonic findings in screening and diagnostic CTC cohorts

Screening CTC		Diagnostic CTC	
Extracolonic finding type	No. of findings	Extracolonic finding type	No. of findings
Category E4 (20 patients)	24	Category E4 (8 patients)	8
Lung nodule[a]	7	Lung nodule[a]	2
AAA	2	AAA	1
Common iliac aneurysm	3	Lymphadenopathy	2
Other vascular aneurysm	3	Lung opacity	1
Renal mass	3	Renal mass	1
Urolithiasis or hydronephrosis	2	Cortical nephrocalcinosis	1
Liver mass	1		
Mediastinal mass	1		
Lung opacity	1		
Avascular necrosis of hip	1		
Category E3 (9 patients)	9	Category E3 (8 patients)	9
Indeterminate renal lesion	3	Indeterminate renal lesion	3
Lung opacity	2	Lung opacity or nodule[a]	2
Lymphadenopathy	2	Lymphadenopathy	2
Liver mass	1	Liver mass	1
Pericardial effusion	1	Pleural effusion	1

C-RADS, CT colonography reporting, and data system; CTC, CT colonography; AAA, abdominal aortic aneurysm
[a]Lung nodules ≥ 5 mm were considered for category E3 and E4

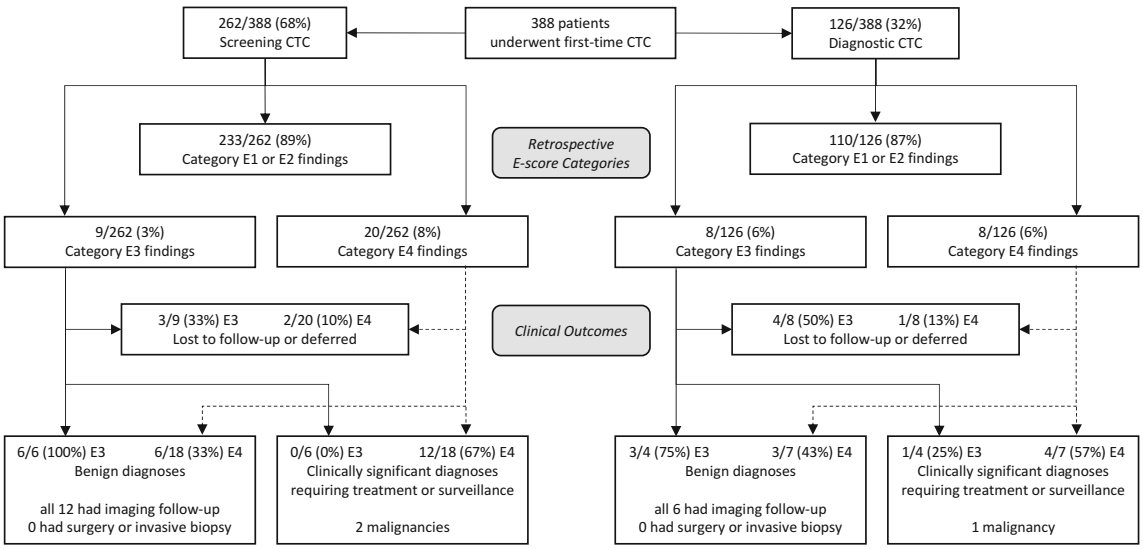

Fig. 1. Flow chart of CT colonography reporting and data system (C-RADS) extracolonic finding categories and clinical outcomes in each study cohort. Category E1, normal examination, or anatomic variant; E2, clinically unimportant finding; E3, likely unimportant finding; E4, potentially important finding; CTC, CT colonography.

comes, and one follow-up deferral (Table 4). The PPV of a significant outcome given an initial diagnostic E4 was 4/7 (57%). The six patients with E3 and E4 scores receiving a benign diagnosis experienced the following additional imaging studies after their initial CTC: 5 CT chest, 3 renal ultrasound, 1 CT abdomen/pelvis, 1 PET/CT, and 1 upper GI air contrast. No patients with either E3 or E4 scores in this diagnostic CTC cohort required an invasive procedure for diagnosis of a benign condition.

There was no statistically significant difference between screening and diagnostic CTC cohorts in proportions of clinically significant outcomes (12/262 vs. 5/126, $p = 0.78$) or benign outcomes (12/262 vs. 6/126, $p = 0.94$). The E3 PPV and E4 PPV of a clinically significant outcome were not statistically significantly dif-

Table 4. Clinical outcomes of screening and diagnostic CTC cohorts with C-RADS category E3 and E4 extracolonic findings

Screening CTC		Diagnostic CTC	
I. Benign outcomes	No. of outcomes	I. Benign outcomes	No. of outcomes
Category E4 (6 patients)	6	Category E4 (3 patients)	3
Stable lung nodule	5	Pulmonary hamartoma	1
No liver mass	1	Hemorrhagic renal cyst	1
Category E3 (6 patients)	6	Inflammatory pulmonary nodule	1
Simple liver cyst	1	Category E3 (3 patients)	4
Lung scar	1	Simple renal cyst	2
Resolving infection	1	Stable pulmonary nodule	1
Bosniak 1 renal cyst	1	Asymptomatic minimal aspiration	1
Reactive lymph node	1		
No pericardial effusion	1		
II. Lost to follow-up or deferred	No. of outcomes	II. Lost to follow-up or deferred	No. of outcomes
Category E4 (2 patients)	2	Category E4 (1 patient)	1
Lung nodule	1	Cortical nephrocalcinosis	1
Mediastinal mass	1	Category E3 (4 patients)	4
Category E3 (3 patients)	3	Lymphadenopathy	2
Indeterminate renal lesion	2	Indeterminate renal lesion	1
Lymphadenopathy	1	Liver mass	1
III. Clinically significant outcomes	No. of outcomes	III. Clinically significant outcomes	No. of outcomes
Category E4 (12 patients)	14	Category E4 (4 patients)	4
Non-small cell lung cancer	1	Pneumonia	1
Renal cell carcinoma	1	AAA	1
AAA	2	Progressive ILD	1
Common iliac artery aneurysm	2	Stable lymphoma	1
Renal artery aneurysm	1	Category E3 (1 patient)	1
Splenic artery aneurysm	1	Malignant pleural effusion	1
Ascending thoracic aortic aneurysm	1		
Bosniak 2F renal cyst	2		
Urolithiasis with hydronephrosis	1		
Bladder outlet obstruction	1		
Femoral head avascular necrosis	1		
Category E3 (0 patients)	0		

ferent between the screening and diagnostic CTC cohorts (Table 5; E3: 0.00 vs. 0.25, $p = 0.20$; E4: 0.67 vs. 0.57, $p = 0.64$).

Discussion

This study is the first to directly compare the distribution of extracolonic findings and clinical outcomes in a diagnostic vs. a screening CTC population. Our results showed no statistically significant difference in E-score or clinical outcomes of extracolonic findings between screening CTC and diagnostic CTC patient cohorts.

The E-scores in our population were overall congruent with most published data [4, 5, 9]. Our combined E1 and E2 prevalences (89%) were congruent with the largest study of 7952 screening patients that reported a prevalence of 88.4% [5]. However, our E3 prevalence (4%) was lower than two other studies reporting 9.1% and 9.3% [4, 9], whereas our E4 prevalence (7.2%) was higher than two other studies reporting 2.5% and 1.7% [5, 9]. Other studies of screening CTC populations report prevalences ranging from 9% to 13.9% for E3 and 2% to 2.9% for E4 [8, 9]. Yet, our E3 and E4 scores were congruent with other studies of diagnostic CTC populations where E3 prevalence ranged from 8.4% to 23% and E4 prevalence ranged from 2% to 7% [7, 10, 12]. Our relatively high E4 prevalence could be due to our predominantly male and older population, factors associated with increased incidence of extracolonic findings [7, 13–15]. Conversely, our relatively lower E3 prevalence of 4.4% was likely due to an under-representation of women in our study, as adnexal or uterine abnormalities account for nearly 25% of E3 findings [4].

For both screening and diagnostic CTC, we found that the presence of prior imaging was associated with significantly increased odds of a category E3 or E4 score relative to E1 (RRR 4.4–9.4, $p < 0.001$). This is not surprising as patients with normal imaging exams are less likely to require follow-up imaging than those with abnormalities. Although our results suggested that patients undergoing diagnostic CTC have a greater proportion of category E2–4 findings than E1 compared to patients undergoing screening CTC (RRR 1.43–2.55), our sample size was too small to detect a statistically significant difference.

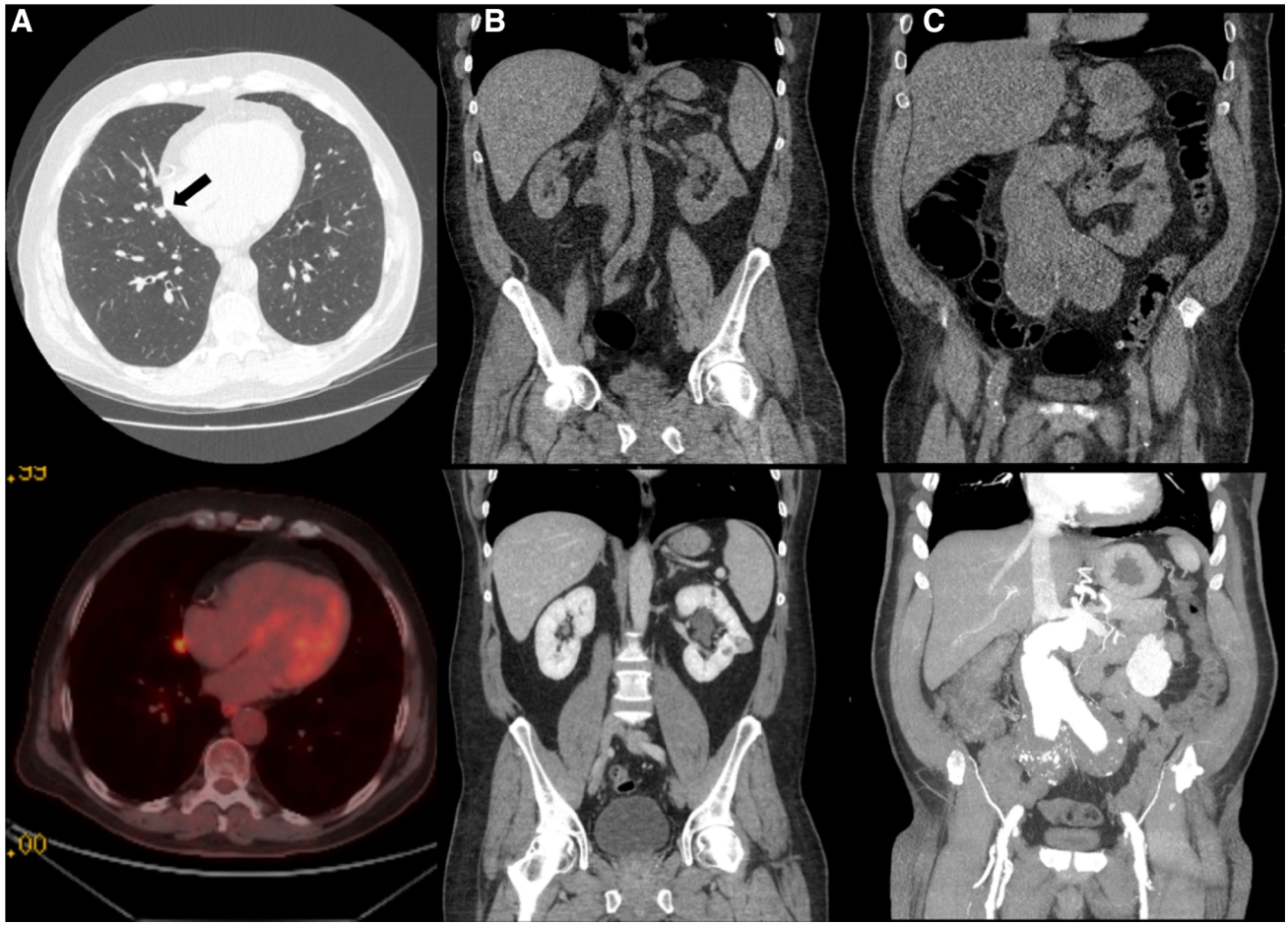

Fig. 2. Three patients with unsuspected clinically significant extracolonic findings on screening CT colonography (CTC). **A** A 61-year-old man with a growing right middle lobe lung nodule on CTC (top) found to be hot on subsequent PET CT (bottom); resection revealed well-differentiated squamous cell carcinoma. **B** A 53-year-old man with indeterminate left renal lesion on CTC (top) that enhances on follow-up contrast-enhanced CT (bottom); partial nephrectomy confirmed stage 1 renal cell carcinoma. **C** A 69-year-old man 6 cm abdominal aortic aneurysm and up to 5 cm bilateral common iliac artery aneurysm (top) confirmed on CT angiography (bottom); the patient postponed elective surgery and died 2 months later from rupture.

Table 5. Clinical outcomes of screening and diagnostic CTC cohorts with C-RADS category E3 and E4 extracolonic findings who had imaging follow-up

Clinical outcomes, no. (%)	Category E4		Category E3	
	Screening	Diagnostic	Screening	Diagnostic
Benign	6 (33%)	3 (43%)	6 (100%)	3 (75%)
Clinically significant	12 (67%)	4 (57%)	0 (0%)	1 (25%)
Total, no.	18	7	6	4
Clinically significant PPV	0.67	0.57	0.00	0.25
p[a]	0.64		0.20	

[a]Based on two-sample test of proportions comparing screening to diagnostic PPV
C-RADS, CT-colonography reporting and data system; PPV, positive predictive value

Regarding clinical outcomes in this study population, 4.6% (18/388) required follow-up imaging to confirm benign outcomes after detection of a category E3 or E4 finding on initial CTC, which was not statistically significantly different between screening and diagnostic cohorts (4.6% vs. 4.8%, $p = 0.94$). Similarly, the prevalence of clinically significant outcomes leading to treatment or surveillance was not statistically significantly

different between screening and diagnostic CTC cohorts (4.6% vs. 4.0%, $p = 0.78$). The positive predictive value of a clinically significant outcome given an initial E4 finding was 67% in the screening cohort and 57% in the diagnostic cohort. This closely matches the value of 68% reported by Pooler et al. [5]. Our results confirm and strengthen the validity of the C-RADS E-score in accurately discriminating between clinically important and unimportant findings. In our population, three extracolonic malignancies and three abdominal aortic aneurysms (AAAs) were detected, leading to expedited treatment. Two early-stage malignancies underwent curative resection. In a recent study where CTC was found to be more cost-effective than colonoscopy due to its higher participation rates, sensitivity analysis including AAA detection showed a further increase in the cost-effectiveness of CTC [16]. Since ''identifying abnormalities outside the colon'' was reported as the chief reason for selecting CTC among 43.3% of 1417 patients surveyed [17], and because CTC is estimated to be 29% less expensive than optical colonoscopy in a Medicare population cost-effectiveness analysis [18], the benefits of detecting extracolonic findings deserve continued attention.

We acknowledge limitations of our study. The higher than expected proportion of category C0 examinations were mostly attributable to inadequate bowel prep and arose in situations where patients underwent CTC shortly after incomplete optical colonoscopy. The inclusion of patients referred after incomplete optical colonoscopy, a population typically excluded in benchmark studies reporting C0 rates as low as 0.7%, likely accounts for our observed rate [14]. Since the majority of patients in our study were men, we found a lower prevalence of E3 findings than in other studies where up to 25% of E3 findings are adnexal cystic lesions or uterine abnormalities [4]. Our estimated prevalence of clinically significant and benign findings was affected by deferral or loss to follow-up of 41% (7/17) of E3 and 11% of (3/28) E4 findings, although these rates were similar in both screening and diagnostic cohorts. The absence of prospectively available E-scores and reliance on a retrospective classification method introduces subjectivity that limits the generalizability of our results. However, the use of a consistent algorithm between screening and diagnostic populations within our cohort and single rater blinded to clinical outcomes strengthens the internal validity of our study with respect to the primary objective of comparing distributions between the two groups.

In summary, the distribution of extracolonic findings did not differ significantly comparing screening and diagnostic CTC populations. The proportion of extracolonic findings warranting potential follow-up investigation (category E3 and E4) was low at 11%, with 4.4% of the total population benefiting by detection of a clinically significant outcome, including treatable malignancies and aneurysms. CTC confers a meaningful benefit to patients by successful detection of clinically significant extracolonic findings in both screening and diagnostic populations.

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Compliance with ethical standards

Disclosures Judy Yee, MD, FACR has received research Grants from Echopixel and Philips. No other author has disclosures.

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