Eur Radiol (2012) 22:1195–1204
DOI 10.1007/s00330-011-2367-0

GASTROINTESTINAL

CT colonography without cathartic preparation: positive predictive value and patient experience in clinical practice

Carmen Zueco Zueco · Carolina Sobrido Sampedro · Juan D. Corroto · Paula Rodriguez Fernández · Manuela Fontanillo Fontanillo

Received: 11 August 2011 / Revised: 9 November 2011 / Accepted: 11 December 2011 / Published online: 14 January 2012

Abstract
Objective To determine the positive predictive value (PPV) for polyps ≥6 mm detected at CT colonography (CTC) performed without cathartic preparation, with low-dose iodine faecal tagging regimen and to evaluate patient experience.
Methods 1920 average-risk patients underwent CTC without cathartic preparation. Faecal tagging was performed by diatrizoate meglumine and diatrizoate sodium at a total dose of 60 ml (22.2 g of iodine).The standard interpretation method was primary 3D with 2D problem solving. We calculated per-patient and per-polyp PPV in relation to size and morphology. All colonic segments were evaluated for image quality (faecal tagging, amount of liquid and solid residual faeces and luminal distension). Patients completed a questionnaire before and after CTC to assess preparation and examination experience.
Results Per-polyp PPV for detected lesions of ≥6 mm, 6–9 mm, ≥10 mm and ≥30 mm were 94.3%, 93.1%, 94.7% and 98%, respectively. Per-polyp PPV, according to lesion morphology, was 94.6%, 97.3% and 85.1% for sessile, pedunculated and flat polyps, respectively. Per-patient PPV was 92.8%. Preparation without frank cathartics was reported to cause minimal discomfort by 78.9% of patients.
Conclusion CTC without cathartic preparation and low-dose iodine faecal tagging may yield high PPVs for lesions ≥6 mm and is well accepted by patients.

C. Zueco Zueco (✉) · C. Sobrido Sampedro · J. D. Corroto · P. Rodriguez Fernández
Complexo Hospitalario Universitario de Vigo - CHUVI, c/Pizarro 22, 36204 Vigo, Pontevedra, Spain
e-mail: carmen.zueco.zueco@sergas.es

M. Fontanillo Fontanillo
Complexo Hospitalario Universitario de Vigo - CHUVI, H Meixoeiro, 2ªpl. s/n, 36214 Vigo, Pontevedra, Spain

Key Points
- *Computed tomographic colonography (CTC) without cathartic preparation is well accepted by patients*
- *Cathartic-free faecal tagging CTC yields high positive predictive values*
- *CTC without cathartic preparation could improve uptake of colorectal cancer screening*

Keywords CT-colonography · Faecal tagging · Patient acceptance · Colorectal cancer · Bowel preparation colorectal polyp · Adenoma

Introduction

Despite being a preventable neoplasia, colorectal cancer is the second leading cause of cancer death in the developed world. Early detection and removal of the precursor lesion significantly reduces the incidence and mortality associated with this neoplasia [1]. CT colonography (CTC) is increasingly accepted by both patients and professionals [2], owing to its non-invasiveness and high sensitivity for polyp and neoplasia detection. This sensitivity is comparable to that obtained using optic colonoscopy (OC) [3, 4]. However, the need for thorough colonic cleansing by means of cathartics still remains a major barrier limiting patient acceptance [5–7]. Tagging of faecal matter has been a substantial improvement in this line, as the need for exhaustive colonic cleansing is relaxed, while allowing good discrimination between polyps and faeces [3, 7–9].

Iodine or barium solutions have been used for faecal tagging. In some reports, they are used with no additional colonic preparation [8, 10, 11], while in other studies they were associated with low residue diets [12–15], stool softening or reduced catharsis with a variety of doses and

administration patterns [16–19]. Some researchers conclude that lowering the dose, or even abolishing the use of cathartics, combined with faecal tagging, increases patient acceptance of CTC [14, 15, 18], achieving, in some instances, a sensitivity for polyp detection comparable to that of conventional cathartic preparation. [12]. There has been no general agreement as to which tagging agent to use or on quantity and timing of contrast medium administration, so far. However, the prospect of replacing conventional preparation with cathartics drives research to find a new method combining diagnostic reliability, ease of preparation and patient acceptance. Barium agents have the advantage of not producing diarrhoea. Nevertheless they suffer from the important drawback of primarily tagging the solid stools rather than the liquid components [9]. High-osmolarity iodine contrast medium, if used at low doses, softens the stools and provides a more homogeneous mix, with limited collateral effects. This reduction of side effects, especially diarrhoea, can lead to an improvement in the experience of CTC both for diagnosis and screening purposes. The essential factor is to achieve good quality colon cleansing and tagging of residual stool, which guarantees accuracy in the diagnosis, permitting its use in a real clinical setting. Performance measures which can be obtained in routine clinical CTC practice include the test-positive rate, the false-positive rate (FPR), and the positive predictive value (PPV) as only CTC with positive results made OC [20].

To our knowledge, no previous study, with a large series of patients, has evaluated the PPV and FPR for lesions ≥6 mm detected at CTC without laxatives and faecal tagging using low iodine doses (22.2 g).

The objective of our study was to retrospectively assess the PPV and FPR as performance measures for lesions ≥6 mm detected at CTC performed in clinical practice without cathartic preparation and faecal tagging with low-dose iodine and evaluate clinical experience.

Materials and methods

The present retrospective study was approved by the Institutional Ethics Committee for Clinical Research with waiver of informed consent.

Study population

Our retrospective study group was composed of 1920 patients (1191 women and 729 men; mean age 64.4) referred for CTC by physicians in our hospital over a 36-month interval. This group included 1600 asymptomatic average-risk adults between 50 and 79 years old who underwent CTC screening, and 320 adults between 29 and 90 years old who presented minor abdominal symptoms (changes in intestinal function, abdominal discomfort) and underwent CTC because of a relative contraindication to cathartic preparation or rejection OC. Patients with rectal bleeding or hematochezia within previous 12 months, colo-rectal cancer or polyp surveillance, family history of colo-rectal cancer, polyposis syndrome, inflammatory bowel disease or hereditary non-polyposis colo-rectal syndrome were excluded.

Bowel preparation

All patients received the same preparation, consisting of a two-day low-fibre diet, avoiding intake of all foods high in fibre, including fruits, vegetables, whole-grain bread and whole-grain cereals (no specific meal kit was used) and a liquid diet on the day before CTC examination, consisting of a enteral liquid diet (1500 ml) (Iso Source standard, Nestlè, Frankfurt, Germany, supplied by the hospital's pharmacy) and clear liquids.

For faecal tagging, an oral iodinate contrast agent (diatrizoate meglumine and diatrizoate sodium) with an iodine concentration of 370 mg/ml (Gastrografin; Schering, Berlin, Germany, supplied by the hospital pharmacy), was administered at a total dose of 60 ml (22.2 g of iodine) over 42 h according to the following pattern:

First day, low fibre diet; second day, low fibre diet and a dose of Gastrografin (7.5 ml) diluted in 250 ml of water at each of the three main meals starting at lunch time (lunch, snack and dinner); third day, enteral liquid diet (300 ml) and a dose of Gastrografin (7.5 ml) diluted in 250 ml of water at each of the five main meals (breakfast, lunch, dinner, mid-morning and mid-afternoon snacks). At least, 2 L of water per day must be drunk. No full cathartic preparation was used before CTC. Trained nurses, dedicated to CTC, thoroughly instructed patients on this preparation (typical instruction time was≤5 min).

CTC examination

Images were made with 16-slice CT (SOMATOM Sensation, Siemens Medical Solutions, Erlangen, Germany). The imaging parameters include a 16×0.75-mm collimation, a slice thickness of 1 mm, reconstruction increment 0.7 mm and 0.5-s rotation time. A low-dose protocol was used with a tube current of 25 mAs and a kilovoltage of 100 kV. In all patients supine and prone acquisitions were performed. Colonic distension for supine imaging was begun in left lateral decubitus. Then patients were instructed to roll into the supine position until completion. Approximately 30–40 puffs of room air were carefully insufflated using a manual balloon via a flexible rectal catheter. Colonic distension was assessed on the scout view and additional insufflation was performed if there was insufficient colonic distension. All CTC examinations were performed under direct radiologist supervision to ensure

optimal image quality. No spasmolytic agents were used. The typical in-room time for CTC was 11 min.

Patient compliance

The first 700 patients completed two self-administered questionnaires (following prior consent from the Hospital's Clinical Research Ethics Committee), one, before CTC, covering: a) assessment of the preparation discomfort on a four-point scale (1: minimum, 2: mild, 3: moderate, 4: severe), b) presence of diarrhoea, number of stools, abdominal discomfort or other side effects. In the second questionnaire, after CTC, patients assessed the distress associated with the examination on a four-point scale (1: minimum, 2: mild, 3: moderate, 4: severe).

CTC analysis

Imaging processing and interpretation were performed on a Wizard workstation (Siemens Medical Solutions, Erlangen, Germany) with specialised software: Syngo-colonography CT2006G-W, by one of the two radiologists with prior experience in reading more than 300 colonoscopically verified CTCs. Our standard interpretation method was primary 3D fly-through with 2D problem solving [21]. Electronic cleansing software was not available. Lesions were measured with an electronic calliper at the multiplanar reformation (MPR) setting, which showed the maximal diameter of the colonic lesion detected. The colon was divided into six segments for lesion location (caecum, ascending, transverse, descending, sigmoid, rectum). The location, morphology and size were noted for every polyp to be at least 6 mm in diameter. Polyp size was categorised as small (for 6- to 9-mm lesions) or large (for all lesions measuring 10 mm or more). Polyp morphology was classified as sessile, pedunculate or flat (lesions protruding less than 3 mm from the mucosa) [22]. Masses were defined as ≥3 cm (30 mm) and described as polyps, carpet lesions, annular or hemi-circumferential.

Preparation analysis

The interpreting radiologist scored:

a) Consistency of faecal residue (solid, liquid, solid/liquid).
b) Total amount of liquid residue per segment (five-point scale) assessed in axial sections in supine decubitus: as the largest air fluid level relative to the maximum antero-posterior diameter in the same segment: 1: > 75%, 2: 50–75%, 3: 25–50%, 4: <25%, 5: no residual fluid [23]. For segments with several different levels, only the largest was considered.
c) Residual stool, graded as 1: greater than 75% of the lumen filled with stool, 2: 50–75% of the lumen filled with stool, 3: 25–50% of the lumen filled with stool, 4: less than 25% of the lumen filled with stool, 5, no stool.
d) Quality of faecal tagging (visual five-point scale): 1: completely untagged, 2: poorly tagged, 3: average tagging, 4: well tagged, 5, excellent tagging.
e) Distension (five-point scale): 1: collapsed, 2: poor, 3: adequate, 4: good, 5: excellent (Fig. 1).

Polyp matching

Fibre-optic colonography was performed on patients with positive findings for polyps or masses 3–92 days after positive CTC. Lesion measurement at OC was performed using visual comparison against an open forceps or another endoscopically inserted device.

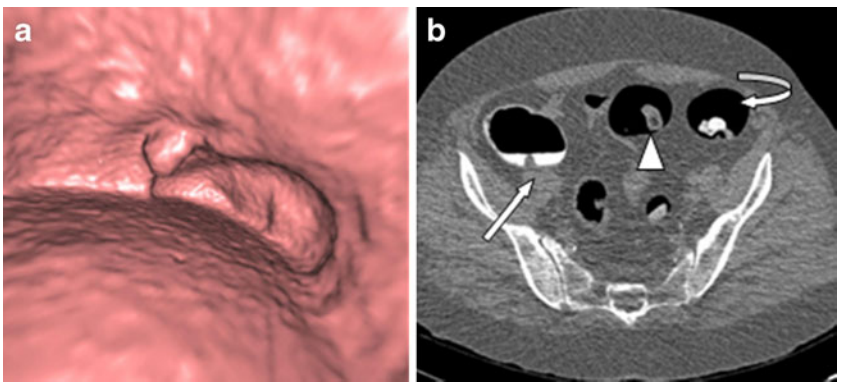

Fig. 1 A 68-year-old woman at average risk of a colorectal neoplasm, who was asymptomatic. **a** 3D endoluminal image shows a 9-mm sessile polyp. Histology confirmed a tubular adenoma located in the caecum. **b** 2D axial image confirms that the polyp identified in (**a**) is a soft-tissue lesion (*arrow*). Axial image shows a residual fluid score of 4, a tagging residual fluid score of 5 and a distension score of 5 in the caecum (*arrow*). In the descending colon (*curved arrow*) a residual stool score of 4, a tagging residual fluid score of 3 and a distension score of 4. In the sigmoid (*arrowhead*) a residual stool score of 4, a tagging residual stool of 1 and a distension score of 4 were found

The records and reports from both examinations were retrospectively reviewed from June to December 2010 for the evaluation of CTC–OC agreement on lesions≥6 mm. This data collection was performed by two radiologists not involved in the readings. Findings were categorised as matched lesions OC-CTC if their size measurements were within a 50% margin of error and if they were located in the same or in an adjacent segment [3, 24].

Pathological analysis

Pathological analysis classified adenomas as tubular, tubullo-villous, villous, serrated, high-grade dysplasia or adenocarcinoma. Neoplastic lesions were defined as adenoma or adenocarcinoma. Advanced adenomas were defined as tubular adenomas (≥ 10 mm diameter) or adenomas of any size with more than 25% villous component or high-grade dysplasia [25]. Advanced neoplasia included both advanced adenomas and adenocarcinomas. Invasive carcinoma was defined as a malignant extension past the muscularis mucosae.

A follow-up of clinical histories and histological registries of all 1920 patients was performed in order to identify subsequent clinical events or diagnosis related to polyps or colonic neoplasias.

Statistical analysis

Matched lesions were considered as CTC true-positive (TP). Lesions were categorised as CTC false-positive (FP) if detected on CTC but without matching OC, and as CTC false-negative (FN) when polyps were detected on OC but not on CTC. Subjects with at least one TP lesion per size category were classified as CTC–TP cases; those with no TP and one or more FP polyps were classified as FP cases. The positive predictive values (PPV) of CTC findings were calculated per polyp in relation to size and morphology and per patient. The Statistical Package for Social Sciences, version 17.0 (SPSS, Chicago, IL, USA) was used for data recording and analysis.

Descriptive statistics were computed for quantitative (mean and standard deviation) and qualitative variables (frequency, percentage and confidence intervals). The Student *t*-test was used to analyse differences between means and the Chi-squared test for the association between qualitative variables. PPV and their confidence intervals were used for comparison of the two examination procedures. Effects were considered statistically significant when $P<0.05$.

Results

A total of 287 patients out of our 1920 average-risk adult population had at least one lesion≥6 mm in diameter. The overall test positive rate was, therefore, 14.9% (287/1920). A total of 369 polyps were found in our positive patients. Polyps ≥10 mm were found in 125 patients (6.5%, 95% CI: 5.5–7.5%), 85.6% of which (107) underwent OC. No OC was performed in 18 patients with large polyps owing to several patient-related issues (comorbidities, patient refusal). Small polyps (6–9 mm) were found in 170 patients (8.8%, 95% CI: 7.6–10.0%); 129 of which (78.2%) had OC examinations, while 37 decided to have CTC follow-up. Histological diagnoses for matched neoplasias are shown in Table 1.

Per-patient PPV

Out of 236 patients undergoing OC, 219 had matched findings with CTC, yielding an overall per patient PPV of 92.8% (219/236) at the 6-mm size threshold (Table 2). At least one of these matching lesions was neoplastic in 199 patients and an advanced neoplasia in 97 patients. Consequently the PPV was 84.3% (199/236) and 41.1% (97/236) for adenomatous polyps and advanced neoplasia, respectively.

A total of 20 false-positive≥6-mm polyps were found in 14 patients obtaining a per-patient FPR of 5.9% (14/236). Only 1 false-positive lesion >30 mm, due to endometriosic infiltration, was found (Table 2). OC identified 13 individual polyps ≥6 mm that were not detected in CTC examinations

Table 1 Histopathology of neoplastic polyps and masses detected at CT colonography according to lesion size

Histopathology	Neoplastic polyps 6–9 mm [*n*=124]	Neoplastic polyps≥1 cm [*n*=109]	Masses≥3 cm [*n*=46]
Tubular adenoma	109 (87.9)[a]	58 (53.2)[a]	1 (2.2)[a]
Tubulo-villous adenoma	9 (7.2)	16 (14.7)	5 (10.9)
Villous adenoma	1 (0.8)	5 (4.6)	2 (4.3)
Serrated	2 (1.6)	4 (3.7)	1 (2.2)
HDG	2 (1.6)	4 (3.7)	11 (23.9)
Adenocarcinoma	1 (0.8)	22 (20.2)	26 (56.5)
Advanced neoplasia	13 (10.5)	109 (100)	46 (100)

[a]Numbers in parentheses are %

Table 2 Positive predictive value (PPV) and false-positive rate (FPR) for polyps ≥6 mm detected at CT colonography

Variable	Positive predictive value (PPV)	CI 95%	False positive rate (FPR)	CI 95%
By-patient assessment				
	92.8% (219/236)	89.3–96.3	5.9% (14/236)	3.7–10.7
By-polyp assessment				
All polyps(≥6 mm)	94.3% (332/352)	91.9–96.7	5.7% (20/352)	3.3–8.1
According to lesion size				
Small (6–9 mm)	93.1% (162/174)	89.0–97.2	6.9% (12/174)	2.8–10.9
Large(≥10 mm)	94.7% (124/131)	90.4–98.9	5.3% (7/131)	1.1–9.6
Mass (≥3 cm)	97.9% (46/47)	88.7–99.9	2.1% (1/47)	0.05–11.3
According to lesion morphology				
Sessile	94.6% (175/185)	91.1–98.1	5.4% (10/185)	1.9–8.9
Pedunculated	97.3% (71/73)	90.4–99.7	2.7% (2/73)	0.3–9.5
Flat	85.1% (40/47)	73.9–96.3	14.9% (7/47)	3.6–26.1

in 10 out of 236 patients (4.2%) undergoing complete OC examination. All these polyps were small polyps (6–9 mm). In each of these patients additional polyps of similar or larger size were found at prospective CTC, showing concordant OC findings.

Per-polyp PPV

Out of 174 small polyps detected by CTC, 162 matched OC findings, yielding PPVs of 93.1% (162/174) for 6–9 mm individual polyps and 94.7% (124/131) for those larger than 10 mm. PPV for individual masses was 97.9% (46/47) (Table 2). There were no significant differences in PPV with respect to polyp sizes. Furthermore, there was no significant effect of polyp size on PPV (P=0.751). On the contrary, lesion morphology significantly affected PPV of CTC, which was higher (P=0.019) for sessile (94.6%; 175/185) and pedunculated polyps (97.3%; 71/73) than for flat lesions (85.1%; 40/47; Figs. 2, 3).

Three patients showed mild vasovagal reactions, which were all resolved in the radiology service in 30–45 min. No allergic reactions occurred.

Preparation results

The consistency of the faecal matter was liquid in 86.0% of colonic segments, solid in 9.5% and liquid–solid in 4.5%. The mean score for all segments with residual fluid was 4.73±0.64 (five-point scale; Fig. 4) and 4.26 ±0.55 for those with residual stool (Table 3). The segment with the worst score was the sigmoid, both for residual fluid (4.69 ±0.77) and residual stool (3.71±1.02). Faecal tagging scores were excellent for all segments both in segments with residual fluid (mean 4.80±0.45) and those segments with residual stool (mean 4.66±0.49) even in the rectum (Fig. 3, 4.43 ±1.23 and 4.14 ±1.15, respectively; Table 3). The mean distension for all segments was 4.87±0.30, which reached a maximum in the caecum (4.99±0.14).

Questionnaire results

Diarrhoea occurred in only 7.4% (52/700) of patients at some point (during the first, second or both days) after Gastrografin intake. All but 12 patients described the diarrhoea as mild with three or fewer stools per day. Abdominal discomfort occurred

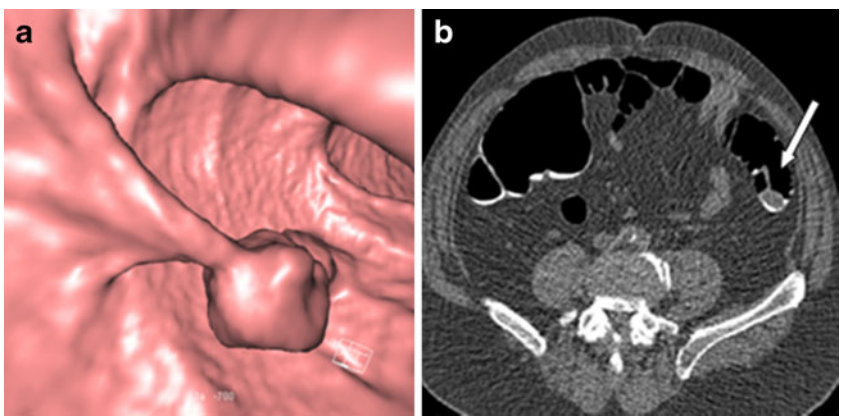

Fig. 2 A 67-year-old man at average risk of a colorectal neoplasm, who was asymptomatic. **a** 3D endoluminal image shows a 19-mm pedunculated polyp. Histology confirmed a tubular adenoma located in the sigmoid. **b** 2D axial image confirms that the polyp identified in (**a**) is a soft-tissue lesion (*arrow*). In the sigmoid (*arrow*) the polyp is outlined by residual fluid (score of 5), excellent tagging (score of 5) and good distension (score of 4)

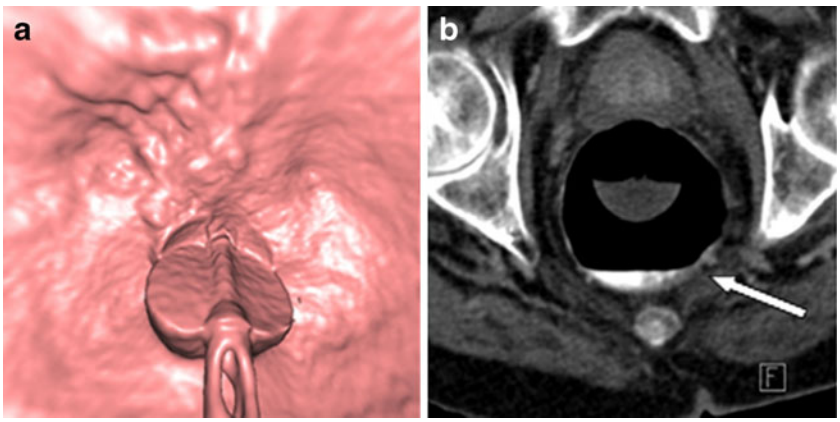

Fig. 3 A 77-year-old man at average risk of a colorectal neoplasm, who had changes in intestinal function. **a** 3D endoluminal image shows a 23-mm flat lesion. Histology confirmed a tubulo-villous adenoma located in the rectum. **b** 2D axial image confirms that the lesion identified in (**a**) is a soft-tissue lesion protruding less than 2.5 mm from the mucosa (*arrow*). Axial image shows a residual fluid score of 4, a tagging residual fluid score of 5 and a distension score of 5 in the rectum

in 7.6% of patients. The preparation was classified as causing minimal discomfort by 78.9% (552/700) of patients, and as being severely unpleasant by only 2.9% (20/700 Fig. 5).

The CTC examination was minimally unpleasant for 55.0% (385/700) of patients surveyed and severely unpleasant for 6% (42/700 Fig. 5).

Discussion

In our study, comparison with other diagnostic approaches was based on indirect quality measures such as the test positive rate, false-positive rate and positive predictive value, as, in clinical practice, only positive CTC findings are referred for OC for polypectomy or for biopsy [20, 26, 27]. A high PPV is essential for CTC to be considered as an efficient, non-invasive technique, since it protects against unnecessary duplicities in screening or diagnostic tests. The high overall per-patient PPV, 92.8% at the 6-mm size threshold, reflects a very good agreement in positive findings between CTC and subsequent OC. This result is in line with recent previous studies in clinical practice with conventional preparation with laxatives showing a 90–92% PPV [20, 27] and substantially outperforms a large published multi-centre CTC screening trial [3]. The low per patient FPR (5.9%), also in line with these studies [20, 27, 28], makes our CTC screening approach highly cost-effective. It could be argued that in a clinical practice set-up, where false negative rates cannot be assessed, high PPV could result from only truly relevant lesions being detected. However, out of 236 patients who underwent OC after positive CTC findings, only in 10 (4.2%) were diagnosed additional polyps not previously detected by CTC. Of the 33 FP and FN polyps, 5 were due to differences in localisation and 6 to differences in size which broke the matching rules, while 22 were undetected in CTC or OC. Besides, the follow-up of clinical histories and cancer registries of all patients did not reveal any clinical events related to polyps or neoplasia. Out of 167 patients who had an OC or a new CTC since the

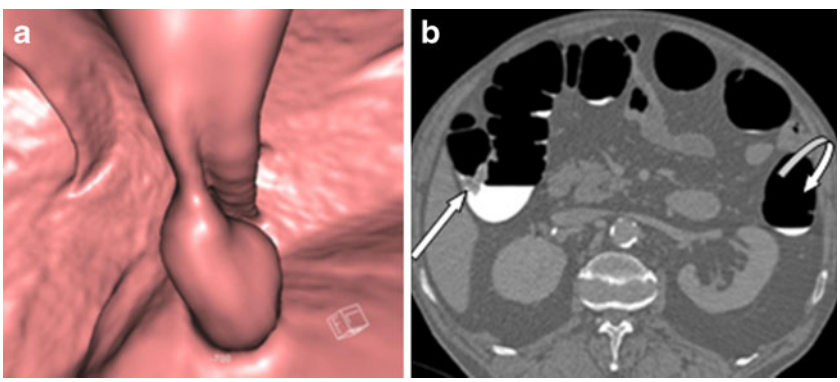

Fig. 4 A 71-year-old man at average risk of a colorectal neoplasm, who was asymptomatic. **a** 3D endoluminal image shows a 23-mm sessile polyp. Histology confirmed a tubular adenoma located in the ascending colon. **b** 2D axial image confirms that the polyp identified in (**a**) is a soft-tissue lesion. In the ascending colon (*arrow*) the residual fluid, tagging residual fluid and distension scores are of 2, 5 and 4 respectively. In the descending colon (*curved arrow*) the residual fluid, tagging residual fluid and distension scores are 4, 5 and 4 respectively

Table 3 Qualitative analysis for faecal residue, tagging and distension across the six different colonic segments

	C1	C2	C3	C4	C5	C6	Mean score
Residual fluid[a]	4.77±0.64	4.75±0.67	4.72±0.69	4.70±0.72	4.69±0.77	4.78±0.62	4.73±0.64
Residual stool[b]	4.41±0.58	4.64±0.52	4.48±0.64	4.23±0.76	3.71±1.02	4.11±0.86	4.26±0.55
Fluid tagging[c]	4.97±0.21	4.97±0.22	4.95±0.28	4.85±0.60	4,63±1.00	4,43±1.23	4.80±0.45
Solid tagging[d]	4.71±0.76	4.88±0.37	4.91±0.29	4.80±0.61	4.58±0.88	4.14±1.15	4.66±0.49
Distension[e]	4.99±0.14	4.98±0.18	4.92±0.47	4.78±0.68	4,57±0.82	4,97±0.24	4.87±0.30

C1: caecum, C2:ascending colon, C3: transverse colon, C4: descending colon, C5: sigmoid, C6: rectum

[a] Total amount of liquid residue per segment (five-point scale) as the largest air fluid level relative to the maximum antero-posterior diameter in the same segment: 1: >75%, 2: 50–75%, 3: 25–50%, 4: <25%, 5: no residual fluid

[b] Residual stool, graded as 1: greater than 75% of the lumen filled with stool, 2: 50–75%, 3: 25–50%, 4: less than 25% of the lumen filled with stool, 5: no stool.

[c] Quality of faecal tagging (five-point scale) 1: completely untagged, 2: poorly tagged, 3: average tagging, 4: well tagged, 5: excellent tagging

[d] Distension (five-point scale) 1: collapsed, 2: poor, 3: adequeate, 4: good, 5: excellent

initial CTC was performed (6 to 42 months earlier), only 2 subjects had two small polyps (6–9 mm) detected which were either not present or undetected in the initial CTC. If they were really false-negatives, would increase our FN rate by only 1.2%. No large polyps or colonic neoplasia were found.

Our CTC positive rate for lesions ≥6 mm, and the prevalence of advanced neoplasia (8.7%), were slightly higher than in others screening trials [4, 20, 28]. This could be due to the higher mean age in our series, since the prevalence of advanced neoplasia increases from 5.7% in patients aged 50–59 to 13% in patients aged 70–75 [29]. However, this can be taken as an indication that relative performance of CTC is not lessened when no cathartics are used in patient preparation. The relative high rate of cancer in this population could also be attributed to the same factor, since 56% of these lesions were found in patients over 79 years.

As in studies with a conventional preparation with laxatives in our study there were no significant differences in PPV with respect to polyp sizes [20], nevertheless per polyp PPV was very significantly (P=0.019) affected by morphology of the lesion, being poorer for flat (85.1%) than for pedunculated or sessile polyps (97.3 and 94.6%, respectively, Fig. 6), although this effect of morphology was less pronounced than in a previous study [20]. In our opinion, the improved reliability for flat lesions should be attributed to specific conditions, such as liquid consistency and optimal tagging of residual faecal matter, which facilitate flat lesion detection both on endoluminal 3D and on 2D viewing (Figs. 3, 7), therefore allowing discrimination of small variations in thickness and relief of the colonic wall [30].

Ionic iodinated agents such as diatrizoate meglumine and diatrizoate sodium are hypertonic and exert a mild osmotic laxative effect because of an increased colonic fluid load, resulting in liquid faeces with homogeneous tagging and, therefore, allowing for better detection of lesions. Moreover, when the patient shifts from supine to prone decubitus, or between oblique positions, the residual liquid or semi-liquid faecal material is readily redistributed, offering a larger area of "clean" mucosa for the study as a whole. On the contrary, solid faeces tend to form an irregular layer that adheres to the mucosa. In our study, 86.2% of patients had liquid faeces, which we believe, in agreement with Zalis et al. makes interpretation easier [31] and reduces reading time (< 10 min in our study).

Since residual stool is generally recognised as a major source of potential error at CTC, the scarce faecal residue, either liquid or solid, along with the excellent labelling achieved with the iodine faecal tagging preparation in our

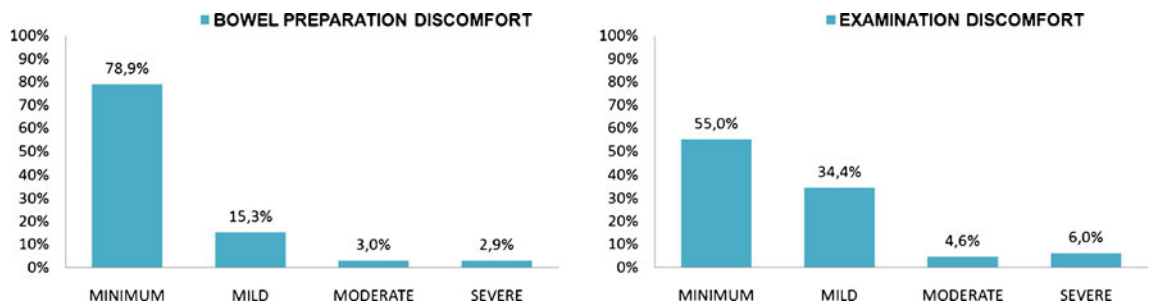

Fig. 5 Bar graphs show **a** the level of bowel preparation discomfort and **b** the level of CTC examination discomfort reported by patients

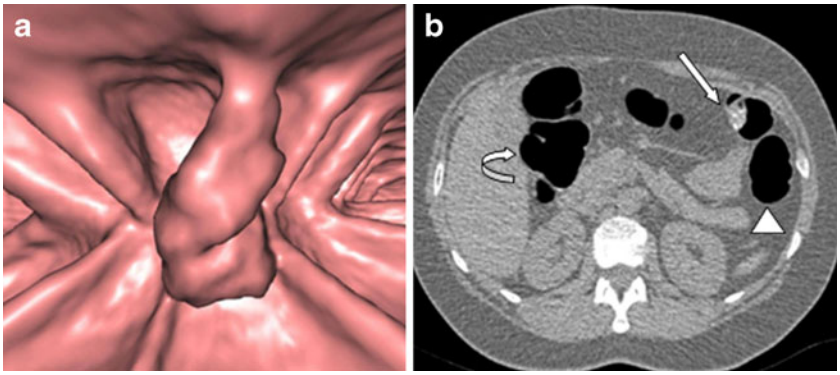

Fig. 6 A 72-year-old man at average risk of a colorectal neoplasm, with abdominal discomfort. **a** 3D endoluminal image shows a 21-mm pedunculated polyp. Histology confirmed a villous adenoma located in the transverse colon. **b** 2D axial image confirms that the polyp identified in (**a**) is a soft-tissue lesion (*arrow*). In the ascending (*curved arrow*), transverse (*arrow*) and descending colon (*arrowhead*), a residual fluid score of 5, a tagging residual fluid score of 5 and a distension score of 4 were found

study are remarkable results, especially so given the small volume of iodine applied with regard to that used in other studies. The fact that patients took diatrizoate meglumine and diatrizoate sodium in small doses over 42 h was probably essential for the high level of efficiency in tagging. Although recent studies [32–36] report good results when iodinated faecal tagging agents are administered over 24 h, in our opinion, the need for adequate tagging in all segments should prevail over the benefits of a reduced period of iodine administration, since the latter is not among the main sources of distress for patients. Moreover, side effects of the iodinated agent (diarrhoea, abdominal pain, nausea and vomiting) may be reduced when administered at lower doses, even if this is over a longer period of time. Few studies have been conducted with iodine tagging as the sole preparation [10, 12, 15, 19, 32–37], each of these used different doses of iodine. Iannaccone et al. [12] administered 200 ml of diatrizoate meglumine and diatrizoate sodium (total of 74 g iodine over 48 h), achieving faecal tagging judged as excellent in 98.5% of patients and episodes of diarrhoea or abdominal discomfort reported in 10.3% of patients. Other researchers applied smaller quantities (60 g of iodine) over 24–48 h [10, 19, 34], but, when side effects were assessed, a large percentage of patients was affected, particularly by diarrhoea. In our study, the amount of iodine used (60 ml of diatrizoate meglumine and diatrizoate sodium, containing 22.2 g of iodine) was substantially lower than in any previous study, except those of Keeling et al. [32] who used 15 g of iodine in frail elderly patients with a limited objective of ruling out gross pathological conditions and Liedenbaum et al. [37] who compared the effects of different doses of iodine (45 g–22.5 g). In our study, diarrhoea, with a maximum of three stools per day and graded as mild by all except 12 patients, was declared by only 7.4% (52/700) of patients. This is probably one of the key reasons why the preparation experience in our study was graded as excellent, since 94% of patients found it minimally or mildly unpleasant and non-interfering with their common daily activity, while only 5.9% considered it moderately to severely upsetting. This remarkable result indicates that this protocol enables high

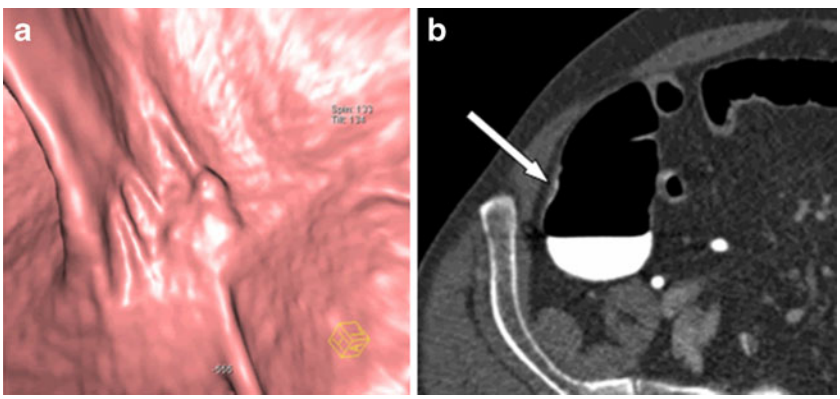

Fig. 7 A 63-year-old woman at average risk of a colorectal neoplasm, who was asymptomatic. **a** 3D endoluminal image shows a 21-mm flat polyp (protruding less than 2.5 mm from the mucosa). Histology confirmed a tubulo-villous adenoma located in the caecum. **b** Axial 2D view confirms that the polyp identified in (**a**) is a soft-tissue lesion (*arrow*). Axial image shows a residual fluid score of 3, a tagging residual fluid score of 5 and a distension score of 4 in the caecum

quality tagging and faecal cleansing with almost no significant diarrhoea and represents an encouraging outcome in CTC acceptance for screening purposes. Contrary to previous publications in which laxative cleansing before CTC is the most uncomfortable part of the whole procedure [5, 6, 18, 38], in our study the percentage of patients who considered themselves minimally disturbed by the preparation was significantly higher (78%) than those who were minimally disturbed by the examination (55%, Fig. 5). However, 89.6% of patients graded the examination as minimally-mildly unpleasant. Given this good acceptance, the excellent colonic distension achieved (4.87 mean distension) and the absence of complications, the possibility of modifying our colonic distension system, with room air, was not considered. Both techniques, manual room air insuflation and automated CO_2 delivery for CTC are safe techniques, both cause an acceptable level of discomfort during and after the examination, and they produce reliable colonic distension [39]. On similar grounds, we avoided a generalised use of spasmolytics, a more controversial practice as i.v. drug administration lengthens examination time, increases the possibility of additional side effects and adds a new source of discomfort [6, 39].

Several limitations of our study deserve specific discussion. First of all, those stemming from being performed with an observational purpose, thus preventing the estimation of direct performance indexes such as sensitivity or specificity. Nonetheless, the good surrogate performance measures (92.8% CTC-OC concordance rate and 5.9% per patient FPR) suggest that there was no significant underdiagnosis of patients with colonic lesions and that relevant lesions have been adequately detected and removed, since the prevalence of advanced neoplasia obtained in our study is in line with other screening trials.

Secondly, questionnaires about patient experience of preparation and examination were carried out, once only, immediately after the procedures, but not repeated at a later stage as in some other studies [18, 32, 33]. This could have altered patient perception, although we would expect that our conditions would, if they had any effect, bias our results towards poorer acceptance. Thirdly: The CTC reading was performed by one of two experienced radiologists in our service, as double readings would not be feasible in our clinical practice set-up.

The length of the preparation protocol could be an additional concern. Like most studies performed with a tagging-only bowel preparation for CTC [7, 12, 15, 19, 31–33], ours used a low-fibre diet with clear instructions for the patients. Most studies prescribe this diet for 2 or 3 days before the CTC examination. Low-fibre diets reduce residual bowel content and improve subjective tagging quality of residual faeces [37]. They are varied enough to barely cause any burden on patients, as evidenced by Liedenbaum el al who found no significant differences in acceptance, with respect to degree of burden, between patients who followed the restricted diet and those who did not [37]. On the other hand, the enteral liquid diet used on the day before CTC covers all dietary requirements and prevents hunger sensation. The only drawback would be that, as it is furnished by the hospital pharmacy, it adds to the overall cost of the examination, albeit to very limited amount. In this respect, the substitution of this diet for conventional liquid foods is currently under consideration. With regard to the amount of tagging agent (8×7.5 ml over 42 h in our scheme), we find it preferable to administer it in a larger number of small doses provided all segments are adequately clean and labelled and side effects are reduced. Therefore, the assayed regime provides an optimal balance between tolerance and safety, the two key factors for increasing CTC acceptance.

In conclusion, our study shows that CTC without cathartic bowel preparation and iodinated agents for faecal tagging can obtain high PPV values and a low rate of false-positive results for≥6-mm polyps comparable to those obtained with conventional preparation with laxatives. Furthermore, because of a good patients' experience, this method could really improve the acceptance of CTC for colorectal cancer screening.

Acknowledgments We thank C. P. Cadórniga for critical review of this manuscript and A. Salgado for his help with the data analysis.

References

1. Winawer SJ, Zauber AG, Ho MN et al (1993) Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 329:1977–1981
2. Levin B, Lieberman DA, McFarland B et al (2008) Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin 58:130–160
3. Pickhardt PJ, Choi JR, Hwang I et al (2003) Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 349:2191–2200
4. Kim DH, Pickhardt PJ, Taylor AJ et al (2007) CT colonography versus colonoscopy for the detection of advanced neoplasia. N Engl J Med 357:1403–1412
5. Gluecker TM, Johnson CD, Harmsen WS et al (2003) Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences. Radiology 27:378–384
6. Thomeer M, Bielen D, Vanbeckevoort D et al (2002) Patient acceptance for CT colonography: what is the real issue? Eur Radiol 12:1410–1415
7. Jensch S, de Vries AH, Pot D et al (2008) Image quality and patient acceptance of four regimens with different amounts of mild laxatives for CT colonography. AJR Am J Roentgenol 191:158–167
8. Callstrom MR, Johnson CD, Fletcher JG et al (2001) CT colonography without cathartic preparation: feasibility study. Radiology 219:693–698

9. Lefere P, Gryspeerdt S, Marrannes J, Baekelandt M, Van Holsbeeck B (2005) CT colonography after fecal tagging with a reduced cathartic cleansing and a reduced volume of barium. AJR Am J Roentgenol 184:1836–1842
10. Zalis ME, Perumpillichira J, Del Frate C, Hahn PF (2003) CT colonography: digital subtraction bowel cleansing with mucosal reconstruction initial observations. Radiology 226:911–917
11. Johnson CD, Manduca A, Fletcher JG et al (2008) Noncathartic CT colonography with stool tagging: performance with and without electronic stool subtraction. AJR Am J Roentgenol 19:361–366
12. Iannaccone R, Laghi A, Catalano C et al (2004) Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. Gastroenterology 127:1300–1311
13. Dachman AH, Dawson DO, Lefere P et al (2007) Comparison of routine and unprepped CT colonography augmented by low fiber diet and stool tagging: a pilot study. Abdom Imaging 32:96–104
14. Florie J, van Gelder RE, Schutter MP et al (2007) Feasibility study of computed tomography colonography using limited bowel preparation at normal and low-dose levels study. Eur Radiol 17:3112–3122
15. Buccicardi D, Grosso M, Caviglia I et al (2010) CT colonography: patient tolerance of laxative free fecal tagging regimen versus traditional cathartic cleansing. Abdom Imaging. doi:10.1007/s00261-010-9650-4
16. Lefere PA, Gryspeerdt SS, Dewyspelaere J, Baekelandt M, Van Holsbeeck BG (2002) Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. Radiology 224:393–403
17. Neri E, Turini F, Cerri F, Vagli P, Bartolozzi C (2009) CT colonography: same-day tagging regimen with iodixanol and reduced cathartic preparation. Abdom Imaging 34:642–647
18. Jensch S, Bipat S, Peringa J et al (2010) CT colonography with limited bowel preparation: prospective assessment of patient experience and preference in comparison to optical colonoscopy with cathartic bowel preparation. Eur Radiol 20:146–156
19. Campanella D, Morra L, Delsanto S et al (2010) Comparison of three different iodine-based bowel regimens for CT colonography. Eur Radiol 20:348–358
20. Pickhardt PJ, Wise SM, Kim DH (2010) Positive predictive value for polyps detected at screening CT colonography. Eur Radiol 20:1651–1656
21. Pickhardt PJ, Lee AD, Taylor AJ et al (2007) Primary 2D versus primary 3D polyp detection at screening CT colonography. AJR Am J Roentgenol 189:1451–1456
22. Zalis ME, Barish MA, Choi JR et al (2005) CT colonography reporting and data system: a consensus proposal. Radiology 236:3–9
23. Macari M, Lavelle M, Pedrosa I et al (2001) Effect of different bowel preparations on residual fluid al CT colonography. Radiology 218:274–277
24. Pineau BC, Paskett ED, Chen GJ et al (2003) Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. Gastroenterology 125:304–310
25. Winawer SJ, Zauber AG (2002) The advanced adenoma as the primary target of screening. Gastrointest Endosc Clin N Am 12:1–9
26. An S, Lee KH, Kim YH et al (2008) Screening CT colonography in an asymptomatic average-risk Asian population: a 2-year experience in a single institution. AJR Am J Roentgenol 191:W100–106
27. Pickhardt PJ, Taylor AJ, Kim DH, Reichelderfer M, Gopal DV, Pfau PR (2006) Screening for colorectal neoplasia with CT colonography: initial experience from the 1st year of coverage by third-party payers. Radiology 241:417–425
28. Kim DH, Pickhardt PJ, Hanson ME, Hinshaw JL (2010) CT colonography: performance and program outcome measures in an older screening population. Radiology 254:493–500
29. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G (2000) Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 343:162–168, Erratum in: N Engl J Med 343:1204
30. Lostumbo A, Suzuki K, Dachman AH (2010) Flat lesions in CT colonography. Abdom Imaging 35:578–583
31. Zalis ME, Perumpillichira JJ, Magee C, Kohlberg G, Hahn PF (2006) Tagging-based, electronically cleansed CT colonography: evaluation of patient comfort and image readability. Radiology 239:149–159
32. Keeling AN, Slattery MM, Leong S et al (2010) Limited-preparation CT colonography in frail elderly patients: a feasibility study. AJR 194:1279–1287
33. Iafrate F, Hassan C, Zullo A et al (2008) CT colonography with reduced bowel preparation after incomplete colonoscopy in the elderly. Eur Radiol 18:1385–1395
34. Liedenbaum MH, de Vries AH, Gouw CI et al (2010) CT colonography with minimal bowel preparation: evaluation of tagging quality, patient acceptance and diagnostic accuracy in two iodine-based preparation schemes. Eur Radiol 20:367–376
35. Iafrate F, Hassan C, Ciolina M et al (2011) High positive predictive value of CT colonography in a referral centre. Eur J Radiology 66: e289–292
36. Liedenbaum MH, Denters MJ, Zijta FM et al (2011) Reducing the oral contrast dose in CT colonography: evaluation of faecal tagging quality and patient acceptance. Clin Radiol 66:30–37
37. Liedenbaum MH, Denters MJ, de Vries AH et al (2010) Low-fiber diet in limited bowel preparation for CT colonography: Influence on image quality and patient acceptance. AJR Am J Roentgenol 195:W31–37
38. Beebe TJ, Johnson CD, Stoner SM, Anderson KJ, Limburg PJ (2007) Assessing attitudes toward laxative preparation in colorectal cancer screening and effects on future testing: potential receptivity to computed tomographic colonography. Mayo Clin Proc 82:666–671
39. Shinners TJ, Pickhardt PJ, Taylor AJ et al (2006) Patient-controlled room air insufflation versus automated carbon dioxide delivery for CT colonography. AJR Am J Roentgenol 186:1491–1496