Computed tomography of the bowel: a prospective comparison study between four techniques

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Purpose

An important technical requirement for the CT study of the bowel is the distension of a clear lumen with appropriate separation of the intestinal walls, both for the small and large bowel, because collapsed bowel loops can hide lesions and mimic pathologic conditions.

CT techniques designed for bowel imaging are all characterized by the administration of intraluminal contrast material to provide distension of the lumen; the way of contrast administration is the primary distinguishing feature between CT protocols dedicated to examine the small intestine (i.e. CTE and CTe) and that optimized for the study of the colon (CT-WE, also called hydrocolon-CT). In both CTe and CTE small bowel distension is provided by the anterograde administration of intraluminal contrast material (through a nasojejunal tube in CTE and oral ingestion in CTe), while mural enhancement is obtained with the injection of intravenous iodinated contrast media [1, 2]. In CTE technique neutral contrast agents are injected through the naso-jejunal catheter in a variable amount (from 1500 up to 2500 mL) [3]. In CTe negative contrast media that are most widely accepted for oral use include water, oil emulsions, solutions containing sugar alcohols, such as manitol or sorbitol, and polyethylene glycol solutions [4-6]. When performing both CTE and CTe the enteric contrast material may provide a variable grade of large bowel distension, but the real capability of these techniques to allow an adequate exploration of all colonic segments remains largely undetermined.

In some clinical concerns the CT examination has to be focused on the study of the colon. The most widely accepted CT technique for large bowel evaluation is CT-colonography with air or carbon dioxide [7-9], but the colonic distension may also be obtained using water as intraluminal contrast media. This technique, called CT with water enema - CT-WE - is based on colonic distension with water followed by intravenous administration of iodinated contrast media; it offers an excellent visualization of the colonic wall due to parietal enhancement by iodinated contrast, as well as a good contrast between wall, water-filled lumen and pericolic fat [10,11]. The neutral contrast is administered through a rectal enema tube, and it may sometimes reflux through the ileocecal valve from the cecum into the terminal ileum, revealing pathologic findings of the last ileal loop.

More recently a new CT technique, called CTE-WE (CT enterography with water enema), has been proposed to obtain a simultaneous distension of the small and large intestine. This original technique has been employed to evaluate a cohort of 221 patients with Crohn's disease, providing a complete assessment of disease phenotype [12].

The aim of the present study was to prospectively compare the grade of distension of the different bowel segments (including both small and large bowel) obtained using the above mentioned four different CT techniques (CTE, CTe, CT-WE and CTe-WE), providing also data concerning patient's tolerance toward each CT protocol.
Methods and Materials

Inclusion of patients

A total of 120 consecutive outpatients (65 males and 55 females, mean age 51.09 ± 13.36 years) with suspected or known pathologies involving the gastrointestinal tract (including both small and large bowel) were recruited. Inclusion of patients was designed to obtain four groups with the same number (30 subjects each one), each group corresponding to a specific, clinically indicated CT protocol.

The first consecutive 60 patients with a clinical indication for the CT examination of the small bowel were randomly assigned by the study coordinator to undergo either the CTE or the CTe protocol; so, for both CTE and CTe, inclusion criteria were the same: suspected or known Crohn’s disease, suspected carcinoid tumor, abdominal pain of unknown origin, diarrhea, obscure gastrointestinal bleeding in patients with negative upper and lower endoscopy. The first consecutive 30 patients who had to undergo a clinically indicated CT investigation of the large bowel were assigned to the CT-WE protocol; inclusion criteria were as follows: diverticulitis, suspected or known ulcerative colitis, detection of colo-rectal polyps, preoperative localization and staging of colorectal cancer detected at videocolonoscopy, positive fecal occult blood test, chronic iron deficiency anemia, cramping or acute abdominal pain of lower abdominal quadrants, and hematochezia. Inclusion criteria for the CTe-WE group were comprehensive of those of the other three groups, including patients with suspected or known diseases affecting the small and/or the large bowel.

Exclusion criteria included: the clinical suspicion and/or conventional radiographic findings suggestive for bowel (sub-) obstruction, age < 18 years, previous bowel resection, pregnancy, contraindication to intravenous injection of hyoscine-N-butylbromide, and general contraindications to intravenous administration of iodinated contrast media (i.e. EGFR < 45 mL/min and documented previous reaction to iodinated contrast material). The first 120 patients who agreed to participate and provide informed consent were enrolled in the study.

CT protocols

All examinations were performed with a 64-slice multidetector CT scanner with the patient in supine position. Bowel wall enhancement was produced by intravenous injection of iodinated contrast medium with an iodine concentration ranging between 350 and 370 mg/mL. The iodine flow injected per second per kilogram of body weight was maintained constant for all examinations (1.11 g I/s). The flow rate was set at 3.2-3 mL/s with an automatic injector and acquisition was started in the portal phase, 45 s after the arterial peak in the upper abdominal aorta using a bolus-tracking software. Immediately before CT acquisition, bowel hypotonia was obtained by i.v. injection of 2 mL hyoscine-N-
butylbromide 20 mg/mL. Bowel cleaning was standardized for all groups of patients: a low fiber diet for 3 days before the CT examination, and oral administration of 2 L of an isotonic non-absorbable electrolyte solution containing polyethylene glycol the afternoon before examination.

Patients enrolled in the conventional invasive CTE protocol underwent nasojejunal intubation, which was followed by injection of 1800-2000 mL of neutral contrast material (0.5% methylcellulose) administered at a rate of approximately 60 mL/min before CT acquisition. In the CTe protocol small bowel lumen distension was achieved by oral administration of 1500-2000 mL of a non-absorbable isotonic solution containing polyethylene glycol 45 min prior to CTe-WE. All the volume of neutral enteral contrast material had to be drunk in a time interval not superior to 15-20 min. All CT-WE examinations were performed with the following technique. A lubricated enema tube was inserted into the rectum. The tube was connected to a bag containing 2000 mL of lukewarm tap water, which was gently infused through gravity in 3-4 min, with the patient placed supine on the CT table. When performing CTe-WE both small and large bowel were distended with neutral enteral contrast material.

Image analysis

All CT examinations were reviewed on a dedicated workstation. Both quantitative and qualitative analyses were performed in consensus by two radiologist with a 5-year and 10-year experience in abdominal imaging respectively. They were blinded to the type of CT protocol of each examination, and CTs were reviewed in a random order.

For purposes of analysis, the small bowel was divided into jejunum, ileum, and terminal ileum according to Arslan et al. [13]. Jejunal loops may be distinguished from that of the proximal ileum due to their anatomical localization and for the presence of more circular folds (valvulae conniventes) per centimeter. It is known that, on average, the jejunum presents four to seven folds every 2.5 cm, and the ileum, three to five folds in the same length [14]. Distal jejunal loops continue as the proximal ileum. The last ileal loop has usually a right cephalic orientation and it may be correctly visualized on the coronal plane. The large intestine was divided into six segments: rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and cecum, as proposed by Ajaj et al. [15]. In order to identify a potential source of bias in the assessment of true luminal filling, CT examinations were preliminarily analyzed to find out the presence of inflammatory or neoplastic strictures of the small intestine that may have artificiously improved the distension proximally. A prestenotic dilatation was considered significant when the small bowel lumen (proximal to a luminal narrowing) exceeded a 2.5-cm diameter [12].

The quantitative analysis of intestinal distention was performed measuring the largest cross-sectional diameter (from outer wall to outer wall) of each bowel segment. Distension measurements were carefully made in correspondence to healthy, unaffected bowel segments.
The qualitative analysis was also performed on a per segment basis using a continuous 3-point scale (0, poor; 1, good; 2, optimal), as described by Megibow et al. [16]. An optimal score meant that the segment was distended, the wall was uniformly visualized, and a fold pattern could be recognized. A score of 0 meant that the segment was collapsed without any luminal separation, the walls could not be seen, and a fold pattern could not be recognized. The percentage of bowel segments with an adequate distension for diagnostic purposes was obtained summing the relative percentages of segments that received both good and excellent scores.

**Statistical analysis**

Statistical analysis was performed to assess the presence of a significant difference between the grade of bowel distension obtained with the four CT protocols on a per segment basis.

The normality of data derived from quantitative per segment analysis was assessed. It was observed that measurements of the largest cross-sectional diameter of some bowel segments did not follow the normal distribution, so all these quantitative data were considered as non-parametric and expressed as medians and range (minimum to maximum). The Kruskal-Wallis test for non parametric data was used to assess the presence of a significant difference among the medians of measurements obtained from the four groups. After obtaining a significant Kruskal-Wallis test, the Mann-Whitney U-test was applied for pairwise comparisons. The type I error was protected by using the Bonferroni adjustment, and the "a priori" alpha level (0.05) was divided by the number of pairwise comparisons (6), thus resulting in a level of significance of 0.0083.

Frequencies obtained from qualitative per segment analysis were compared using the Chi-square test, while pairwise comparisons were conducted by means of the Fisher's exact test. In this case also, type I error was protected by using the Bonferroni adjustment, setting the level of significance at 0.0083.
Results

Quantitative analysis

Distension of the jejunum was significantly different among the four CT protocols (p<0.0001), and CTE provided the best distension of jejunal loops among all the other techniques (p<0.0001). There was no significant difference between CTe and CTe-WE (p=0.1453). CT-WE provided the lowest median value of distension of jejunal loops (10 mm, range 6-15 mm).

Distension of the ileum was significantly different among the four CT protocols (p<0.0001), and no significant difference was found between the median values of ileal distension provided by CTE, CTe and CTe-WE (CTE vs CTep= 0.0811; CTE vs CTe-WEp= 0.234; CTe vs CTe-WEp= 0.579). CT-WE provided the lowest median value of distension of the ileum (10 mm, range 4-22 mm), which was significantly inferior to that provided by the other CT protocols (p< 0.001 for all pairwise comparisons).

No significant difference was found among the median values of distension of the terminal ileum provided by the four CT protocols, despite the p-value tended to reach the level of significance (p< 0.0608). In particular the comparison between CTe and CTe-WE gave the lowest p-value (p= 0.0292), which was otherwise not significant due to the Bonferroni adjustment for pairwise comparisons (adjusted level of significance p= 0.0083).

The median values of distension of cecum, ascending, transverse, descending colon and sigma provided by CT-WE and CTe-WE were significantly higher than those provided by the other two techniques. The p-value was < 0.0001 for all the following comparisons: CT-WE vs CTE, CT-WE vs CTe, CTe-WE vs CTE, CTe-WE vs CTe, for all segments of the large bowel.

Qualitative analysis

Jejunum

CTE determined a significantly higher frequency of patients with an optimal jejunal distension (90%; 27/30 patients) when compared to CTe (3.3%; 1/30 patients; p < 0.001), CT-WE (0%), and CTe-WE (20%; 6/30; p < 0.001) (Fig. 1). In this regard there was no significant difference between CTe and CTe-WE protocols (3.3% vs 20%, respectively; p = 0.1). The frequency of patients with an adequate distension obtained with CTE (30/30; 100%) was significantly higher than that achieved by CTe (13/30 patients [43.3%]; p < 0.001) and CTe-WE (8/30 patients [26.7%]; p < 0.001) (Fig. 2). In no patient of the CT-WE group the jejunum was adequately visualized. Concerning the percentage of examinations with an adequate luminal filling, no significant difference was found between CTE and CTe-WE groups (26.7% vs 43.3%; p= 0.28).
Ileum

The frequency of patients with an optimal distension of the ileum was not significantly different between CTE (27/30 patients; 90%), CTe (21/30 patients; 70%) and CTe-WE groups (24/30 patients; 80%) (p= 0.15), but it was significantly lower in the CT-WE group (4/30, 13.3%) when compared to other groups (p< 0.001 at all pairwise comparisons). Ileal distension was adequate in all patients who had undergone CTE (30/30; 100%), in 28/30 patients (93.3%) who were submitted to CTe, in 29/30 patient (96.6%) of the CTe-WE group, and in 10 patients (33.3%) of the CT-WE group; in this regard there was no significant difference between CTE, CTe and CTe-WE protocols (p= 0.35), but the difference was significant when comparing CT-WE group with all the other groups (p< 0.001).

Terminal Ileum

The frequency of patients with an optimal distension of the terminal ileum was different between the CTE (16/30 patients; 53.3%), CTe (9/30 patients; 30%), CT-WE (8/30 patients; 26.6%), and CTe-WE protocols (23/30 patients; 76.7%) (p < 0.001); pairwise comparisons showed a significant difference with regard to CTe-WE vs CTe and CTe-WE vs CT-WE (p < 0.001 in both cases) (Fig. 3). No difference was found between the CTE and CTe-WE protocols (p= 0.1). The frequency of examinations with an adequate luminal filling of the terminal ileum was not significantly different between CTE (27/30 patients; 90%), CTe (25/30 patients; 83.3%), CT-WE (21/30 patients; 70%) and CTe-WE groups (28/30; 93.3%) (p= 0.066).

Cecum and other colonic segments

The frequency of examinations with an optimal visualization of the cecum was almost the same for the CT-WE (29/30, 96.6%) and CTe-WE (28/30, 93.3%) protocols, but it was largely inferior in the CTE (8/30, 26.6%) and CTe (9/30, 30%) groups (p< 0.0001 at all pairwise comparisons [CT-WE vs CTE, CT-WE vs CTe, CTe-WE vs CTE and CTe-WE vs CTe]). There was also a significant difference among the four CT techniques in the frequency of patients with an adequate luminal filling of the cecum (p< 0.0001), with CT-WE and CTe-WE determining the highest percentages (30/30, 100% in both cases). In 15/30 patients (50%) CTE determined an adequate distension of the cecum, which was obtained in 21/30 patients (70%) who had undergone CTe, thus resulting in no significant difference between these two techniques (p= 0.18).

All the other colonic segments distal to cecum (ascending, transverse, descending colon and sigma) were optimally distended by both CT-WE and CTe-WE with very high frequencies (>86.6% for each colonic segment with both techniques) (Fig. 4). For all colonic segments distal to cecum CTE and CTe provided lower frequencies of patients with an adequate luminal filling than those obtained with the other techniques. CTe
provided a higher frequency of adequate distension than that obtained by CTE for cecum (21/30 vs 15/30, not significant), ascending colon (19/30 vs 17/30, not significant), descending colon (12/30 vs 6/30, not significant), sigma (11/30 vs 1/30, p< 0.0024) and rectum (0/30 vs 10/30, p< 0.00032).
Fig. 1: Volume-rendered CT reconstruction (A) and coronal reformatted CTE image (B) which show the position of the nasojejunal enteroclysis catheter with the tip at the duodeno-jejunal passage (arrow).

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Fig. 2: Coronal oblique reformatted CTe-WE image shows simultaneous distension of ileum (i), cecum (C) and ascending colon (ac).

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Fig. 3: Coronal reformatted CTe-WE image with optimal distension of the ileocecal area, including both cecum (C) and last ileal loop (i), which is affected by Crohn’s disease.

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**Fig. 4:** Coronal reformatted CTe-WE images (A and B) show optimal simultaneous distension of both small and large bowel. Legend: J, jejunum; i, ileum; ac, ascending colon; tc, transverse colon.

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Conclusion

Luminal distention is very important for CT imaging of the bowel, because collapsed bowel loops can hide even large lesions and may falsely mimic wall thickening [2], and such a requisite is valid for both the small and large bowel. Macari et al. [14] have considered that appropriate luminal distension is achieved when the small bowel diameter corresponds to at least 2 cm, and intraluminal contrast material separates the intestinal walls and allows the identification of folds (valvulae conniventes), without collapsed loops.

In our work, we found that CTE provides better distension of jejunal loops at both qualitative and quantitative analysis (p< 0.001). In both CTE and CTe the prominent mechanism responsible for small bowel distension is the antegrade administration of contrast material; when performing CTE, the direct infusion of methylcellulose in the jejunal loops results in a better distension of this bowel tract than that provided by CTe. On the other hand, CTE is characterized by an additional radiation dose given to the patient due to the fluoroscopically guided placement of the nasojejunal tube. However, the optimal distension of jejunal loops, which is constantly provided by CTE, may be particularly important to diagnose pathologies that selectively affect this segment of the small bowel (i.e. celiac disease) and their complications (i.e. lymphoma and adenocarcinoma in celiac patients) [17]. A particular clinical indication to perform CTE is the detection and characterization of lower ileocolic inflammatory lesions in patients with stricturing Crohn's disease involving the gastric antrum or the duodenal bulb and determining a gastric outlet syndrome [18].

The jejunum is not adequately distended by CTe (and CTe-WE) because the duodenum and proximal jejunal loops distend earlier than terminal ileum (15-20 min vs 45-60 min after the ingestion of oral contrast), and the large majority of CTe protocols, including that of our study, are designed to explore the ileum and the terminal ileal loop [2, 3]. So, the major limitations of CTe include the ingestion of a large volume of fluid in a relatively small amount of time, the need for a precise timing of the CT scan in relation to the oral contrast intake, and the lack of a simultaneous visualization of jejunum and ileum.

With regard to the ileum, the median values of luminal distension obtained with CTE, CTe and CTe-WE were not significantly different between each other, and high frequencies of optimal distension were found at qualitative analysis with all these CT techniques. CT-WE technique allowed an adequate distension of the ileum only in 1/3 of patients. The terminal ileum is an important, but sometimes difficult area to adequately examine on both small bowel barium follow-through (SBFT) and enteroclysis examinations. The degree of contrast opacification and luminal distension of the terminal ileum can vary widely with both techniques.

In our study we found that there is no significant difference among all CT techniques in regard to the frequencies of patients with an adequate distension of the terminal ileum,
with the greatest median value of luminal distension provided by CTe-WE and the lowest one obtained with CT-WE.

When performing CTe-WE, the terminal ileum is distended with a double mechanism: the anterograde passage of oral contrast and the retrograde passage of trans-rectally injected water through the ileocecal valve, which is incompetent in a large number of patients [12]. This second mechanism of distension of the terminal ileum (reflux of water through the ileocecal valve) may be quite consistently observed also when performing CT-WE (21/30, 70%). The incompetence of the ileocecal valve and the likelihood ileocecal reflux are increased by the pharmacological effect of the smooth muscle relaxant (hyoscine-N-butylbromide), which is administered before CT acquisition (Fig. 5).

In the CTe-WE technique the reflux of water from the cecum through the ileocecal valve into the terminal ileum combined with the orally ingested contrast material results in excellent luminal distension of both sides of the ileocecal area [12]. This simultaneous and combined distension of terminal ileum and cecum is not so consistent with the other techniques, as we observed a significant difference among the four CT protocols in the frequency of patients with an adequate distension of cecum (p< 0.0001). In particular, the anterograde passage of oral contrast through the ileocecal valve was not sufficient for an adequate separation of cecal walls in 15/30 patients belonging to the CTE group and in 9/30 patients of the CTe group. On the contrary, CTe-WE and CT-WE provided very high frequencies of patients with adequate distension of the cecal lumen (100% in both cases), thus underlining the advantage of techniques that include a retrograde colonic distension for a comprehensive assessment of the ileocecal area. The main advantage of CTe-WE over CT-WE is that CTe-WE provides an adequate demonstration of the entire ileum, and not only of the last ileal loop.

To our knowledge only one work examined the grade of distension and contrast opacification of large bowel loops obtained with CTe technique. In this work Johnson et al. [20] evaluated the grade of colonic distension in 70 CTe of patients with Crohn’s granulomatous colitis and ulcerative colitis performed either with (33/70, 47%) or without (37/70, 53%) intravenous administration of 0.5 mg of glucagon. Interestingly they found a relative high frequency of patients with an adequate colonic distension for diagnostic purposes in both groups (66% of patients who received glucagon and 63% of patients who did not receive glucagon), but their assessment was not made on a per-segment basis.

In our group of patients who had undergone CTe we found a trend of progressive decrease in the frequency of colonic segments with an adequate distension from the cecum (70%) to the rectum (33.3%). In the CTE group results concerning colonic distension were even more inconsistent. On the other hand the trans-rectal introduction of a 1500-2000 mL water enema allowed to obtain a colonic distension suitable for image assessment in all patients belonging to the CT-WE and CTe-WE groups.
Up to date CT-WE has received little attention in the radiological literature. Two precedent works were focused on the ability of CT-WE to detect colorectal cancer and polyps using colonoscopy as reference standard. Ridereau-Zins et al. [10] reported an overall CT-WE sensitivity and specificity of 98.6 and 95.0%, respectively, while Soyer et al. [11] provided a sensitivity of 95% for tumors ≤6 mm. Soyer et al. performed also a semi-quantitative analysis of their CT-WE examinations using a tree-point scale, depending on the grade of colorectal distension. Image analysis revealed optimal colon distension in all but three cases of their study cohort (98/101, 97%), and, in the remaining three cases (3/101, 3%), colonic distension was acceptable but this did not hamper the diagnostic capabilities of the CT examinations.

A drawback of the quantitative analysis performed in our study is that the widest wall-to-wall diameter is only a surrogate measure of the overall distention within a segment of the gastrointestinal tract. Currently there is no readily available method that would allow us to measure the exact volume of the entire segment of interest. The quantitative findings, however, were found to parallel those of qualitative assessment, thus supporting reader’s qualitative impression of the entire segment.

CT studies of the bowel should be tailored to answer the clinical question. CTE is the only CT protocol that guarantees a constantly good distension of the jejunum, but the positioning of the nasojejunal tube is labor-intensive and exposes patients to an additional radiation dose. CT-WE may be considered a useful CT protocol to explore the large intestine, including inflammatory and neoplastic pathology, with the advantage of providing retrograde distension of the last ileal loop in a high percentage of patients. CT-WE allows a simultaneous, combined and constant distension of both small and large bowel.
**Fig. 5:** CTe-WE coronal reformatted image which shows optimal distension of the ileocecal area with patency of the ileocecal valve (arrow). Legend: c, cecum; i, terminal ileum.

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