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Multi-detector CT enterography in active inflammatory bowel disease: Image quality and diagnostic efficacy of a low-radiation high contrast protocol

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ABSTRACT

Purpose: To prospectively evaluate image quality and diagnostic efficacy of a low radiation-high contrast (LR-HC) CT Enterography (CTE) in active Inflammatory Bowel Disease (IBD).

Materials and methods: Eighty-five (36M; 49F; 17–75 yrs) patients with active IBD underwent contrast-enhanced CTE and were stratified in two groups according to age (< or ≥45 yrs): Group A (N = 45; 32 ± 9 yrs; 58 ± 10 kg) and Group B (N = 40; 58 ± 10 yrs; 61 ± 13 kg). Each group received a different amount of radiation (Noise Index, NI) and non-ionic iodinated contrast media (LOCM) as follows: Group A (NI = 15; 2.5 ml/kg) and Group B (NI = 12.5; 2 ml/kg). Thyroid functional tests were performed in all patients of group A at 4–6 wks. Signal- and contrast-to-noise ratios were calculated for liver (L) and abdominal aorta (A). Statistical analysis was performed by Student's *t*- or Chi-square test for continuous and categorical data, respectively.

Results: No patient of Group A developed signs of thyrotoxicosis. SNR_L, CNR_L and diagnostic accuracy of CTE were 8.4 ± 1.7 vs 8.9 ± 2.1 ($p = 0.256$), 5.4 ± 1.5 vs 5.6 ± 1.7 ($p = 0.486$) and 91.1 vs 92.5% ($p = 0.764$) whereas the effective dose and the LOCM administered were 6.7 ± 2.2 vs 13.9 ± 6.0 mSv ($p < 0.001$) and 144 ± 25 vs 122 ± 25 ml ($p < 0.001$) for Group A and B, respectively.

Conclusion: LR-HC CTE is a dose-effective protocol in the evaluation of active IBD in young patients.

1. Introduction

Contrast-enhanced multi-detector CT-enterography (CTE) is currently regarded as the CT technique of choice to evaluate active Crohn's disease [1] as no significant differences have been observed in its diagnostic accuracy compared to CT enteroclysis [2] and it is also considered useful in the evaluation of colonic involvement [3]. Indeed, as it is less time consuming than Magnetic Resonance Enterography (MRE) and widely available, CTE has also emerged in clinical practice as the imaging modality of choice in the assessment of Inflammatory Bowel Disease (IBD) in the acute setting [4]. Moreover, as CTE usually results in a more reproducible image quality than MRE [5], the American College of Radiology guidelines recommend it as the initial diagnostic step in patients with only a clinical suspicion of Crohn's disease [6].

However, there are major concerns about the radiation exposure resulting from multi-detector CT technology due to the average age of patients and the relapsing-remitting course of IBD [7]. As a result, several dose-reduction strategies have been successfully applied to CTE protocols such as the use of iterative reconstruction (IR) algorithms in place of the filtered back-projection (FBP) to reduce the image noise associated to either low-dose [8,9] or low-voltage settings [10,11]. These strategies have resulted in a significant reduction of the estimated effective dose (ED) absorbed by patients compared to that delivered by standard CTE protocols with a comparable image quality and diagnostic accuracy [8–11].

Nonetheless, radiologists should be aware that improvement in the quality of CT images obtained using low dose protocols may also be achieved by increasing the amount of iodinated contrast media

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administered as first suggested by Watanabe et al. [12].

Indeed, the possibility of balancing the effects of radiation and contrast media dose on the image quality of contrast-enhanced abdominal CT scans has been reported both in an experimental [13] as well as in a clinical setting [14]. In this latter study, an increased amount of non-ionic iodinated contrast media (LOCM) was safely and effectively administered in young patients with normal thyroid and renal function to compensate for the lower image quality resulting from a low dose protocol performed by simply selecting a higher noise index (NI) in the automated tube-current modulation (ATCM) system [14]. As the image noise is inversely related to the square root of the radiation dose [15], this protocol resulted in a significant reduction of the estimated ED compared to a standard protocol with a comparable image quality as evaluated by both qualitative and quantitative analysis [14]. More recently, the diagnostic efficacy of such a low radiation - high contrast (LR-HC) CT protocol has been evaluated in selected young patients with non-traumatic acute bowel disease [16].

In the present study, we prospectively investigated both the effects on image quality as well as the diagnostic accuracy of a LR-HC CTE performed in selected young patients with active IBD in comparison to a standard protocol performed in adult patients in the same clinical context.

2. Materials and methods

This prospective study was approved by the local Ethical Committee Board on February 26th 2014 and written informed consent was obtained from all patients.

2.1. Population

From November 2014 to October 2015 ninety-five (45M; 50F; aged 17–81 yrs) consecutive patients were referred from the Department of Gastroenterology of our Institution to undergo contrast-enhanced CTE for either a clinical and ultrasonographic suspicion of active Crohn's disease (CD) or an exacerbation of known IBD (either CD or Ulcerative Colitis). As 8 patients were not considered eligible for the presence of either thyroid ($n = 2$), renal ($n = 2$) or cardio-vascular co-morbidities ($n = 4$) and two patients were lost to follow-up, final population included 85 patients (36 M; 49F; aged 17–75 yrs). As radiation and contrast media are commonly regarded as age-specific risks [13], patients were stratified in two groups according to age with a threshold set at 45 yrs ($<$ or $\geq$): Group A (17–44 yrs; N = 45; 32 ± 9 yrs; 58 ± 10 kg) and Group B (45–75 yrs; N = 40; 58 ± 10 yrs; 61 ± 13 kg).

For all patients, Body Mass Index (BMI, kg/m^2) and Glomerular Filtration Rate (GFR, ml/min) based on the Cockcroft-Gault formula [17] were calculated.

2.2. CTE protocol

Most (68/85, 80%) patients underwent a contrast-enhanced multidetector (Aquilion 64,Toshiba, Japan) CTE performed after oral administration of 1200–1400 ml of a 7% polyethylene-glycol (PEG) solution from 45 to 60 min prior to the CT examination followed by ingestion of 500 ml of tap water prior to CT acquisition [18]. In seventeen patients (7 in Group A and 10 in Group B) with known CD presenting with signs and symptoms of small bowel obstruction fractionated oral administration of the 7% PEG solution had to be aborted after 500–750 cm^3 and ingestion of tap water was not undertaken.

2.3. CT technique

In all patients a caudo-cranial acquisition from the pubic symphysis to the diaphragm was performed in the portal venous phase with the following scanning parameters: detector configuration = 1 × 32 mm; table feed 36 mm/s; rotation time 0.75 s; helical pitch = 27; section thickness = 5 mm; 120 kVp; ATCM (*Sure Exposure 3D*). All images were reconstructed with a standard (*kernel = 3*) FBP algorithm.

In each patient the scan delay (T_{delay}) was calculated according to the following formula [14]:

$$T_{delay} = CI + 25 - T_{SD}$$

where CI is the duration of contrast injection, T_{SD} is the scan duration and 25 is the average of the sum of the abdominal aortic (15 s) and the hepatic arrival times (35 s) [19].

For each group a different Noise Index (NI = 12.5 vs 15) was selected in the ATCM system and a different amount (2.0 vs 2.5 ml/kg) of LOCM (Iopamiro 370 mgI/ml; Bracco Imaging S.p.A., Milan, Italy) was administered as follows: Group A (NI = 15; 2.5 ml/kg) and Group B (NI = 12.5; 2 ml/kg). In all patients, i.v. contrast injection was followed by 100 ml of saline solution administered at the same rate with an automated dual-head injector (Enpower CTA, Bracco Imaging S.p.A., Milan, Italy).

All patients of Group A underwent evaluation of thyroid function (*TSH*, *FT3*, *FT4*) at four to six weeks to exclude an Iodine-induced thyrotoxicosis [20]. In all patients, the radiation dose delivered was reported as both volumetric CT Dose Index ($CTDI_{vol}$, *mGy*) and Dose-Length Product (DLP, *mGy *cm*) whereas the estimated ED (*mSv*) was calculated by applying a conversion factor of 0.015 to the DLP [21].

2.4. Image analysis

Image analysis was performed by two senior radiology residents on both axial as well as 5 mm thick coronal reformatted images using a dedicate Workstation (OsiriX Imaging Software, Geneve, Switzerland) with standard window settings (WW = 450 HU; WL = 50 HU).

Readers were asked to independently score the grade of luminal filling of small bowel loops according to a 5-point scale: *5 = Excellent*; *4 = Good*; *3 = Fair*; *2 = Poor*; *1 = Inadequate*. In both groups, anatomic criteria were used to distinguish jejunal (*left hypocondrium and left flank*) from proximal (*right flank*) and pelvic ileal loops (*pelvic inlet*) [22]. In twelve patients (4 in Group A and 8 in Group B) previously submitted to surgical resection, proximity to the ileo-colic anastomosis was used to identify the neo-terminal ileum and the different number of folds per 2.5 cm of length (*4–7 for jejunum and 3–5 for ileum*) was used as a criteria to distinguish jejunal from proximal ileal loops [22]. Confident recognition of folds was also used as the imaging criteria for an optimal distention of either jejunal or proximal ileal loops whereas a caliber of at least 1.5 cm was chosen as a marker of an adequate distension for pelvic ileum [23].

In all patients, Signal-to-Noise ratios (SNR) were calculated for both hepatic parenchyma and abdominal aorta as previously described [14]. Four circular (1 cm^2) regions of interest (ROI) were also placed within the psoas muscles at mid-lumbar level (L3) and the values in Hounsfield Units were averaged to obtain the mean of muscle tissue (μ_M). Values of the standard deviation measured in each ROI were also recorded and averaged to obtain the image noise (σ). Contrast to noise ratio of the liver (CNR_L) and of the abdominal aorta (CNR_A) were then calculated with the following formula:

$$CNR_L = (\mu_L - \mu_M)/\sigma;\ CNR_A = (\mu_A - \mu_M)/\sigma$$

In addition, to normalize the CNR_A for the mean ED in each group, the relative figure of merit (FOM) [24] was calculated with the following formula:

$$FOM_A = CNR_A{}^2/ED$$

2.5. CTE diagnosis

In all patients, the CTE diagnosis of IBD was based on established CT signs of active inflammatory bowel involvement such as wall thickening (>3 mm), mural hyper-enhancement (*increased attenuation of the inner*

layer), mural stratification (*bilaminar or trilaminar appearance of the bowel wall*), prominence of the vasa recta (*comb sign*) and mesenteric lymph nodes [25–27]. In patients with active CD, the pattern of disease was further classified as nonstricturing/nonpenetrating (B1), stricturing (B2) or penetrating (B3) according to established criteria [27].

2.6. Reference standard

Original non structured CTE reports were compared with reference standard diagnoses based on open ($n = 29$) or laparoscopic surgery ($n = 10$), ileo-colonoscopy with ($n = 28$) or without biopsy ($n = 6$) and clinical follow-up ($n = 12$) performed at 12 ± 4 months (range 4–18 mo.).

2.7. Statistical analysis

Statistical analysis was performed by using MedCalc 2.1 and the Statistical Package for the Social Sciences (SPSS, Chicago, Ill) version 20.0 for Windows. Differences in continuous variables were analyzed by the unpaired Student's *t*-test whereas non parametric tests were used for categorical data. In detail, the Mann-Whitney *U* test was used to assess the differences in the grade of luminal distension of small bowel loops and the Chi-square test was used to assess the differences in the diagnostic performance of the two protocols, both with a level of significance of 0.05. Finally, inter-observer agreement was evaluated by the Cohen's *k*-analysis [28]. A *k* value of 0.00 indicates no agreement whereas k values of 0.1–0.2, 0.21–0.40, 0.41–0.60, 0.61–0.80 and 0.81–1.00 indicate a poor, fair, moderate, good and perfect agreement, respectively.

3. Results

3.1. Patients' characteristics

Patients' features (age, gender, body weight and height, BMI) are summarized in Table 1 along with the serum creatinine (mg/ml) and GFR (ml/min) values. Gender distribution was similar in group A whereas a higher but not significantly different ($p = 0.453$) numbers of females was observed in group B. No significant differences were also observed between patients' weight ($p = 0.378$) and height ($p = 0.085$). As a result, BMI values were also lower but not significantly different in Group A than in Group B ($p = 0.078$) (Table 1). Conversely, although no significant differences were observed between serum creatinine levels ($p = 0.772$), GFR values were significantly higher in patients of Group A than in those of Group B (Table 1).

3.2. Non-ionic iodinated contrast media

No adverse reactions to the LOCM used were observed in both groups and none of the patients of Group A developed clinical and/or laboratory signs of thyroid dysfunction at follow-up. The amounts of LOCM injected were significantly different with 144 ± 25 vs 122 ± 25 ml ($p < 0.001$) in Group A and B, respectively, corresponding to an Iodine load of 53.6 ± 9.2 and 45.1 ± 9.2 g (Table 2).

Table 1
Patients' anagraphic and physical characteristics as well as serum creatinine and GFR values are reported for both groups along with the levels of significance (*p*) according to the unpaired Student's *t*-test. BMI = Body Mass Index: GFR = Glomerular Filtration Rate. Data are reported as mean ± 1 sd.

Patients' features	Group A ($n = 45$)	Group B ($n = 40$)	*p*
Age (years)	32 ± 9	58 ± 10	–
Gender (M/F)	23/22	14/26	0.453
Weight (kg)	58 ± 10	61 ± 13	0.378
Height (cm)	167 ± 8	164 ± 7	0.085
BMI (kg/m^2)	20.5 ± 2.8	22.3 ± 3.9	0.078
Serum creatinine (mg/dl)	0.75 ± 0.15	0.76 ± 0.20	0.772
GFR (ml/min)	109 ± 20	88 ± 31	<0.001

Table 2
Effective tube current (ETC), Volumetric Computed Tomography Dose Index ($CTDI_{vol}$), Dose-Length products (DLP), Effective dose (ED), volumes of contrast media (ml) and Iodine load (gr) administered to patients of both groups are reported along with the scan delays of multi-detector CTE acquisitions and the levels of significance (*p*) according to the unpaired Student's *t*-test. For only dose metrics, data are reported as both mean ± 1 standard deviation as well as median with 1st and 3rd quartile.

Parameter	Group A	Group B	*p*
ETC (mAs)	73 ± 28	125 ± 70	<0.001
Median	76	119	
1st quartile	46	84	
3rd quartile	96	163	
$CTDI_{vol}$ (*mGy*)	11.9 ± 3.1	18.9 ± 6.3	<0.001
Median	11.0	19.7	
1st quartile	9.7	17.9	
3rd quartile	13.6	22.4	
DLP (*mGy*cm*)	450 ± 146	928 ± 398	<0.001
Median	435	856	
1st quartile	343	620	
3rd quartile	529	1172	
ED (*mSv*)	6.7 ± 2.2	13.9 ± 6.0	<0.001
Median	6.8	12.8	
1st quartile	5.3	9.3	
3rd quartile	8.2	17.6	
Contrast media (*ml*)	144 ± 25	122 ± 25	<0.001
I (*g*)	53.6 ± 9.2	45.1 ± 9.2	<0.001
Scan Delay (*s*)	72 ± 7	75 ± 8	0.141

3.3. Effective absorbed dose

The ATCM system resulted in an effective tube current of 73 ± 28 mAs (*range 40–272 mAs*) in patients of Group A and of 125 ± 70 mAs (*range 60–394 mAs*) in patients of Group B ($p \leq 0.001$). As a result, both $CTDI_{vol}$ (*mGy*) and Dose-Length Products (*mGy*cm*) were significantly different with an estimated ED (*mSv*) of 6.7 ± 2.2 vs 13.9 ± 6.0 ($p < 0.001$) for Group A and B, respectively (Table 2).

3.4. Scan delays

In each patient the duration of contrast injection (CI) was equal to the body weight as the rate of the injection was kept identical to the amount of LOCM administered/kg of body weight. As a result, scan delays were only affected by scan duration (12–15 s) and ranged between 60 and 90 with mean values of 72 ± 7 vs 75 ± 8 s ($p = 0.141$) for Group A and B, respectively (Table 2).

3.5. Luminal distension

No significant differences were observed in the grade of luminal distension of small bowel loops between patients of Group A and B. In detail, while luminal distension of jejunal loops was mostly scored as fair or poor (2.82 ± 1.54 vs 2.94 ± 1.23; $p = 0.770$) by both readers ($k = 0.62$) for Group A and B, respectively, that of both proximal and pelvic ileum was mostly scored as good or excellent (4.39 ± 0.66 vs 4.25 ± 0.74, $p = 0.650$ and 4.58 ± 0.67 vs 4.49 ± 0.61, p 0.720) for Group A and B respectively, both with good inter-observer agreements ($k = 0.67$ and 0.70, respectively).

3.6. Image quality

Quantitative evaluation of image quality is reported in Table 3. Whereas peak hepatic enhancement was significantly higher in patients

Table 3
Attenuation values (HU) of liver, abdominal aorta and psoas muscles are reported along with the Signal-to-Noise Ratios (SNR) and Contrast-to-noise Ratios (CNR) for the liver (L) and abdominal aorta (A), the image noise (σ) for each group, the Figure of Merit (FOM) for the CNR_A and the *p* value according to the unpaired Student's *t*-test. Data are reported as mean ± 1 sd.

Parameter	Group A	Group B	*p*
Liver (HU)	150 ± 20	131 ± 17	< 0.001
SNR_L	8.4 ± 1.7	8.9 ± 2.1	0.265
CNR_L	5.4 ± 1.5	5.6 ± 1.7	0.486
Aorta (HU)	217 ± 22	233 ± 51	0.130
SNR_A	11.1 ± 2.2	15.3 ± 3.9	< 0.001
CNR_A	9.9 ± 2.4	13.6 ± 4.2	< 0.001
Psoas muscles (HU)	70 ± 9	56 ± 12	< 0.001
Sigma (σ)	15.0 ± 3.0	13.0 ± 2.0	0.004
FOM	16.5 ± 13.2	18.9 ± 15.8	0.562

of Group A, no significant differences were observed in the SNR_L ($p = 0.265$) and CNR_L ($p = 0.486$). By contrast, mean attenuation values of the abdominal aorta were not significantly different between patients of Group A and B ($p = 0.130$). As a result, both SNR_A and CNR_A were significantly higher in patients of Group B. However, when the CNR_A was normalized to the effective dose, no significant differences were observed between the corresponding FOMs of Group A and B (Table 3).

3.7. Diagnostic accuracy

According to the reference standards, 56 patients (33 in Group A and 23 in Group B) had active CD as assessed by open ($n = 25$) or laparoscopic surgery ($n = 10$) and ileo-colonoscopy with biopsy ($n = 21$) whereas 8 patients (4 in Group A and 4 in Group B) had Ulcerative Colitis (UC) as assessed by open surgery ($n = 2$) and colonoscopy with biopsy ($n = 6$). Seventeen patients (8 in Group A and 9 in Group B) had either functional disorders such as irritable bowel syndrome (IBS) or an undetermined colitis as assessed by clinical follow-up ($n = 10$) and colonoscopy ($n = 7$) whereas four patients (1 in Group A and 3 in Group B) had miscellaneous diseases such as auto-immune enteritis, celiac disease, small bowel lymphoma and parasitic enteritis as assessed by clinical follow-up ($n = 2$) and open surgery ($n = 2$).

The diagnostic accuracies of CTE in both groups are reported in Table 4. No significant differences were observed in sensitivity (91.6 vs 92.8%, $p = 0.820$), specificity (88.9 vs 91.6%, $p = 0.591$) and diagnostic accuracy (91.1 vs 92.5%, $p = 0.764$) of CTE in Group A and B, respectively.

In detail, CTE performed with a LR-HC protocol (Group A) correctly identified twenty-nine patients with active CD with either a penetrating (Fig. 1a), a stricturing (Fig. 2a) or a nonstricturing/nonpenetrating phenotype (Fig. 3a) and four patients with UC (Fig. 4a). True negative findings were observed in 8 patients as assessed by either ileo-colonoscopy w/out biopsy ($n = 2$) or by clinical follow-up ($n = 6$). There were three false negative findings in patients with Crohn's disease as assessed by open surgery ($n = 1$) and ileo-colonoscopy with biopsy ($n = 2$) and 1 false positive finding as assessed by clinical follow-up.

Table 4
Sensitivity, specificity, diagnostic accuracy, positive (PPV) and negative (NPV) predictive values of multi-detector CTE are reported for both Group A and B along with the 95% confidence intervals (CI) and the levels of significance (*p*) according to the Chi-square test.

Diagnostic performance	Group A ($CI_{95\%}$)	Group B ($CI_{95\%}$)	*p*
Sensitivity	91.6% (76.3 to 98.1%)	92.8% (76.5 to 99.1%)	0.820
Specificity	88.9% (51.7 to 99.7%)	91.6% (61.5 to 99.8%)	0.591
Accuracy	91.1% (78.6 to 96.3%)	92.5% (79.3 to 98.3%)	0.764
PPV	97.0% (83.8 to 99.9%)	96.3% (81 to 99.1%)	0.548
NPV	72.7% (39.0 to 93.4%)	84.6% (54.5 to 98.1%)	0.833

In group B, CTE correctly identified twenty-one patients with active CD with either a penetrating (Fig. 1b), a stricturing (Fig. 2b) or a nonstricturing non-penetrating phenotype (Fig. 3b) and four patients with UC (Fig. 4b). True negative findings were observed in 8 patients as assessed by either endoscopy w/out biopsy ($n = 4$) and clinical follow-up ($n = 4$). Two false negative findings in patients with Crohn's disease and one false positive finding were also observed as all assessed by ileo-colonoscopy with biopsy.

4. Discussion

Cross-sectional imaging techniques play a pivotal role in the detection and staging of CD as well as in the evaluation of its complications and both CTE and MRE are currently considered complementary to ileo-colonoscopy [1]. In the acute setting, however, CTE appears to be more suited than MRE to evaluate patients with active IBD (either CD or UC) because it is less time consuming and widely available [4]. Moreover, as CTE usually results in a more reproducible image quality than MRE [5], it is also recommended as the initial diagnostic step in the evaluation of patients with only a clinical suspicion of CD according to the American College of Radiology guidelines [6].

There are, however, major concerns regarding the radiation exposure resulting from multi-detector CT technology which are mainly due the average age of patients and the relapsing-remitting course of IBD [7]. As a result, several dose-reduction strategies have been successfully applied to CTE protocols such as the use of IR algorithms to reduce the image noise associated to either low-dose [8,9] or low-voltage settings [10,11].

However, improvement in the quality of CT images obtained using low dose protocols may also be achieved by increasing the amount of LOCM administered as first suggested by Watanabe et al. [12] and later confirmed both in an experimental [13] as well as in a clinical setting [14].

In the present study, we prospectively investigated both the effects on image quality as well as the diagnostic efficacy of a CTE performed according to a LR-HC protocol in the evaluation of selected young patients (< 45 yrs) with IBD in the acute setting. While the age-threshold chosen to stratify patients in our study has to be considered arbitrary, it is very close to the value (*40 yrs*) adopted by the Montreal classification to distinguish young (A2) from adult patients (A3) with IBD [29]. As we stratified patients by age, however, minor differences were noted in their physical characteristics (Table 1) which can be largely accounted for by the demographic features (e.g. young patients tend to be taller than adult patients).

Conversely, significant differences were observed both in the volume of LOCM administered as well as in the estimated ED delivered to both groups (Table 2). Indeed, the estimated mean ED delivered to patients of Group A in the present study (6.7 *mSv*) compares favorably with the data reported by Ippolito et al. using a low-dose CTE [9] and is in perfect agreement with the value reported by Johnson et al. using a low-voltage (100 kVp) CTE [10]. However, mean ED as low as 4.6 *mSv* have been reported by Kaza et al. using a 80 kVp voltage [11] and values in the order of 2–3 *mSv* have been reported by Lee et al. who also claimed that the diagnostic accuracy of CTE may not be affected by image quality given its intrinsic luminal contrast [30].

As far as the mean estimated ED delivered to patients of Group B (13.9 *mSv*) is concerned, our results are in overall accordance with the values reported using standard CTE protocols [8–11]. Similarly, the mean $CTDI_{vol}$ observed in our control group is not only in agreement with the data reported by both Ippolito et al. [9] and Kaza et al. [11] using standard CTE protocols but also compliant with the current diagnostic reference level (19 *mGy*) of an adult contrast-enhanced CT examination of the abdomen and pelvis [31].

We are indeed aware that the amount of LOCM administered to

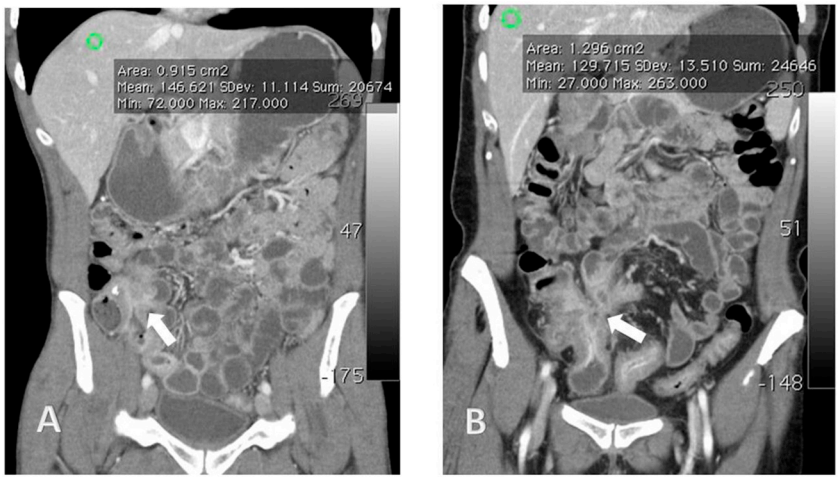

Fig. 1. Multi-detector CTE in a 36 yrs old male (Group A, 62 kg, BMI 21) and in a 51 yrs old female (Group B, 62 kg, BMI 23.6) with acute abdominal pain and spiking fever: 5 mm thick coronal reformatted images are shown. In both patients stratified thickening of the bowel wall and mural hyper-enhancement can be appreciated at the level of terminal ileum along with entero-enteric (A) and entero-colic (B) fistulous tracts (arrows). CTE findings were both true positive as assessed by open (A) and laparoscopic surgery (B). Dose-Length Products (*mGy*cm*) were 353 and 783 corresponding to an ED of 5.3 *mSv* (A) and 11.7 *mSv* (B), respectively.

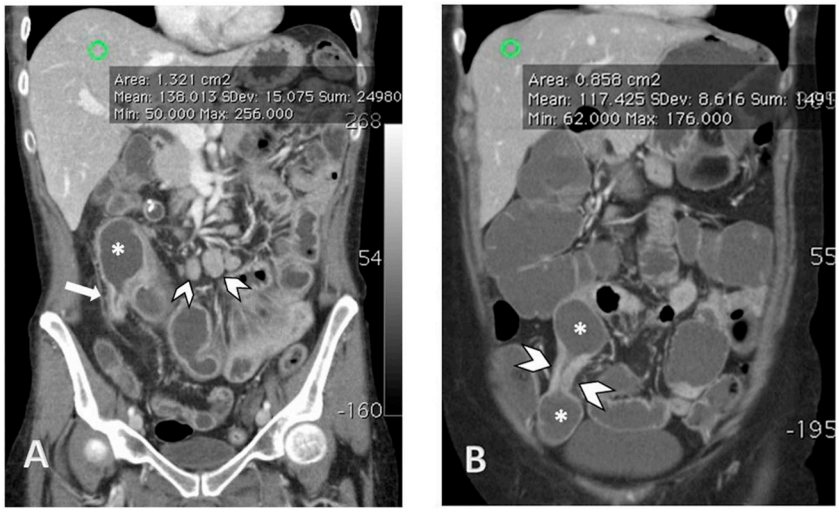

Fig. 2. Multi-detector CTE in a 39 yrs old (Group A, 53 kg, BMI 22) and in a 54 yrs old female (Group B, 60 kg, BMI 23.4) with a small bowel obstruction: 5 mm thick coronal reformatted images are shown. In A severe narrowing of the bowel lumen can be appreciated at the level of an entero-enteroanastomosis (arrow) with mild thickening of the bowel wall and marked up-stream dilation (*) of the bowel lumen. A cluster of enlarged mesenteric lymph nodes is also depicted (arrow-heads). In B segmental and homogeneous thickening (arrow-heads) of the bowel wall is depicted at the level of the pelvic ileum with associated up-stream as well as down-stream dilation of the bowel lumen (*). CTE findings were both true positive as assessed by laparoscopic (A) and open (B) surgery. Dose-Length Products (*mGy*cm*) were 322 and 843 corresponding to an ED of 4.8 *mSv* (A) and 12.6 *mSv* (B), respectively.

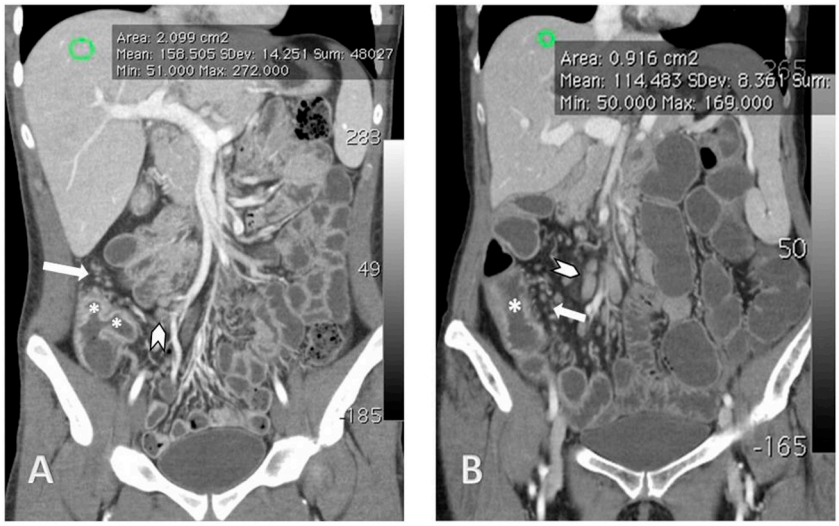

Fig. 3. Multi-detector CTE in a 17 yrs old male (Group A, 60 kg, BMI 20.7) and in a 64 yrs old female (Group B, 62 kg, BMI 21.7) with acute abdominal pain: 5 mm thick coronal reformatted images are shown. Mild thickening of the bowel wall with mural hyper-enhancement (*) are depicted at the level of the terminal ileum and ascending colon in A and of the neo-terminal ileum in B along with engorgement of the vasa recta (arrows) and ileo-colic lymph nodes (arrow-heads). CTE findings were both true positive as assessed by ileo-colonoscopy with biopsy. Dose-Length Products (mGy*cm) were 469 and 834 corresponding to an ED of 7 *mSv* (A) and 12.5 *mSv* (B), respectively.

patients of Group A (0.92 gI/kg) is far above the recommended values [32] resulting in an Iodine load of 53.6 ± 9.2 g (Table 2) and in a higher peak hepatic enhancement compared to patients of Group B as assessed by quantitative analysis (Table 3). As this latter finding was largely expected [33], surprising similar SNR_L and CNR_L were observed in both groups (Table 3) confirming the balancing effects of contrast media and radiation dose on the image quality of abdominal CT scans [14]. Indeed, the SNR_L observed in present study are in complete agreement with the data reported by Ippolito et al. [9] and are also consistent with our previous investigation [14] whereas the CNR_L are considerably lower as we used as reference tissue the para-spinal muscles instead of the sub-cutaneous fat. As both choices were

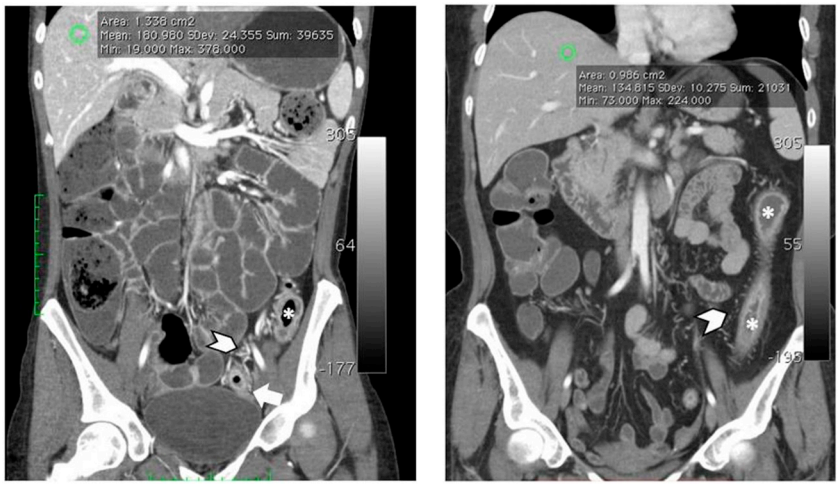

Fig. 4. Multi-detector CTE in a 27 yrs old (Group A, 50 kg, BMI 17.3) and in a 55 yrs old female (Group B, 68 kg, BMI 25.0) with acute abdominal pain and diarrhea: 5 mm thick coronal reformatted images are shown. Stratified thickening of the bowel wall can be appreciated at the level of the descending (*) and sigmoid colon (arrow) in A and descending colon (*) in B along with engorgement of the vasa recta (arrow-heads). CTE findings were considered consistent with a left ulcerative colitis and were both true positive as assessed by colonoscopy and biopsy with ED of 4.6 mSv (A) and 17.4 mSv (B), respectively.

arbitrary, they are well supported by the literature [9,30].

Conversely, as the CTE acquisitions were performed during the venous phase, no significant differences were observed in the mean attenuation values of abdominal aorta [19] and both SNR_A and CNR_A were higher in Group B as a result of the significantly lower image noise (Table 3). However, when CNR_A was normalized for the mean ED delivered in each group, no significant differences were observed in the corresponding FOM (Table 3) underscoring the overall comparable image quality of both CTE protocols (Figs. 1–4). FOM are indeed acknowledged to be an effective mean to compare the effects on image quality of different CT protocols [24]. Besides, luminal distension of small bowel loops was also scored similar in both groups as assessed by semi-quantitative analysis with a good inter-observer variability (k = 0.6–0.7).

As far as the Iodine load is concerned, this should not be considered an issue in patients with normal thyroid [20] and renal function [34]. While subtle alterations of thyroid hormone synthesis are indeed expected to occur soon after Iodine administration, they are transitory and a normal thyroid function is usually resumed within 24–48 h [35]. Indeed, none of the patients of Group A showed signs of contrast-induced thyrotoxicosis both at laboratory analysis performed 4–6 wks after CTE as well as at a further clinical follow-up and it could even be argued that the urinary excretion of LOCM has been facilitated in patients of Group A by the significantly higher GFR values (Table 1). Although there is currently a trend to reduce the amount of iodinated contrast media administered to patients using low-voltage CT protocols [36], these technologies are still not widely available in clinical practice whereas our LR-HC CTE simply relies on standard kilo-voltage settings, FBP algorithms and ATCM systems.

As far as our CTE protocol is concerned, the formula used to calculate the scan delay in each patient was largely derived from the data of Bae et al. [19] with the only difference that the total rather than half of the scan duration was subtracted as a result of the caudo-cranial acquisition [14]. However, the mean scan delays observed in each group (Table 2) are close to the 65–70 s adopted for a venous phase acquisition in other CTE protocols [8–11]. While previous studies have emphasized the diagnostic role of an enterographic phase performed at 45–50 s. [26], this has to be supported by an high (4–5 cm^3/s) rate of injection and usually triggered by bolus tracking which, albeit performed with low dose scans, is still a source of radiation exposure that can be effectively spared in patients with normal transit times [16]. Moreover, as a result of the caudo-cranial acquisition in our protocol vascular enhancement is more conspicuous in the pelvis (Figs. 1–4) and this can be considered beneficial for the detection of most signs of active inflammatory bowel involvement [24–26].

Finally, both CTE protocols resulted in a similar diagnostic accuracy (91.1 vs 92.5%, p = 0.764) which is not only in agreement with the values reported in the literature [8–11] but also consistent with our preliminary observations in patients with non-traumatic acute bowel disease [16].

Our prospective study has several limitations. First, no attempts were made to correlate CTE findings with clinical (CDAI) or endoscopic indices (CDEIS) of disease severity as the study was performed in the acute setting and only aimed at evaluating the diagnostic efficacy of a LR-HC CTE in comparison to a standard CTE protocol. Second, there was a selection bias as patients with either thyroid, renal or cardiac co-morbidities were excluded. However, as we did not use a bolus tracking technique patients with cardiac diseases could not be enrolled because of unpredictable transit times [19] whereas the presence of thyroid or renal co-morbidities represented a contra-indication for being included in Group A given that the amount of Iodine administered (0.92 gI/kg) was far above the recommended values [31]. Third, as we stratified patients by age, some obvious differences were observed in their physical characteristics which may be largely accounted for by demographic features and could only be amended by an intra-patient comparison [10]. Lastly, we are aware that the amount of LOCM injected according to the standard protocol (Group B) is indeed higher (0.74 gI/kg) than the recommended dose of 0.5–0.6 gI/kg of total body weight [31]. However, it is close to the maximum dose of 0.75 gI/kg of lean body weight and such an assumption appears to be reasonable considering the body habitus and the nutritional status of most patients with active IBD [37].

Despite these limitations, our results indicate that LR-HC CTE can be safely and effectively performed to evaluated active IBD in young patients with normal thyroid and renal function showing the highest benefit to risk ratio according to the AHARA principle [38] with a similar diagnostic accuracy as a standard protocol but a significantly lower ED falling in the range of values reported using IR algorithms combined to either low-dose [8,9] or low-voltage CTE protocols [10,11].

As a further reduction of the radiation dose could be achieved combining this protocol with the use of IR algorithms, prospective studies addressing this issue are warranted.

Declaration of Competing Interest

All authors have no conflicts of interest to declare.

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