The Egyptian Journal of Radiology and Nuclear Medicine (2015) **46**, 315–323

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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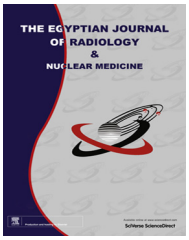

ORIGINAL ARTICLE

Local staging of rectal cancer: Diagnostic potential of endorectal contrast agent and MPRs with 64-MDCT compared with the pathologic staging

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Received 25 October 2014; accepted 20 January 2015
Available online 7 February 2015

KEYWORDS

Local staging;
Rectal cancer;
Endorectal contrast agent;
MPRs;
MDCT

Abstract *Purpose:* To assess the diagnostic potential of endorectal contrast agent and multiplanar reconstructed images (MPRs) with MDCT in local staging of rectal cancer compared with the pathologic staging.

Patients and methods: This study included 30 patients with biopsy-proven rectal cancer (age range 18–84 years, mean 46.7 ± 19). Preoperative MDCT examinations were performed to all patients using a 64-row multidetector scanner. The examination was carried out in two steps, firstly using oral contrast agent only, secondly using endorectal contrast agent. Images were reconstructed in axial, coronal, and sagittal planes. MDCT staging was compared with pathologic staging.

Results: For T-staging, MDCT using endorectal contrast was more sensitive (75.8%), specific (90%) and accurate (86.7%) than using oral contrast only (43.3%, 88.1%, 74.4%) respectively ($p = 0.001$). The sagittal and coronal MPRs were more sensitive, specific and accurate than the axial images with diagnostic accuracy 64.4% for axial, 75.5% for coronal, and 81.1% for sagittal MPRs. There were statistically significant differences between axial and coronal MPRs ($p = 0.02$), and between axial and sagittal MPRs ($p = 0.002$). Diagnostic accuracy for N-staging was 80%.

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Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

http://dx.doi.org/10.1016/j.ejrnm.2015.01.006

Conclusion: 64-MDCT with endorectal contrast agent and MPRs, mainly sagittal images is a reliable accurate technique for the preoperative local staging of rectal cancer.

1. Introduction

Worldwide, incidence of colorectal cancer ranks fourth in men (after lung, prostate and stomach) and third in women (after breast and cervix uteri) with over 1 million new cases occurring every year worldwide. The majority of cancers occurring in the colon and rectum are adenocarcinomas, which account for more than 90% of all large bowel tumors (1). In Egypt, they represented 6.53% of all incident cancers, accounting for 4.00% and 2.55% of male and female cancers respectively according to National Cancer Institute (NCI) registry.

The prognostic factors of rectal cancer are several, such as depth of tumor invasion, the percentage of the circumference of rectal involvement by the tumor, regional lymph node metastasis, blood or lymphatic vessel invasion, residual tumor following surgery with curative intent, tumor grade, histologic type, tumor border configuration, tumor size and gross tumor configuration (2).

Optimal management of rectal cancer requires accurate preoperative staging that includes assessment of the tumor extent, depth of cancer invasion (T-stage), tumor location, size, configuration and lymph node involvement (N-stage) with subsequent improvement of survival and reduction of the frequency of local recurrence (3).

A variety of examinations have been used for the preoperative planning of rectal cancer management (4), including digital rectal examination, endorectal sonography, CT, and MRI (5). The current role of CT in patients with rectal cancer is controversial. Accuracy rates for pre-operative staging of rectal cancer with CT were less satisfactory with accuracy rates ranging between 41% and 82% (6–8) for helical CT staging, however the accuracy rate obtained for local staging of rectal cancer is improved with the use of multidetector CT (3,9).

The aim of this study was to evaluate the benefits of adding endorectal contrast as well as reconstructed images to MDCT examination in improving the diagnostic accuracy of local staging of rectal cancer.

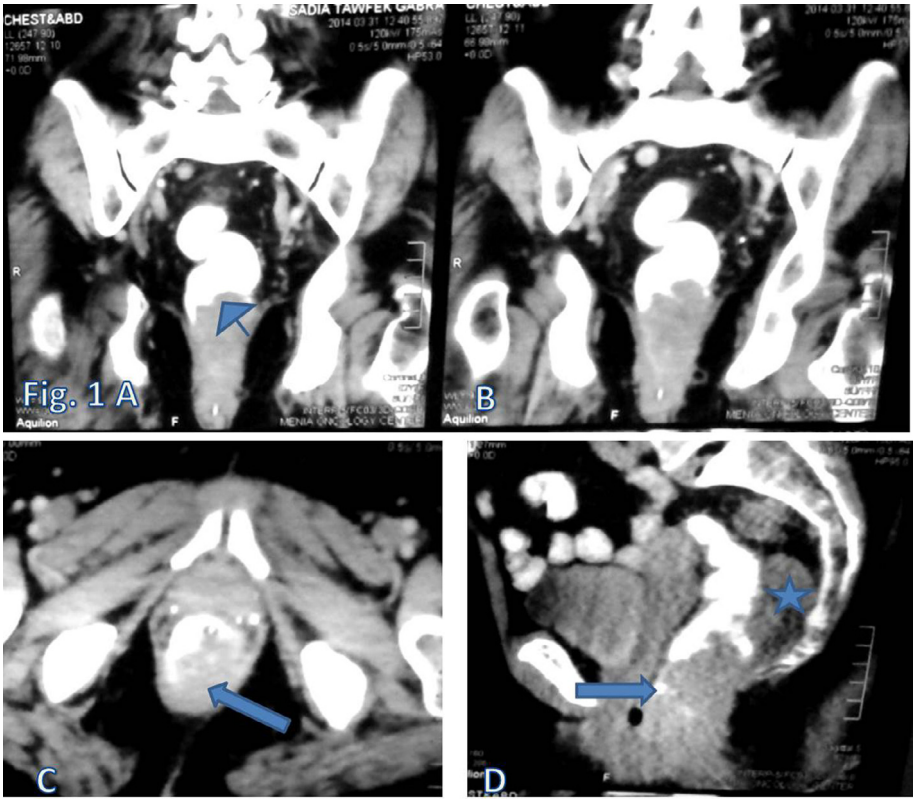

Fig. 1 82 year old female patient: MDCT with endorectal contrast coronal MPR (A & B) revealed a large irregular soft tissue rectal mass lesion eccentric and markedly attenuating rectal lumen, proximal shouldering is seen (arrow on A). (C) Axial CT MDCT (MPR images) with endorectal contrast, the eccentric mass lesion is noted at the Lt. postero-lateral aspect (arrow). (D) Sagittal CT MPR images, here the lesion and mucosal destruction were noted with haziness of the peri-rectal fat planes, enlarged peri-rectal LNs were seen (asterisk on D), and the lesion was inseparable from the uterus anteriorly (arrow on D).

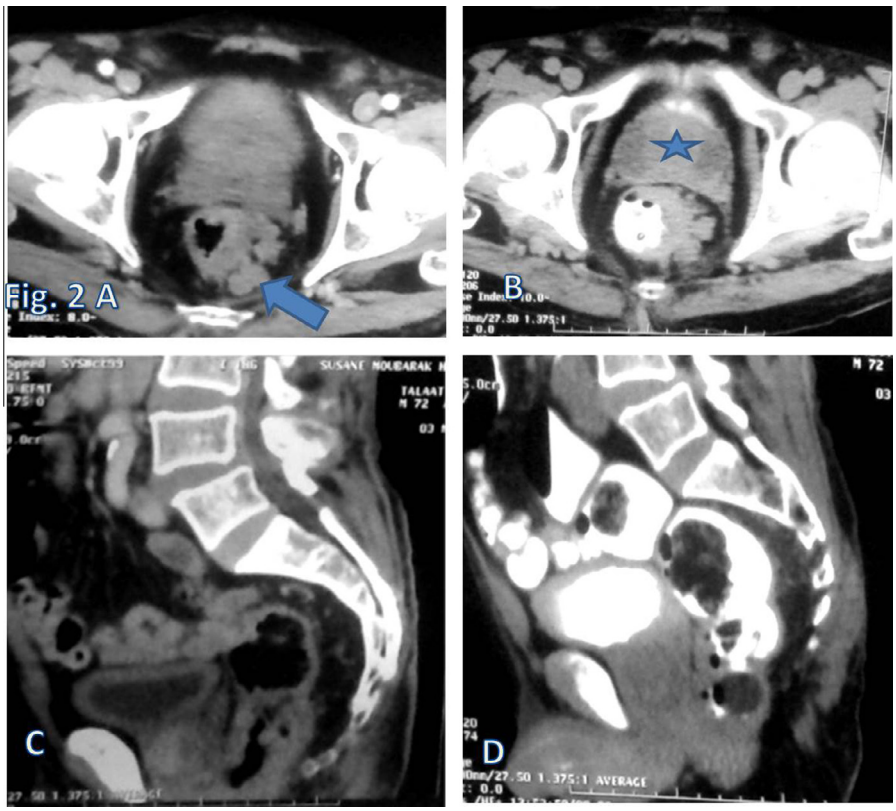

Fig. 2 72 year old male patient: Axial CT MPR image with only oral contrast (A) revealed irregular thickening of the Lt. lateral rectal wall with peri-rectal enlarged LNs (arrow). After endorectal contrast (B) the lesion became more defined with irregular eccentric filling defect and haziness of the peri-rectal fat planes. Sagittal MPR image with oral contrast only (C) revealed the irregular rectal wall thickening that encroaches on rectal lumen after endorectal contrast (D) The rectum became fully distended with contrast and the lesion appeared more obvious with evident proximal shouldering. Also, the lesion appeared inseparable from the prostate anteriorly.

2. Patients and methods

2.1. Patients

This study was approved by the ethics committee of our institution during the period between January 2013 and April 2014. It included 30 patients with biopsy-proven rectal cancer. Written informed consent was obtained from each patient prior to the examination. Patients with obstructive lesions were excluded from the study. The patients included did not receive preoperative neoadjuvant chemotherapy.

2.2. Imaging and image processing techniques

2.2.1. Imaging acquisition and scanning parameters

Preoperative MDCT examinations were performed to all patients in this study using a 64-row multidetector scanner (Aquilion64; Toshiba Medical Systems Corporation, Otawara, Japan). The examination was carried out in two steps, firstly using the oral contrast agent only, and the second step using the endorectal contrast. Firstly, the patients were fasting about 6 h before the examination. They were given 1000 mL of oral contrast agent [Diluted water soluble iodinated contrast agent, meglumine diatrizoate (Gastrographin)] over 2 h. To reduce colonic motility, 20 mg of scopolamine butyl-bromide (Buscopan) was injected intramuscularly 15 min before the examination.

All patients underwent the same MDCT examination protocol using 64×0.5 mm collimation scanner with a gantry rotation speed of 400 ms/rotation, range of box 450–500, image thickness 0.5 mm, standard pitch factor of 0.641, reconstruction interval 0.5 mm. and total exposure time 6.949. Each scan was obtained with a tube voltage of 120 kV and 250 mA s. All patients received 100 mL of nonionic water soluble IV contrast agent at a flow rate of 3 mL/s (300 mg I/mL, Omnipaque 300). The scanning was initiated after a delay of 65 s.

Secondly, the patients received endorectal contrast agent (diluted water soluble iodinated contrast agent: 15 cc of Gastrographin diluted in 300–500 cc of saline) using an enema syringe or Foley's catheter while the patient was on the CT table in the right lateral decubitus position with the knees on the chest to ensure adequate filling. The administration was stopped immediately if the patient experienced intolerable pain. After the administration, the catheter was removed and the patient was placed in a supine position. Before rectal filling, the patients were asked to empty their rectums. The above described MDCT examination protocol then was repeated.

2.2.2. Image reconstruction

For image reconstruction, the axial source images were transferred to Vitrea workstation (Toshiba Medical Systems). Multiplanar reformatted images (MPRs) were obtained in axial, coronal and sagittal planes with a section thickness of 5 mm, and a section reconstruction interval of 5 mm.

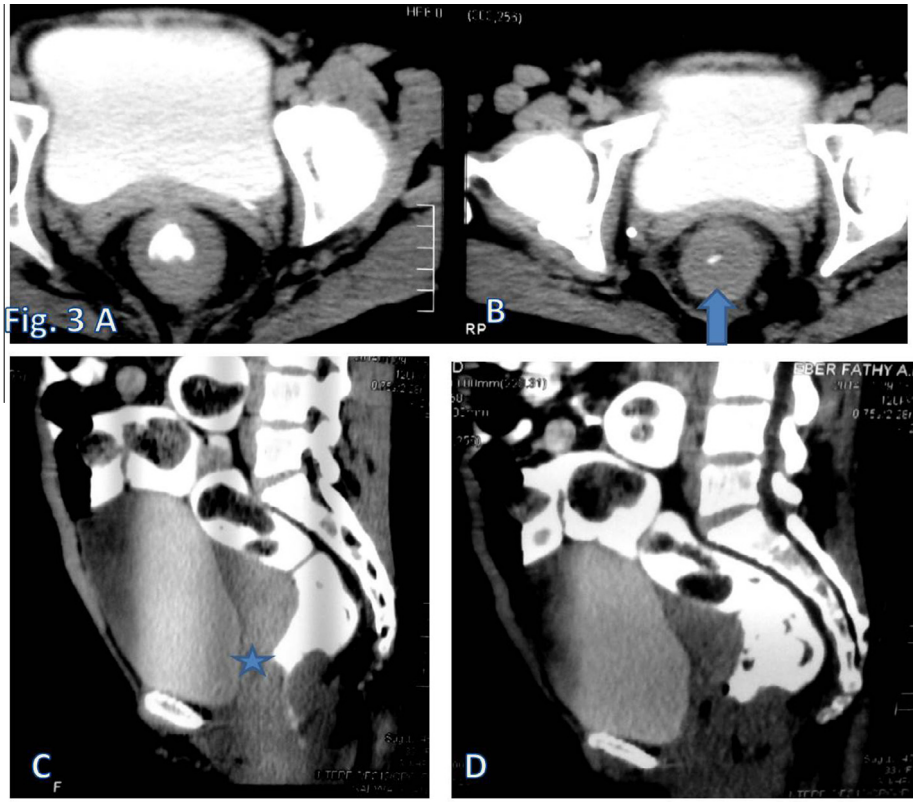

Fig. 3 33 year old female patient: MDCT with endorectal contrast axial MPR images (A & B) revealed a circumferential rectal wall thickening with irregular encroachment on the rectal lumen (arrow on B) and no peri-rectal extension seen. On sagittal MPR images (C & D), the marked mucosal destruction and irregularities were detected clearly with proximal shouldering and haziness of the peri-rectal fat planes, the lesion appeared inseparable from the uterus anteriorly (asterisk on C).

2.2.3. Image analysis

All the images obtained were assessed for delectability of the tumor location, depth of tumor infiltration, tumor configuration and regional lymph nodes. For local tumor staging by MDCT we followed the scheme used by Kulinna et al. (3) in which tumors on MDCT were classified by a modified TNM stage: tumors confined to the bowel wall were classified as T1or T2. An indistinct or speculated border between the outer rectal wall and the surrounding fat at the level of the tumor was considered as evidence of perirectal invasion (T3). Tumor infiltration into adjacent organs was considered stage T4. Lymph nodes were considered to be positive for metastases if at least one perirectal lymph node with a short-axis diameter of more than 3 mm was found.

2.2.4. Surgical interference and pathologic examination

Surgical resection was done for all patients, for the recto-sigmoid cases (10 patients) anterior low resection was done and for the remaining cases (20 patients) abdomino-perineal resection was done with meso-rectal excision. The resected tissues were examined histopathologically for pathologic staging.

2.2.5. Statistical analysis

Data entry was done by SPSS version 17 and analyzed by the same software. MDCT staging using oral and endorectal contrast agents as well as MPR images (axial, coronal and sagittal) was compared with pathologic TNM staging with calculation of the sensitivity, specificity, positive predictive valve (PPV), negative predictive value (NPV), and accuracy. The probability (p value) of less than 0.05 was used as a cutoff point to determine whether there is statistically significant improvement in local tumor staging by adding endorectal contrast agent and reconstructions images (coronal and sagittal) to the routine examination.

3. Results

This prospective study included 30 patients with biopsy-proven rectal cancer (8 males, 22 females). Their ages ranged from 18 to 84 years (mean age was 46.7 ± 19). The majority of our patients were females (73.3%), this was statistically significant (p = 0.001). Histo-pathologic examination of the biopsied specimen was performed for all patients. The most common pathologic type was adenocarcinoma, it was detected in 26 (86.7%) out of 30 patients, most of them were well-differentiated type (40%), the least common pathologic types were malignant lymphoma (10%) and malignant mucosal melanoma (3.3%) Table 1.

The MDCT characterization of rectal lesions showed that, the most common tumor location was the ano-rectal region represented (56.6%). The lesions were limited to the bowel wall in 56.7% of the patients, (33.3%) were extended to the peri-rectal fat, while (10%) invaded the adjacent structures (uterus in 2 patients and prostate in 1 patient). The most common

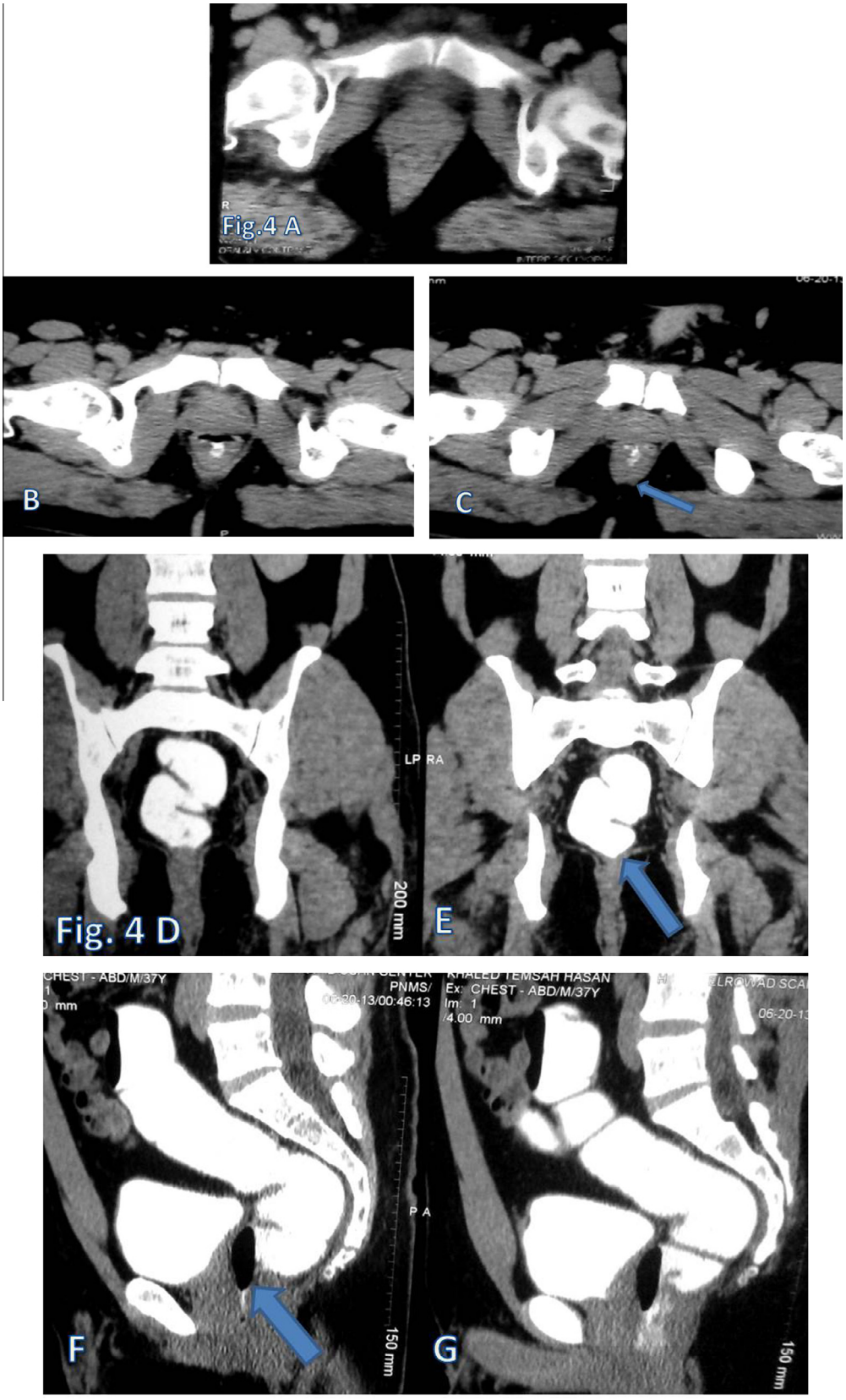

Fig. 4 38 year old male patient: Axial CT, MPR image (A) with oral contrast only, no definite rectal lesion identified. After endorectal contrast (B & C) no significant lesion could be identified, only, minute focal bulge on Lt. postero-lateral wall (opposite 5 O'clock position), with preserved related peri-rectal fat planes (arrow on C). On coronal cuts after endorectal contrast (D & E), there is abrupt cutting to contrast at the distal rectal region with significant proximal shouldering (arrow on E) and this could not be detected on axial images. On sagittal MPR image after endorectal contrast (F & G), the mucosal destruction and irregularity appeared clearly with preserved peri-rectal fat planes and proximal shouldering (arrow on F).

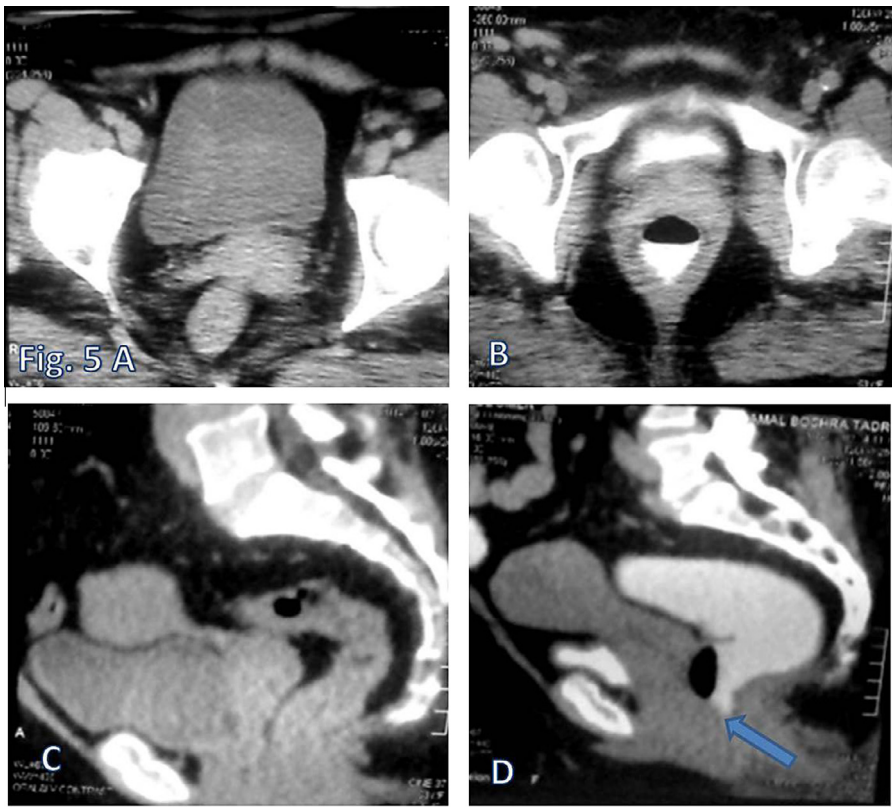

Fig. 5 63 year old female patient: Axial & sagittal MDCT, MPR images with oral contrast only (A & C) the rectal lumen was collapsed with preserved peri-rectal fat planes and no definite lesions identified. After endorectal contrast axial and sagittal MPR images (B&D) there were circumferential wall thickenings. The proximal shouldering was detected clearly on sagittal MPR image (arrow on D).

Table 1 Histopathologic types and grading of rectal cancer (n = 30).

Pathologic type	No.	%
Adenocarcinoma:	26	86.7
Grading		
– Well differentiated	12	40
– Moderately differentiated	4	13.3
– Poorly differentiated	5	16.7
Subtypes		
– Mucinous	4	13.7
– On top of villous adenoma	1	3.3
Malignant lymphoma	3	10
Malignant mucosal melanoma	1	3.3
Total	30	100

Table 2 MDCT characterization of rectal lesions; location, extension and configuration (n = 30).

Lesion characterization by MDCT	No.	%
Location		
Recto-sigmoid	10	33.3
Ano-rectal	17	56.6
Rectal	3	10
Extension		
Bowel wall	17	56.7
Perirectal fat	10	33.3
Adjacent structure (uterus)	2	6.7
Adjacent structure (prostate)	1	3.3
Configuration		
Diffuse wall thickening	7	23.3
Focal wall thickening	6	20
Irregular circumferential soft tissue lesion	11	36.7
Smooth circumferential soft tissue lesion	6	20

tumor configuration was the irregular circumferential soft tissue lesion represented (36.7%) Table 2.

A comparison between oral and endorectal contrast agents for T-staging in correlation with the postoperative pathologic TNM staging revealed that using endorectal contrast agent was more sensitive (75.8%), specific (90%) and accurate (86.7%) than using oral contrast agent only (43.3%, 88.1%, 74.4%) respectively, this was statistically significant (p = 0.001) Table 3. MDCT with oral contrast only could not detect the tumor in 13 patients, correctly staging the tumor in 12 patients, and underestimate the staging in 5 patients while adding the endorectal contrast to the MDCT examination correctly staging the tumor in 24 patients and underestimate the staging in 3 patients Tables 4 and 5.

For T-staging (see Figs. 1–5) with regard to reconstruction images, the coronal and sagittal reconstructed images were more sensitive, specific and accurate than the axial images. The sensitivity for axial images was (41.2%), (65.7%) for additional coronal images, and (70%) with additional sagittal

images. The specificity for axial images was (73.3%), (85.3%) for coronal images, and (90%) for sagittal images. The overall accuracy was (64.4%) for axial images, (75.5%) for additional coronal images, and (81.1%) for additional sagittal images. There were statistically significant differences between axial and coronal reconstructions ($p = 0.02$) and between axial and sagittal reconstructions ($p = 0.002$) Table 6.

Regarding N-staging, MDCT was accurate (80%) in nodal staging with a sensitivity of (71.5%) and specificity of (66.7%) as compared with the pathologic staging Table 7.

4. Discussion

Local tumor staging is crucial for the prognosis and planning of therapy in the individual patient and aims at precisely determining the extent of the tumor as a basis for deciding whether surgery alone or surgery in combination with neoadjuvant therapy is the most suitable strategy (10). In this study it was of practical interest to determine the diagnostic potential of endorectal contrast agent and reconstruction images with MDCT in local staging of rectal cancer.

Our study showed female predominance in rectal cancer incidence (73.3%) with a male to female ratio of 1:2.8 this was in contrary to the ratio (1.2:1) previously reported by Egyptian National Cancer Registry, El Minia Profile 2009 (1). We found no obvious cause or explanation to this unusual ratio, it may be due to the small number of the studied group, underlying genetic abnormality or other leading risk factors should be stressed in the future researches.

Among this studied group that included 30 patients with biopsy-proven rectal cancer, the most common pathologic type was adenocarcinoma representing 86.7%, this was in agreement with Fleming et al. (11) and Hamilton et al. (12) who reported that more than 90% of colorectal carcinomas were adenocarcinomas originating from epithelial cells of the colorectal mucosa.

Determination of the depth of tumor invasion is not only crucial for local staging but also influence the prognosis. In one of the largest series published, T3 tumors with extramural spread of more than 5 mm were associated with a 5-year survival rate of only 54%, but T3 tumors with 5 mm or less of

Table 3 Comparison between MDCT with oral and endorectal contrast agents for T-staging in rectal cancer ($n = 30$).

MDCT T-staging	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Endorectal Contrast	75.8	90	81.3	88.1	86.7
Oral contrast	43.3	88.1	73.3	72.3	74.4

Note. PPV = positive predictive value, NPV = negative predictive value. $p = 0.001$.

Table 4 Correlation between MDCT with oral contrast and pathologic T-staging.

MDCT T-staging with oral contrast	No. of patients	Pathologic staging			CT accuracy (%)
		Correct	Under estimation	Over estimation	
T1–2	10	7	3	0	36.8
T3	4	2	2	0	33.3
T4	3	3			100
Total	17	12	5	0	74.4

Table 5 Correlation between MDCT with endorectal contrast and pathologic T-staging.

MDCT T-staging with endorectal contrast	No. of patients	Pathologic staging			CT accuracy (%)
		Correct	Under estimation	Over estimation	
T1–2	17	16	1	0	84.2
T3	10	5	2	3	85.1
T4	3	3	0	0	100
Total	30	24	3	3	86.7

Table 6 Comparison between axial, coronal and sagittal reconstruction images for T-staging in rectal cancer ($n = 30$).

MDCT T-staging	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Axial	41.2	73.3	41.6	67.7	64.4
Coronal	65.7	85.3	52.7	80.6	75.5
Sagittal	70	90	80.5	81	81.1

Note. PPV = positive predictive value, NPV = negative predictive value. Statistical differences between axial and coronal reconstructions ($p = 0.02$), and between axial and sagittal reconstructions ($p = 0.002$).

Table 7 Sensitivity, specificity and accuracy of MDCT for N-staging in rectal cancer ($n = 30$).

MDCT N-staging	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
	71.5	66.3	63.7	72.7	80

extramural spread were associated with 5 year survival rate of greater than 85% (13). The challenge for preoperative imaging in rectal cancer is to accurately determine the depth of mural involvement by the tumor (T stage), and the distance from the tumor to the circumferential mesorectal resection plane. Duman et al. (14) and Dar et al. (15) had addressed the impact of MDCT in preoperative evaluation of tumor invasion (T-staging) and lymph node metastasis (N-staging). They proposed that MDCT is a reliable radiological tool for local staging of rectal cancer. In this study extramural tumor extension was detected in 13 patients, 10 of them extend to the perirectal fat. It was identified as small strands of tumor tissue extending beyond the external surface with irregular, nodular or spiculated configuration of tumor margin. The other 3 patients showed tumor invasion of the surrounding structures, it was diagnosed when the fat plans in-between the tumor and adjacent structures were obliterated.

Luminal distention of the rectum with contrast material is essential for optimal assessment of the rectal wall. Various materials had been used to induce rectal distension including positive agents such as barium sulfate or iodinated solutions, neutral agents such as water or negative agents such as air or carbon dioxide. The iodinated contrast agent meglumine diatrizoate (Gastrographin) is the most widely used agent for CT, it had wide acceptance and a low adverse-event rate (16). In our study we use a positive endorectal contrast agent [Diluted water-soluble iodinated contrast agent meglumine diatrizoate (Gastrographin)] to determine whether this agent can increase the T-staging accuracy or not. We found that using endorectal contrast agent improved the diagnostic accuracy for the T-staging, with a higher sensitivity (75.8%), specificity (90%) and diagnostic accuracy (86.7%) than using oral contrast agent only (43.3%, 88.1%, 74.4%) respectively. Our overall diagnostic accuracy (86.7%) was in agreement with Kulinna et al. (17) who reported that the accuracy for T-staging using MDCT was 86%, and Filippone et al. (18) who found an accuracy of 83%. Sibileau et al. (19) assessed the accuracy of water-enema multidetector computed tomography in rectal cancer staging; this recent study reported a high sensitivity (97.7%) and specificity (88.1%) for T3 and T4 stage.

Our diagnostic accuracy of each individual stage was 84.2%, 85.1%, 100% for T1–2, T3 and T4 respectively, this was conceded with Dar et al. (15) who reported excellent accuracy rates for T and N-staging of rectal cancer, with the diagnostic accuracy for T1/T2, T3 and T4 lesions was 77%, 86.5% and 100%, respectively. MDCT is more accurate in detecting T4 and T3 stages than T2 and T1 stages. This can be explained by that CT is not able to differentiate and distinguish different layers of the rectal wall despite of major improvements in its technology that allowed faster scanning, thinner slice, increased spatial resolution and better image quality. It is still impossible to differentiate T1 from T2 tumors on MDCT (15,20).

Multiplanar reconstruction images serve as a cross-sectional technique that optimally displayed the longitudinal extent, intraluminal disease, and intramural involvement of rectal disease (3). In our study, a high quality, high resolution multiplanar reconstruction images were created by the 64-row multidetector scanner through using a narrow collimation (64×0.5 mm collimation) and a thin-slice isotropic scanning technique which completely eliminates stair-stepping artifacts that distort the multiplanar reformatted images. The MPR images in different planes (axial, coronal, and sagittal) were evaluated for their diagnostic accuracy for the T-staging. We found that MDCT had a diagnostic accuracy of only 64.4% for axial, 75.5% for coronal and 81.1%for sagittal MPR images in T-staging. The differences in diagnostic accuracy was of statistical significance, between axial and coronal reconstructions ($p = 0.02$) and between axial and sagittal reconstructions ($p = 0.002$). These results matched with that of Kulinna et al. (3) who addressed the importance of MPR in improving local staging of rectal cancer. He reported that optimal sections through the tumor were obtained with sagittal and coronal reconstructions and sagittal images also have major implications for improving the delineation of the tumor as opposed to adjacent organs or vessels. His results showed that, the accuracy rate was only 81% for axial evaluation and 98% for combined evaluation with MPR in T-staging. Sinha et al. (21) concluded that the overall accuracy of T-staging on MPR images was 87.1% versus 73.0% for axial images alone.

Prediction of nodal staging in patients with primary rectal carcinoma is important for prognosis, and preoperative assessment of lymph node involvement has important value in developing the therapeutic schedule and a new auxiliary treatment (22). CT criteria for metastatic lymph nodes included size, border, shape and enhancement. In our study, we relied on the size of perirectal lymph nodes based on a modified TNM stage (3). We used a 3 mm cut-off value and had an overall diagnostic accuracy of 80%, this was consistent with findings from a previous studies. Kulinna et al. (3) used a 3 mm cut-off value and reported that two reviewers had 96% and 80% accuracy rates. Sinha et al. (21) used a 5 mm cut-off value and reported an 84.8% overall accuracy rate in the N-staging. Dar et al. (15) used a 3 mm cut-off value and had an overall accuracy rate of 84%, Ahmetoğlu et al. (23) also obtained the same overall accuracy (84%) in N staging. The accuracy rates reported in the literature for N-staging vary widely (22–73%). The inability to assess the internal architecture of lymph nodes, lack of reliable CT criteria for metastatic lymph nodes, and variable cut-off values of their size may explain the wide variability of the diagnostic accuracy of the CT in N-staging. One of the drawbacks of CT is the difficulty in distinguishing normal sized nodes with microscopic tumor involvement from enlarged benign reactive nodes (14).

5. Conclusion

Adding endorectal contrast agent as well as high-quality MPRs mainly the sagittal images to the routine 64-MDCT

examination provides definite improvements in the diagnostic accuracy for local staging of rectal cancer.

Conflict of interest

We have no conflict of interest to declare.

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