The accuracy of endorectal ultrasonography and high-resolution magnetic resonance imaging for restaging rectal cancer after neoadjuvant chemoradiotherapy



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AIM: Endorectal ultrasonography (ERUS) and high-resolution Magnetic Resonance Imaging (HR-MRI) are two frequently used techniques for the preoperative staging of rectal cancer to offer proper neoadjuvant or surgical treatment. Because tumor restaging after neoadjuvant therapy using ERUS and HR-MRI remains challenging the aim of this study is to determine which of the two imaging methods used in restaging rectal cancer has the highest accuracy.

MATERIAL AND METHODS: We included patients with rectal cancer who underwent ERUS and HR-MRI scans before and after neoadjuvant chemo-radiotherapy (n-CRT). The n-CRT was followed by imagistic restaging at 6 weeks after the last therapy session and by surgical resection. The pathology stage from the surgical sample was compared with the HR-MRI and ERUS restaging.

RESULTS: Fifty-four patients underwent n-CRT and 47 were restaged by both ERUS and HR-MRI. ERUS was accurate in tumor restaging after n-CRT in 29 cases (61.7%) and HR-MRI in 32 cases (68%). Regarding lymphatic node status, ERUS was accurate for 34 patients (72.3%) and had an overall rate of over-staging of 12.8% and 14.9% of under-staging. HR-MRI was accurate for 30 patients (63.8%) in restaging the lymph nodes after n-CRT and had an overall rate of over-staging of 25.5% and 10.7% of under-staging.

CONCLUSION: Restaging rectal cancer after n-CRT remains difficult because of radiotherapy tissue alteration, which results in low diagnostic accuracy for both methods.

KEY WORDS: Endorectal Ultrasonography (ERUS), High-Resolution Magnetic Resonance Imaging (HR-MRI), Neoadjuvant Chemo-Radiotherapy, Rectal Cancer Restaging,

Introduction

Rectal cancer is one of the most common cancers of the digestive tract: second after lung cancer in men and third after breast and genital cancer in women from Romania. It is known that radical surgery is the best curative treatment option for rectal cancer but neoadjuvant chemoradiotherapy (n-CRT) can help by down-staging the rectal tumor ¹.

Because of recent advances in oncology and the availability of therapeutic options, primary surgery is no longer the only recommended treatment. The main goals of preoperative treatment are to shrink the tumor and thereby enhance the resectability rate and facilitate sphincter-saving surgery, to reduce local recurrences and perhaps improve long-term survival ².

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Preoperative staging of rectal cancer includes several imaging investigations, of which the most used are endorectal ultrasonography (ERUS) and magnetic resonance imaging (MRI). By correctly staging the rectal cancer, patients can benefit from optimal treatment. Namely, early tumors may be eligible for local excision, whereas for advanced cancers, short- or long-term chemo-radiotherapy is indicated prior to full-scale surgical resection ¹. Several studies have reached the conclusion that MRI is superior to ERUS in the staging of rectal tumors ³⁻⁵. However, Bipat et al. found that ERUS was more accurate than MRI for perirectal tissue invasion and that the assessment of lymph nodes and invasion of adjacent organs was comparable in a meta-analysis that included all stages ⁶. Other studies have shown that MRI is preferable in advanced and stenosis tumors and in the assessment of lymph node involvement, whereas ERUS has advantages in assessing the wall penetration of the early stages of rectal cancer ⁷. Some authors have argued that a combination of both MRI and ERUS may increase the accuracy of the preoperative staging 7-9.

Restaging rectal cancer after n-CRT remains difficult. Although MRI is considered the first imaging modality choice after preoperative n-CRT, its reliability is debatable ¹⁰. Moreover, some recent studies using ERUS demonstrated higher accuracy in restaging rectal cancer compared with MRI ¹¹.

The accurate restaging of rectal cancer is becoming increasingly important because of the "wait and see" approach and active surveillance strategies in complete response. Moreover, correct and accurate imagistic description and staging offer valuable information for complete surgical resection ^{12, 13}.

The aim of this study was to evaluate the diagnostic accuracy of ERUS and HR-MRI in local restaging of rectal cancer after n-crt.

Material and methods

PATIENTS

The present prospective study was conducted in a single university hospital profiled in hepatic, biliary and

TABLE I - MRI parameters

digestive surgery, where the patients were diagnosed with and treated for rectal cancer. All the patients included in this study underwent ERUS and HR-MRI scans before and after n-CRT. The neoadjuvant treatment was followed by restaging at 6 weeks after the last therapy session and then by surgical resection at 2 or 4 days after restaging. The stage obtained from analysis of the surgical specimen was compared with the stage obtained from ERUS and HR-MRI. The imagistic investigations were scheduled before and after chemo-radiotherapy to enable a comparison between imagistic and surgical pathology staging. All included patients were informed about the study and gave their signed consent. Subjects were selected using the following inclusion criteria: patients with recently diagnosed rectal cancer, with no metastasis at the moment of staging. Exclusion criteria were patients under 18 years old, refusal of the surgical treatment, history of recurrent rectal cancer and mental health problems that affected their discernment.

MRI TECHNIQUE AND IMAGE INTERPRETATION

For the HR-MRI native pelvic examination, anti-spasmolytic drugs (Drotaverine Hydrochloride 40mg i.v., Nospa Chinoin Pharmaceutical and Chemical Works Co. Ltd. - Hungary) were administered before the start of the examination. The examination was performed on a 1.5T MRI scanner (Symphony TIM upgrade, Siemens AG, Erlangen, Germany) with an 8-chain Body Coil. There was no bowel preparation of the patients. The protocol included three T2-weighted turbo spin-echo sequences in the sagittal, oblique HR axial and oblique HR coronal planes. DWI were obtained in axial planes using EPI sequences at three b-values (b50, b400 and b800 s/mm²) and restriction of diffusion was quantified by ADC value. T2WI parameters and DWI parameters are shown in Table I.

Image interpretation was done on a PACS station (KODAK Carestream Version 10.2) by two radiologists with 5 years' experience in pelvic and gastrointestinal imaging in consensus. The readers were unaware of the pathological or ERUS results.

| | TSE T2 – Weighted imaging | | | | |
|------------------------|---------------------------|---------|--------------------|------------------|---------|
| MRI Parameter | Sagital | Axial | HR Coronal oblique | HR axial oblique | DWI |
| TR(ms) | 3500 | 3320 | 3500 | 4000 | 5800 |
| TE(ms) | 91 | 91 | 91 | 80 | 96 |
| Slice no | 28 | 40 | 25 | 25 | 30 |
| Bandwidth (Hz/pixel) | 391 | 391 | 391 | 391 | 1132 |
| FOV(mm) | 220 | 220 | 220 | 200 | 250 |
| Slice thickness (mm) | 3 | 4 | 4 | 3 | 4 |
| Matrix | 256x256 | 256x256 | 256x256 | 256x256 | 136x160 |
| Acquisition time (min) | 4 | 5.5 | 4 | 6 | 4.5 |

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The T-restaging was performed using the following criteria: – T0: Tumor redaction of more than 70% combined with evident fibrotic changes and no restricted diffusion was considered as a complete response;

- T1-2: Tumor reduced in size but still visible on T2 and DWI associated with intact low T2 signal outside the layer of the rectum wall;

- T3: Tumor reduced or not visible in size on T2 and DWI associated with breaching of the rectum wall and presence of neoplastic tissue in the mesorectal fat;

– T4: Tumor reduced or not visible in size on T2 and DWI with penetration of the visceral peritoneum or direct invasion of adjacent organs 14 .

Nodal involvement was considered by using a size threshold of > 5 mm and heterogeneous signal or ill-defined margins ¹⁵. Nodes below the inferior margin of the tumor were not taken into account. The measurements were recorded in millimeters (mm). However, it must be stressed that unlike for ultrasound, there are a number of absolute and relative contraindications for MRI. The examination can be performed in pregnant women, but without contrast substance administration and using a limited number of sequences ¹⁶⁻¹⁹.

ERUS TECHNIQUE AND IMAGE INTERPRETATION

ERUS was performed using a Logiq E9 BT15 (General Electric, Boston, USA) and an IC 5-9D of 4-9 MHz rigid endocavitary probe was used. The ERUS was performed by one of two investigators with more than 5 years' experience. The preparation included two enemas, one the prior evening and one on the morning of the examination. The investigation was conducted in the left lateral position using the endocavitary probe covered by a condom filled or not with water and introduced through the anal canal. Conventional gray-scale mode was used to characterize the morphologic changes visible after n-CRT and vascular Doppler examination was used to highlight tumor vasculature if present.



Fig. 1: T3 rectal cancer. The tumor infiltrates all layers of the rectum and spreads into the perirectal fat tissue.



Fig. 2: Doppler window outlines the rectal highly vascularized tumor.



Fig. 3: Lymph node measured in the perirectal fat tissue, considered to be malignant.

T-restaging was performed using the following criteria: – T0: Homogenous hypoechoic movable lesion, important redaction in size, intact wall structure and the absence of perirectal fat infiltration. No vascularization present on Doppler examination;

- T1-2: Reduction in tumor volume, but tumor still visible on gray-scale mode infiltrating the sub-mucosa or muscularis propria associated with reduction or not of vascular signal on Doppler examination;

- T3: Reduction or not in tumor volume visible on gray-scale mode infiltrating the rectal wall through serosa or perirectal fat associated with reduction or not of vascular signal on Doppler examination (Figs. 1, 2);

– T4: Reduction or not in tumor volume visible on gray-scale mode infiltrating the visceral peritoneum or directly invading adjacent organs.

For N staging, the following criteria were used: For grayscale mode lymph nodes larger than 5 mm in diameter, those that were hypoechoic and round in shape were considered malignant (Fig. 3), and for Doppler exam, lymph nodes with a resistance index ≥ 0.61 and peak systolic velocity ≥ 20 cm/second were also considered malignant.

HISTOPATHOLOGICAL ANALYSIS

TABLE II - Distribution by age.

Pathological examinations of the resected surgical specimens were performed after fixation in formaldehyde. The obtained specimens were then cut, embedded in paraffin and sectioned. Routine staining was used. The slices were analyzed by a specialist pathologist according to the routine protocol used in the pathology department. The diameter in three directions and the T and N staging were recorded, and the staging results were given at about 2 weeks after surgery.

Pathological T and N staging was performed using the following criteria: 20

- T0: No evidence of primary tumor;
- T1: Tumor invades submucosa;
- T2: Tumor invades muscularis propria;

- T3: Tumor invades through muscularis propria into subserosa or into non-peritonealized pericolic or perirectal tissues;

- T4: Tumor directly invades other organs or structures and/or perforates visceral peritoneum;

- N0: No regional lymph node metastasis;

- N1: Metastasis in one to three regional lymph nodes;
- N2: Metastasis in four or more regional lymph nodes.

STATISTICAL ANALYSIS

All statistical calculations were performed using SPSS v.24 software. Sub-staged predictions that were lower were considered and these were divided by the total. HR-MRI and ERUS results were compared with histopathology (considered as the gold standard). Descriptive analysis was conducted according to the type of variable. Bivariate assessment of variables was performed. Bivariate distributions were constructed first. Afterwards, two types of approaches were used: (1) correlation analysis to see if any relationship exists between the variables and (2) non-parametric evaluation to assess differences between distributions. Taking into account the types of variables used, the Kendall correlation coefficient in the tau-b form, the Mann-Whitney and the Wilcoxon tests were employed. Statistical significance was considered at the 0.05 critical level (p-value < 0.05). Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were analyzed for all stages.

Results

ERUS and HR-MRI have become the state of the art in radiological examination of the terminal part of the digestive tract ²¹. The main limitation of ERUS application is tumors located close to the sigmoid colon or infiltrating adjacent organs.

Of a total of 90 patients, 54 (60%) received n-CRT as a preoperative treatment and 36 (40%) did not. Because

| | Age group | Frequency | Percent |
|-------|-----------|-----------|---------|
| Valid | <=50 | 7 | 7.8% |
| | 51-60 | 32 | 35.6% |
| | 61-70 | 34 | 37.8% |
| | 71-80 | 15 | 16.7% |
| | >80 | 2 | 2.2% |
| _ | Total | 90 | 100% |

TABLE III - Localization of rectal cancer

| | Frequency | Percentage |
|------------------------|-----------|------------|
| Interior rectal cancer | 34 | 37.8% |
| Middle rectal cancer | 38 | 42.2% |
| Superior rectal cancer | 18 | 20% |
| Total | 90 | 100 |

we analyzed the restaging of rectal tumor after n-CRT, those 36 patients without neoadjuvant treatment were also excluded from the final results. From these 54 patients, we analyzed 47 of them because they had both of the imaging investigations. One patient refused the HR-MRI for restaging, arguing that he suffered from claustrophobia the first time, and five patients refused ERUS, arguing that at staging it caused them pain. One patient had an inconclusive result at ERUS restaging and he was also excluded from the final analysis. A total of 47 patients met our selection criteria and were included in the study.

The mean patient age was 62.1 years, with a minimum of 28 years and a maximum of 82 years. Most of the patients diagnosed with rectal cancer were between 51 and 70 years old, as seen in Table II.

After diagnosis, subjects were grouped in patients with superior, middle and inferior rectal cancer. The majority of the patients were diagnosed with middle rectal cancer (42.22%), which is the most frequent site of cancer at the rectum, followed by those with inferior rectal cancer (37.78%) and superior rectal cancer (20.00%) as seen in Table III.

Fifty-four patients underwent n-CRT and 47 were restaged by both ERUS and HR-MRI, 6 weeks after the last chemo-radiotherapy session, prior to surgery, so we were able to calculate the accuracy of restaging diagnostic for rectal cancer.

T and N stages obtained by ERUS and HR-MRI after n-CRT were analyzed and the results were compared with T and N stages obtained by the pathologist after examining the resected tumor.

The final valid sample consisted of 47 patients for the ERUS and HR-MRI analysis. Because T1 tumors are difficult to detect imagistically, we decided to combine them with T2.

TABLE IV - "T" accuracy over-staging and under-staging of rectal cancer by ERUS after nCRT

| T Stage | Accuracy | Over-staging | Under-staging | |
|---------|---------------|---------------|---------------|--|
| T0 | 1/5 (20%) | 4/5 (80%) | 0/5 (0%) | |
| T1-2 | 7/15 (40.6%) | 8/15 (53.5%) | 0/15 (0%) | |
| T3 | 19/25 (76%) | 4/25 (8%) | 4/25 (16%) | |
| T4 | 2/2 (100%) | 0/2 (0%) | 0/2 (0%) | |
| Total | 20/47 (61.7%) | 14/47 (29.8%) | 4/47 (8.5%) | |

TABLE V - "T" accuracy, over-staging, under-staging of rectal cancer by HR-MRI after nCRT

| T Stage | Accuracy | Over-staging | Under-staging |
|---------|---------------|--------------|---------------|
| T0 | 3/5 (60%) | 2/5 (40%) | 0/5 (0%) |
| T1-2 | 10/15 (66.6%) | 2/15 (13.3%) | 3/15 (20%) |
| Т3 | 17/25 (68%) | 0/25 (0%) | 8/25 (32.3%) |
| Τ4 | 2/2 (100%) | 0/2 (0%) | 0/2 (0%) |
| Total | 32/47 (68%) | 4/47 (8.5%) | 11/47 (23.4%) |

ERUS was accurate in tumor restaging after n-CRT in 29 cases (61.7%) and HR-MRI in 32 cases (68%), as seen in Tables IV and V.

As seen in Tables IV and V, five patients had a complete response after n-CRT, which was confirmed through the pathology result. Prior to surgery, at restaging, ERUS identified one with a complete response and HR-MRI three.

Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated for ERUS, as seen in Table 6, and for HR-MRI, as seen in Table 7, for all stages. ERUS found the highest sensitivity in stage T3 (Se=80.65%) and the highest specificity in stage T4 (Sp=95.74%).

HR-MRI found the highest sensitivity and specificity in stage T4 (Se and Sp = 100%) because two patients did not respond to n-CRT and were diagnosed as stage T4 and confirmed by the pathology result. Otherwise, the highest sensitivity found for HR-MRI was still in stage T3 (Se=80.65%) and the highest specificity in stage T0 (Sp=89.36%).

In the following figures HR-MRI demonstrates the differences between the initial staging and restaging after neoadjuvant treatment. An axial T2-weighted HR image in a 61-year-old woman demonstrates a circumferential irregular thickening of the inferior rectal wall. White arrows indicate breaching of the outer muscular layer and invasion of perirectal fat. This patient was primary stage T3b (Fig. 4a).

A sagittal T2-weighted image in the same patient shows extension of the tumor from above the anal verge to the middle rectum (white lines) (Fig. 4b).

ADC maps shows restricted diffusion in the site of the tumor (Fig. 4c).

An axial T2-weighted HR image in the same patient after neoadjuvant CRT demonstrates extensive fibrosis at the site of the primer tumor (white arrows). No residual tumor was observed (Fig. 5a).

A sagittal T2-weighted image shows fibrosis of the anterior wall (white arrows) and edema of the posterior wall (arrow heads) (Fig. 5b).

The ADC maps show no diffusion restriction after n-CRT. This patient was restaged as complete response (Fig. 5c). Regarding lymphatic node status, ERUS was accurate for 34 (72.3%) out of 47 patients (100%) and had an overall rate of over-staging of 12.8% and 14.9% of understaging. It is shown that most of the patients at restaging were classified as being in stage N0 (38 patients), of whom 32 (84.2%) were confirmed to be in this stage by the pathology result, as seen in Table VIII.

HR-MRI was accurate for 30 (63.8%) out of 47 patients (100%) in restaging the lymph nodes after n-CRT and



Fig. 4: A) T3b rectal tumor highlighted by HR-MRI at staging; B) HR-MRI T3b rectal tumor coronal section at staging; C) HR-MRI T3b rectal tumor - ADC map.



Fig. 5: A) HR-MRI complete response after nCRT showed at restaging; B) HR-MRI TO rectal tumor coronal section at restaging; C) HR-MRI T0 rectal tumor - ADC map.

| Table | VI | - | Se, | Sp, | PPV | and | Npv | for | all | Τ | stages | diagnosed | with |
|-------|----|---|-----|-----|-----|-----|-----|-----|-----|---|--------|-----------|------|
| ERUS | | | | | | | | | | | | | |

| T Stage | Sensitivity | Specificity | NPV | PPV |
|---------|-------------|-------------|--------|--------|
| Т0 | 55.56% | 95.5% | 91.3% | 71.45% |
| T1-2 | 65.22% | 91.43% | 80% | 85.33% |
| T3 | 80.65% | 64.71% | 78.57% | 67.57% |
| T4 | 100% | 95.7 | 100% | 100% |

TABLE IX - "N" over-staging and under-staging of rectal cancer by HR-MRI after nCRT.

| N Stage | Accuracy | Over-staging | Under-staging |
|---------|---------------|---------------|---------------|
| N0 | 26/38 (68.4%) | 12/38 (31.5%) | 0/38 (0%) |
| N1 | 2/4 (50%) | 0/4 (0%) | 2/4 (50%) |
| N2 | 2/5 (40%) | 0/5 (0%) | 3/5 (60%) |
| Total | 30/47 (63.8%) | 12/47 (25.5%) | 5/47 (10.7%) |

TABLE VII - Se, Sp, PPV, and NPV for all T stages diagnosed with HR-MRI

| T Stage | Sensitivity | Specificity | NPV | PPV |
|---------|-------------|-------------|--------|--------|
| Т0 | 71.43% | 89.36% | 95.45% | 50% |
| T1-2 | 75% | 82.05% | 86.4% | 68.18% |
| T3 | 75.76% | 88% | 73.55% | 89.29% |
| Τ4 | 100% | 100% | 100% | 100% |

TABLE X - Se, Sp, PPV and NPV for all N stages diagnosed with ERUS.

| N stage | Sensitivity | Specificity | NPV | PPV |
|---------|-------------|-------------|--------|--------|
| N0 | 86.36% | 64.29% | 60% | 88.37% |
| N1 | 57.14% | 86% | 93.48% | 36.36% |
| N2 | 55.56% | 97.67% | 91.3% | 83.33% |

TABLE VIII - "N" accuracy, over-staging and under-staging of rectal TABLE XI - Se, Sp, PPV and NPV for all N stages diagnosed with cancer by ERUS after nCRT.

| N Stage | Accuracy | Over-staging | Under-staging |
|---------|---------------|--------------|---------------|
| N0 | 32/38 (84.2%) | 6/38 (15.7%) | 0/38 (0%) |
| N1 | 1/4 (25%) | 0/4 (0%) | 3/4 (75%) |
| N2 | 1/5 (20%) | 0/5 (0%) | 4/5 (80%) |
| Total | 34/47 (72.3%) | 6/47 (12.8%) | 7/47 (14.9%) |

HR-MRI.

| N stage | Sensitivity | Specificity | NPV | PPV |
|---------|-------------|-------------|--------|--------|
| N0 | 76% | 69.23% | 42.86% | 90.48% |
| N1 | 66.67% | 84.31% | 95.56% | 33.33% |
| N2 | 62.5% | 89.36% | 93.33% | 50% |

had an overall rate of over-staging of 25.5% and 10.7% of under-staging, as seen in Table IX.

The Se, Sp, PPV and NPV for N stage calculated for ERUS are shown in Table X and for HR-MRI in Table

XI for all stages. Both HR-MRI and ERUS were accurate in restaging 21 tumors: one complete response, five at T1-2 stage, 14 at T3 and two at T4.

Both methods missed restaging in seven cases: two com-

plete responses, three T1-2 tumors, with ERUS overstaging all of them and HR-MRI over-staging one and under-staging two.

ERUS alone correctly restaged eight tumors, seven T3 tumors and one T1-2 tumor. HR-MRI under-staged all tumors (six T1-2 and one T0). HR-MRI alone correctly restaged 11 tumors: two complete responses, five T1-2 tumors and four T3 tumors. ERUS over-staged the two complete response (both were restaged T3), under-staged one T1-2 tumor, over-staged four T1-2 (all were restaged T3), under-staged two T3 tumors (both restaged T2) and over-staged the other two T3 tumors.

Discussion

Treatment options for rectal cancer depend on the stage at presentation ²². Digital rectal examination is useful for detecting lower rectal cancer, but it cannot stage the tumor correctly, thus preoperative staging is mostly based on imaging. Accurate staging is particularly important because stage 1 tumors are best treated with surgery alone, whereas stage 2 and 3 tumors require preoperative n-CRT ²³.

Patients with locally advanced rectal cancer undergoing n-CRT should benefit from restaging imaging before surgery because of the growing number of treatment options and the importance of response assessment in the individualization of cancer management. As in staging rectal cancer, in the restaging phase most patients will benefit either from HR-MRI or ERUS, or in some cases both ²³.

Restaging rectal cancer after n-CRT is challenging for T staging mainly because of the difficulty in differentiating fibrotic changes and reactive inflammatory changes from residual tumor ²⁴.

Although HR-MRI and ERUS are the main imaging tools used in restaging rectal cancer, their diagnostic accuracy is generally low and varies significantly in the literature ²⁵. In a recent study on 94 patients, Zhan et al. reported an overall accuracy for MRI for T-restaging of 49%, with over-staging occurring in 40.4% and under-staging in 10.6%. The author concluded that better methods are urgently required ²⁶.

Another study conducted in a high-volume rectal cancer center by Van den Broek et al. on a consecutive cohort of 48 patients using three independent readers demonstrated an overall accuracy for T-restaging ranging from 47% to 68%. They concluded that MRI has low accuracy in restaging rectal cancer and that the interobserver variability is significant ¹⁰.

In our study, HR-MRI was accurate in 32 (68%) out of 47 (100%) patients for T-restage. Our data are consistent with the results of these two recently published studies.

In contrast with the published data, HR-MRI over-staging in this study was lower than under-staging ("T" overstage = 8.5% and "T" under-stage = 23.4%). This large number of under-staged tumors can be explained by the presence of numerous cases of extensive fibrotic changes in the mesorectal fat with no evident restricted diffusion, which were interpreted as T0-T2 stage (11 tumors), but in the histology report malignant cells were identified outside the rectum wall.

The HR-MRI accuracy of N-restage was 63.82% in this study. Our results were consistent with those published in a meta-analysis including 12 MRI studies reporting an accuracy ranging from 60% to 88% with an average of 72% 27 .

In a recent study on 139 patients, Dickman et al. reported an ERUS accuracy of 44.6% in T-restaging for rectal cancer after n-CRT and an accuracy of 78.41% in N-restaging ²⁸. Moreover, in a meta-analysis on 18 restaging ERUS studies, Memon et al. reported an ERUS T stage restaging accuracy that ranged between 56% and 72% ²⁷. In our study ERUS was accurate in tumor restaging after nCRT in 29 cases (61.7%) from 47 (100%) and for N-restage in 34 cases (72.34%).

The over- and under-staging of ERUS was, according to the published data, over-staging more tumors than under-staging ("T" over-staging = 29.8% and "T" understaging = 8.5%). This can be explained by the tendency of the examiner to over-stage the irradiated tumor formation because of important fibrosis at the level of the tumor bed.

After searching the database on PubMed from 2004–2017 and introducing the key words MRI, ultrasound, and restaging rectal cancer, we could not find any study comparing MRI and ERUS in the same group of patients. In this study all subjects underwent both examinations; no subject was examined by only one method. From our point of view this is an important advantage over other studies because we were able to compare between the two imaging modalities in the most objective way.

Overall, in this study HR-MRI showed slightly higher accuracy in T-restaging rectal cancer after n-CRT than ERUS (68% vs. 61.7%), while for N-restaging ERUS showed higher accuracy (72.34% vs. 63.82%).

HR-MRI demonstrated high specificity (T0 - 89.36%, T1 - 2 82.05% and T3 - 88%) but low sensitivity for all three groups (T0 - 71.43%, T1-2 - 75% and T3 - 75.76%), while ERUS showed very high specificity for T0 and T1-2 stages (95.45% and 91.43%) but much lower for T3 stage (64.71%), while sensitivity was low for T0 and T1-2 stages (55.56% and 65.22%) but highest for both methods for T3 stage (80.65%). T4 tumors were not discussed because of the low number of cases in this study (two).

Both methods together missed the T-restaging of seven tumors. ERUS alone correctly restaged eight tumors, all of them being under-staged by HR-MRI, while HR-MRI alone correctly restaged 11 tumors, ERUS over-staging eight and under-staging three. These are interesting





results because HR-MRI missed all tumors staged correctly by ERUS by under-staging them, while most of the stages missed by ERUS were due to over-staging.

ERUS can also be done in 3D and used for spatial representation and precise measurement of tumor formations, using CT and/or MRI image reconstruction ²⁹. In this study investigators were blinded to the results of each imaging modality, but in everyday practice radiologists should benefit from any important information regarding the patient. We believe that performing both examinations, comparing results and determining the final stage in consensus will boost the diagnostic accuracy of rectal cancer restaging.

Our study has two important limitations. First, the sample size for this study is relatively small and second this study had only a few patients with complete response. This are the patients which will benefit the most form an accurate restaging. Therefore, further larger prospective studies are needed to find determinant criteria for this multimodality approach for each of the imaging modalities, and to confirm these results.

As a final statement, we propose a restaging imaging algorithm (Fig. 6).

Conclusion

In conclusion, ERUS and HR-MRI are two imaging methods used for restaging rectal cancer with close sensitivity and specificity and a moderate diagnostic. Restaging rectal cancer after n-CRT remains difficult because of radiotherapy tissue alteration, which results in low diagnostic accuracy for both methods.

However, because of the different advantages and characteristics of each imaging method, we suggest that multimodal assessment with rectal HR-MRI and ERUS may be the best option for local restaging of locally advanced rectal cancer after n-CRT.

Riassunto

L'ultrasonografia endorettale (ERUS) e la risonanza magnetica ad elevate risoluzione (HR-MRI) sono le due tecniche usate di frequente per la stadiazione preoperatoria del cancro del retto per permettere l'adeguato trattamento neoadiuvante o chirurgico. Dato che la restadiazione del tumore con ERSU e con HR-MRI dopo trattamento neoadiuvante rappresenta una problematica, lo scopo del nostro studio era quello di stabilire quale dei due metodi di indagine per imaging avesse la maggiore accuratezza per la restadiazione del cancro del retto.

Lo studio ha preso in considerazione pazienti con cancro del retto sottoposti ad ERUS e a HR-MRI prima e dopo trattamento chemioterapico neoadiuvante (n-CRT). La restadiazione per imaging è stata eseguita 6 settimane dopo l'ultima sessione del trattamento chemioterapico e prima dell'intervento chirurgico. Lo studio anatomo-patologico del pezzo chirurgico è stato messo in relazione con i referti di restadiazione con ERUS e HR-MRI.

Di 54 pazienti sottoposti a n-CRT, 47 sono stati restadiati sia con ERUS che con HR-MRI. ERUS si è dimostrata adeguata nella restadiazione del tumore dopo n-CRT in 29 casi (61,7%) e la HR-MRI in 32 casi (68%). Per quanto riguarda lo stato linfonodale ERUS è stata accurata in 34 pazienti (72,3%) con una incidenza di sopra-stadiazione del 12,8% e una di sottostadiazione del 14,9%. La HR.MRI si è dimostrata accurata nella restadiazione linfonodale dopo n-CRT in 30 pazienti (63,8%) con una incidenza di soprastadiazione del 25,5% e del 10,7% di sottostadiazione.

In conclusione la restadiazione del cancro del retto dopo n-CRT rimane difficoltosa per il sovvertimento tissutale dovuto alle radiazioni, con la conseguente scarsa accuratezza diagnostica con entrambi i metodi.

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