UNIVERSITÀ DI PISA

Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia

Scuola di Specializzazione in Radiodiagnostica

Direttore: Prof. Carlo Bartolozzi

TESI DI SPECIALIZZAZIONE

3-Tesla Magnetic Resonance Imaging vs Endorectal Ultrasound in the preoperative staging of rectal cancer: a correlation analysis

Relatore:

Chiar.mo Prof. Carlo Bartolozzi

Candidata:

Dr.ssa Elisa Guidi

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INDEX

ABSTRACT

Purpose: To evaluate the correlation between endorectal ultrasound (ERUS) and magnetic resonance imaging (MRI) in preoperative staging of rectal cancer.

Materials and Methods: Fifty patients with rectal cancer underwent ERUS and 3-Tesla MRI for preoperative staging. With both imaging techniques were evaluated the following features: lesion site, tumour longitudinal extent, distance between lesion distal margins and puborectalis muscle, levator ani muscles infiltration, depth of extramural spread, mesorectal lymph nodes involvement and pelvic organs infiltration.

MRI evaluated also the following features: maximum thickness of the lesion, distance between externa margins of the lesion and mesorectal fascia and overcoming of the peritoneal reflection. All MR studies were evaluated by two experienced professionals board certified in radiology and experts in gastrointestinal imaging.

The correlation between MRI and ultrasound data was calculated for each measure using the Spearman rank test (p-values <0.05 were considered statistically significant).

The interobserver agreement for MRI was assessed by using the Cohen's kappa statistics.

Eleven patients underwent directly to surgical resection without neoadjuvant therapy, and the surgical specimen was

used as standard of reference for determination of depth of invasion (T stage) and perirectal nodal involvement (N stage).

Results: ERUS and MRI showed a statistically significant correlation for the lesion site (MRI observer A vs ERUS: r_s=0.873, p<0.000001/ MRI observer B vs ERUS: r_s=0.8485, p<0.000001), the tumour longitudinal extent (MRI observer A vs ERUS: r_s=0.378, p=0.010393/ MRI observer B vs ERUS: r_s=0.3794, p=0.010131), the distance between lesion and puborectalis muscle (MRI observer A vs ERUS: r_s=0.7954, p<0.000001/ MRI observer B vs ERUS: r_s=0.7989, p<0.000001) and the depth of extramural spread (MRI observer A vs ERUS: r_s=0.5107, p=0.000149/ MRI observer B vs ERUS: r_s=0.5046, p=0.000186).

Moreover, TRUS and MRI were able to demonstrate the levator ani muscles infiltration with an overall agreement of 82% for MRI reader A and 80% for MRI reader B, the lymph nodes involvement with an agreement of 68% for MRI reader A and 76% for MRI reader B and the pelvic organs infiltration with an agreement of 80% for both MRI reader.

MRI allowed, however, the evaluation of other staging parameters, as the distance between lesion and mesorectal fascia.

The interobserver agreement between MRI reader A and B was 0.91 for the lesion site, 0.914 for the distance between

lesion and puborectalis muscle, 0.791 for the tumour longitudinal extent, 0.758 for the depth of extramural spread, 0.734 for the maximum thickness of the lesion and 0.48 for the distance between lesion and mesorectal fascia.

There was also an agreement between the two observers of 100% for the pelvic organs involvement, of 96% for the overcoming of the anterior peritoneal reflection, of 88% for the mesorectal lymph nodes involvement and of 82% for the levator ani muscles infiltration.

Conclusions: The good agreement between MRI and TRUS in preoperative staging of rectal cancer argues in favor of the use of MRI, because it also allows a more comprehensive local assessment.

INTRODUCTION

Colorectal cancer is an important public health problem: there are nearly one million new cases of colorectal cancer diagnosed world-wide each year and it is the third leading cause of death with over half a million deaths [1,2].

In particularly, rectal cancer, defined as a tumor with its lower edge within 15 cm from the anal verge, account for about a third of all colorectal malignancies [3].

In the last decades, we have seen dramatic improvements in the outcomes of patients with rectal cancer. The rate of local recurrence has decreased, the probability of survival has increased, and the quality of life has improved. Advances in surgical pathology, refinements in surgical techniques, and the widespread use of preoperative chemo-radiotherapy (CRT), have all contributed to these improvements. Advances in imaging have also played a pivotal role in identifying the rectal tumors at risk for recurrence, helping in planning surgical procedures and selecting patients for neoadjuvant therapy [4].

RECTAL ANATOMY

The rectum varies in lenght from 10 to 15 cm, from the upper end of anal canal to the recto-sigmoid junction, and can be divided into three segments from the anal verge: lower rectum, middle rectum, and upper rectum. The rectal wall is

composed of three layers: mucosa, submucosa and muscularis layer, that are best visualized on ERUS.

The rectum is surrounded by mesorectal fat (mesorectum) containing lymph nodes, superior hemorrhoidal vessels and fibrous tissue, and it is bordered by a thin membrane called mesorectal fascia [2].

The mesorectum is thick posteriorly but either almost absent anteriorly where it is separated from the urogenital organs by the Denonvillier's fascia.

Distally the rectum is in direct contact with the levator ani muscles, and this relationship must be taken into consideration when deciding between an abdominoperitoneal excision or a sphincter-sparing procedure for rectal cancers located at or below the level of the anorectal ring [4].

LOCAL STAGING OF RECTAL CANCER

The diagnosis is usually established by means of clinical examination (rectal digital examination), endoscopy (sigmoidoscopy and colonoscopy), double-contrast enema examination, and histologic confirmation, supplemented by biochemistry (eg, blood carcinoembryonic antigen measurement).

Unfortunately, all these techniques are poor indicators of the depth of invasion (T stage) and lymph node involvement (N stage), which are both important features for prognosis [5].

Computed Tomography (CT)

CT is used for pre-operative assessment of distant metastases, but don't have a role in local staging because it does not distinguish rectal wall layers, however it can evaluate lymph nodes (mesorectal but also iliac and mesenteric or retroperitoneal) [6].

Endorectal Ultrasonography (ERUS)

ERUS has the advantage to visualize all layers of the rectal wall and can demonstrate other anatomical structures, such as seminal vescicles, prostate, cervix, vagina, blood vessels and perirectal nodes situated into the field of view of the probe, also the puborectalis muscle and the anal sphincters are clearly visualized on ERUS [4].

On ERUS imaging, the rectal wall is visualized according to the Beynon five-layers model described below:

- first hyperechoic layer - interface between the balloon and its contained water and the mucosal surface;
- second hypoechoic layer - mucosa and muscolaris mucosae;
- third hyperechoic layer – submucosa;
- fourth hypoechoic layer – muscularis propria;
- fifth hyperechoic layer – interface between the muscularis propria and perirectal fat or serosa if present [7] (Fig.1).

Rectal tumors appear as expansions of the first hypoechoic layer of the rectal wall, distorting and interrupting the other layers of the rectal wall from the inside out.

An ultrasound T classification, similar to the T classification of the AJCC TNM staging system is based on tumor disruption of the different echographic layers.

Metastatic lymph nodes appear as hypoechoic deposits, with an echogenicity similar to that of the primary tumor.

ERUS is a very accurate tool for measuring size, circumference and distance of the tumor from various anatomic landmarks (eg, sphincters, prostate, etc), and it can delineate the relationship of distal rectal cancer with internal and external anal sphincters [4].

Magnetic Resonance Imaging (MRI)

The introduction of phased-array coils and the use of T2-weighted fast spin echo thin-section sequences have enabled accurate determination of prognostic factors and anatomic assessment of the pelvis by delineating rectal tumors through increases in spatial and contrast resolution.

MRI can accurately predict the depth of extramural penetration, and more importantly, predict the relationship between tumor and mesorectal fascia, which is an important risk factor for local recurrence.

T2-weighted images are the most suitable for depicting the

rectal wall anatomy, and MRI can distinguish:

- inner hyperintense layer – mucosa and submucosa (no differention is possible between these two components);
- intermediate hypointense layer – muscularis propria;
- outer hyperintense layer – perirectal fat tissue.

The mesorectal fascia can be identified as a thin, low-signal-intensity structure that envelops the mesorectum and the surrounding perirectal fat (Fig.2).

The anal canal can be easily visualized in MRI of the lower rectum with clear depiction of the levator ani muscle, the puborectalis muscle, and the internal and external anal sphincters [8].

On T2-weighted images, the tumour appears as epithelial-based thickening with a signal intensity slightly higher than the muscularis propria [6].

Metastatic lymph nodes appear as hypointense deposits into the mesorectal fat, and the use of border contour and signal intensity characteristics in addition to size criteria can improve the accuracy of nodal staging [9].

Rectal MRI with phased-array coil provides a full evaluation of the rectal wall layers, mesorectal fat and fascia and it improves patient comfort compared with the use of an endorectal coil or ERUS. Moreover, stenosing lesions and tumors at the rectosigmoid junction can be evaluated in all cases by MRI.

TNM STAGING

The more recent clinical staging classification from the American Joint Committee on Cancer (2010) takes into account the subclassification of T3 tumors (Tab.1).

Moreover, we can distinguish between "T3 early" if tumor extends ≤5 mm beyond muscularis propria and "T3 advanced" if tumor extends >5 mm.

SURGICAL TREATMENT

At the present total mesorecal excision (TME) is the surgical approach of choice for rectal cancer, because is able to reduce the local recurrence rate to less than 10% [10], improving the 5-year survival rate if compared with conventional surgery.

TME is achieved by means of a dissection along the plane that separates the visceral from the parietal layers of the perirectal pelvic fascia, thus allowing radical removal of the rectum and its surrounding mesorectum [11].

The circumferential resection margin (CRM) is the lateral or radial resection margin created by the surgeon and the ideal plane of resection is just outside the mesorectal fascia.

RISK FACTOR FOR LOCAL RECURRENCE

In large databases, the risk factors associated with local recurrence are generally similar to the risk factors for distant

recurrence: T stage, N stage, distance to the CRM, perineural invasion, lymph node and blood vessel invasion, and histologic grade. Of these risk factors, the T and N stage are commonly used for (neo) adjuvant treatment decisions, and recently also the distance to the CRM [12].

Incomplete removal of the lateral spread of the tumour is now generally accepted as the reason for most of local recurrences that may be reduced thanks to perioperative radiotherapy.

In Europe there is a preference for preoperative radiotherapy, based on the results of several trials, among which the most important is the Swedish Rectal Cancer Trial that showed the most convincing results, with a local recurrence rate of 11% after radiotherapy compared with a rate of 27% in the controls, and improved survival [13].

Attention has also been directed at the surgical technique itself as a determinant of local recurrence rates. Histology of resection specimens has shown that the frequency of local recurrence greatly decreases when a tumour-free circumferential resection margin of more than 1 mm can be obtained [14].

Tumor stage

Transrectal ultrasound (TRUS) is very accurate for staging of superficial rectal tumors but is not as useful for staging of

advanced rectal cancers, so it is the gold standard for discriminating stage T1 from T2 [2].

Instead MRI is very accurate for identifying large T3 and T4 tumors and invasion of mesorectal fascia [5].

Most staging failures with MRI occur in the differentiation between T1 and T2 lesions and between T2 and borderline T3 lesions [12].

Nodal stage

Nodal disease is one of the most important risk factors for both local and distant recurrence, but identifying nodal involvement with imaging remains difficult because size criteria used on its own result inaccurate. In addition to size with 5 mm as a cut-off, roundness, border irregularity and hypoehoic nature (ERUS)/ heterogeneus signal (MRI) can provide additional accuracy.

Circumferential Resection Margin (CRM)

The association of CRM with local recurrence was first demostrated in 1986 by Professor Quirke's group [15] and some trials have demonstrated that patients with CRM involvement have 3.5 times the risk of local recurrence and double the risk of death [16].

The CRM is identified with the mesorectal fascia and a positive CRM is defined as a closed distance of 1 mm or less

between tumor and resection margin and, it can be the result of an inadequate total mesorectal excision (TME) surgery or an advanced tumor that comes close to or invades the mesorectal fascia.

The mesorectal fascia is very difficult to identify with ERUS, except when there is an invasion of vagina, prostate, or seminal vesicles, instead many single center studies have shown that MRI is highly accurate for the prediction of an involved CRM [12,14].

MATERIALS AND METHODS

Patients

From May 2011 to May 2013, fifty patients with biopsy proved rectal cancer were submitted to MRI and ERUS. All patients underwent colonoscopic examination in which a bioptic procedure was performed.

The inclusion criteria were (1) histologically confirmed rectal adenocarcinoma and (2) distal end of tumor located within 15 cm from the anal verge.

The study consisted of 32 (64%) men and 18 (36%) women with a mean age of 68.3 years (range 34-87 years).

Thirty-nine patients (78%) underwent to preoperative chemoradiotherapy (CRT) followed by surgical treatment, instead eleven patients (22%) underwent immediately to surgical treatment (TME) without CRT.

Following surgery, operative specimens were analysed by a pathologist.

MRI technique and parameters

All MRI examinations were performed with a 3-Tesla scanner (Discovery 750, General Electric, Milwaukee, Wisconsin, USA) using a pelvic phased-array surface coil (8US TORSOPA).

The night before the MR study, the patients were given a water enema to clean the rectum, and the examinations were

performed after luminal distension with rectal gel in a variable quantity from 60 to 120 mL relating to the location of the lesion. It is important not to overdistend the rectum with rectal gel since this could distort the anatomy and reduce the ability to interrogate the surrounding mesorectum, which would be compressed by overdistension.

The patient is positioned supine, and the phased-array surface coil is placed on the pelvis in such a way that the lower edge of the coil lies below the pubic bone.

The following sequences were acquired:

- axial T2-weighted Fast Spin Echo (FSE) (repetition time [TR]/ echo time [TE] 3500-6000/ 90-150 ms), field of view 24 cm, section thickness 5 mm, interval 0.5 mm, matrix 384x224;
- sagittal T2-weighted Fast Spin Echo (FSE) (repetition time [TR]/ echo time [TE] 3500-6000/ 90-150 ms), field of view 24 cm, section thickness 5 mm, interval 0.5 mm, matrix 384x224;
- coronal T2-weighted Fast Spin Echo (FSE) (repetition time [TR]/ echo time [TE] 3500-6000/ 90-150 ms), field of view 24 cm, section thickness 5 mm, interval 0.5 mm, matrix 384x224;
- oblique-axial T2-weighted Fast Spin Echo (FSE) (repetition time [TR]/ echo time [TE] 3500-6000/ 90-150 ms) on a plane perpendicular to the long axis of the

tumor as visualized in the sagittal sequences, field of view 22 cm, section thickness 3 mm, interval 0.2 mm, matrix 384x224;

- sagittal 3D T2-weighted Fast Spin Echo (CUBE) (repetition time [TR]/ echo time [TE] 1600/ 85-95 ms), field of view 24 cm, section thickness 0.9 mm, no interspace, matrix 288x256;
- axial diffusion-weighted (DWI) (repetition time [TR]/ echo time [TE] 2000-6000/ 50-55 ms), field of view 30-32 cm, section thickness 5-6 mm; interval 1-1.2 mm; b-value 0-500-800 sec/mm^2.

No contrast enhancement was used and the overall acquisition time varied between 20 and 30 minutes.

MR images analysis

All MR examinations were interpreted by two experienced gastrointestinal radiologists blinded to each other and to the endosonographic findings.

The following features were described:

- lesion site (distance from the anal verge);
- tumour longitudinal extent;
- maximum thickness of the lesion;
- distance between lesion and puborectalis muscle;
- levator ani muscles infiltration;
- depth of extramural spread;

- distance between lesion and mesorectal fascia;
- overcoming of the anterior peritoneal reflection;
- mesorectal, iliac and obturatory lymph node involvement;
- pelvic organs infiltration.

Local MR staging was established according to the TNM system.

Positive (N1-N2) lymph nodes were considered if greater than 5mm in diameter, with an irregular border and mixed-signal intensity.

The mesorectal fascia was demostated as a low-intensity fine structure enveloping the mesorectum.

ERUS technique and parameters

ERUS was performed by an experienced operator, using a Pro Focus BK Medical ultrasound machine with a rigid rotating probe (Type 2050) and a 6/16 MHz transducer (BK Medical, Wilmington, Massachusetts, USA) that provided a 360° radial scan of the rectal wall and surrounding structures.

All patients received an enema to clean the rectum the night before the examination.

The procedure was performed with patients in the left lateral decubitus position without sedation. A digital rectal and proctoscopic examination was performed to assess the distance from the anal verge and the longitudinal extent. The

proctoscope permitted the passage of the ultrasound probe to facilitate positioning of the probe above the lesion; this facilitated complete imaging of the lesion from its most proximal to distal extend as well the proximal mesorectum, which may harbor involved lymph nodes.

The transducer rotated inside the head of the probe to provide a 360° field of view and the advantage of 3D ERUS was that the volume could be freely rotated, rendered, tilted and sliced, providing the operator with an infinite variety of section parameters, as well as visualization of the lesion at different angles and in different planes (coronal, frontal, axial). Multiplanar reformatting was probably the most useful way to demonstate the adjacent structures in several planes.

ERUS images analysis

All ERUS examinations were performed by a single operator, who evaluated the following features:

- lesion site (distance from the anal verge);
- tumour longitudinal extent;
- distance between lesion and puborectalis muscle;
- levator ani muscles (puborectalis muscle) infiltration;
- depth of extramural spread;
- mesorectal lymph node involvement;
- pelvic organs infiltration.

On ERUS imaging, rectal tumors appear as expansions of the

first hypoechoic layer of the rectal wall, distorting and interrupting the other layers of the rectal wall from the inside out.

The sonographic criteria for identifying involved lymph nodes consist in size greater than 5mm, mixed signal intensity, irregular margins and spherical rather than ovoid or flat shape.

Standard of reference

For patients who proceeded directly to surgical resection without neoadjuvant therapy (n=11), the surgical resection specimen was used as standard of reference for determination of depth of invasion (T stage) and perirectal nodal status (N stage).

Pathological examination was done without knowledge of the results of ERUS and MRI, and the surgical specimen was staged (TNM) according to the guidelines of the American Joint Commitee on Cancer (AJCC).

Statistical analysis

The correlation between MRI and ultrasound data was calculated for each parameter using two-tailed Spearman's rank-order correlation coefficient and a *p*-value of less than 0.05 was considered statistically significant.

The interobserver agreement for MR imaging was assessed

by using the Cohen's kappa statistics. Kappa values were interpreted in the following way: absence of agreement 0, slight agreement 0.20, fair agreement 0.21-0.40, moderate agreement 0.41-0.60, substantial agreement 0.61-0.8, and almost perfect agreement 0.81-1 as proposed by Landis et al. [17]. Confidence limits were set at 95 percent.

Descriptive statistics were also used.

All calculations were done by using SPSS statistical software (SPSS Inc, Chicago, Ill, USA).

RESULTS

From May 2011 to May 2013, fifty patients (39 treated with neoadjuvant chemoradiotherapy followed by surgery and 11 with surgical resection alone) were evaluated with MRI and ERUS.

Characteristics of the patients and tumors are described in Table 2.

Thirty-two patients (64%) were men and 18 (36%) women with a mean age of 68.3±12.2 years (range, 34-87 years).

The mean distance of the tumor from the anal verge was 8.26±2.87 cm (range, 2-14 cm); ten cancers (20%) were in the lower third of the rectum, twenty-nine cancers (58%) were in the middle third of the rectum and eleven cancers (22%) were in the upper third of the rectum. Forty-two tumors (84%) were below the peritoneal reflection.

The pathological T stage of the eleven patients who underwent to surgical resection alone was: pT2 in 4 patients, pT3 in 6 patients and pT4 in 1 patient and, lymph nodes were involved by the tumor in 8 patients.

Patient acceptance of ERUS and MRI was good in all cases, and there were no complications.

Correlation between TRUS and MRI

TRUS data and MRI data of reader A, showed a statistically significant correlation for the lesion site (r_s=0.873,

$p<0.000001$), the tumour longitudinal extent ($r_s=0.378$, $p=0.010393$), the distance between lesion and puborectalis muscle ($r_s=0.7954$, $p<0.000001$) and the depth of extramural spread ($r_s=0.5107$, $p=0.000149$).

Also, TRUS data and MRI data of reader B revealed a statistically significant correlation for the lesion site ($r_s=0.8485$, $p<0.000001$), the tumour longitudinal extent ($r_s=0.3794$, $p=0.010131$), the distance between lesion and puborectalis muscle ($r_s=0.7989$, $p<0.000001$) and the depth of extramural spread ($r_s=0.5046$, $p=0.000186$).

Moreover, TRUS and MRI were able to demonstrate the levator ani muscles infiltration with an overall agreement of 82% for MRI reader A and 80% for MRI reader B, the lymph node involvement with an agreement of 68% for MRI reader A and 76% for MRI reader B and the pelvic organs infiltration with an agreement of 80% for both MRI readers.

Correlation between TRUS and MRI are scheduled on Table 3.

MRI interobserver agreement

The interobserver agreement between MRI readers A and B was almost perfect for the lesion site (k=0,91; 95% CI: 0,882-0,937) and the distance between lesion and puborectalis muscle (k= 0,914; 95% CI: 0,878-0,950), there was a substantial agreement for the tumour longitudinal

extent (k= 0,791; 95% CI: 0,700-0,882), the depth of extramural spread (k= 0,758; 95% CI: 0,672-0,844) and the maximum thickness of the lesion (k= 0,734; 95% CI: 0,625-0,844), instead there was only a moderate agreement for the distance between lesion and mesorectal fascia (k= 0,48; 95% CI: 0,312-0,649).

There was also an agreement between the two observers of 100% for the pelvic organs involvement, of 96% for the overcoming of the anterior peritoneal reflection, of 88% for the mesorectal lymph nodes involvement and of 82% for the levator ani muscles infiltration.

Distance between tumor and mesorectal fascia

The relationship between tumor and mesorectal fascia is an important risk factor for local recurrence, but its involvement can correctly visualized only on MRI.

In our study the mesorectal fascia was visualized on MRI in all patients.

For MRI observer A the mean distance between lesion and mesorectal fascia was 0.74 cm (range, 0-2.2 cm), and for observer B it was 0.59 cm (range, 0-1.8 cm).

The distance between lesion and mesorectal fascia was <5 mm in seventeen patients (34%) for MRI reader A and in twenty-two patients (44%) for MRI reader B with a moderate interobserver agreement.

Agreement between MRI/ERUS and histologic examination

Eleven patients underwent to surgical resection alone and the agreement between MRI and histologic examination (HE) was 45.5% for T stage and 63.6% for N stage, instead the agreement between ERUS and histologic examination was 27.3% for T stage and 63.6% for N stage.

T stage was overestimated in 7 cases (63.6%) with TRUS and in 6 cases (54.5%) with MRI, and it was underestimed in 1 cases (9.1%) with TRUS and in any case with MRI (Tab. 4,5).

N stage was overestimated in 3 cases (27.3%) with TRUS and MRI, and it was underestimed in 1 cases (9.1%) with TRUS and MRI.

Overstaging and understaging of MRI and ERUS in term of predicting T and N stage are summarized in Table 6.

DISCUSSION

The correct staging of rectal cancer is of high relevance since the treatment options depend on the stage at presentation. The common practice (on the basis of oncologic guidelines) is to administer neoadjuvant therapy followed by surgery to patients with T3 and T4 tumors or any tumor with positive locoregional lymph nodes, instead patients with T2 tumors are treated with surgical resection (TME) and T1 tumors may be correctly resected either by endoscopic techniques (mucosectomy) or minimally invasive surgical procedures (transanal endoscopic microsurgery).

Although rectal tumors can be diagnosed using digital examination, barium enema, and colonoscopy/ sigmoidoscopy, these endoluminal techniques do not provide sufficient information about the extraluminal spread of the tumor for preoperative planning. Therefore CT, ERUS and MRI are the imaging modalities predominantly utilized in the preoperative staging of rectal cancer.

CT is unable to differentiate the different layers of the rectal wall and has lower overall predictive accuracy than ERUS and MRI in locoregional staging, however it is used to search for distant metastasis (e.g. lung, liver).

Bipat et al. [5] published an extensive meta-analysis in 2004 comparing ERUS, CT and MRI, including a variety of MR techniques and coils, they found that ERUS was the best

technique for assessing local invasion, with a sensitivity and specificity of detecting muscularis propria invasion of 94% and 69% for MRI and, 94% and 86% for ERUS and a sensitivity and specificity of detecting perirectal tissue invasion of 82% and 76% for MRI and, 90% and 75% for ERUS.

Later, in 2013, Beaumont et al. [18] compiled the results of several large studies (n=40 or greater) suggested that ERUS was significantly more sensitive than MRI for the assessment of T1 and T2 tumors, with no significant difference between the two modalities in the staging of T3 and T4 tumors.

In fact it has been demonstrated that the most staging failures with MRI occur in the differentiation between T1 and T2 lesions and between T2 and “T3 early” lesions. A T1 tumor cannot be reliably distinguished from T2 because the submucosal layer is generally not visualized on phased-array MRI and the difficulty in determining T2 from “T3 early” lesions is often caused by the presence of desmoplastic reaction within the peritumoral tissues that made difficult the MR differentiation between perirectal fat spiculation, caused by fibrosis alone from those containing tumour cells. ERUS has the same difficulty in distinguishing T2 from “T3 early”, and this often involves an overstaging [14].

In our study, considering only the eleven patients who underwent surgery without CRT, T stage was overestimated

in 7 cases (63.6%) with ERUS and in 6 cases (54.5%) with MRI, in particularly ERUS has not been able to distinguish T2 from T3 in 3 cases (42.9%) and MRI in 2 cases (33.3%).

Distinguish between T2 from T3 tumors at the immediate interface between the muscle coat and the extramural fat is of little importance in preoperative clinical decision making because the outcome of patients with “early T3” tumors is good with surgery alone [11], instead is important evaluate the depth of extramural spread in tumors that are clearly T3, whether or not the tumour threatens the mesorectal fascia, and whether the tumour has any other markers of aggressiveness, such as nodal metastases, vascular invasion or local peritoneal involvement, because they are important in determining prognosis and stratifying patients for preoperative therapy [19].

In fact, tumors with 5 mm or less of extramural spread regardless of lymph node status have an 85% 5 year cancer-specific survival rate compared with poorer prognosis of tumors with more than 5 mm spread, which have only a 54% 5 year cancer-specific survival rate [20].

Unfortunately our study did not demonstrate an high accuracy of preoperative MRI or ERUS in the prediction of correct T stage, since the agreement with histopathology was about 45.5% for MRI and only 27.3 for ERUS and it did not correlate with the data reported in the most of the studies

published in literature (65%-100%) [21].

The single most important element in the realization of local control is a free circumferential resection margin (CRM) and Quirke et al. [15] already in 1986 demonstrated that microscopically inadequate radial margins lead to a recurrence rate of 86% and many subsequent studies have confirmed the importance of a free CRM.

It has been suggested that circumferential resection margin status is even more informative in treatment planning than T stage, so the currently TNM classification, based on depth of bowel infiltration, does not distinguish between primary resectable tumors and locally advanced tumors infact a T3 tumor can be either primary resectable with a wide tumor-free CRM or locally advanced with a close or involved CRM [22].

For the prediction of the CRM, the radiologists assessed the MRI scans for the shortest distance from the outermost part of the tumour to the adjacent mesorectal fascia [14], so positive margins can be due to main tumor extension, tumor deposits, extramural vascular invasion, or suspicious lymph nodes. [23].

Beets-Tan et al. [14] in a study of preoperative MRI in 76 patients, concluded that a tumour-free zone of 1 mm by histology could be predicted with a high degree of certainty when the measured distance on MRI was at least 5 mm, and a

histological margin of at least 2 mm when the MRI distance was at least 6 mm.

Histology of resection specimens has shown that the frequency of local recurrence greatly decreas when a tumor-free CRM of more than 1 mm can be obtained.

With ERUS it is very difficult to identify the mesorectal fascia in patients with a “threatened CRM,” except when it shows invasion of vagina, prostate, or seminal vesicles. Many single-center studies have shown that MRI is highly accurate for the prediction of an involved CRM [14].

Lymph nodes assessment remains an unresolved problem in the preoperative staging of rectal cancer for both ERUS and MRI.

In the meta-analysis of Bipat et al. [5], the sensitivity and specificity of detecting lymph node involvement was 66% and 76% for MRI and, 67% and 78% for ERUS.

Although short axis diameter greater than 5 mm was the criterion most commonly used to predict lymph node metastases on MRI, our review found little evidence to support this particular cut-off and Brown et al. [9] suggested that the use of border contour and signal intensity characteristics, in addition to size criteria, can improve the accuracy of nodal staging.

Our study, considering only the 11 patients who underwent surgery without CRT, addresses an overall agreement for lymph nodes involvement of 63.6% for ERUS and MRI.

Due to its wide field of view, MRI can also predict the peritoneal involvement, that represents an independent risk factor for intraperitoneal recurrence after surgery.

Moreover, the identification of the peritoneal attachment and its involvement is important because tumors with peritoneal reflection invasion (T4a) are treated as colon cancers and these tumors should be reported at MR imaging as circumferential resection margin (CRM) negative because CRM corresponds to the cut of surgical resection margin and does not cover the anterior aspect of the upper rectum [23,24].

In our study, ERUS and MRI have a statistically significant correlation for the assessment of lesion site, tumour longitudinal extent, distance between lesion and puborectalis muscle, depth of extramural spread, and an overall good agreement for the levator ani muscles infiltration, the mesorectal lymph nodes involvement and the pelvic organs infiltration.

MRI also allowed to evaluate the maximum thickness of the lesion, the distance between lesion and mesorectal fascia, the overcoming of the anterior peritoneal reflection and the iliac and obturatory lymph nodes involvement.

Although, ERUS can distinguish tumor T1 stage from T2 because it shows all the different layers of the rectal wall, it is operator dependent and requires a learning curve for correct staging of rectal cancer.

Moreover, the accuracy of ERUS in the staging of rectal cancer has been highly variable, with values ranging anywhere from 69%-89% and the study of Harewood et al. [25] on the potential biases have showed an inverse relationship between study size and reported ERUS accuracy, as well as higher reported accuracy values in older studies and this study also noted that most published studies utilized very experienced operators, so actual accuracy of ERUS is probably much lower in common practice than in publication.

ERUS can not assess stenotic tumors or lesions located in the upper rectum and it can not visualize mesorectal fascia and tumor extension into surrounding organs because of the limited field of view.

Endorectal MRI has the same limitations of ERUS and it has been almost completely replaced by phased-array coils that have made better spatial resolution with improved signal-to-noise ratio, without the limitations of endorectal MRI and they have the advantage of having a larger field of view of the mesorectal fascia [26].

Downsides of MRI remain the limited availability, the high cost, the need to obtain good standard high-resolution

sequences and the interpretation of the images that depends on the knowledge and expertise of the radiologist [27].

With routinary use of MRI, approximately 40-50% of patients can be treated successfully with primary surgery without significant risk of local recurrence or systemic failure. For the remaining patients, the use of preoperative-CRT is aimed at reducing the size of the primary tumour and making irresectable tumour resectable with tumour free circumferential margins to reduce the risk of recurrence [24].

CONCLUSIONS

With the development of the technique (faster acquisitions, dedicated external coils, contrast agents, etc.), MRI has achieved almost the same accuracy as ERUS for local staging of rectal cancer.

In this study comparing those two modalities we can state that phased-array MRI is slightly superior in determining the depth of transmural tumor invasion (T stage) and it has the same value in detecting lymph node metastasis (N stage) as compared to ERUS.

MRI has also an additional value in the preoperative evaluation of other markers of tumour aggression such as iliac and obturatory nodal involvement, overcoming of the peritoneal reflection, and especially the involvement of the mesorectal fascia, which represents the CRM.

In conclusion, there was a very good intermodality agreement between TRUS and MRI and because the extramural spread is the most important prognostic indicator with regard to T stage, we suggest the routinary use of MRI for the staging of rectal cancer with the use of ERUS only in preoperative staging of patients with early tumors (T1-T2) who can be avoided from unnecessary TME.

Table 1: TNM staging of rectal cancer.

	T staging
T1	Tumor invades mucosa and submucosa
T2	Tumor invades but does not penetrate muscularis propria
T3	Tumor invades subserosa through muscularis propria T3a: tumor extends <1 mm beyond muscularis propria T3b: tumor extends ≥1-5 mm beyond muscularis propria T3c: tumor extends >5-15 mm beyond muscularis propria T3d: tumor extends ≥15 mm beyond muscularis propria
T4	Tumor invades peritoneal reflection (T4a) or other organs (T4b)
	N staging
N0	No metastatic lymph nodes
N1	Metastasis in 1-3 perirectal nodes
N2	Metastasis in 4 or more perirectal nodes
	M staging
M0	No distant metastasis
M1	Distant metastasis

Table 2: Characteristics of the patients and tumors.

Variable	**N**
Age	68.3±12.2 years (range, 34-87)
Gender • male • female	 • 32 (64%) • 18 (36%)
Distance from anal verge	8.26±2.87 cm (range, 2-14)
Location • upper third of the rectum • middle third of the rectum • lower third of the rectum	 • 11 (22%) • 29 (58%) • 10 (20%)
Location in relation to peritoneal reflection • below • above	 • 42 (84%) • 8 (16%)

Table 3: Correlation between TRUS and MRI.

	TRUS–MRI reader A	TRUS–MRI reader B
Lesion site	r_s=0.873 p<0.000001	r_s=0.8485 p<0.000001
Tumour longitudinal extent	r_s=0.378 p=0.010393	r_s=0.3794 p=0.010131
Distance lesion-puborectalis muscle	r_s=0.7954 p<0.000001	r_s=0.7989 p<0.000001
Depth of extramural spread	r_s=0.5107 p=0.000149	r_s=0.5046 p=0.000186
Levator ani muscles infiltration	82%	80%
Lymph node involvement	68%	76%
Pelvic organs infiltration	80%	80%

Table 4: Accuracy of ERUS examination to predict the correct T stage.

	T1	T2	T3	T4	Tot	HE
T1	0	0	0	0	0	
T2	0	0	0	0	0	
T3	0	3	3	1	7	
T4	0	1	3	0	4	
Tot	0	4	6	1	11	
ERUS						

Table 5: Accuracy of MRI examination to predict the correct T stage.

	T1	T2	T3	T4	Tot	HE
T1	0	0	0	0	0	
T2	0	0	0	0	0	
T3	0	2	4	0	6	
T4	0	2	2	1	5	
Tot	0	4	6	1	11	
MRI						

Table 6: Comparison of overstaged and understaged cases by MRI and ERUS.

	T stage		N stage	
	Overstaged	Understaged	Overstaged	Understaged
ERUS	7 (63.6%)	1 (9.1%)	3 (27.3%)	1 (9.1%)
MRI	6 (54.5%)	0	3 (27.3%)	1 (9.1%)

Fig.1: 3D ERUS image of the rectal wall layers.

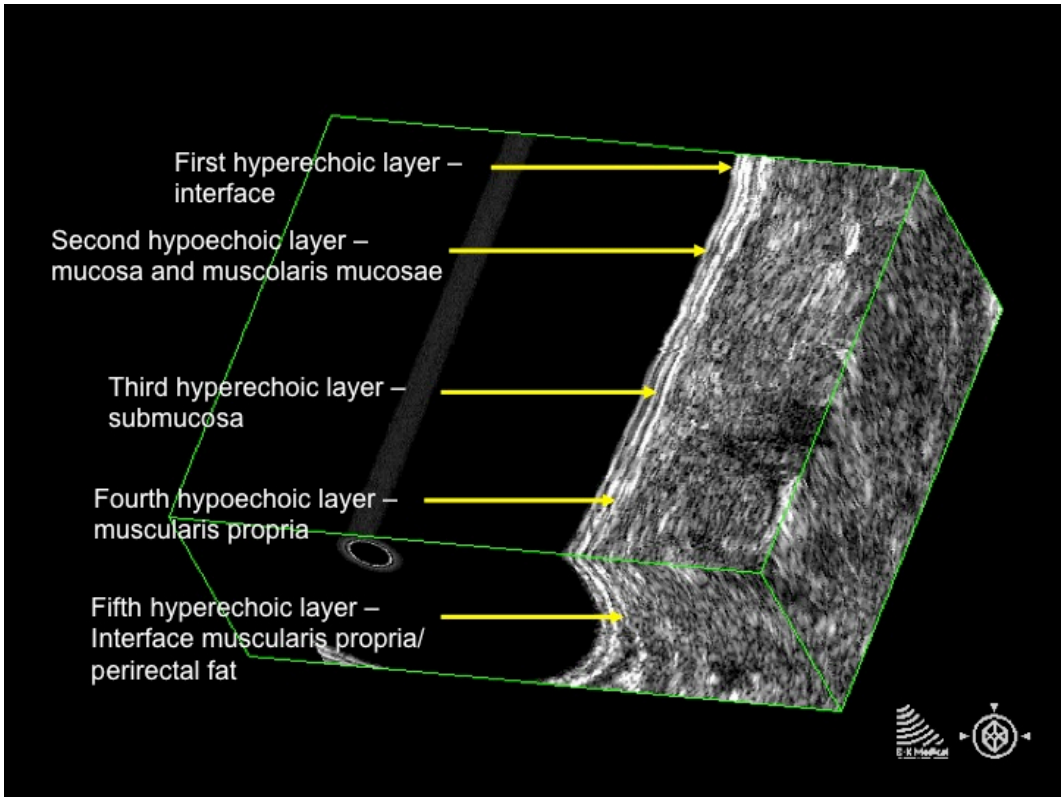
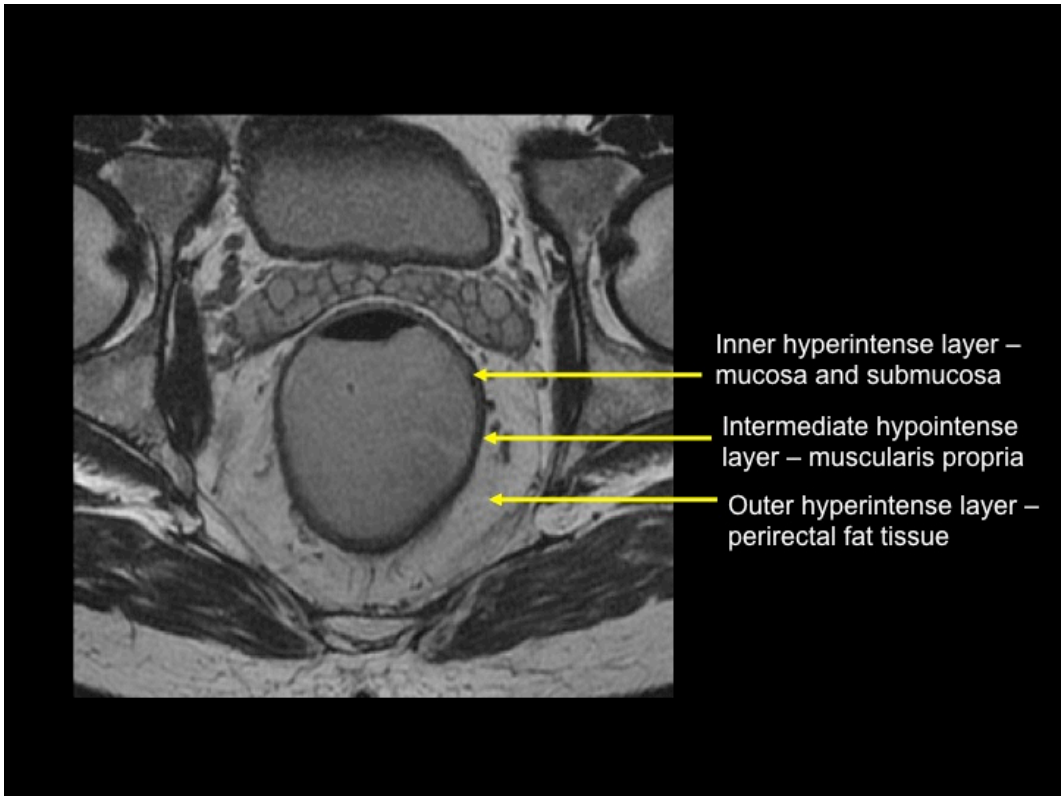


Fig.2: MR image of the rectal wall layers.



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