A prospective comparison of endorectal ultrasound and pelvic Magnetic Resonance in the preoperative staging of rectal cancer

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Paolo Bianchi, Chiara Ceriani, Angela Palmisano, Giovanni Pompili*, Giovanni Rubis Passoni**, Matteo Rottoli, Andrea Cappellani***, Marco Montorsi

*Cattedra e Unità Operativa di Chirurgia Generale, Università degli Studi di Milano, Istituto Clinico Humanitas.IRCCS, Rozzano (Milano) Italy; *Divisione di Radiologia, Università di Milano, Ospedale "San Paolo", Milano, Italy; **Unità Operativa di Endoscopia Digestiva, Ospedale "San Paolo", Milano, Italy; ***Cattedra di Chirurgia Generale, Università di Catania, Italy.*

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BACKGROUND: *The developement of new surgical modalities (local excision, coloanal-anastomosis) and the diffusion of preoperative neoadjuvant therapy, has increased the importance of an accurate preoperative staging in patients with rectal cancer. The aim of this study was to compare the accuracy of endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI) in the local preoperative staging of rectal carcinoma; moreover the two methods were assessed with a concordance K test.*
METHODS: *Twenty-nine patients with rectal carcinoma were staged with EUS and body coil MRI and then underwent radical surgery. The preoperative staging was compared with the histologic findings of the operative specimen.*
RESULTS: *EUS was more accurate (79.3%), with better sensibility (90%), positive predictive value (PPV) (85.7%) and negative predictive value (NPV) (25%) than MRI in the evaluation of T parameter. MRI was more accurate (72.4%), with better specificity (81.2%), PPV (72.7%) and NPV (68.4%) than EUS in the evaluation of N parameter. The concordance test obtained a K value of 19.8% for the T parameter and 34.2% for the N parameter.*
CONCLUSIONS: *EUS and MRI are complementary methods in the preoperative staging of rectal cancer. EUS is more accurate in determing bowel wall penetration of the tumor, while MRI is more accurate in the evaluation of lymphnode involvement. The low value of the K index confirms the complimentarity of the two examinations. Further studies with new imaging techniques such as endocoil MRI, external phase-arrayed coil MRI and threedimensional ultrasound are needed to identify the most effective single examination in the preoperative staging of rectal cancer.*

KEY WORDS: Endorectal ultrasound, Magnetic Resonance, Rectal cancer, Preoperative staging.

Introduction

In recent years there has been an increase in the use of sphincter-saving procedures for the treatment of low rectal neoplasms such as low anterior resection with coloanal- anastomosis and local excision; moreover preoperative neoadiuvant chemo-radio therapy has gained increased attention in selected patients [1-3]. Therefore an accurate preoperative staging of rectal tumors has become even more important for planning the treatment and for achieving a good outcome in patients with rectal tumors [4]. Three main modalities are currently used for the preoperative staging of rectal cancer: computed tomography (CT), endorectal ultrasonography (EUS) and magnetic resonance imaging (MRI). CT was the first modality to be used and proved useful in demonstrating advanced disease and distant metastases, but less useful in determing the degree of tumor extension through the bowel wall, a microscopic perirectal fat involvement (T parameter) and lymph node metastases (N parameter [5-7]. EUS can better assess the extent of tumor invasion and measure the longitudinal and circumferential extention of the tumor. Moreover EUS can visualize the perirectal lymphnodes and a fine needle biopsy can be performed; on the other hand, neither liver metastases nor distant nodal involvement can be assessed. MRI is a relative new imaging technique which, through an high soft tissues contrast, can assess wall penetration, perirectal nodal involvement and distant metastases. The uti-

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For correspondence: Paolo Pietro Bianchi,MD, Università di Milano, Istituto Clinico "Humanitas IRCCS", Via Manzoni 56, 20089 Rozano(Milano), Italy.

lity of EUS and MRI for staging rectal cancers has been demonstrated in many studies [8-12], but few prospective studies comparing EUS and MRI are available [13-15]. The purpose of the present study was to compare the accuracy of EUS and MRI in the preoperative local staging of rectal carcinoma in patients candidates for radical surgery. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated on the basis of the final histologic findings of the operative specimen. Moreover the statistical significance of a concordance K test between the two methods was calculated with the aim to evaluate the diagnostic concordance of the two methods.

Patients and Methods

Patients

Patients with histologically proven rectal carcinoma by endoscopic biopsy were included in the study. Rectal carcinoma was defined as a tumor located at any level from the anal verge to the rectosigmoid junction. Exclusion criteria were: patients submitted to emergency surgery, those without an adequate preoperative staging for any reasons, such as incomplete EUS or MRI examination, and those with unresectable neoplasms. All EUS and MRI examinations were independently performed by a single experienced operator, EUS by a good expereienced endoscopist and MRI by a radiologist dedicated to MRI. Surgical operations included low anterior resection or abdominoperineal resection with total mesorectal excision (TME). The surgical technique included an high vascular ligation of the inferior mesenteric vessels, radical lymphoadenectomy and total mesorectal excision [16]. When an abdominoperineal resection was performed, the perineal cavity was closed as first intention with a drainage tube left in the perineal space for the first postoperative days. Pathologic examination of the specimen was obtained according to the TNM classification of malignant tumors [17].

Methods

EUS examination was routinely performed with a standard multidisciplinar flexible ultrasound scanner with a flexible convex probe and a 7.5 MHz transducer (Pentax FG36UX, Pentax Precision Instruments, New York, USA or Olympus GF-UM20, Tokyo, Japan). The operator was an endoscopist experienced with flexible instrument. Each patient received a cleaning enema two hours before the examination. The patients were examined in the left lateral decubitus position. A latex balloon attached to the tip of the transducer was filled with degassed water to prevent interfaces between endoluminal stool or mucus and imaging. After the introduction of the instrument, the exam was performed with a probe withdrawn technique. T stage was assessed following the common criteria of division in layer of the wall of the rectum. The sonographic criteria for N stage were: size (>1 cm), hypoechoic echodensity, sharply demarcated borders and round (rather than ovoid or flat) shape. MR imaging of the pelvis was performed with a 1.0 T unit (Philips Gyroscan, General Electric Medical Systems. Milwaukee, USA) using a body coil. The operator was a single radiologist. In order to localize the tumor a sagittal T2 turbo spin echo scan was at first performed. T2 turbo spin echo scans, even with fat suppression, and T1 spin echo scans paratrasversal to the tumor were then performed. After the injection of paramagnetic contrast, the examination was completed with sagittal and paratrasversal T1 scans. The use of coronal scans was limited to the study of the ischio-rectal fossa and perianal lesions. T1 scans, especially after paramagnetic contrast, were useful in evaluation of perirectal fat tissue, lymphnodes and outer contour of the rectum. T2 scans were more useful in the evaluation of anatomic layers of the rectal wall and in the study of involvement of other pelvic structures. Statistical analysis was performed with evaluation of Kendall coefficient of concordance (K value), usually used for expressing inter-rater agreement among independent judges who are rating the same stimuli. In our study this method was applied to evaluate the concordance among the two diagnostic methods.

Results

Twenty-nine consecutive patients (22 males, 7 females) with a mean age of 58.5 years (range 27-84) with rectal adenocarcinoma were included in the study. The distribution of rectal cancer was: 12 (41.4%) in the upper third, 10 patients (34.4%) in the middle third and 7 (24.2%) in the lower third. All the patients were operated on: 25 (86.2%) had a low anterior resection, while 4 (13.8%) had an abdominoperineal resection. Five patients (17.2%) were submitted to a neoadjuvant chemoradiotherapy before surgery. The mean time elapsed between preoperative staging and surgery was 7.5 days in patients without neoadjuvant therapy. Histopathological results, according to TNM classification, are listed in Tab. I.

Table I – *Histopathological staging and grading of rectal tumors*

Stage	Patients (%)
T1N0	4 (13.8)
G1	2 (6.9)
T2N0	4 (13.8)
G2	23 (79.4)
T3N0	8 (27.6)
G3	4 (13.7)
T3N1	10 (34.5)
T2N2	1 (3.4)
T3N2	2 (6.9)

The total number of lymphnodes examined was 514 (range 4/53 - average 17.7) and the positive lymphnodes were 46 (8.9%). The overall accuracy rate in determination of wall invasion (T parameter) obtained by EUS was 79.3% (23 patients). Tables II and III show the comparative results of EUS and MRI in assessing T parameter. For statistical reasons T1 and T2 stages were grouped together. EUS understaged 2 patients (6.9 %) from T3 stage to T1-2 stage and overstaged 4 patients (13.8%) from T1-2 stage to T3 stage (Tab. II). Sensitivity was 90.0%, specificity 60.0%, PPV 85.7%, NPV 25.0% (Tab. III). MRI yelded an overall accuracy of 51.7% (15 patients); 5 patients (17.3%) were overstaged from T1-2 stage to T3 stage and 9 patients (31.0%) were understaged from T3 stage to T1-2 stage (Tab. II). Sensitivity of MRI was 38.5%, specificity 66.6%, PPV 44.4%, NPV 50.0% (Tab. III).

TABLE II. *Comparative results of EUS and MRI (T parameter)*

	EUS		MRI	
	N°	Percent	N°	Percent
Overstaging	4/29	13.8%	5/29	17.3%
Understaging	2/29	6.9%	9/29	31.0%

EUS = Endoscopic Ultrasound;
MRI = Magnetic Resonance Imaging.

TABLE III – *Comparative results of EUS and MRI in assessing T parameter*

	EUS %	MRI %
Sensitivity	90.0	38.5
Specificity	60.0	66.6
PPV	85.7	44.4
NPV	25.0	50.0
Accuracy	79.3	51,7

EUS = endoscopic ultrasound;
MRI = magnetic resonance imaging;
PPV= positive predictive value;
NPV= negative predictive value.

Tables IV and V showed the results in assessing N parameter. Four patients (13.8 %) were overstaged from N0 stage to N1-2 stage and 8 patients (27.6 %) were understaged from N1-2 stage to N0 stage [Tab. 4]. EUS sensitivity was 75.0 %, specificity 35.7 %, PPV 55.5 %, NPV 57.1 % [Tab. 5] with an overall accuracy of 58.6 % (17 patients). MRI obtained an overall accuracy of 72.4 % (21 patients). Three patients (10.4 %) were overstaged and 5 patients (17.2 %) were understaged (Tab. IV). Sensitivity of MRI was 57.1 %, specificity 81.2 %, PPV 72.7 %, NPV 68.4 % (Tab. V).

TABLE IV – *Comparative results of EUS and MRI (N parameter)*

	EUS		MRI	
	N°	Percent	N°	Percent
Overstaging	4/29	13.8%	3/29	10.4%
Understaging	2/29	27.6%	5/29	17.2%

EUS = endoscopic ultrasound;
MRI = magnetic resonance imaging.

TABLE V – *Comparative results of EUS and MRI in assessing N parameter*

	EUS %	MRI %
Sensitivity	75.0	57.1
Specificity	35.7	81.2
PPV	55.5	72.7
NPV	57.1	68.4
Accuracy	58.6	72.4

EUS = endoscopic ultrasound;
MRI = magnetic risonance imaging;
PPV= positive predicive value;
NPV= negative predicitive value.

The concordance test between the two methods revealed an overall concordance for T stage of 62 % and for N stage of 72.4 %. The expected case accord was 55.4 % for the T stage and 67.2 % for the N stage. Therefore the K value or according index was 14.7 % for T stage and 15.8 % for N stage (Tab.VI).

TABLE VI – *Statistical concordance test among EUS and MRI*

	T parameter %	N parameter %
Overall Concordance	58.6	72.4
Expected case Accord	50.5	54.4
K value	19.8	34.2

EUS = endoscopic ultrasound;
MRI = magnetic resonance imaging.

Discussion

An accurate preoperative staging is crucial in order to select the best strategy in patients with rectal cancer. Multimodality treatment and new surgical options have gained increased attention for these patients. Conservative surgery of the sphincter function has progressively replaced the abdominoperineal resection in patients with mid and low rectal cancer [18]. Moreover an early, small rectal cancer confined to mucosa or submucosa can be excised locally by conventional or with transanal endoscopic

microsurgery techniques (T.E.M.). Neoadjuvant preoperative chemoradiotherapy can now be recommended for advanced rectal cancer in order to downstage the lesion [20-21]. Therefore an accurate evaluation of the depth of rectal wall invasion and pararectal lymph node involvement became crucial in the choice of treatment [19]. EUS and MRI are the more accurate methods in assessing wall penetration, with an overall higher accuracy than computed tompography (CT) [5]. CT is not able to accurately determine the depth of tumor invasion within the bowel wall and its value in assessing early tumor is limited. While the benefits of EUS over CT has been demonstrated in many studies [22-24], few prospective data are available comparing EUS and MRI directly [12-14]. In our study, the overall accuracy of EUS (79.3%) was superior to MRI (51.7%). The main problem of EUS in assessing T parameter was the overstaging (13.8% of cases), this may be related to different causes: the perineoplastic inflammatory cell aggregation, a prior endoscopic biopsy that can induce necrotic and hemorragic microfoci within the rectal wall, the preoperative radiotherapy that can modifies echogenicity of the parietal layers of the rectum and a common trend of the operator, also if well experienced, to overstage the neoplasm more than to understage it [25-28]. Moreover it must be remembered that two of the four patient overstaged from a T1-2 to a T3 stage by EUS in our study were submitted to preoperative chemoradiotherapy. The main reason of the low accuracy of MRI in assessing T parameter was the understaging of the tumor (9 out of 29 patients from T3 to T1-2 stage). This is not always found in the literature and may be related to the limited experience of the operator with this particular examination. The understaging effect of EUS (6.9%) is less frequent; it can be related to the same causes of the overstaging and, for the obstructive neoplasms, to the difficulties of the normal linear or convex probe to perform an accurate study of the wall. Herzog et al. [29] and Jochem et al. [30] described the technical difficulties in the examination of the inferior third of the rectum, with a 16% diagnostic error. The recent availability of new tridimensional probes, microprobes and anterior ultrasonic probes is expected to reduce this problem [30]. MRI is more accurate, such as CT, in advanced stages. In early stages the trend of MRI is to overstage the neoplasm, particulary in tumor surrounded by fibrotic (desmoplastic) tissue and by an high inflammatory cell aggregation. The difference, in this study, can be related to the initial experience of the operator, with a trend to understage the lesions. EUS showed an higher sensitivity (90%) and a better PPV (85.7%) then MRI; on the contrary MRI showed a better NPV (50%), while specificity is similar: 60% for EUS and 66.6% for MRI. The present study confirms that EUS is better than MRI in assessing wall penetration, as already stated by other authors [13 - 15]. This is not unexpected because MRI using body coils suffers the same limitations as CT in determining the correct extent of tumor infiltration within the rectal wall. However, newer MRI techniques using an endorectal coil or with a phase-arrayed body coil appears to be able to overcome these limitations [31-32], even if MRI with endocoil still has some problems; these are related to the site of the tumor and to the dimension of the coil. Lesions close to the anal verge cannot be studied with endocoil because of the difficulty to introduce the coil.

Because of the lacking of good diagnostic imaging criteria [15–25-26] to differentiate inflammatory from neoplastic lymphnodes, Heriot et al.[4] argued that nodal involvement cannot be accurately assessed by any modality. Our criteria of lymphnodes involvement were: size superior to 10 mm and irregular borders. In the evaluation of lymphnodes involvement MRI showed an overall accuracy (72.4%) higher than EUS (58.6%). The overstaging rates are similar, but EUS has an higher percentage of understaged cases (27.6%) than MRI (17.2%). EUS yelded an higher sensitivity (75.0%), but specificity (81.2%), PPV (72.7%) and NPV (68.4%) were better with MRI. Due to this conflicting difference in values, a specific test, that aims to investigate the concordance among different examinations, was applied. The concordance test between EUS and MRI showed that, once eliminated the expected casuality accord, the according index (K value) was only 14.7 (Tab. VI). The low value of the test is important in the overall evaluation of these two methods, which proves to be more complementary than supplemental.

Conclusions

EUS and MRI are both relevant procedures in the preoperative staging of rectal cancer. EUS has an high accuracy in the evaluation of T parameter. Neoadjuvant therapy impairs staging accuracy resulting in high percentage of overstaging for T parameter. To this regard, MRI appears to be less affected by radiotherapy [32].

The crucial problem of staging lymphnodal involvement is still open, while MRI seems to be superior to EUS. The present study demonstrates the complementarity of the two procedures: EUS is more accurate, with better sensitivity, PPV and NPV than MRI in T parameter evaluation. MRI is more accurate, with better specificity, PPV and NPV than EUS in N parameter evaluation. Because of the small group of patients the statistical concordance test, that reveals a very low K index value, has an unclear significance. Probably the best statitistical results can be obtained comparing the imaging examinations of a larger group of patients with the gold standard of histology. This is the purpose of our incoming study, including external MRI phase-arrayed body coil and endo coil. At present the two methods analyzed in this study should be used together to correctly stage a rectal tumor. Some technological progresses (MRI with

endo-coil; three dimensional ultrasonographic probes) can modify these results in the near future.
The study confirm the well-known better accuracy of EUS in T parameter assessement and otherwise better accuracy of MRI in N staging. The complentarity of the 2 methods is confirmed by the low value of k test. Our results confirm that, at the moment, we do not have a single preop. stage exam to purpose. Morover a high number of patients have been excluded by the study because technical and organizative problem, stressing how can be difficult is to perform both examination.

Riassunto

RAZIONALE: Lo sviluppo di nuovi trattamenti chirurgici (escissione locale, coloano-anastomosi) e la diffusione della terapia neoadiuvante, ha reso ancora più determinante l'accuratezza della stadiazione preoperatoria dei tumori del retto. Scopo di questo studio è confrontare l'accuratezza dell'ecografia endoscopica (EUS) e della risonanza magnetica nucleare (MRI) nella stadiazione locale preoperatoria del carcinoma rettale; inoltre le due metodiche sono state confrontate con un test di concordanza del k.
METODI: Ventinove pazienti con tumore rettale sono stati stadiati con EUS e MRI con bobina body coil e quindi trattati con chirurgia radicale. La stadiazione preoperatoria è stata confrontata con l'esame istologico dei pezzi operatori.
RISULTATI: L' EUS è risultata più accurata (79.3%), con migliore sensibilità (90%), valore predittivo positivo (PPV) (85.7%) e valore predittivo negativo (NPV) (25%) della MRI nella valutazione del parametro T. La MRI è risultata più accurata (72.4%), con migliore sensibilità (81.2%), PPV (72.7%) e NPV (68.4%) dell'EUS nella valutazione del parametro N. Il test di concordanza ha rivelato un valore di k del 19.8% per il parametro T e del 34.2% per il parametro N.
CONCLUSIONI: EUS e MRI sono metodiche complementari nella stadiazione preoperatoria del cancro del retto. EUS è più accurata nella valutazione della penetrazione parietale del tumore, mentre la MRI è più accurata nella valutazione dell'interessamento linfonodale. Il basso valore del test di concordanza (k test) conferma la complementarità delle due metodiche. Ulteriori studi con l'impiego delle nuove tecniche di imaging quali la MRI con bobina endocoil, o bobina esterna phase d'array e l'ecografia endorettale tridimensionale, sono necessari per poter identificare il singolo esame più efficace nella stadiazione preoperatoria del cancro rettale.

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