MRI and correlation between TNM and CEA, CA19.9, AFP in rectal cancer

Experience of a single academic surgical center

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MRI and correlation between TNM and CEA, CA19.9, AFP in rectal cancer. Experience of a single Academic Surgical Center.

In our study we examined 75 patients treated for rectal cancer in the period between 01/01/2011 and 31/12/2014. Out of these 75 patients, we considered those 36 staged through MRI. We then compared the TNM stage obtained through MRI with the one emerged from histological examination. The correlation between the two TNM stages was assessed considering all patients staged through MRI and dividing the cases according to the submission or not to a neoadjuvant treatment. Finally, we analyzed serum levels of tumor markers CEA, CA 19.9 and AFP, relating them with the final disease stage.
Data analysis showed a statistically significant correlation in the T stages, especially in the population not subjected to neoadjuvant treatment. Instead, for N, we found no statistically significant correlation. Similarly, none of the tumor markers presented a statistically significant correlation with disease stage. However, according to the positivity of tumor markers, we associated the following score: 0, (no positive marker)1 (only one marker positive) 2 (two markers positive) 3 (three markers positive). In presence of three markers positive, meaning the highest score, we found a statistically significant correlation with N + staging of the disease, obtained by postoperative pathologic examination.
The conclusion is that MRI is certainly effective in T stage evaluation. Probably, for limph node involvement evaluation, more reliable parameters for establishing possible lymph node malignancy need to be found.
The role of the tumor markers CEA, CA 19.9, AFP during preoperative evaluation of rectal tumors remains undefined.

KEY WORDS: MRI, Rectal cancer, Tumor markes, Tumor regression, T stage

Introduction

In Europe colorectal cancer is the third malignancy for incidence in men, behind prostate and lung tumors, and the second for mortality, preceded by lung cancer. In female sex this cancer is the second either for incidence and mortality, preceded in both cases by breast cancer [1].
Of all colorectal cancers, 28% originate in rectum, with a greater incidence in men than in women (31% vs. 24%) [2]. This change in incidence appears to be mainly due to some differences in lifestyle and diet between the two sexes, such as lower consumption of alcohol and tendency of women to eat less fatty food. In women there are also few evidences of a protective role by hormonal balance.
While colon cancer is usually diagnosed at an average age of 69 years in men and 73 in women, rectal cancer is usually diagnosed at younger age such as 63 years in men and 65 in women [2]. It has been registered an increasing incidence of colorectal cancer in the population aged

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under fifty and a decrease in over fifty, although advanced age is itself a risk factor for the development of this disease. This could be due to the effects of screening programs, in fact individuals under fifty with no risk factors are not included in screening programs for colorectal cancer and this could lead to diagnostic delays [4]. Other factors such as spread of obesity, low physical activity and Western diet, seem to be also involved in this turnaround [4,5]. In addition, some recent studies have shown that smokers have a greater risk of developing rectal cancer, while smoking seems not to increase the risk for colon cancer [6,7].

In Italy there is a different distribution between north and south, probably due to regional differences in diet and lifestyle, such as higher consumption of foods rich in fiber and low in fat in the south of the country. These differences are likely to decline because of increasing dietary approval [8].

From the surgical point of view, rectal cancer is staged according to the TNM system.

The TNM staging has been firstly proposed in 1988; nowadays the one published by AJCC (American Joint Commision on Cancer) in 2010 is the most widely used version [9,10].

The TNM system is used for both clinical staging of cancer (cTNM), through the use of diagnostic tests, and pathological staging (pTNM). Concerning nodal pathological staging, removal of at least fifteen-twelve lymph nodes is necessary [10].

TNM staging of AJCC does not take into account the depth of tumor invasion of the muscularis propria. The majority (80%) of rectal cancer is diagnosed in stage T3, but the 5-year survival rate decreases from 85% to 54%, when tumor invasion beyond the muscularis propria is more than 5 mm, regardless of lymph node involvement [11]. To achieve a more accurate radiological staging of rectal cancer through MRI, stage T3 has been divided into four categories according to tumor extention beyond muscularis propria:

– T3a < 1 mm
– T3b 1-5 mm
– T3c 5-15 mm
– T3d > 15 mm [12]

Although not included in TNM staging, an important parameter for rectal cancer staging is circumferential resection margin of the tumor (CRM). CRM is defined as the minimum distance between the tumor and the mesorectal fascia [13], and it is an important predictor of locoregional disease recurrence and survival [14,15]. Usually CRM is considered positive when ≤ 1 mm and negative when > 1 mm. To evaluate the CRM, MRI appears to be the most appropriate instrumental diagnostic investigation [16].

After neoadjuvant therapy, the various categories staging pTNM should be expressed with a prefixed "y"; therefore here we speak ypTNM [17]. This addition is used to indicate that pathological evaluation of the tumor could be influenced by possible effects of neoadjuvant therapy on surgical specimen. The pathologist should also indicate the extent of tumor response to neoadjuvant therapy, that appears to be an important prognostic factor. Any tumor regression (TRG) can be indicated according to the following scheme, proposed by Dworak et al. in 1997:

– TRG0: absence of tumor regression;
– TRG1: fibrosis < 25% of the tumor;
– TRG2: fibrosis in 26-50% of the tumor;
– TRG3: fibrosis > 50% of the tumor;
– TRG4: fibrotic mass without cancer cells[18]

Pathologic examination of resection margins is considered extremely important [19].

Despite the therapeutic approach to rectal cancer is becoming increasingly multi-modal, nowadays surgery remains the main treatment with curative intent. Surgical options can use either "open" techniques and laparoscopy as well as minimally invasive techniques, including robotic surgery.

To plan a correct surgical treatment of rectal cancer, it is essential to achieve a correct preoperative staging. For this tumor, in addition to distant metastasis identification, it is essential to define the extent of the tumor and to identificate the possible involvement of regional lymph nodes, both for prognostic and therapeutic purposes.

Integrated multidisciplinary treatment uses MRI study of the pelvis to identify patients in need of receiving neoadiuvant therapy [20].

The aim of our study was to evaluate the efficacy of MRI in locoregional staging of rectal cancer.

In particular, we compared the factors T (tumor extension) and N (regional lymph nodes involvment) obtained through MRI staging, with the same factors evaluated by histological examination, in order to assess the correlation between preoperative and postoperative staging.

We also assessed whether serum levels of the following markers, Carcino-Embryonic Antigen (CEA), CA 19.9, alpha-fetoprotein (AFP), correlated with cancer stage and whether there was a possible increase of their serum levels according to the tumor stage.

Materials Methiods

In our study we examined cases of rectal cancer operated in the period between 1/01/2011 and 31/12/2014.

All 75 cases have followed a company procedure that, in presence of rectal carcinoma, provides for a collegial multidisciplinary discussion of every clinical case among specialized surgeons, oncologists, radiologists and gastroenterologists, for a correct definition of the preoperative study. Based on this, it was determined the most appropriate therapeutic approach to every individual case, considering whether or not to refer the patient to a neoadjuvant therapy. We evaluated the cases that underwent computed tomography (CT) and magnetic resonance imaging (MRI) as preoperative study.

Therefore in these cases we decided to collect personal data, and reports either of chest-abdomen CT and pelvic MRI. We focused on the loco-regional staging of tumors and in particular on the TNM stage expressed by the radiologial report of the MRI examination. We compared the factors T (tumor extension) and N (regional lymph nodes involvement) obtained through MRI staging, with the same factors emerged from the histological examination after pathologic analysis. Since the radiological MRI reports of 10 patients did not specify a TNM staging, they were later reanalyzed by a radiologist in order to have factors T and N expressed in all this patients.
These cases were then further divided according to the submission or not to a neoadjuvant treatment.
We also collected data related to the value of serum tumor markers: Carcino-Embryonic Antigen (CEA), CA 19.9, alpha-fetoprotein (AFP).
To evaluate the serum levels of these markers, we considered normal CEA values between 0.01 and 5.50 ng/ml, those of CA 19.9 between 0.00 and 33.00 IU/ml and those of AFP between 0.00 and 7.50 IU/ml.
We then correlated the serum tumor markers with the factors T (tumor extension) and N (lymph node involvement) emerged by histologic examination.
Also in this case the treated patients were further subdivided according to the submission or not to a neoadjuvant treatment.
The statistical analysis was performed by evaluating the correlation coefficients and the t-test for paired data. P values <0.05 were defined as statistically significant.

Results

The analysis of our data showed that 75 patients were operated, with an average age of 68.58 +/- 12.96 years; 42 (56%) males and 33 (44%) females, with a mean age respectively of 67.48 +/- 10.60 and 70 +/- 13.79.

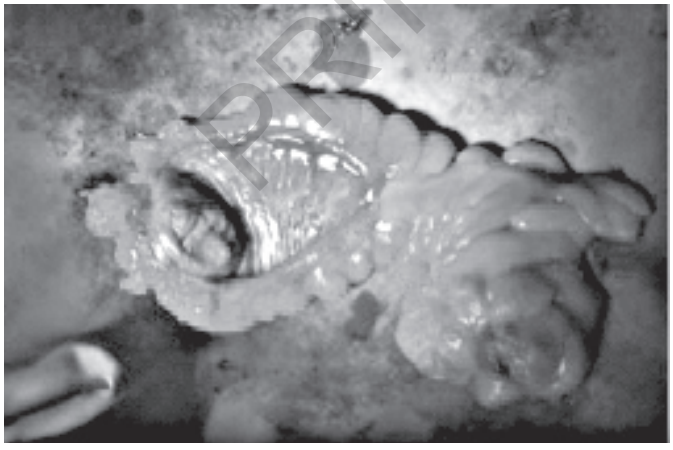

Fig. 1: Specimen of a patient operated for rectal cancer.

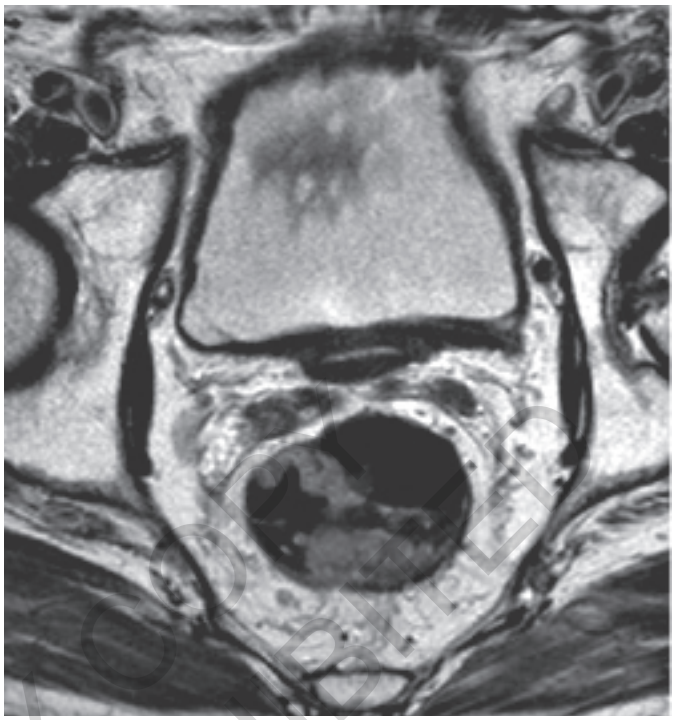

Fig. 2: MRI image with evidence of a T3a stage tumor, with spicolature in the left margin and muscle infiltration on the right side.

Out of these 75 patients: 60 (80%) were treated surgically using the technique of anterior resection, 8 (10.6%) with abdominoperineal resection, 3 (4%) underwent colostomy for palliation, 2 (2.6%) underwent left hemicolectomy in consequence of neoplastic localization at rectosigmoid joint, 1 patient (1.4%) was treated with a proctocolectomy and 1 (1.4%) via transanal excision. (Fig. 1)
All the patients were submitted to a preoperative evaluation; 73 (97,33%) were staged using CT and 36 (48%) through MRI (Figs. 2, 3).
Out of the 36 patients staged by MRI, 21 (58%) were directly addressed to surgical treatment and 15 (42%) were subjected to neoadjuvant treatment before surgery.
Data analysis showed a correlation between preoperative T stage (tumor extension), determined by MRI, and postoperative stage, emerged from the histological examination (correlation coefficient 0.67, p <0.001).
This correlation resulted even higher, if we consider separately the group of patients that didn't receive neoadjuvant treatment (correlation coefficient 0.86, p <0.001), but statistically non-significant (correlation coefficient 0.31) in the cases treated with neoadjuvant therapy (Fig. 4).
T-test analysis for paired data demonstrates the absence of statistically significant difference between T stage, obtained by MRI, and T stage obtained by histological examination, if we cosider all our patients, the group treated with neoadjuvant therapy and the group not treated. Likewise we also found a lack of statistically

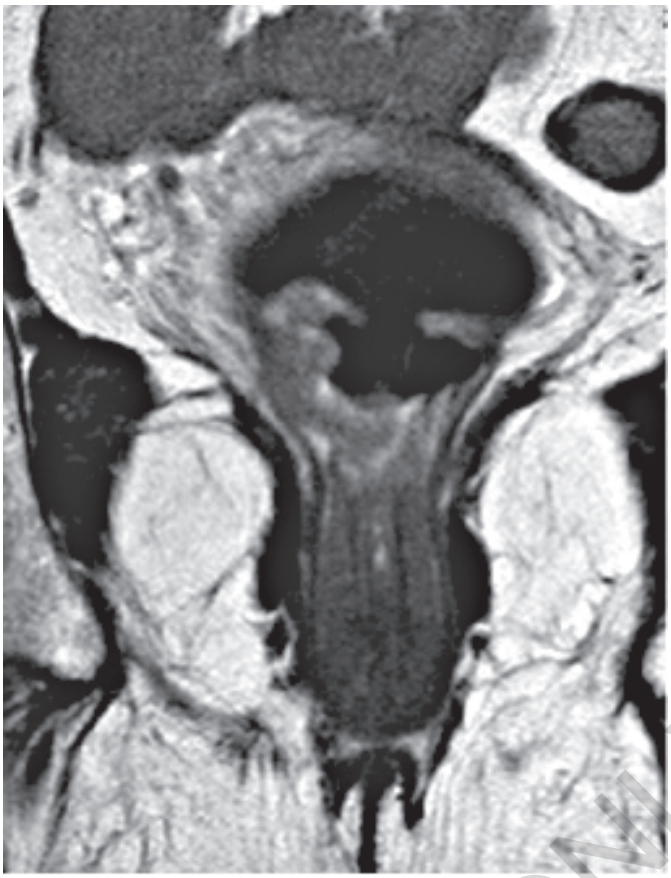

Fig. 3: MRI image with evidence of a T4 stage tumor, with infiltration of the levator ani muscle.

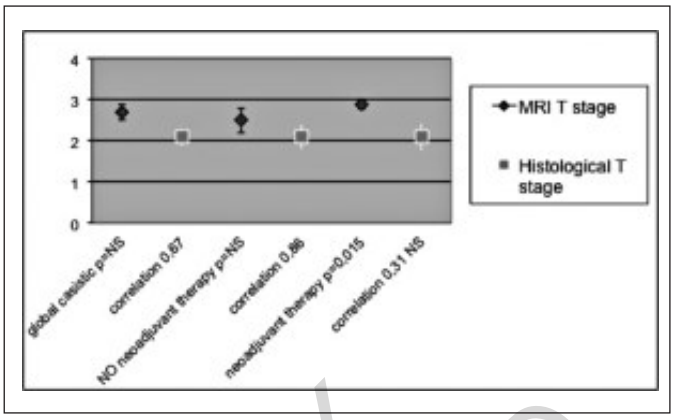

Fig. 4. Evaluation of the correlation between T stage obtained by MRI and the one emerged from pathological examination. There is a statistically significant correlation in the overall population (correlation coefficient 0.67); this correlation is even higher if we consider just the cases not-submitted to neoadjuvant treatment (correlation coefficient 0.86). However, there is no significant correlation in patients submitted to neoadjuvant treatment (correlation coefficient 0.31).

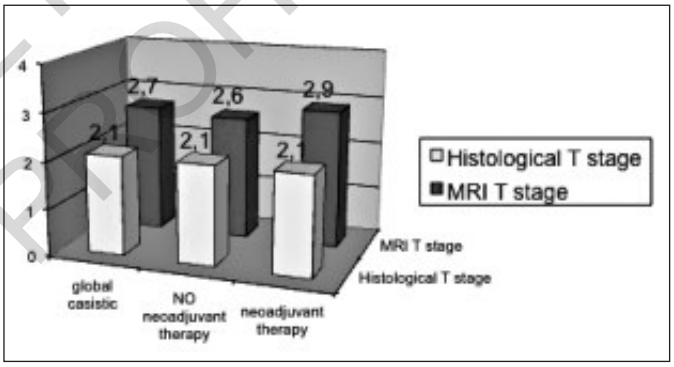

Fig. 5: Median T stages according to the type of treatment.

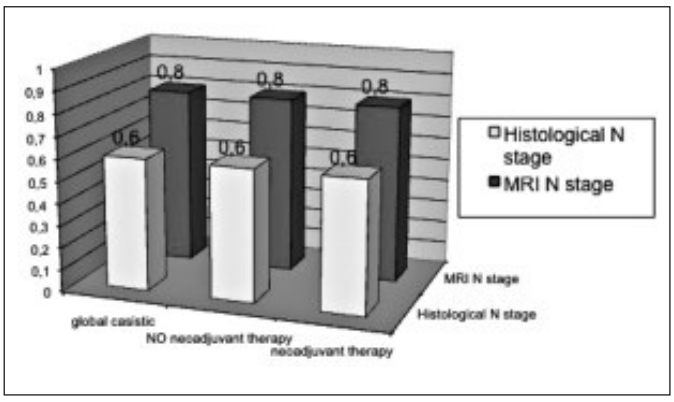

Fig. 6: Median N stages according to the type of treatment

significant difference between preoperative stage, determined by MRI, and histologic examination, in the group of patients that didn't undergo neoadjuvant treatment.

In contrast, in patients undergone neoadjuvant therapy, there was a statistically significant difference between pre and post-operative stage, with a reduction of the stage in reference to the histological examination.

After neoadjuvant treatment, 15 patients were re-evaluated by CT before surgery.

One of these 15 patients was restaged also through MRI. The stage given by the radiological report prior to neoadjuvant treatment was T3dN0; the one given by the revaluation after neoadjuvant treatment was T2N0; the one emerged by the postoperative histological evaluation was T2N0. From this case a correlation between the preoperative stage obtained by MRI (T2N0) and postoperative histological evaluation (T2N0) has emerged. There was also evidence of a downstaging (change from stage T3dN0 to stage T2N0) as a consequence of neoadjuvant treatment.

Our study did not show any statistically significant correlation between preoperative N stage (lymph node

involvement), obtained by MRI, and postoperative N stage, emerged from pathological examination. We did not find any correlation neighter considering the overall series (group treated with neoadjuvant therapy and group non-treated with neoadjuvant therapy), nor considering patients treated with neoadjuvant therapy and those that did not undergo this treatment as separate populations.
In our series preoperative T stage was found to be on average 2.7 in the overall series, 2.6 in patients without neoadjuvant treatment, 2.9 in those having received such a treatment. The average postoperative stage was 2.1 taking in consideration the overall series and 2.1 even considering separately the patients with and without neoadjuvant treatment (Fig. 5).
Concerning the evaluation of lymph node involvement, preoperative N stage was found to be on average 0.8 in the overall series, the same value was found in patients not submitted to neoadjuvant treatment and patients undergone such treatment. The postoperative median stage resulted 0.6 either considering the overall series or considering separately the patients submitted and those not submitted to neoadjuvant treatment (Fig. 6).
The serum levels of the tumor markers Carcino-Embryonic Antigen (CEA), CA 19.9, alpha-fetoprotein (AFP), were not evalueted in all 75 patients. In 61 patients all these three markers were tested, in 1 just CEA and CA 19.9, in 1 just CA 19.9; therefore CEA was determined in 62 (82.6%) patients, CA 19.9 in 63 (84%), the AFP in 61 (81.3%).

We found the following results:
CEA: out of 62 patients, 45 (72.5%) were found to have values in the normal range, and 17 (27.5%) values exceeding the limits.
CA 19.9: out of 63 patients, 52 (82.5%) were found to have values in the normal range, and 11 (17.5%) values exceeding the limits.
AFP: out of 61 patients, 55 (90.2%) were found to have values in the normal range, and 6 (9.8%) are higher than the limits (Table I).
Again we took in consideration either all cases globally (group treated with neoadjuvant therapy and group not treated with neoadjuvant therapy), or separately, depending on whether or not they had undergone neoadjuvant treatment.

TABLE 1 - *Tumor makers measurements*

Tumor Marker	N° patients	Patients with n.v.	Patients with v. superior than ranges
CEA	62	45 (72,5%)	17 (27,5%)
CA 19.9	63	52 (82,5%)	11 (17,5%)
AFP	61	55 (90,2%)	6 (9,8%)

Out of the 61 patients tested for all the 3 markers, 17 (27.8%) underwent neoadjuvant treatment, 44 (72.2%) didn't. The single case assayed only for CEA and CA 19.9 has not been subjected to neoadjuvant treatment, while the case assessed only for CA 19.9 was submitted to neoadjuvant treatment.
Matching serum levels of tumor markers CEA, CA 19.9, AFP, considered individually, with factors T (tumor extension) and N (lymph node involvement) emerged from histological examination, no statistically significant correlation between markers and disease stage was found. According to the positivity of tumor markers, we associated the following score:
– 0, no positive marker
– 1, only one marker positive
– 2, two markers positive
– 3 three markers positive
In presence of three markers positive, meaning the highest score, we found a statistically significant correlation (correlation coefficient 0.41, $p < 0.001$) with N + staging of the disease, obtained by postoperative pathologic examination.

Discussion

Adequate and accurate staging is essential to set correct therapeutic treatment of rectal tumors. In recent years, it has been attempted to identify the most appropriate diagnostic investigations especially in order to provide the most correct loco-regional staging. Thus it emerged the strategic role of MRI.
Various studies have been conducted with the aim to evaluate efficacy of MRI in the preoperative staging of rectal tumors.
The use of MRI for rectal cancer staging began in 1986 [21]; over the years this method has gained more and more ground, becoming a milestone of the preoperative study of these tumors.
To stage primary tumor, the first scan is performed with high-resolution T2-weighted sequences [22]. Use of bowel preparation, antispasmodic drugs and rectal gel, with diagnostic intent, is still controversial [23].
For restaging tumors previously treated with neoadjuvant chemo-radio therapy, high-resolution T2-weighted sequences seem to lose in accuracy; this appears to be due to the intense fibrotic process determined by therapy, that makes difficult to distinguish the residual tumor. Following neoadjuvant treatment, in addition to a marked fibrosis, a peritumoral infiltration of inflammatory cells and an intense vascular proliferation are frequently found. All these elements contribute to a possible overstaging. In contrast, microscopic residual of tumor cells within the rectal wall is the main factor that leads to an understaging [24].
The use of diffusion-weighted MRI is more suitable for the staging of rectal cancers previously undergone

neoadjuvant treatment, since it gives a better characterization of any residual cancer cells [25].

In a recent meta-analysis on the staging through MRI, it has been observed that for the evaluation of tumor extent (T), MRI resulted to have a sensitivity around 87% and specificity around 75% [16].

The stadium T1 and T2 are hardly distinguishable on MRI, because it results difficult to get a clear image of submucosal layer. In stage T2, the tumor is confined to the muscular layer, that appears to be hypointense. In MRI sequences, stadium T3 is defined as tumor invasion through the hypointense muscular layer within the hyperintense perirectal fat [26]. The distinction between T2 and T3 stage is not always easy, because of a frequent desmoplastic reaction in tissues surrounding the tumor, that can lead to a possible overstaging [27].

From the clinical point of view, the depth of the invasion in the extramural perirectal fat is considered more important than the distinction between stage T2 and T3. Actually it has been observed that, T2 stage cancers have the same prognosis of T3 stage malignancies with an infiltration into the perirectal fat less than 1 mm [28]. The prognosis instead has a wide variability in T3 stage tumors with different mesorectal infiltration; in fact five-year survival rate decreases from 85% to 54% when tumor invasion beyond the muscularis externa is more than 5 mm, regardless of lymph node involvement [1].

MRI results to be very accurate in the identification of T3 and T4 stages. This is very important for therapeutic treatment planning, because these two particular stages will be addressed to neoadjuvant therapy [29].

Concerning lymph node involvement, there is a great debate about MRI reliability. On the basis of a recent meta-analysis, MRI shows a sensitivity of 77% and a specificity of 71% [16]. The main problem seems to be represented by the difficulty in finding reliable parameters for identifying possible lymph node malignancy. The use of the single dimensional parameter, placing 5 mm as cut-off, was shown to have a sensitivity of 66% and a specificity of 76%. The use of a contrast agent increases the predictive value of malignancy, allowing to evaluate also contours irregolarities and heterogeneous intensities [30].

A study of 2013 has demonstrated the utility of the use of lymph node-specific contrast agents, like as suspensions of ultra-nanoparticles of iron oxides (USPIO-ultra-small superparamagnetic particle iron oxides) or gadofosveset trisodium, for lymph node study. These contrast agents, used in diffusion-weighted MRI, improve the visualization of suspicious lymph nodes, but unfortunately it remains problematic their finding, especially for a possible large-scale use [31].

However, MRI is certainly more reliable than CT in detecting lymph node metastases; in fact the reliability of the latter is quite poor, with oscillations between a 22 to 73% [32].

Therefore MRI is a diagnostic tool particularly suitable for locoregional staging of rectal neoplasms, on the contrary it isn't the first choice test for identifying the presence of distant metastases. For this purpose, CT at first and possibly PET are more indicated.

From our study it emerged a close correlation between T stage, determined by MRI, and T stage found by histological examination, particularly in cases that hadn't received neoadjuvant treatment. This findings are in agreement with other studies of the literature, including a report published by Jiang JB et al [33]. in 2006, conducted on 53 patients, where MRI turned out to have an accuracy of 77.4% in determining T stage. Moreover, similarly to our results, they showed a statistically significant correlation between pathological and MRI stage ($p < 0.001$).

In a 2015 study conducted by Algebally A.M. et al. [34] on 56 patients, the accuracy of MRI in determining the T stage was even higher, reaching 85.7%.

In our study, no statistically significant correlation emerged from the separate analysis of the cases subjected to neoadjuvant treatment; this is probably ascrivable to the fact that 14 out of the 15 patients submitted to this treatment, had not been restaged through MRI, but only using CT. Therefore the lack of correlation might be attributable to the downstaging determined by neoadjuvant treatment; this interpretation is supported by the study of our only patient restaged also through MRI. In fact the data of this patient show a significant correlation between the preoperative stage (T2N0), given by MRI performed at the end of the neoadjuvant treatment, and postoperative histologic stage (T2N0). In this patient there was also evidence of a downstaging as a consequence of neoadjuvant treatment; in fact we found a transition from stage T3dN0, assessed by radiological investigationt prior to such treatment, to stage T2N0, emerged from MRI performed after neoadjuvant treatment. Since this is a single case, it is not possible to determinate its statistical significance.

On a wider casistic, it would be useful to assess more reliably the accuracy of MRI in the evaluation of tumor regressions after neoadjuvant treatment. Indeed the assessment of tumor regression following such treatment results to be of great importance, since it was observed that eventual regression significantly increases the disease-free interval [35]. However, evaluation by means of MRI of the possible downstaging following neoadjuvant treatment, results not to be as accurate as the evaluation previous to the treatment. From a study conducted by Zhan S. et al. in 2015 [36], evaluating 94 patients submitted to neoadjuvant treatment, it emerged how the restaging throught MRI still remains a challenge. It appears particularly difficult to assess the possible involvement of the mesorectal fascia, because of the frequent development of fibrotic tissue in response to neoadjuvant treatment. This fibrotic tissue, as it emerges from a 2008 study of Viliegen RF et al. [37] is hardly distinguishable from the possible presence of small tumor foci. The final histological stage remains the best predictor for disease-free interval since affected both by

the preoperative stage and the neoadjuvant therapy response [38].

Our study did not show any statistical significant correlation between preoperative N stage (lymph node involvement), obtained by MRI, and postoperative N stage, emerged from pathologic examination, neither considering the overall cases, nor analyzing separately patients treated and not treated with neoadjuvant therapy. This figure is quite in agreement with the study of Jiang JB et al. [33] of 2006, where a poor correlation between pathological N stage and MRI N stage ($p = 0.003$) was demonstrated. We can hypotize that our data have been influenced by the number of cases, although surely the identification of lymph node involvement, using high-resolution T2-weighted MRI sequences, results overall difficult. This is mainly due to the difficult finding of reliable diagnostic parameters for lymph node malignancy. In order to better characterize lymph node involvement, Heijnen LA et al. [33] have demonstrated the value of diffusion-weighted MRI in association with lymph node-specific contrast agents.

Utility of the assay of tumor markers in preoperative rectal cancer staging is still debated. In clinical practice we dose Carcino-Embryonic Antigen (CEA) and CA 19.9 [39].

The prognostic value of CEA for rectal cancer has long been debated. In recent years it has been observed that patients with elevated CEA serum levels, either before or after chemo-radio therapy, appear to have a lower response to chemo-radio-therapy and seem to have a higher risk of local recurrence [40]. Besides, those patients with pre-operative CEA levels superior than 6 ng/ml showing a reduction in CEA levels after chemo-radio-therapy, have a better prognosis [41]. Surely in postoperative follow-up the determination of CEA appears to be very useful to monitor possible recurrences, since they are usually accompanied by an increase of its serum levels.

Inspite of the fact that the value of CA 19.9 is not supported by the same evidence of CEA, their dosage is usually coupled [39].

In clinical practice normally also alpha-fetoprotein (AFP) levels are measured; generally high levels of AFP are linked to the presence of liver metastases.

Our analysis did not reveal any statistically significant correlation between serum levels of CEA, CA 19.9, AFP, considered individually, and T and N tumor stages. This figure was probably influenced by the fact that, in most of the cases treated in our study, tumor markers levels were in normal range. It is also possible that this lack of correlation is connected to the downstaging due to the neoadjuvant treatment, that some of our patients were submitted to, since marker levels were measured prior to neoadjuvant therapy.

On the basis of our experience, we find the utility of these tumor markers in preoperative evaluation of rectal cancer rather doubtfull.

Alpha-fetoprotein was the marker less frequently found higher than threshold values, probably because its elevated levels are mainly determinated by the presence of liver metastasis and not by the primitive rectal cancer mass.

Finally, we found a statistically significant correlation of a concomitant positivity of CEA, CA 19.9, AFP with high N stages. However, given the low frequency of this finding in our series, further evaluation on a wider scale are probably needed.

From our study we have concluded that, in the preoperative evaluation of rectal cancer, MRI is effective in determining T stage, expecially in patients not submitted to neoadjuvant treatment. However in patients submitted to this treatment, MRI is probably useful either for revaluating the stage of the tumor before surgery and for assessing the extent of tumor regression; therefore, a presurgical restage of these patients is recommendable. Probably, for limph node involvement evaluation, more reliable parameters for establishing possible lymph node malignancy need to be found.

The role of the tumor markers CEA, CA 19.9, AFP during preoperative evaluation of rectal tumors remains undefined.

Riassunto

Nel nostro studio abbiamo esaminato 75 pazienti trattati per carcinoma del retto nel periodo dal 1 gennaio 2011 al 31 dicembre 2014. Di questi 75 casi abbiamo considerato 36 casi stadiati con RMN , Abbiamo confrontato la stadiazione ottenuta con lo studi oRMN con quella evidenziatasi dallo studio istologico. La correlazione tra le due stadiazioni TNM è stata ulteriormente analizzata in base all'esecuzione o meno di trattamento neoadiuvante.

Abbiamo, infine, analizzato i valori sierici di marcatori tumorali di CEA, Ca 19.9, AFP correlandoli alla stadiazione.

I dati hanno dimostrato una correlazione statistiacmente significativa per il T specialmente nella popolazione che non aveva eseguito terapia neoadiuvante.

Per il parametro N non abbiamo evidenziato correlazioni statisticamente significative; nessuno dei marcatori tumorali presentava un correlazione con lo stadio di malattia. Analizzano ulteriormente nei pazienti i marcatori tumorali positivi abbiamo associato il seguente score: 0 (assenza di marcatori positivi),1 (solo un marcatore positivo), 2(due marcatori positivi),3 /tre marcatori positivi).

In presenza di tre marcatpori positivi abbiamo trovato una correlazione statisticamente significativa con N+ in base all'esame istologico.

La conclusione è che la RMN è efficace nella valutazione del T. Per stabilire il coinvolgimento linfonodale necessitiamo di ulteriori parametri. Il ruolo dei marcatori tumorali CEA, CA 19.9, AFP durante la valutazione preoperatoria dei tumori del retto rimane non ben definito.

References

1. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al.: *Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012.* Eur J Cancer, 2013; 49(6):1374-403.

2. Siegel R, Desantis C, Jemal A: *Colorectal cancer statistics.* CA Cancer J Clin, 2014; 64(2):104-17.

3. Fernandez E, Bosetti C, La Vecchia C, Levi F, Fioretti F, Negri E: *Sex differences in colorectal cancer mortality in Europe, 1955-1996.* Eur J Cancer Prev, 2000; 9(2):99-104.

4. Bailey CE, Hu CY, You YN, et al*: Increasing disparities in age-related incidences of colon and rectal cancers in the United States, 1975-2010.* JAMA Surg, 2015; 150(1):17-22.

5. Aleksandrova K, Pischon T, Buijsse B: *Adult weight change and risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition.* Eur J Cancer, 2013; 49(16):3526-536.

6. Tárraga López PJ, Albero JS, Rodrìguez-Montes JA: *Primary and Secondary Prevention of Colorectal Cancer.* Clin Med Insights Gastroenterol, 2014; 7:33-46.

7. Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P: *Smoking and colorectal cancer: A meta-analysis*. JAMA: the journal of the American Medical Association, 2008; 300(23):2765-778.

8. Grande E, Inghelmann R, Francisci S: *Regional estimates of colorectal cancer burden in Italy.* Tumori, 2007; 93(4):352-59.

9. Edge SB, Compton CC: *The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM.* Annals of surgical oncology, 2010; 17(6):1471-474.

10. Tepper JE, O'Connel MJ, Niedzwiecki D, et al.: *Impact of number of nodes retrieved on outcome in patients with rectal cancer.* J Clin Oncol, 2001; 19(1):157-63.

11. Merkel S, Mansmann U, Siassi M, Papadopoulos T, Hohenberger W, Hermanek P: *The prognostic inhomogeneity in pT3 rectal carcinomas*. Int J Colorectal Dis, 2001; 16(5):298-304.

12. Taylor F, Mangat N, Swift IR, Brown G: *Proforma-based reporting in rectal cancer.* Cancer Imaging, 2010; 10(1A):142-50.

13. Nagtegaal ID, Quirke P: *What is the role for the circumferential margin in the modern treatment of rectal cancer?* J Clin Oncol, 2008; 26(2):303-12.

14. Nagtegaal ID, Marijnen CA, Kranenbarg EK, et al.: *Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma: Not one millimeter but two millimeters is the limit.* Am J Surg Pathol, 2002; 26(3):350-57.

15. Wibe A, Rendedal PR, Svensson E, et al.: *Prognostic significance of the circumferential resection margin following* total *mesorectal excision for rectal cancer.* Br J Surg, 2002; 89(3):327-34.

16. Al-Sukhni E, Milot L, Fruitman M, et al.: *Diagnostic accuracy of MRI for assessment of T category, lymph node metastases, and circumferential resection margin involvement in patients with rectal cancer: A systemic review and meta-analysis.* Ann Surg Oncol, 2012; 19(7):2212-223.

17. Fleming ID, Cooper JS, Henson DE, et al.: A*JCC manual for staging of cancer.* 5th ed. Philadelphia, PA: Lippincott-Raven; 1997.

18. Dworak O, Keilholz L, Hoffmann A: *Pathological features of rectal cancer after preoperative radiochemotherapy*. Int J Colorectal Dis, 1997; 12(1):19-23.

19. Hermanek P, Wittekind K: *Residual tumor ® classification and prognosis. S*emin Surg Oncol, 1994; 10(1):12-20.

20. Glimelius B, Tiret E, Cervantes A, Arnold D: ESMO Guidelines Working Group: Rec*tal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. A*nnals of Oncology, 2013; 24(supplement 6):81-88.

21. Hodgman CG, MacCarty RL, Wolff BG, et al.: *Preoperative staging of rectal carcinoma by computed tomography and 0.15T magnetic resonance imaging. Preliminary report.* Dis Colon Rectum, 1986; 29(7):446-50.

22. Suzuki C, Torkzad MR, Tanaka S, et al.: *The importance of recral cancer MRI protocols on interpretation accurancy.* World J Surg Oncol, 2008; 6:89.

23. Dewhurst CE, Mortele K: *Magnetic resonance imaging of rectal cancer.* Radiol Clin North Am, 2013; 51(1):121-31.

24. Kuo LJ, Chern MC, Tsou MH, et al., *Interpretation of magnetic resonance imaging for locally advanced rectal carcinoma after preoperative chemoradiation therapy.* Dis Colon Rectum, 2005; 48(1):23-8.

25. Song I, Kim SH, Lee SJ, Choi JY, Kim MJ, Rhim H: *Value of diffusion-weighted imaging in the detection of viable tumour after neoadjuvant chemoradiation therapy in patients with locally advanced rectal cancer: Comparison with T2 weighted and PET/CT imaging.* Br J Radiol, 2012; 85(1013):577-86.

26. Heo SH, Kim JW, Shin SS, Jeong YY, Kang HK: *Multimodal imaging evaluation in staging of rectal cancer.* World J Gastroenterolog, 2014; 20(15):4244-55.

27. Laghi A, Ferri M, Catalano C, et al.: *Local staging of rectal cancer with MRI using a phased array body coil.* Abdom imaging, 2002; 27(4):425-31.

28. Burdan F, Sudol-Szopinska I, Staroslawska, et al.: *Magnetic resonance imaging and endorectal ultrasound for diagnosis of rectal lesions.* Eur J Med Res, 2015*;* 20(1):4.

29. Bertini L, Casciani E, Masselli G, Lanciotti S, Polettini E, Gualdi GF: *MRI of extraperitoneal rectal carcinoma*. Ann Ital Chir, 2010; 81(4):239-46.

30. Brown G, Richards CJ, Bourne MW, et al.: M*orphologic predictors of lymph node status in rectal cancer with use of high-spatial-resolution MR imaging with histopathologic comparison.* Radiology, 2003; 227(2):371-77.

31. Heijnen LA, Lambregts DM, Mondal D, et al.: *Diffusion-weighted MR imaging in primary rectal cancer staging demonstrates but does not characterise lymph nodes*. Eur Radiol, 2013; 23(12):3354-360.

32. Muthusamy VR, Chang KJ: *Optimal methods for staging rectal cancer.* Clin Cancer Res, 2007; 13(22 Pt2): 6877-884.

33. Jiang JB, Day Y, Zhang XM, et al.: *Accuracy of preoperative magnetic resonance imaging in prediction of pathological stage and circumferential resection margin in rectal cancer. Z*honghua Yi Xue Za Zhi*,* 2006; 86(14):961-64.

34. Algebally AM, Mohey N, Szmigielsky W, Yousef RR, Kohla RR: *The value of high-resolution MRI technique in patients with rectal carcinoma: pre-operative assessment of mesorectal fascia involvment, circumferential resection margin and local staging.* Pol J Radiol, 2015; 80:115-21.

35. Rödel C, Martus P, Papadoupolos T, et al.: *Prognostic significance of tumor regression after preoperative chemoradiotherapy for rectal cancer.* J Clin Oncol, 2005; 23(34):8688-696.

36. Zhan S, Wang X, Huang X, Zhu H: *Magnetic resonance imaging in restaging rectal cancer after neoadjuvant chemoradiotherapy.* J Buon, 2015; 20(1):62-7.

37. Viliegen SF, Beets GL, Lammering G, et al.: *Mesorectal fascia invasion after neoadjuvant chemotherapy and radiation therapy for locally advanced rectal cancer: Accuracy of MR imaging for prediction*. Radiology, 2008; 246(2):454-62.

38. Quah HM, Chou JF, Gonen M, et al.: *Pathologic stage is most prognostic of disease-free survival in locally advanced rectal cancer patients after preoperative chemoradiation.* Cancer, 2008; 113(1):57-64.

39. Bast RC Jr, Ravdin P, Hayes DF, et al.: *2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology.* J Clin Oncol, 2001; 19(6):1865-878.

40. Ishihara S, Watanabe T, Kiyomatsu T, Yasuda K, Nagawa H: P*rognostic significance of response to preoperative radiotherapy, lymph node metastasis, and CEA level in patients undergoing total mesorectal excision of rectal cancer*. Int J Colorectal Dis, 2010; 25(12):1417-425.

41. Kim CW, Yu CS, Yang SS, et al.: Clinical significance of pre- to post-chemoradiotherapy s-CEA reduction ratio in rectal cancer patients treated with preoperative chemoradiotherapy and curative resection. Ann Surg Oncol, 2011; 18(12):3271-727.