Chapter

The Utility of Magnetic Resonance Imaging in the Multidisciplinary Treatment of Patients with Rectal Cancer

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Abstract

Rectal cancer is one of the most common types of cancer in both men and women. In recent years, the importance of magnetic resonance imaging (MRI) has greatly increased in the multidisciplinary treatment of patients with rectal cancer. MRI has a particularly important role in the most accurate preoperative staging of these patients, both in terms of assessing the local invasion of the tumor and in terms of assessing the status of pelvic lymph nodes. Many patients with rectal cancer, especially those in the advanced stage of the disease, in the preoperative period undergo neoadjuvant radio chemotherapy. The evaluation of the clinical response of these patients to neoadjuvant therapy is of crucial importance both in terms of personalized treatment and in terms of their prognosis. In this regard, MRI has its clearly defined role at present in evaluating the efficacy of neoadjuvant therapy, as well as in postoperative follow-up.

Keywords: MRI, rectal cancer, staging, lymph nodes, multidisciplinary treatment

1. Introduction

Rectal cancer is currently a real public health problem, being the second most common type of cancer in women and the third most common type of cancer in men. Surgical treatment with curative intent (rectal resection with total mesorectal excision - TME) is the only therapeutic possibility that can ensure the healing of these patients [1].

In recent decades, the prognosis of these patients has significantly improved following the introduction in clinical practice of neoadjuvant radio chemotherapy, both to improve the life expectancy and to reduce the incidence of local recurrence. In this regard, studies show that in 15–27% of patients with rectal cancer, neoadjuvant radio-chemotherapy has caused a significant decrease in the size of tumors [2]. Therefore, a particularly important role in clinical practice is the

response identification to neoadjuvant therapy in these patients. At the same time, a particularly important role in the prognosis of patients, in addition to the response to neoadjuvant radio chemotherapy, is the surgery itself and especially the achievement of a total mesorectal excision (TME) as accurate as possible and obtaining negative surgical resection margins [3, 4].

2. The utility of magnetic resonance imaging in patients with rectal cancer

In recent years, abdominal and pelvic magnetic resonance imaging (MRI) has established itself as a gold standard method in the evaluation of patients with rectal cancer because of its crucial role in identifying non-responsive patients to neodjuvant radio chemotherapy [5, 6]. However, a particularly important role in the preoperative and postoperative clinical evaluation of these patients is played by accurate images of the anatomical structures of the pelvis, rectal tumor and their relationship with the surrounding anatomical structures [7].

In this sense, the most used MRI sequence in the preoperative evaluation of these patients for visualization of the rectum, tumor, and its relationship with surrounding tissues is High-spatial-resolution T2-weighted imaging [7]. On the other hand, one of the major advantages of rectal MRI scanning in T2 sequences is that 3 layers of the rectal wall can be differentiated. The inner layer is represented by the mucosa and submucosa, the middle layer is represented by the muscularis propria, and the outer layer is represented by the mesorectal fat. This allows for a much more accurate understanding of tumor invasion of the rectal wall and surrounding structures compared to other imaging studies [8, 9].

One of the disadvantages of MRI is the rather long time required to perform this investigation and therefore it is recommended that patients be positioned in a supine position for maximum comfort. But despite this inconvenience the benefit of this imaging method is major [10]. Current studies debate the optimal MRI resolution in the evaluation of patients with rectal cancer (1.5 T or 3 T). While 3 T cameras provide much better spatial resolution, they also have a higher susceptibility to artifacts during diffusion-weighted imaging (DWI) [10–12].

2.1 Local staging in rectal cancer using MRI

Newer studies have shown that MRI can identify patients who are at increased risk of local recurrence. In this sense, it has been shown that patients with tumors that invade only the rectal mucosa have a good long-term prognosis, while patients with invasion of the mesorectal fascia and pelvic organs in the vicinity of the rectum have a particularly high risk of recurrence [13–15]. In this respect MRI has a special utility for the detection of extramural tumor invasion as well as mucin deposits at this level [16]. On the other hand, more and more studies have shown that, in the case of superficial rectal tumors, EUS (endorectal ultrasound) has a special value in the identification of tumors and invasion of surrounding structures, while EUS is less useful in the case of tumors that penetrate the mesorectal fascia, respectively the anatomical structures in the vicinity of the rectum [17, 18].

Regarding the technique of performing MRI in these patients, in order to obtain good quality anatomical images, most authors recommend that the scan plane be perpendicular to the rectal wall at the level of the tumor with a slice thickness of maximum 3 mm. The sections are made in coronal, sagittal and axial plane [19]. On the other hand, there are debates in the literature regarding the use of intravenous contrast in these patients. Most authors do not recommend the routine use of

intravenous contrast [16]. However, there are authors who consider that the use of gadolinum contrast increases the accuracy of detecting transmural tumor invasion as well as vascular invasion [9, 20, 21].

There is further controversy in regards to patient preparation for MRI. Some authors recommend the administration of spasmolytic drugs prior to imaging studies especially in patients with upper rectal tumors and if 3 T devices are used. Other authors recommend that the use of diffusion-weighted MRI be preceded by endorectal filling. But in these cases, dilation of the rectum can affect the measurement of the distance between the mesorectal fascia and the tumor [22, 23]. To eliminate this inconvenience, some authors recommend that a maximum of 60 ml of gel be used for endorectal filling [24].

One of the major advantages of performing MRI in patients with rectal cancer is that it is possible to accurately identify both the circumferential invasion of the tumor in the rectal mucosa and its transmural invasion. This fact is especially important because newer studies have shown that one of the main factors that can lead to local recurrence is incomplete resection, especially in the lateral aspect of the resection specimen [25]. At the same time, pelvic MRI has the ability to accurately detect the macroscopic type of rectal tumor (polypoid, ulcerative) and the presence or absence of mucin at this level [9].

When performing rectal MRI in T2 sequences, the rectal mucosa appears hypointense, the submucosa hyperintense, and the muscularis propria appears as a circumferential hypersignal. Precise identification of the layers of the rectal wall thus allows a precise location of the tumor at the level of the rectal wall [26]. According to the TNM classification of rectal cancer, in stage T1, the tumor is limited to the mucosa and submucosa, in stage T2, the tumor does not extend beyond the muscularis propria, in stage T3, the tumor exceeds muscularis propria and in stage T4, the tumor extends beyond the rectal wall [19] (**Figure 1**).

If the tumor invades the mesorectal fat it is considered to be stage T3 and if it invades the peritoneum of the pelvic cavity, it is interpreted as stage T4. The invasion of intersphincter space is considered a T3 stage. and the invasion of the external anal sphincter is considered a T4 stage [27–29] (**Figure 2**).

A limiting factor in these cases is the existence of fibrous tissue in the rectal wall or in the tissues around the tumor. The existence of fibrosis at this level can make it difficult properly stage the patient, especially by over staging [30]. In this respect, there are studies in the literature which have shown that it is sometimes difficult to differentiate by MRI, peritumoral fibrosis from residual tumor deposits, especially in patients who have undergone neoadjuvant radiochemotherapy. Therefore, most

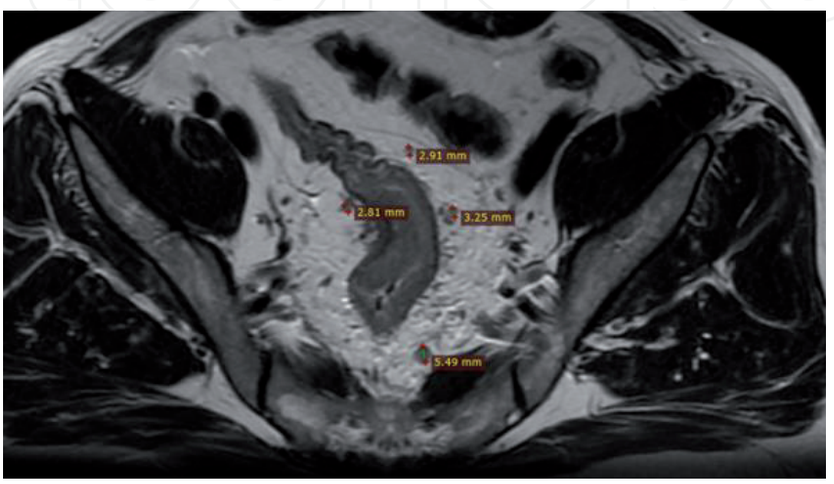

Figure 1.
MRI image, axial view, the tumor invades the mesorectal fascia.

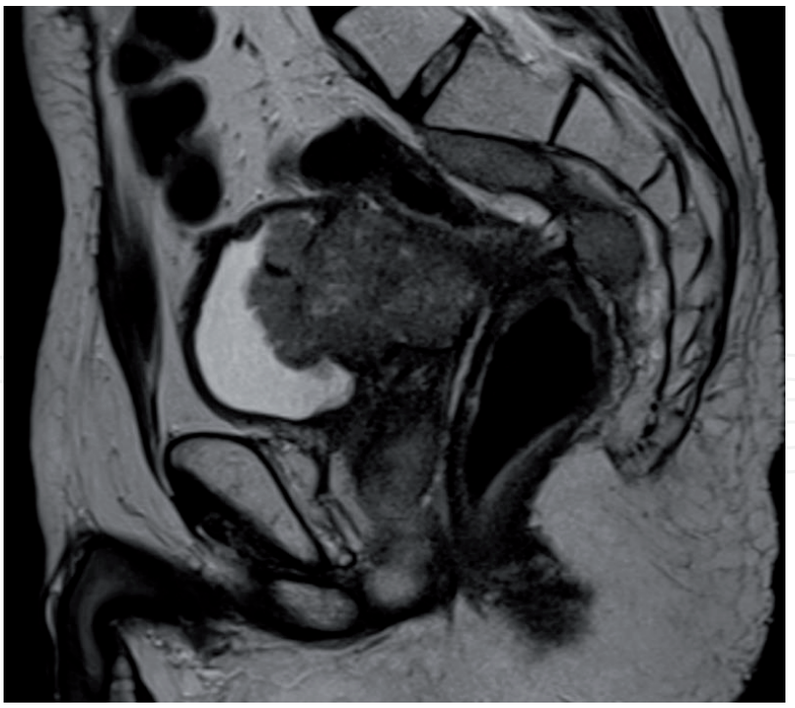

Figure 2.
MRI image, sagital view – tumor recurrence invasive in the bladder and prostate.

authors in the literature recommend that, in patients who have undergone neo-adjuvant radio-chemotherapy, MRI examination should be performed by physicians experienced in this type of pathology [31].

Further MRI findings regard the relationship of the tumor with the anal sphincter as well as the distance between the tumor and the anocutaneous line. Tumors located less than 6 cm are considered low rectal tumors, tumors whose lower edge is located 7–11 cm from the ano-cutaneous line are considered medium rectal tumors, and tumors whose lower limit is located more than 11 cm from the ano-cutaneous line are considered superior rectal tumors [29]. The precise location of the tumor and its relationship to the anal sphincters are particularly important in determining the type of surgery to be performed in these patients (abdomino-perianal resection, abdominal resection) and the extent of the surgery to be performed.

Given the importance of precise localization of the rectal tumor relative to the anocutaneous line in determining the subsequent therapeutic decision in these patients, there are many studies that have investigated the specificity and sensitivity of MRI compared to colonoscopy in establishing the exact distance between the lower edge of the tumor and ano-cutaneous line.

In this regard, there are studies that have shown that MRI cannot rule out performing colonoscopy in these patients, especially because of the fact that colonoscopy offers the possibility of collecting biopsies for histopathological examination. But in many cases the assessment of the distance between the lower edge of the rectal tumor and the anocutaneous line during colonoscopy is subjective, both due to local anatomical details and the experience of the person performing colonoscopy, so many authors conclude that pelvic MRI it is much more useful in establishing the distance between the lower edge of the tumor and the ano-cutaneous line [32–35].

In patients with rectal cancer, a particularly important factor that determines their long-term prognosis, both in terms of the occurrence of local recurrence and survival is represented by extramural vascular invasion (EMT). Recent studies have shown that, T2-weighted MRI was able to identify EMT in 80–90% of cases. EMT is manifested by the existence of morphological changes in the blood vessels adjacent to the tumor [29, 36–38].

Another particularly important prognostic factor that can be identified in these patients using MRI and is represented by the distance between the tumor margin and the mesorectal fascia. Thus, it has been shown that in patients in whom the distance between the rectal tumor and the mesorectal fascia is less than 1 mm, the risk of local recurrence is approximately 22%; if the distance is greater than 1 mm, the risk of local recurrence is only 5% [39, 40]. Regarding the assessment of the distance between the tumor edge and the mesorectal fascia, a factor that may limit the effectiveness of MRI is the existence of a low layer of mesorectal fat between the anterior wall of the rectum and the seminal vesicles in men, respectively the posterior wall of the vagina in women. In these cases, it has been shown that MRI sensitivity and specificity may be affected [41].

Regarding the accuracy of MRI, in the correct evaluation of the T descriptor of the TNM classification of rectal cancer, a very important role is played by the experience of the radiologist performing the investigation [42, 43]. Thus, population studies have shown that the sensitivity of MRI in the correct evaluation of the T descriptor varies between 29 and 57% and the specificity varies between 50 and 83% [43–47]. These results are due, in part, to the experience of the examining physician and, on the other hand, to the difficulty of differentiating in some cases a stage T1 tumor from a stage T2 tumor. In some cases, the desmoplastic reaction of the tumor makes a tumor look like T3 stage on MRI when in fact, following surgical specimen examining the surgical resection piece is actually a T2 stage [48].

Last but not least, the knowledge of local anatomical details, of the relations of the rectal tumor formation with the surrounding structures, allows the surgical team an adequate programming of the resection surgery, thus diminishing the possible intraoperative surprises regarding local invasion of the rectal tumor. In this way, the morbidity and postoperative mortality of these patients can be significantly reduced.

2.2 Detection of lymph node metastases using MRI in patients with rectal cancer

The existence of loco-regional lymph node metastases at the time of diagnosis is a poor prognostic factor in patients with rectal cancer, the first lymph nodes affected being those located in the mesorectum. In the case of rectal cancer, loco-regional lymph nodes are considered to be the obturator lymph nodes, internal iliac lymph nodes and the ones located in the mesorectum [49–51]. Therefore, the correct assessment of the existence of lymph node metastases in patients with rectal cancer is of particular importance in the preoperative assessment of these patients, the experience of the examining physician having a particularly important role in these cases [52, 53] (**Figure 3**).

It is often difficult to assess the status of loco-regional lymph nodes using MRI and it has been found that in about 25% of cases loco-regional lymphadenopathy which were considered as lymph node metastases were not confirmed positive on the histology report [54, 55]. However, some studies have shown that the use of high-resolution T2-weighted sequences can improve the sensitivity and specificity of MRI in the detection of lymph node metastases. These results are due to the fact that, especially in the case of patients undergoing neo-adjuvant radiochemotherapy, local fibrosis makes it difficult to correctly assess the status of loco-regional lymph nodes [56–58].

A much debated topic in the literature is the diagnostic criteria for lymph node metastases based on MRI examination. Thus, there are authors who consider that lymph node adenopathy with a diameter larger than 5 mm represents malignant lymphadenopathy, and those with a diameter below 5 mm are benign [59]. On the other hand, other authors consider that the most faithful sign of suspicion for malignancy is represented by the fact that the diameter of the loco-regional lymph

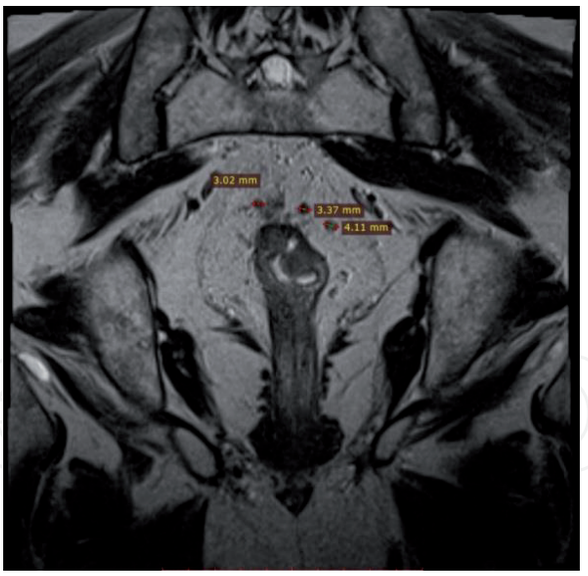

Figure 3.
Adjacent lymph nodes in mesorectal fat up to 4 mm in size. 4 mm extramesorectal lymph node.

nodes decreases in size or increases in size after the practice of neo-adjuvant radio-chemotherapy [60, 61]. On the other hand, other authors consider as criteria for malignancy of the lymph nodes, based on MRI examination, the existence of extracapsular invasion or enlargement of the lymph nodes located on the walls of the pelvic cavity (extramesorectal), or changes in their morphology (presence or absence of heterogeneity) [62, 63].

However, the specificity of the diagnosis of malignant lymphadenopathy with MRI is around 70%, mainly due to fibrotic changes or mucinous degeneration of these lymph nodes, these results being due also to the fact that there are studies that have shown the existence of fibrotic changes also in case of benign lymphatic nodules [64]. There are also studies in the literature that recommend the practice of MRI with dynamic contrast-enhanced, in patients with rectal cancer, in order to increase the accuracy of MRI diagnosis of lymph node involvement. In the case of the administration of dynamic contrast, it is considered that, usually, the malignant lymph nodes, when examined in T2 sequences, have edges in hypersignal, and their center presents hyposignal [65].

2.3 Detection of distant metastases using MRI in patients with rectal cancer

Recently, the importance of MRI in the preoperative evaluation of rectal cancer patients has increased greatly despite the abdominal CT examination, especially due to the fact that diffusion-weighted MRI is much more effective in detecting small liver metastases compared to abdominal CT imaging [66]. There are also studies in the literature that have shown that the sensitivity and specificity of MRI in the detection of liver metastases is superior even to PET-CT [67, 68]. Therefore, there are authors who recommend performing a whole body MRI, in patients with rectal cancer [69]. On the other hand, the sensitivity and specificity of the detection of pulmonary metastases, in patients with rectal cancer, is lower in the case of MRI compared with chest CT scan [70].

Recently, in order to detect the existence of distant metastases, in patients with rectal cancer, PET-MRI is increasingly used. This method eliminates the lower sensitivity and specificity of MRI in the detection of lung metastases and brings in addition the increased sensitivity and specificity of MRI for the detection of liver metastases, compared to abdominal CT scan [71].

2.4 Evaluation of the response to neo-adjuvant radiochemotherapy

The prognosis of patients with rectal cancer has significantly improved, in recent years, on the one hand by introducing the neo-adjuvant radiochemotherapy in their treatment, as well as by improving imaging methods that allow a more accurate preoperative staging of these patients [72, 73]. Thus, it has been shown that the introduction of neo-adjuvant radiochemotherapy in patients with advanced loco-regional forms of rectal cancer has led to an improvement in their survival, decreased the risk of local recurrence and, in some cases, has even been recorded a complete pathological response, improving as well the postoperative morbidity and mortality of these patients. Also, for these patients it was found a better compliance to postoperative radio-chemotherapy [74–76].

With the initiation of neo-adjuvant radio-chemotherapy of particular clinical importance is the identification of patients with no response to this therapy, with incomplete clinical response or with a complete clinical response (the absence of residual tumor, the absence of neoplastic lymph nodes in the mesorectum). The identification of these groups of patients is very important given the principles of personalized medicine. It is also of crucial importance to identify patients who do not respond to radiochemotherapy, in which case it is beneficial for them to initiate the surgical treatment as soon as possible [77–80].

In this regard, in recent years there are authors who, in rectal cancer patients with neo-adjuvant radiochemotherapy to whom a complete clinical response is recorded, recommend either the practice of a resection surgery with preservation of the rectum or only the clinical follow-up of these patients, without the indication of a surgical treatment. In these situations, a complete clinical response is recorded in approximately 24% of cases [80, 81]. Some authors have shown that the usual MRI techniques (T2 weighted) cannot always correctly assess the clinical response to neo-adjuvant radiochemotherapy, recommending in these cases the use of functional MRI techniques (dynamic contrast-enhanced MRI - DCE-MRI and diffusion-weighted imaging - DWI). These techniques have the advantage of providing much more accurate information about the existence of the residual tumor.

In this sense, in the case of the use of DWI-MRI, the so-called diffusion coefficient that evaluates the diffusion capacity of water at the tissue level is particularly important in evaluating the tumor response to neo-adjuvant radiochemotherapy. This coefficient is inversely proportional to tissue cellularity. Usually, viable tumor cells prevent the diffusion of water to the tissues, while necrotic tumor cells allow the diffusion of water at this level [82, 83]. The diffusion coefficient is also particularly useful in differentiating viable tumor tissue from inflamed areas, respectively necrosis areas. Thus, some authors consider that the value of this coefficient has predictive value in terms of response to neo-adjuvant radiochemotherapy of these patients [84].

DCE-MRI can provide important information about the vascularization of the tumor, the permeability of these vessels, as well as about the structure of the extracellular space. Also, this method has the possibility to identify the areas of hypoxia as well as the intensity of the microvascularization at the level of the tumor formation, both from a quantitative and a qualitative point of view. In this regard, there are studies in the literature that have shown that the existence of increased vascular permeability in the tumor before initiating neo-adjuvant radiochemotherapy is associated with a good therapeutic response, in these cases. Other authors have also shown that the existence of mucin at the level of the tumor formation is associated with a poor therapeutic response in these cases [84–87].

The major advantages of using MRI in evaluating the clinical response to neo-adjuvant radiochemotherapy are represented on the one hand by highlighting the

morphological changes that occur at the level of the rectal tumor (size, vascularity, structure) as well as the changes that occur in the pelvic lymph nodes. The limiting factor that may influence the accuracy of the method in these cases is the occurrence of local fibrosis after radiotherapy or post irradiation proctitis [88].

2.5 The utility of MRI in the postoperative follow up of the patients with rectal cancer

Local recurrence occurs in approximately 30% of patients operated for rectal cancer. Early identification of local recurrence in these patients is of particular importance both for the therapeutic management of these patients as well as for their long-term prognosis [89]. Local recurrence is characterized by the appearance of a tumor formation at the level of the anastomosis, at the level of the operating bed or at the level of the pelvic lymph nodes. At the time of local recurrence, only about 20% of these patients are still suitable for surgical treatment [90].

Although currently the most used imaging method in postoperative follow-up of patients with operated rectal cancer is abdomino-pelvic CT scan, recently there are more and more studies in the literature that recommend performing abdominal-pelvic MRI in these patients. Those who promote this method are based on the fact that in the detection of pelvic neoplasms, the specificity and sensitivity of pelvic MRI in differentiating areas of fibrosis from tumor recurrence is much higher than pelvic CT scan [91, 92]. At the same time, it has been shown that, in the case of small liver metastases, abdominal MRI has a better detection rate compared to abdominal CT. Also, another argument for the utility of pelvic MRI in these cases is given by the fact that, compared to the pelvic CT, MRI offers a much better spatial resolution, and can also provide functional information (tissue diffusion, local vascularization) [93]. Recent studies have shown that when using diffusion-weighted MRI (DWI-MRI) there is the possibility of identifying tumor recurrence, in these cases, faster than when using conventional MRI techniques or when using abdominal CT [94, 95].

3. Conclusions

The pelvic MRI examination has a special utility both in the preoperative evaluation of the patients with rectal cancer and in the postoperative follow-up of these patients. Nowadays, this method represent the “gold standard” imagistic method in the evaluation of these patients.

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