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ORIGINAL RESEARCH ARTICLE

Colorectal cancer staging with magnetic resonance imaging

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ABSTRACT

Colorectal cancer is the fourth leading cause of death worldwide and the fifth leading cause of cancer death in Colombia. Magnetic resonance imaging is the ideal modality for the evaluation of colorectal cancer, since it allows staging by determining invasion beyond the muscularis propria, extension towards adjacent organs, identification of patients who are candidates for chemotherapy or pre-surgical radiotherapy and planning of the surgical procedure. The key point is based on the differentiation between T2 and T3 stages through the use of sequences with high-resolution T2 information. In addition to this, it allows the assessment of the size and morphology of the lymph nodes, and considerably increases the specificity for the detection of lymph node involvement. MRI is a technique with high specificity and high reproducibility.

Keywords: Magnetic Resonance Imaging; Colon Neoplasms; Rectal Neoplasms; Staging of Neoplasms

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1. Introduction

Colorectal cancer is the fourth leading cause of cancer death worldwide[1,2]. In Colombia, its frequency has been increasing and it is currently the fourth type of neoplasm with the highest incidence and the fifth cause of cancer death[2-4].

MRI was first introduced for the evaluation of rectal cancer in 1986[5-7] and is currently considered the ideal technique for the evaluation of the pelvis in patients with rectal cancer[8-12]. This imaging modality is based on visualization in multiple planes, as well as on images with high contrast of soft tissues[13,14], which allow local staging by identifying invasion beyond the muscularis propria; in addition, it classifies patients who are candidates for chemotherapy or pre-surgical radiotherapy and helps in the planning of the surgical procedure[15,16]. It is a reliable technique, with good reproducibility and high specificity, which reaches 92%, especially for predicting negative resection margins by determining the relationship of the tumor with the resection margin or the commitment beyond the muscularis propria layer[13,15,16]. The presence of tumor or nodule within 1 mm from the resection margin increases the risk of recurrence[15].

The advantage of magnetic resonance lies in the use of sequences that allow an adequate contrast between the tumor and the surrounding soft tissues, which is not possible through the use of other imaging techniques such as computed axial tomography[8,17]. It has been shown that the distance of the tumor to the resection margin is the most important predictor of local recurrence[13,18-21]. It is also the method of

choice for patients who received radiotherapy[22].

High resolution sequences with T2 information are the key for the evaluation of rectal cancer[8,15]. These sequences consist of fine axial images (smaller than 3 mm), obtained orthogonally to the plane of the tumor, with a resolution of 0.5 to 0.8 mm[15]. By means of this sequence it is possible to differentiate between a T2 stage tumor (confined to the rectal wall) and a T3 tumor (with extension beyond the muscularis propria)[10,15]. The evaluation of the involvement and extension towards the lymph nodes continues to be a determining and controversial factor[15]. MRI allows not only the assessment of lymph node size, but also the identification of nodal morphology, which considerably increases the specificity for the detection of lymph node involvement[15].

The sensitivity and specificity of MRI for the detection and staging of rectal cancer depend on the experience of the radiologist[8,10,15,23,24]. In the study by Rafaelsen *et al.*[25], it was shown that the sensitivity in tumor staging for an expert radiologist is 96%, while for a general radiologist it is 77%, and the specificity was 74% and 40%, respectively. The elements that should be assessed in an MRI for primary rectal cancer are the stage, the depth of invasion beyond the muscularis propria and the relationship of the tumor with the mesorectal fascia (**Figure 1**), the presacral fascia (**Figure 2**), the anal sphincter and the walls of the pelvis[15].

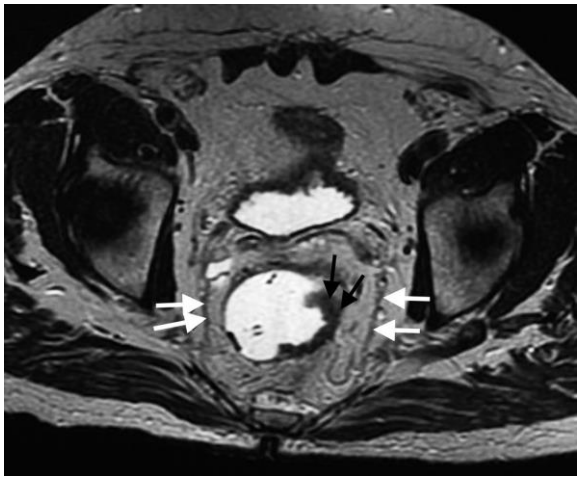

Figure 1. Axial MRI sequence with T2 information. The normal arrangement of the mesorectal fascia is seen on both sides of the pelvis (white arrows) in a patient with a thickening and irregularity of the left lateral wall of the rectum due to a T2 stage colorectal cancer (black arrows).

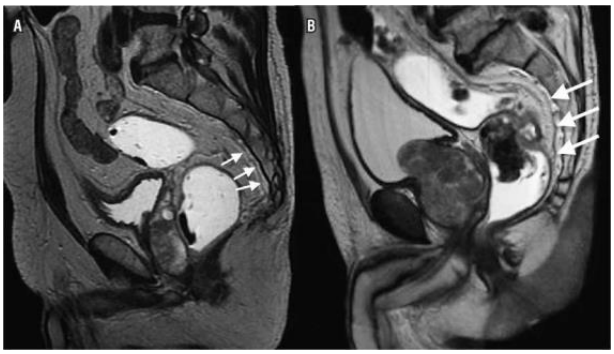

Figure 2. (A) and **(B)** Magnetic resonance sagittal sequence with T2 information. The normal arrangement of the presacral fascia is appreciated (white arrows).

2. Structures to be assessed by magnetic resonance imaging

2.1 Tumor staging (T)

Tumor staging depends directly on its relationship with the muscularis propria and invasion with adjacent organs[8]. A T1 tumor is one that is confined to the mucosa, a T2 tumor is one that extends to the muscularis propria (**Figure 3**), a T3 tumor invades and extends beyond the muscularis propria (early T3 less than 5 mm or advanced T3 greater than 5 mm) (**Figures 4** and **5**) and a T4 tumor is one that invades the pelvic organs (**Figure 6**)[15]. Pelvic vessels, pelvic parietal fascia and mesorectal fascia are not considered organs[8].

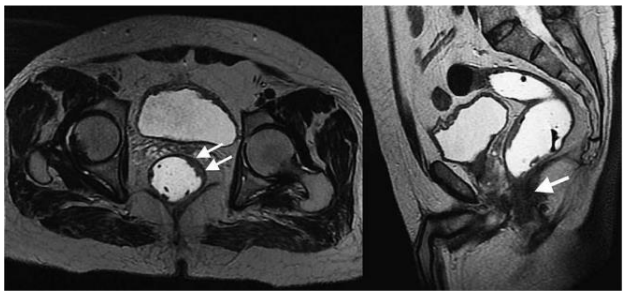

Figure 3. MRI axial sequence with axial T2 information**.** A mass is identified in the anterior wall of the rectum between 12 and 4 o'clock, 7 cm from the anal flange, approximately 40 mm long and 7 mm thick, extending to the muscle, compatible with a T2 stage cancer.

The TNM staging definitions for rectal cancer were taken from the *Radiological Society of North America's standardized MR reporting criteria incorporated into the Radiological Society of North America's radiology reporting template for primary rectal cancer*[26]. Clinicians and radiologists should be aware of the type of TNM classification being used to facilitate interpretation and unify

terms in imaging reports[8].

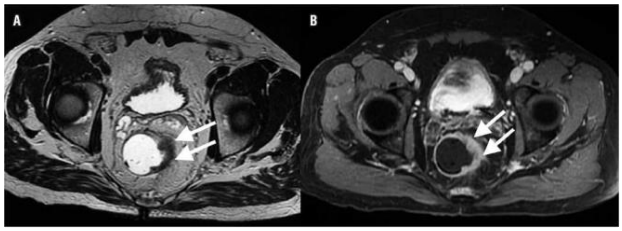

Figure 4. (A) Axial sequence MRI with T2 information and **(B)** axial sequence MRI with T1 information after contrast medium administration. At 7 cm from the anal flange a mass is identified in the left lateral wall of the rectum (white arrows) between 1 and 6 hours, 36 mm long and 9 mm thick, transmural, with a 7 mm component that infiltrates the mesorectal fat between 1 and 3 hours, 21 mm from the mesorectal fascia. There is heterogeneous enhancement after administration of intravenous contrast medium.

80% of rectal tumors are T3 tumor stage lesions, this being a heterogeneous group of lesions that present variable survival rates depending on the extension of the invasion beyond the muscularis propria[15]. T3 stages with invasion of less than 5 mm have a similar survival to T2 tumor stages, which is why they can be grouped together for prognostic and therapeutic purposes[15].

The use of intrarectal contrast is controversial[27]. From 60 to 100 mL of rectal contrast medium can be used, which is composed of ultrasound gel at body temperature, which improves the visualization of polypoid tumors or tumors smaller than 3 cm[15,27]. There is still no consensus on the use of intravenous contrast medium[16,27,28].

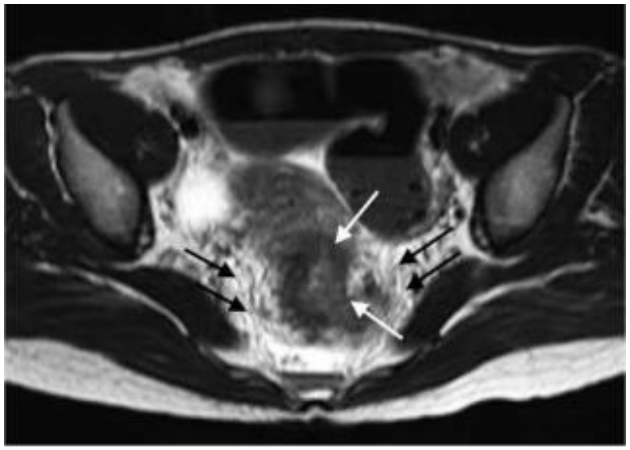

Figure 5. MRI axial sequence with T2 information**.** Mass is identified occupying the entire circumference of the rectum (white arrows), with alteration of the fat and involvement of the mesorectal fascia (black arrows) by tumor extension, associated with tumor ulceration, a finding related to colorectal tumor stage T3a.

To avoid errors due to the partial volume, the images must be obtained in a perpendicular plane to the muscularis muscularis layer[8], recognizing the muscularis propria as a hypointense (black), thin structure that surrounds the rectum[8]. Among the signs that suggest an extension beyond the muscularis propria (advanced T3) (**Figure 5**) are tumor ulceration, a tumor that occupies more than half of the circumference, a tumor with greater longitudinal involvement, lymph node metastases or distant metastases[8].

The demonstration of fat between the tumor and adjacent structures indicates that there is no invasion[8]. The most reliable signs for the detection of invasion are nodular growth towards adjacent organs or ureteral obstruction that generates hydronephrosis[8,29].

Differentiating between stage T2 and T3 lesions is not always easy, since desmoplastic reactions or fibrosis changes generate spiculation of the perirectal fat and it is not always possible to differentiate whether or not there is a tumor component in these lesions, which leads to an overestimation of the staging[14,18,23,30-32]. This situation is particularly important in patients who have been treated with radiotherapy; in this scenario the presence of nodular lesions, unlike spiculation, favors the diagnosis of tumor residue or recurrence over changes due to radiotherapy.

2.2 Relationship of the mass to adjacent structures

The relationship of the tumor with adjacent structures such as the mesorectal fascia, the peritoneal reflection, the pelvic organs, the anal sphincter and the lateral wall of the pelvis must be taken into account[8,15].

2.2.1 Mesorectal fascia

The mesorectal fascia is an anatomical reference point for the diagnostic evaluation of tumor extension[33,34]; this is the most important factor in terms of prognosis[8] since the involvement of the mesorectal fascia increases the risk of local and distant recurrence[8]. The mesorectal fascia corresponds to the visceral layer of the intrapelvic fascia[15]. It composes a distinct anatomical unit by surrounding the rectum and containing the mesorec-

tal fat, nodes and lymphatic vessels[15]. In high-definition images with T2 information, it is visualized as a hypointense image lateral to the rectum (**Figure 1**)[15].

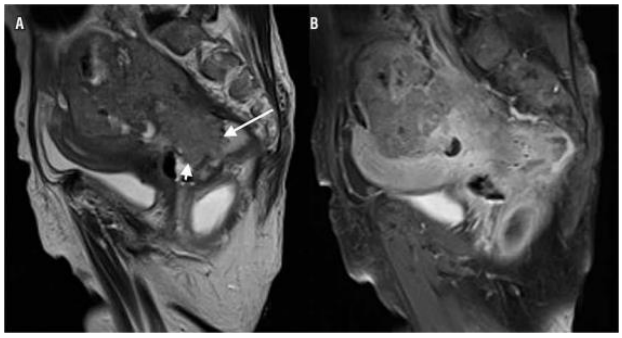

Figure 6. (A) MRI sagittal sequence with T2 information and **(B)** sagittal sequence with T1 information after intravenous administration of contrast medium. Heterogeneous mass involving the wall of the rectum (long white arrow), the vaginal vault (short white arrow) and the posterior wall of the uterus with growth towards the abdominal cavity, which presents heterogeneous enhancement with contrast medium.

The relationship between the mesorectal fascia and the tumor is essential for surgical planning[15]. In histology, a distance greater than 1 mm between the tumor and the resection margin correlates with a lower probability of local recurrence[15,35]. The smaller the distance, the greater the possibility of compromise[8,36]. For this reason, in sequences with high-resolution T2 information, a distance of less than 1 mm between the tumor and the meso-rectal fascia indicates compromise; however, this margin can change according to different centers[8,15,37-39]. This measurement can be taken from any of the following sites: (1) the tumor margin from its extension beyond the muscularis propria; (2) tumor deposits in the mesorectum; (3) tumor thrombus inside a vascular structure or (4) a tumor-like lymph node[8,15].

It should be taken into account that the administration of a rectal enema at the time of the examination with overdistension of the rectum may affect the distance between the tumor and the mesorectal fascia; however, there are no studies that demonstrate that this factor is relevant and instead the use of rectal enema improves the visualization of the lesions[8,40].

2.3 Peritoneal reflection

It is located from the superior aspect of the bladder to the anterior aspect of the rectum, forming the rectovesical sac[15]. In high-definition images with T2 information, it is visualized as a hypointense image in the form of a "V" in axial images[15]. The involvement of this fascia by the tumor causes it to be staged as a T4a stage[15].

2.3.1 Pelvic organs

The pelvic organs most frequently involved in rectal cancer are the uterus, vagina, prostate and seminal vesicles[15]. The assessment of tumor involvement of these structures, as well as of the presacral fascia and the involvement of the sacral nerves, has a significance in terms of surgical planning, especially because the involvement of any of the latter makes the tumor unresectable[15].

2.4 Anal sphincter

The anal sphincter is composed of an internal sphincter of smooth muscle, a continuation of the circular layer of the rectum, and an external sphincter of striated muscle composed of the elenostic vator of the anus and an extension of the puborectalis muscle[15]. The location of the tumor and the anal sphincter must be visualized in coronal images where it is possible to identify the relationship between the superior margin of the puborectalis muscle with the tumor, in order to determine if it is possible to perform a surgical resection[15]. Describing the relationship of the tumor to the anal sphincter is particularly important in cases of tumors involving the distal rectum.

2.5 Lateral wall of the pelvis

The structures of the lateral wall of the pelvis are in close contact with the rectum[15]. The common, external and internal iliac arteries and veins; the ureters, the piriformis and obturator muscle, and the sacral nerves, can be compromised by tumor[15]. The involvement of the mesorectal fascia, at the level of the superior or inferior rectum (sites where its layers cannot be differentiated) implies commitment of the lateral wall of the pelvis[15]. Coronal and sagittal images are recommended for this assessment, especially using high resolution images[15]. The use of enlarged fields of view leads to an underestimation of the proximity of the tumor to the lateral wall and, therefore, an underestimation of the involvement of the lateral wall structures[15].

2.6 Vascular and lymphatic involvement

The assessment of rectal cancer should include not only tumor staging and the involvement of adjacent structures, but also the assessment of determining structures such as lymph nodes and nearby vascular structures.

2.6.1 Vascular invasion

The invasion of vascular structures is not relevant for treatment; however, it plays an important role in terms of prognosis and therefore must be assessed in the images[15]. Perivascular growth is not synonymous with intravascular growth[8].

Identifying invasion in small vascular structures is not simple[15]. The presence of tumor in the lumen of larger vascular structures, such as the superior rectal or middle rectal artery and vein, are indicative findings of tumor invasion[10,15]. Other findings described are nodular growth at the site of extramural growth, proximity of the tumor to the veins or arteries of the pelvis, heterogeneity of the signal intensity inside the vessels or increase in the size of the vessels[8,12,41]. Smith *et al.*[12,41] concluded in their work that when two of these signs are present, the prognosis is similar to when there is vascular invasion evidenced in histology.

2.6.2 Lymph nodes (N)

The lymph nodes play a decisive role in the assessment of rectal cancer since they affect prognosis[8]. The groups that should be evaluated are: mesorectal, superior rectal, inferior mesenteric, common iliac, internal and external, retroperitoneal and superficial inguinal lymph nodes[15]. The presence of lymph node involvement is a prognostic factor for disease recurrence and for the presence of distant metastases[18,42]. The benign or malignant aspect of the lymph node groups must be identified[15]. If any of the lymph nodes are located less than 1 mm from the mesorectal fascia, they should be included in the resection margins to obtain clean margins[15].

The size of the lymph nodes is of limited value in determining the presence of metastasis[8,15]. It must be taken into account that there are micrometastases in normal sized lymph nodes[5,43,44]. A diameter of 5 mm has a sensitivity of 68% and a specificity of 78% to differentiate malignant from benign lymph nodes[8,10,15,45]. This value is not relevant in rectal cancer, since 30% to 50% of lymph nodes with metastasis occur in nodes smaller than 5 mm[15,46,47]; therefore, the morphology of the lymph node, including the margins or contours and internal characteristics (homogeneity), are the key point to determine metastasis[8,10,48-51]. A lymph node with metastatic aspect presents spiculated margins and heterogeneous content[15]. Calcifications inside the lymph node are suggestive of malignancy[8]. Despite this, the problem with relying on morphology is that in larger lymph nodes, it is not possible to differentiate between neoplastic or reactive lymph nodes, and in smaller lymph nodes micrometastases may not be identified (**Figure 7A**)[18]. It should be noted that the sensitivity of magnetic resonance imaging of smaller lymph nodes to differentiate between neoplastic lymph nodes reported in the lithography for the detection of lymph nodes varies between 39% and 95%[5-7,22,52-55].

Contrast medium (gadolinium) has been used for lymph node assessment with studies reporting an accuracy of up to 70% (**Figure 7B**)[5,8]. Heriot *et al.* report a sensitivity and specificity of over 80% for the detection of lymph node involvement when intrarectal antennae are used[22,56].

3. The present and future of preoperative assessment in magnetic resonance imaging

Images with diffusion information can improve the detection of colorectal tumors[15,57]. This sequence can also help in the identification and localization of the tumor, as well as lymph node metastases[15]. The usefulness of the diffusion sequence as a predictor of response to chemotherapy has even been reported, based on ADC values[8,15,58], as shown by Dzik-Jurasz *et al.*, who found that low ADC values predict a good response to treatment[58]. Some authors have reported the usefulness of response considering that a rapid increase in ADC values may precede changes in tumor size[59]. However, it should be noted that there are authors who have not demonstrated changes in accuracy, sensitivity or specificity between T2 sequences and dif-

fusion sequences with respect to tumor staging[27,60]. The major limitation of diffusion sequences is the presence of artifacts originating in intestinal gas, which can hinder their application for diagnosis[15].

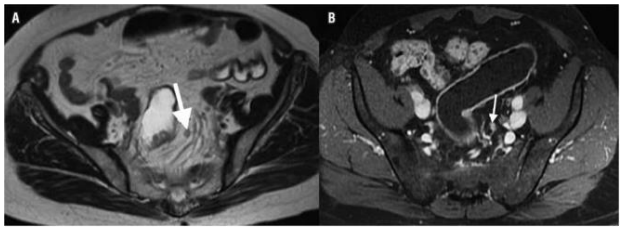

Figure 7. (A) MRI sagittal sequence with T2 information and **(B)** sagittal sequence with T1 information after intravenous administration of contrast medium. A lymph node is identified, rounded, heterogeneous, with apparent spiculated margins, which presents enhancement with intravenous contrast medium (white arrow) related to lymph node with probable micrometastasis.

This sequence can also be used for lymph node assessment; however, the results in rectal cancer have not been fully proven[8]. Hyperintense lymph nodes in the diffusion sequence are considered as metastases[61]. Authors such as Mizukami *et al.* have described a sensitivity of 97% and a specificity of 81%; for this they used magnetic resonance in conjunction with diffusion sequences for the detection of metastatic lymph nodes[61].

4. Assessment of recurrence in magnetic resonance imaging

Tumor recurrence rates range from 70% in the first two years to as high as 85% in three years[62,63]. In cases of recurrence, magnetic resonance allows assessing the extension of the disease, as well as the involvement of adjacent organs[62], with a sensitivity of 80% to 90% and a specificity of up to 100% (**Figure 8**)[62,64-66]. Recurrence can be classified according to the location and involvement of structures in the axial plane (including recurrence at the anastomosis and local recurrence) into: anterior (involves organs located anterior to the rectum in the pelvis such as bladder, uterus, vagina, prostate and/or semi-anal vesicles), posterior (involves structures located posterior to the rectum such as sacrum, coccyx or presacral fascia) and lateral (involves structures located lateral to the rectum such as pelvic wall, iliac vessels, ureters)[62,67].

Post-surgical changes, granulation tissue, residual hematomas, inflammatory changes induced by radiation and neoadjuvant radiotherapy, produce an increase in signal intensity in the sequences with T2 information that can be indistinguishable from a tumor recurrence[62,68]. This increase in signal intensity can persist for up to 2 years after the surgical procedure[62,65]. Because of this, morphologic analysis and contrast enhancement become essentially important to differentiate post-surgical changes from a residual or recurrent tumor. Residual tumor usually has rounded margins while fibrosis causes angular or spiculated margins[62]. In many diagnostic centers it is considered convenient to begin follow-up imaging at least 6 months after surgery or the last radiotherapy session. The use of the diffusion sequence mentioned above demonstrates the benefit for the detection of colorectal cancer[62,64].

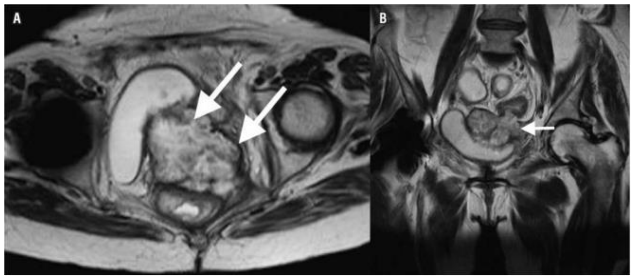

Figure 8. MRI axial sequence with axial **(A)** and coronal **(B)** T2 information. Multiloculated cystic pelvic lesion (white arrows) with thick walls and septa involving the rectal wall, vaginal vault and posterior wall of the bladder, corresponding to a case of a patient with tumor recurrence.

5. Conclusions

MRI is the method of choice for the evaluation of the pelvis in patients with colorectal cancer, since it allows the prediction of negative resection margins, the determination of lymph node metastasis, the involvement of adjacent organs and with the new sequences it can even serve as a predictor of response to chemotherapy management. In addition to these aspects, MRI has a high specificity and high reproducibility, which is why it should be used as the first line for the imaging of rectal cancer, especially when the interpretation of the study is in the hands of an expert radiologist.

Conflict of interest

No conflict of interest is declared during the development of this work.

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