Title: Diagnostic accuracy of MRI in local staging of rectal cancer, and determining the surgical resection margin status; retrospective study. Experience in Oman

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Authors: A. M. A. Al-Hadidi¹, A. Kamona², M. Al Qubtan², J. Al Kalbī², S. Al-Tai³, M. S. al-hanashi⁴, ¹Muscat/OM, ²Muscat/OM, ³Bristol/UK, ⁴Oman/OM
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Aims and objectives

Introduction:

Rectal cancer is one of the most common tumors in industrialized countries and one of the most common malignant tumors of the gastrointestinal tract [1]. Rectal tumor is defined as colorectal tumor which has a distal margin within 15 cm of the anal verge, and these tumors consist around 30%-40% of colorectal cancers [2]. Rectal cancer has a slight male predilection, and its prevalence increases steadily after the age of 50 years. Currently, Magnetic Resonance Imaging (MRI) is the most sensitive and specific modality in staging rectal cancer as it is able to depict the fascia and its relation to the tumor margins precisely [3].

Aims:

In this research, the reliability of MRI in staging rectal cancer is to be examined and its accuracy in determining the mesorectal fascia (MFR) status. Furthermore, the prognostic features of the disease are to be determined by focusing on a subset of patients who had undergone pre-operative CRT or long-course radiotherapy prior to MRI in order to see the effect of the preoperative treatment on the accuracy result of the MRI examination. Discussions of the problem areas, with suggestions to improve overall accuracy are outlined and areas where caution should be exercised are highlighted.
Methods and materials

Inclusion and exclusion criteria:

All medical data of patients who had MRI in the period from 2007 to 2013 who were histopathologically proven rectal cancer with histopathological staging, at the Royal Hospital in Oman, were collected. Any patient with no pre-operative MRI was excluded from the study.

A data of 81 patients who had biopsy proven rectal cancer through colonoscopy were reviewed. Out of the 81 patients, 42 patients either had inoperable rectal cancer, or lost follow up. Only 39 patients were included in the study and met the inclusion and exclusion criteria.

Study population:

From the year 2007 to 2013, we retrospectively reviewed consecutive patients with histological diagnosis of rectal cancer. There were 19 men and 20 women with mean age of 55.21 years (ranging from 26 to 80 years). This study population was subdivided into two groups: the first group included patients who underwent surgery without receiving neoadjuvant therapy (15 patients) and the second group included patients who received neoadjuvant therapy followed by surgery (24 patients). For all patients, MRI examination was performed as part of their staging process before initiating treatment.

Technique:

Bowel preparation, filling of the rectum with contrast agents or air insufflation of the rectum are not recommended in our institution. Intravenous (IV) or intramuscular antispasmodic agents are also not mandatory but can be helpful in improving image quality. IV contrast enhancement with gadolinium is not recommended for the staging of rectal cancer.

MRI was performed with a 3T Philips MRI machine. The patient is positioned comfortably on the back and a phased-array surface coil is placed on the pelvis in such a way that the lower edge of the coil is aligned below the pubic bone. The coil is kept in place with belts and the patient is then advanced head-first into the bore of the magnet.

Sequences:

Initial localization images in the coronal and sagittal planes are needed to plan the images. The first series is the sagittal, T2-weighted, fast (turbo) spin-echo sequence from one pelvic sidewall to the other which enables identification of the primary tumor. The second series consist of large-field-view axial sections of the whole pelvis. The third series consist of the high-resolution images that are T2-weighted thin-section axial
images through the rectal cancer and adjacent tissues. These sequences must be performed perpendicular to the long axis of the rectum and at the level of the tumor (3-mm slices). For patients with low rectal cancers, the fourth series consist of coronal imaging that will optimally show the levator muscles, the sphincter complex, the intersphincteric plane and the relationship to the rectal wall. This sequence is positioned parallel to the longitudinal axis of the anal canal. In our institution, for visualization of more distant lymph nodes, a T1 TSE sequence in axial orientation which covers the entire area up to the aortic bifurcation is used. Diffusion Weighted Images (DWI) with 0, 400 and 800 B factors are routinely performed.

TNM staging:

Assessment of the Primary Tumor

MRI of primary rectal tumors can be used to assess the tumor in terms of T-stage, depth of invasion outside the muscularis propria, relationship to the mesorectal fascia, anal sphincter, and pelvic sidewall, and N-stage.

In our institution, we follow the same MRI criteria for the staging of primary rectal tumors developed by the American Joint Committee on Cancer (tumor-node-metastasis [TNM]) guidelines (Table 1) [4,5]. Figures 1 to 5 show the different T- and N-stages.
**Table 1:** TNM guidelines for staging of rectal cancer

© Adapted from the American Joint Committee on Cancer staging system
Fig. 1: Sagittal T2WI showing a superior rectal tumor confined to submucosa indicating stage T1.

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Fig. 2: Axial (left) and sagittal (right) T2WI showing a large rectal tumor with the origin located at the anterior superior part of the rectum. Even-though the tumor looks large, but the base is not crossing the muscularis propria indicating stage T2.

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**Fig. 3:** Axial (left) and sagittal (right) T2WI showing a rectal tumor which is invading the perirectal fat indicating stage T3

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**Fig. 4:** Upper: Stage T3a tumor with perirectal fat extension of <5mm Middle: Stage T3b tumor with perirectal fat extension of 5-10mm Lower: Stage T3c tumor with perirectal fat extension of >10mm

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**Fig. 5:** Sagittal T2WI showing an upper rectal tumor with invasion of the posterior wall of the uterus indicating stage T4

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Results

For the first group, T stage was correctly determined in 13 out of 15 patients (86.6%) whereas for N stage it was correctly determined in 10 out of 15 patients (66.6%). On the other hand, the second group showed less accurate results. The T stage was correctly determined in 17 out of 24 patients (70.8%) and N stage was correctly determined in 13 out of 24 (54.1%). The status of MRF was also assessed in both groups. In the first group, the status of MRF was correctly assessed in all the patients (100%) with sensitivity of 100% (95% CI: 30.48% to 100%) and specificity of 100% (95% CI: 73.35% to 100%). While in the second group, it was correctly assessed in 17 out of 24 (70.8%) with sensitivity of 100% (95% CI: 40.23% to 100%) and specificity of 65% (95% CI: 40.79% to 84.55%).

Discussion:

T stage/1\textsuperscript{st} group

In first group, the accuracy of the MRI in T staging was 87%, as we failed to correctly stage 2 out of 15 patients. This limitation in T staging was due to over-staging of the two cases from T2 to T3 stage tumors which was attributed to the associated desmoplastic reaction (Fig-6). Our results were in accordance with the data reported in the most of the studies published in the literatures. [6-8]
The most frequent diagnostic error caused by MRI is differentiating T2 from early T3 lesions. This over-staging was often caused by the presence of desmoplastic reaction within the peritumoral tissues that made difficult MRI differentiation between perirectal fat spiculation, caused by fibrosis alone from those containing viable tumor cells [9,11].

T stage/2\textsuperscript{nd} group

Our results showed underestimation in the degree of tumor response to neoadjuvant treatment which led to the inaccurate over-staging of 7 out of 24 patients in the second group with an accuracy rate of about 71%.

A reduction in staging accuracy has been noted which may be as a result of the effects of neoadjuvant treatment due to post-radiation edema, inflammation, fibrosis and necrosis (Fig-7). [10,11,12].

MRF/1\textsuperscript{st} group
Our results showed the high accuracy of MRI in the identification of the Circumferential Resection Margin (CRM) involvement in accordance with many other similar studies. In recent studies, high-spatial-resolution MRI has demonstrated an accuracy of 100% in the identification of CRM involvement. Moreover, this evaluation has shown good reproducibility with complete agreement among those interpreting MR images for the prediction of MRF involvement. This fact indicates that high resolution phased-array MRI is highly accurate in predicting CRM involvement. However, it is less accurate and less consistent in predicting the correct T stage. [3]

**MRF/2nd group**

MRI was highly accurate in the first group, but decreased after neoadjuvant therapy in the second group to 71% which is in accordance with those published in the literature. Indeed, post chemoradiation MRI was not able to discriminate between the fibrotic spiculations in the perirectal fat and spiculations with viable malignant cells at histological analysis [10,11,13].

**N staging, 1st and 2nd groups**

Our results showed that MRI accuracy rate in N staging was low in both groups, achieving 70% and 54% accuracy in the first group and second group, respectively.

The radiologist assessment of nodal involvement generally relies on morphologic criteria such as the size and shape of the node. However, the problem with morphologic imaging is that, with enlarged nodes, it is difficult to distinguish between reactive and metastatic nodes (Fig-8). Also, small nodes micrometastases are easily missed (Fig-9). An additional problem in rectal cancer is the high frequency of micrometastases in normal-sized nodes [11].

Around 30% to 50% of nodal metastases occur in nodes that are less than 5 mm which significantly reduces the accuracy of nodal staging. [14,15].

**Role of DWI in Tumor Staging**

In our study, we found that DWI has an important role in differentiating viable from non-viable tumor at the MRF in the second group. (Fig-10-11).
Fig. 6: Axial (left) and sagittal (right) T2WI showing hyperintensity within the muscularis propria of the rectum, as well as fat stranding. Even-thought the appearance of this tumor is of T3, the histopathological staging came to be stage T2. This finding is due to desmoplastic reaction.

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**Fig. 7:** Axial T2WI of rectal tumor post neoadjuvant treatment showing fibrotic changes in the perirectal fat which is very difficult to differentiate from fat stranding secondary to tumor invasion. This tumor was radiologically over-staged to stage T3. Histopathological staging came to be stage T2.

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Fig. 8: Axial T2WI showing an enlarged perirectal lymph node (9mm) which turned to be a reactive lymph node rather than a metastatic one.

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**Fig. 9:** Axial T2WI showing >5 regional lymph nodes. Non of the lymph nodes measured >4mm. Histopathological staging turned to be N2.

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**Fig. 10:** Post neoadjuvant Axial T2WI (left) showing fat stranding extending from the rectum into the mesorectal fascia anteriorly. Axial DWI (right) show no evidence of restriction at the MRF indicating clear resection margin.

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**Fig. 11:** Axial T2WI (left) and DWI (right) showing a deposit in the left side of MRF which shows diffusion restriction. Histopathological staging showed +ve surgical resection margin for tumor.

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Conclusion

MRI is a valuable tool for the planning of treatment in rectal cancer. It is reasonably accurate, practical, reproducible and a reliable method for pre-operative staging. Despite its known limitations in T-staging, MRI is currently the best available imaging modality that enables highly accurate evaluation of the topographic relationship between lateral tumor extent from the MRF and thus make a prediction about the CRM. Therefore, it is possible to carefully select those patients who will benefit from neoadjuvant therapy and thereby avoiding over- or under-treatment.

With several limitations of MRI in rectal cancer staging, particularly for lymph node staging, it is still increasingly developing and better techniques are implemented. We recommend replacing the sagittal and coronal TSE T2 WI with high resolution sequences to assess the morphology of all the lymph nodes in the pelvic cavity more accurately.

The role of MRI after pre-operative treatment has limitations and more work on functional imaging is recommended which could improve the outcome of the examination in this group of patients, as the DWI in our study showed promising results in 2nd group of patients.
References

1. User's Guide for the Synoptic MRI Report for Rectal Cancerm Canadian Cancer Society