CHAPTER 5

MAGNETIC RESONANCE IMAGING IN RECTUM CANCER STAGING AND EVALUATION OF RESPONSE TO NEOADJUVAN THERAPY

Mehmet Ali İKİDAĞ[1]

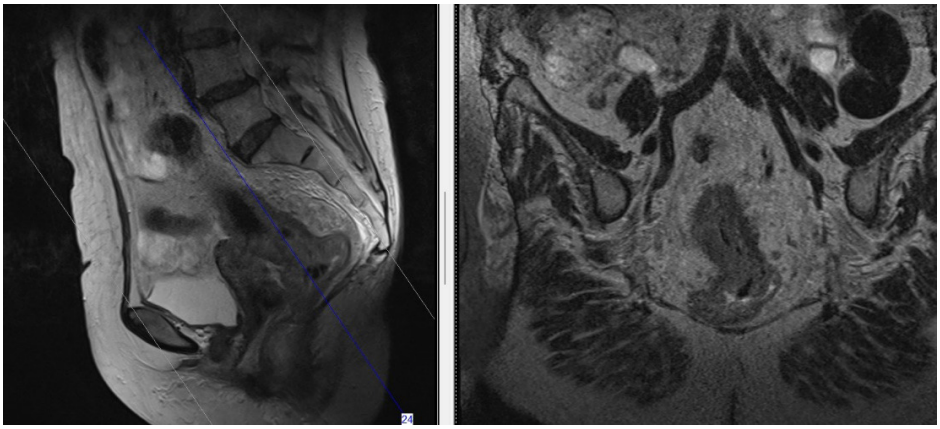
INTRODUCTION

With the developments in surgical and neoadjuvant treatments in rectal cancer, the selection of patients who will be candidates for these treatments is gaining importance. Today, surgical methods such as trans anal excision, trans anal endoscopic microsurgery and trans anal minimally invasive surgery can be applied to low-risk groups, to those who have no lymph node involvement, or no evidence of extramural invasion (1). Magnetic Resonance (MRI) examination is the modality of choice to determine the necessity of neoadjuvant treatment and surgical planning. Radiological TNM classification, extramural venous invasion (EMVI), mucin content in the tumor and mesorectal fascia (MRF) involvement can be determined by MRI.

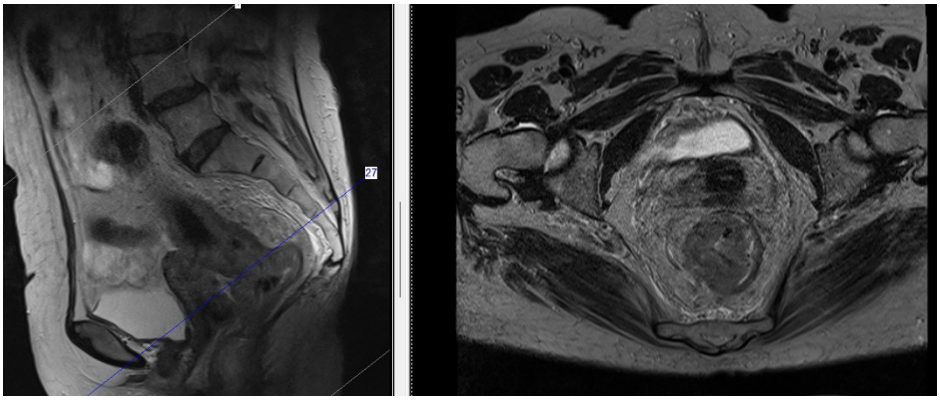
MRI PROTOCOL

According to the 2018 guideline of the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), devices with a magnetic field strength of 1.5 Tesla or higher should be used for imaging rectal cancer (2). After the scout images, T2W sequence should be obtained in the sagittal plane, and the long axis of the tumor should be found over this sequence. High resolution 2D FSE T2W sequences should be obtained in oblique coronal plane parallel to this long axis and in oblique axial plane perpendicular to it (Picture 1,2). Slice thickness should be 3 mm or less, and low field of view (FOV) should be used. Axial diffusion weighed images should be obtained with b≥800 sec/ mm^2. These images are particularly useful for the detection of tumor and lymph nodes in primary staging and restaging after neoadjuvant chemotherapy. In addition to these sequences, it is recommended to obtain T1W images in the axial plane with a wide FOV to evaluate the lymph nodes and bony structures in the pelvic region.

[1] Asst. Prof. , SANKO University Hospital, Department of Radiology, mikidag@hotmail.com



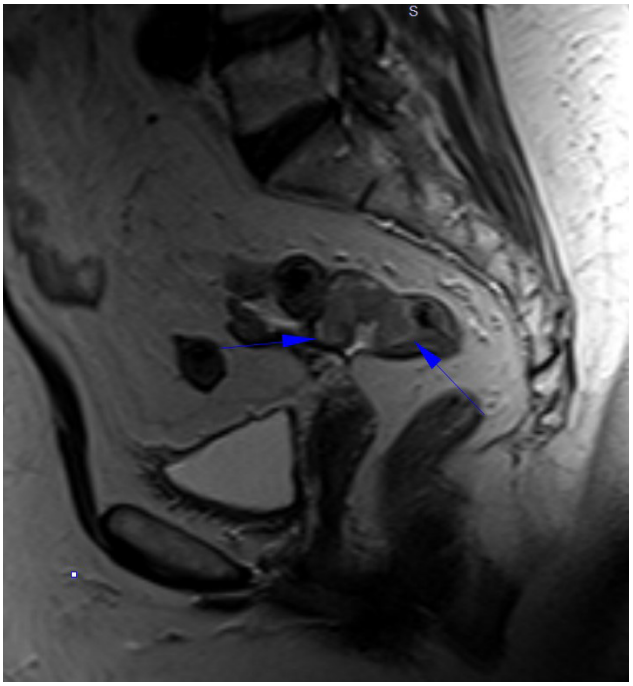
Picture 1: Oblique coronal plane



Picture 2: Oblique axial plane

It has been reported that there is no need to use endorectal coil and fat-suppressed sequences for staging of rectal Ca. Although it has been reported that intravenous contrast agent administration is not necessary, post-contrast images continue to be taken in some centers. Although distension of the rectum with gel and subsequent image acquisition have been suggested, it is not widely used. It should be noted that if more than 60 ml of gel is used, the mesorectal region may be compressed and this may result in misinterpretations. It is also reported that the use of a spasmolytic agent before the examination is beneficial. To determine the relationship of the tumor with the anal canal in distal rectal tumors, it is recommended to obtain thin section images of the anal canal in the coronal plane (2).

In early-stage rectal cancers, it may be difficult to show the primary lesion on sagittal T2W sequence. To determine the location of the tumor, especially in mucinous tumors, planning can be made from T2W hyperintense localizations where there is mucin accumulation. Elevations that may occur at the proximal and distal ends of the tumor can give information about the localization of the tumor (Picture 3).



Picture 3: Elevation at the edges of the tumor localized to the proximal part of the rectum in sagittal T2W image (Arrows).

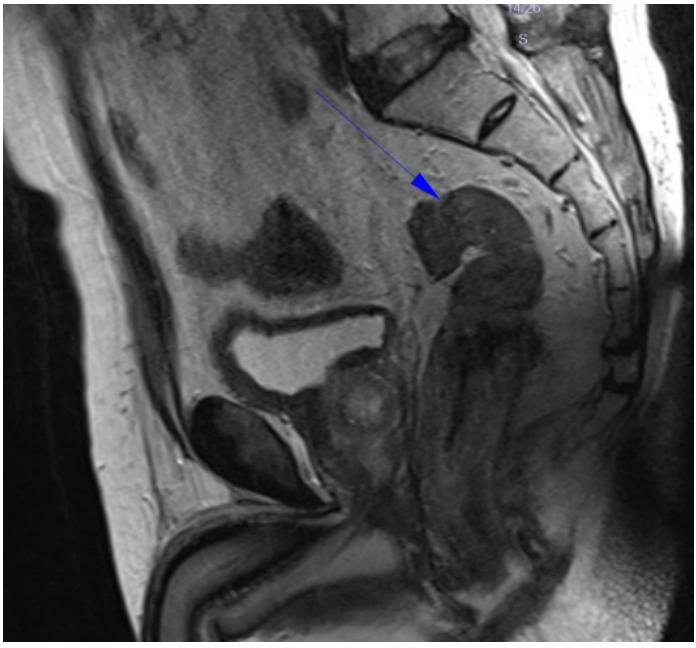
At the ESGAR 2018 meeting, it was recommended to report the findings of the MRI examination as a template. The distance of the tumor from the anal canal, tumor morphology, T staging, anal complex evaluation, nodal staging, evaluation of the circumferential resection margin (CRM), and presence of extramural vascular invasion (EMVI) should be stated in the report (2).

Distance to anal canal and morphology

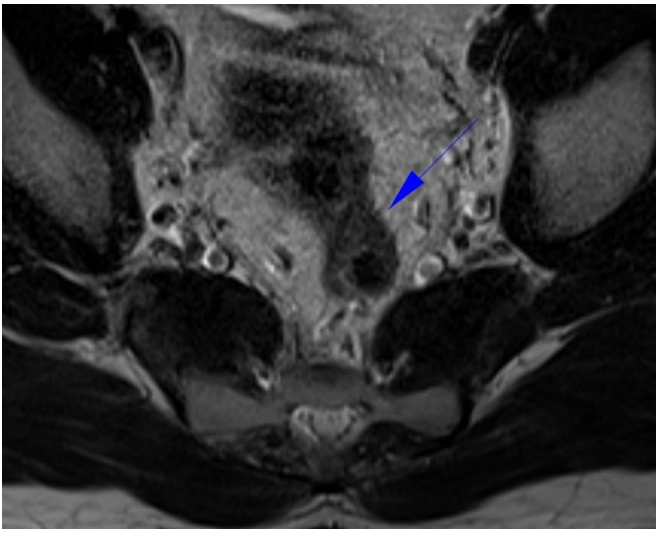
The part of the rectum where the tumor is localized, its distance from the anorectal junction and the size of the long axis of the tumor must be specified. Tumors within 5 cm from the anorectal junction are distal rectum tumors, whereas tu-

mors located in 5 to 10 cm. from anorectal junction are mid-rectal tumors, and tumors located more than 10 cm away from the anorectal junction are proximal rectal tumors. It has been reported that coronal thin section images should be taken parallel to the anal canal in distal rectal tumors, to evaluate the relationship of the tumor with the anal canal.

In proximal rectal cancers, the relationship of the lesion with anterior peritoneal reflection should be evaluated and the presence of anterior peritoneal reflection involvement should be stated in the report. Anterior peritoneal reflection is seen as thin linear structures at the top of the seminal vesicles in men and at the level of the uterocervical junction in women. It is important to determine whether the tumor extends to the sigmoid colon in proximal rectal tumors. Differentiation of the rectosigmoid junction is sometimes difficult. In sagittal T2W images, the point where the rectum moves away from the sacrum and starts to show a horizontal course can be considered as the sigmoid take off point (3). This point can be determined as the point where the superior extension of the rectum ends, and its anterior orientation begins in axial planes (Picture 4,5). Also, the length of the tumor should be specified in images on sagittal planes.



Picture 4: Sigmoid take off in sagittal plane T2W image



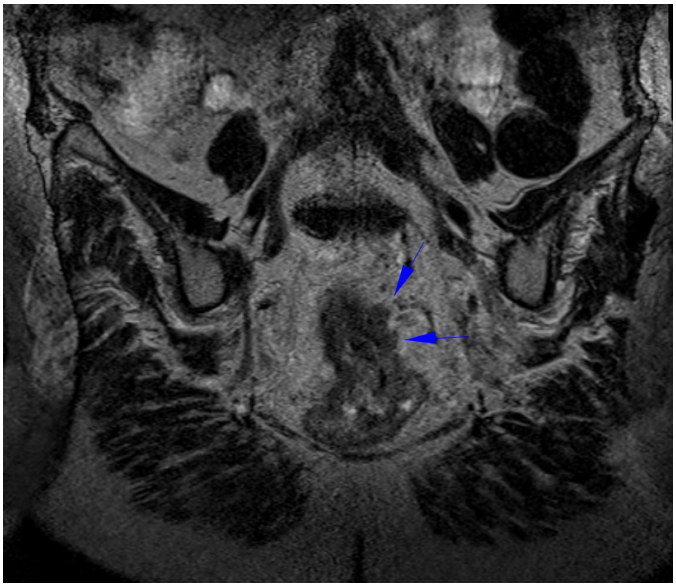
Picture 5: Sigmoid take off in axial plane T2W image

Tumor involvement (circular-semicircular) should be indicated on images in the axial plane. The involved rectum part should be specified according to the clock dial, and whether the lesion contains mucin should be written on the report.

T Staging

Magnetic resonance imaging is a very successful method to show the rectal wall layers. While the mucosa appears hypointense on T2W images, the submucosa appears more hyperintense, especially when edematous, and the muscularis propria appears more hypointense. These features facilitate the evaluation of the extension of the lesion to the mesorectum. If the muscularis propria is intact, the lesion is in either T1 or T2 stage. The biggest limitation of magnetic resonance imaging is to differentiate T1-T2 lesions. Transrectal USG is useful in discriminating T1 and T2 lesions.

Extension of the lesion beyond the rectal wall to the mesorectum is staged as T3. If the extension of the lesion to the mesorectum is less than 1 mm, it is staged as T3a, if it is between 1 mm and 5 mm it is staged as T3b, if it is between 6 mm and 15 mm it is staged as T3c, and if it is more than 16 mm it is staged as T3d (Picture 6). If there is thickening in the anterior peritoneal reflection in superior rectal tumors, the lesion is staged as T4a, and if solid organ involvement is present, the lesion is staged as T4b (Picture 7).

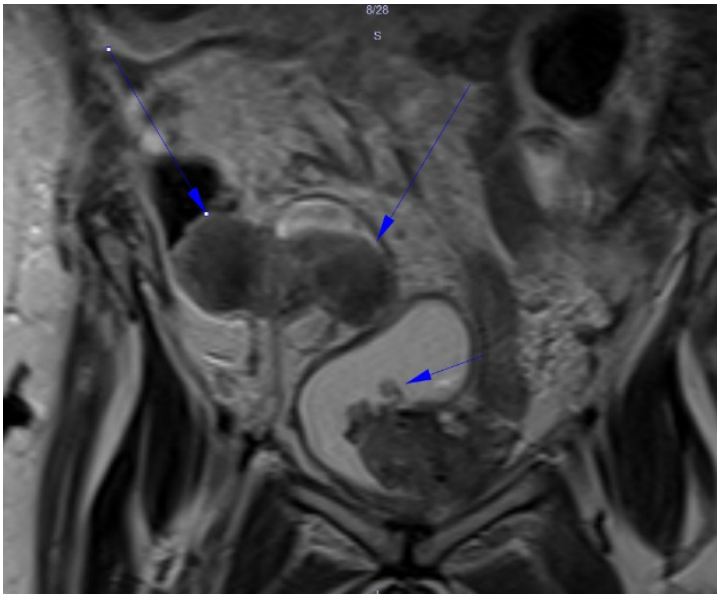


Picture 6: Coronal T2W image shows the extension of the rectal tumor beyond the serosa, into the mesorectal fat planes (T3b).

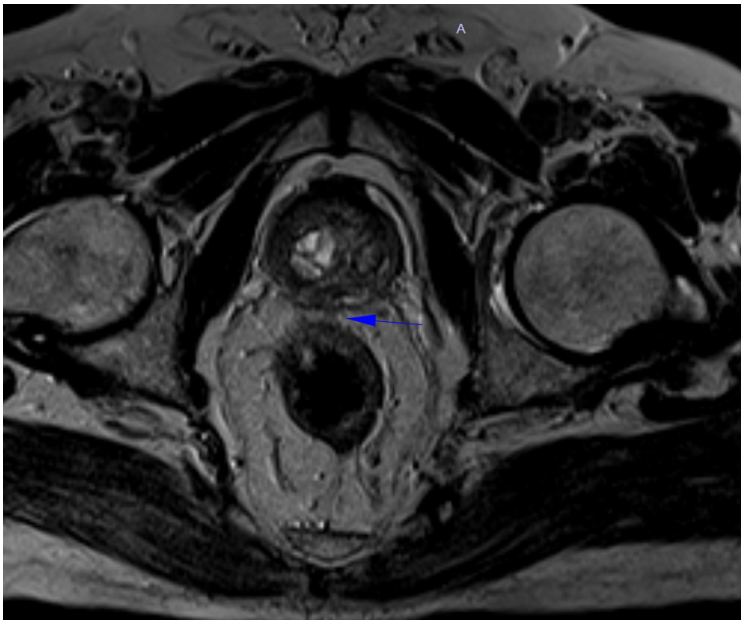
Differentiation of desmoplastic reactions from the primary tumor in the mesorectal planes adjacent to the rectum can be challenging, both at the time of diagnosis and after neoadjuvant therapy. As a rule, rectal tumors are broad-based, while desmoplastic reactions are narrow-based and appear as linear, thin hypointense lines (Picture8) (4).

Evaluation of anal canal invasion

Involvement of anal canal and sphincters changes T staging in rectal cancer. Internal sphincter involvement is seen in T1 and T2 stage tumors, while extension of the lesion to the intersphincteric area is staged as T3, and involvement of the external sphincter is staged as T4b. If anal canal involvement is present, an 'anal positive' note should be added at the end of the radiological staging (5,6).



Picture 7: Rectum tumor bladder invasion (T4b) and right iliac lymph node involvement.



Picture 8: Narrow-based, thin, linear striping indicating desmoplastic reaction in perirectal fat planes.

Evaluation of lymph node involvement

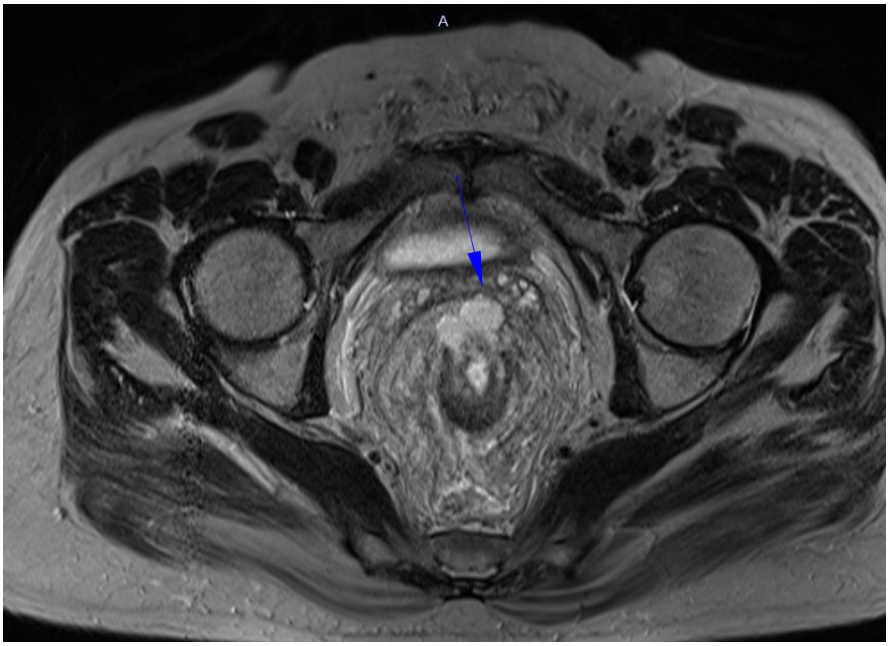
Both size and morphological criteria are used for lymph node staging in rectal cancer. While lymph nodes with a short axis longer than 10 mm are considered as positive, in smaller lymph nodes, it should be evaluated whether the lymph node has a spherical shape, irregular contour or heterogeneous internal structure according to morphological criteria. A lymph node is considered as positive if its short axis is 8 mm and if 2 of the previous mentioned morphological criteria are present. Also, a lymph node larger than 5 mm short axis and having all the 3 criteria are considered as positive. If there are 1 to 3 lymph nodes in the examination area, it is staged as N1, if there are 4 or more lymph nodes, it is staged as N2. For regional lymph nodes, the mesorectum, sigmoid meso, internal iliac, and obturator regions should be evaluated. Involvement of lymph nodes in the external iliac region is considered as M1. Inguinal lymph node involvement in proximal rectum tumors is interpreted as M1, and inguinal lymph node involvement in distal rectum tumors is interpreted as regional lymph node involvement (7).

Evaluation of tumor deposits

Nodular lesions located around the lesion, independent from the main tumor, around the vascular structures are called tumor deposits. These lesions are manifested as a comet sign, especially in coronal sections, and their presence is staged as N1c. Presence of tumor deposits is a poor prognostic factor (8).

Evaluation of the circumferential resection margin (CRM)

Evaluation of mesorectal fascia involvement is important, both in staging and in determining the prognosis. For this reason, the report should indicate whether the tumor infiltrates the mesorectal fascia, approaches the mesorectal fascia up to 1 mm, whether tumor deposits, vascular structures with extramural venous invasion, or lymph nodes infiltrate the mesorectal fascia or approach the mesorectal fascia up to 1 mm. Less than 1 mm distance between the mesorectal fascia and the tumor is considered as positive CRM, and a distance of less than 2 mm is considered as CRM at-risk (Picture 9).



Picture 9: CRM+ tumor on the anterior wall of the rectum, infiltrating the mesorectal fat planes and mesorectal fascia anteriorly (arrow).

Evaluation of extramural venous invasion (EMVI)

Presence of extramural venous invasion is an independent risk factor for local recurrence and poor prognosis. The radiological method with the highest accuracy in determining EMVI is MRI (8-10). It is usually found with T3 and T4 tumors. The proximity of the tumor to the vascular structure should be a suspicious finding in terms of EMVI. Presence of soft tissue signal in the vascular structure, enlargement of the lumen, disruption of the vascular integrity by the tumor are important radiological findings. A positive EMVI tumor and a tumor closer than 1 mm to the mesorectal fascia are considered CRM positive.

EVALUATION AFTER NEOADJUVANT THERAPY

The treatment method of choice in rectal cancer is surgery. However, this method alone is not sufficient, because the incidence of local recurrence is high in patients who only underwent surgery.

The aim of neoadjuvant chemoradiotherapy is to reduce the stage and make the tumor resectable, and to reduce the risk of local recurrence (11). Control MRI should be performed 8 weeks after neoadjuvant therapy, for the regression of in-

flammation and edema occurring in the tissues. Misleading results may occur in MRI examinations that are performed before this period. The purpose of the MRI examination after the treatment is to determine the treatment response and to decide on the surgical approach.

In the MRI examination obtained after treatment, changes in the tumor, mesorectal fascia involvement, lymph nodes, and extramural venous invasion should be evaluated.

Changes in the tumor

The change in the long axis of the lesion in rectal cancer after treatment is determined according to the RECIST criteria. If the tumor shrinks 30% or more, it is defined as partial response, and if there is 20% or more growth, it is defined as progression. If there is no change in the lesion, it is defined as stable disease. A 30% reduction in lesion length corresponds to a 65% reduction in lesion volume. It is emphasized that the most appropriate way to determine the Tumor Regression Degree (TRD) after treatment is to measure the tumor volume in diffusion W images and contrast-enhanced sequences (Picture10) (12).

Morphological changes

Rectal cancer heals with fibrosis after neoadjuvant therapy. Fibrosis is hypointense on T2W images, and iso-hypointense compared to muscle tissue. Desmoplastic reactions can be seen at the level of the lesion after the treatment. Also, T2W hyperintense signal changes can be seen in around the lesion due to edema and submucosal inflammation. It should be noted whether there is necrosis and mucinous degeneration. Three types of mucinous response occur in rectal tumors:

a) In non-mucinous rectal tumors, mucin-containing components may occur in fibrotic areas after treatment. These areas are seen as T2W hyperintense, which means good response to treatment.
b) While solid components regress or disappear after treatment, mucin pools may remain stable, this situation is named as acellular mucin response. It is considered as a good response to treatment.
c) Absence of changes in the mucin compartments before and after treatment is considered as an unresponsive mucinous tumor and is considered as a poor prognostic sign.

The degree of tumor regression after treatment in rectal tumors is shown in Table 1.

Grade	Degree of response	Description
1	Complete	No evidence of treated tumour
2	Good	Dense fibrosis or mucin; no obvious residual tumour
3	Moderate	>50% Fibrosis or mucin and visible intermediate signal intensity
4	Slight	Little areas of fibrosis or mucin; mostly tumour
5	None	Same appearance and signal intensity as original tumour

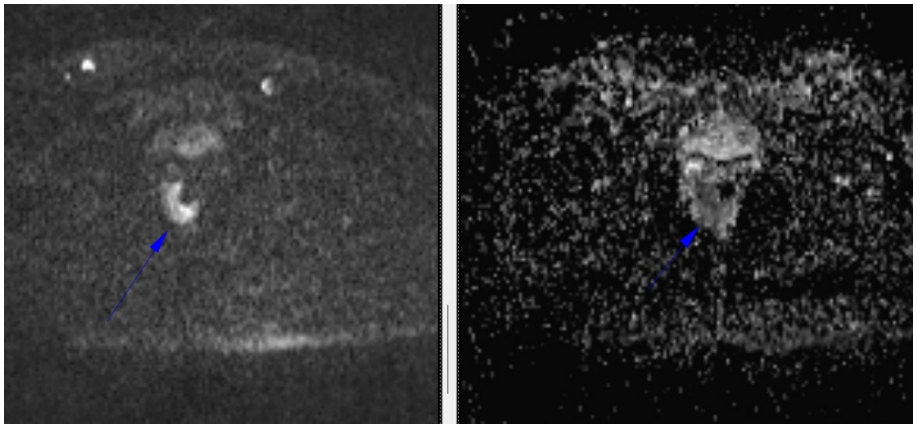
Table1: Tumor regression degree (TRD) after neoadjuvant therapy

Cases with tumor regression degrees 1,2 and 3 are considered to have a good response to treatment, with a higher 5-year survival and a lower recurrence rate.

Cases with tumor regression degrees 4 and 5 are considered as poor response to treatment.

It is emphasized that complete or nearly complete pathological response is important for organ-preserving treatments. While the success of MRI in T staging is higher before treatment (about 85%), it is lower after treatment (about 50%) (13,14).

It has been reported that diffusion W imaging has high sensitivity and specifity in distinguishing post-treatment residual tumor from fibrosis and inflammation (15).



Picture 10: After neoadjuvant chemotherapy, residual tumor is hyperintense in Diffusion W image and hypointense in ADC sequence (arrows).

Evaluation of the mesorectal fascia

Before the treatment, if the distance between the mesorectal fascia and the tumor is less than 1 mm, CRM is positive, if it is less than 2 mm, CRM is considered as at risk. But after treatment, if fatty planes between the tumor and the mesorectal fascia can be distinguished, then CRM should be reported as negative (16).

Evaluation of EMVI

The presence of EMVI is a poor prognostic indicator that affects recurrence and disease-free survival. It may disappear or transform into fibrotic bands after treatment (17).

Nodal involvement

Most of the lymph nodes either disappear or shrink after neoadjuvant chemoradiotherapy. It should be noted that benign lymph nodes may show fibrotic changes and their edges may become irregular. Therefore, morphological criteria are not used in lymph nodes after neoadjuvant therapy. After treatment, lymph nodes with a short diameter less than 5 mm are considered benign, and lymph nodes equal to or larger than 5 mm are considered malignant (18).

CONCLUSION

Correct staging in rectal cancer and correct interpretation of prognostic factors affect treatment selection, success, and recurrence rates. MRI is the method of choice for local staging and surgical planning.

In the evaluation of the treatment response, the distance of the lesion to the anal canal, tumor size, morphological changes in T2 imaging are crucial. Diffusion W imaging should be used as it increases the diagnostic accuracy. In lower rectal tumors, the relationship between the lesion and the anal sphincter must be defined in detail. Morphological criteria should not be considered when evaluating lymph nodes, and it should be decided if the lymph nodes are malignant or benign according to the size criterion, by taking 5mm as a threshold value.

REFERENCES

1. Benson AB, Venook AP, Al-Hawary MM et al. NCCN Guidelines Insights: Colon Cancer, Version 2.2018. *J Natl Compr Canc Netw*. 2018 Apr;16(4):359-369. doi: 10.6004/jnccn.2018.0021. PMID: 29632055.
2. Beets-Tan RGH, Lambregts DMJ, Maas M, et al. Magnetic resonance imaging for clinical management of rectal cancer: Updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. *Eur Radiol.* 2018 Apr;28(4):1465-1475. doi: 10.1007/s00330-017-5026-2. Epub 2017 Oct 17. Erratum in: Eur Radiol. 2018 Jan 10: PMID: 29043428; PMCID: PMC5834554.

3. Bogveradze N, Lambregts DMJ, El Khababi Net al. MRI rectal study group. The sigmoid take-off as a landmark to distinguish rectal from sigmoid tumours on MRI: Reproducibility, pitfalls and potential impact on treatment stratification. *Eur J Surg Oncol*. 2022 Jan;48(1):237-244. doi: 10.1016/j.ejso.2021.09.009. Epub 2021 Sep 20. PMID: 34583878.
4. 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 systematic review and meta-analysis. *Ann Surg Oncol*. 2012 Jul;19(7):2212-23. doi: 10.1245/s10434-011-2210-5. Epub 2012 Jan 20. PMID: 22271205.
5. Shihab OC, Moran BJ, Heald RJ, et al. MRI staging of low rectal cancer. *Eur Radiol* 2009; 19: 643-650 [PMID: 18810451 DOI: 10.1007/s00330-008-1184-6]
6. Lambregts DMJ, Bogveradze N, Blomqvist LK, et al. Current controversies in TNM for the radiological staging of rectal cancer and how to deal with them: results of a global online survey and multidisciplinary expert consensus. *Eur Radiol*. 2022 Mar 7. doi: 10.1007/s00330-022-08591-z. Epub ahead of print. PMID: 35254485.
7. Betge J, Harbaum L, Pollheimer MJ, et al. Lymph node retrieval in colorectal cancer: determining factors and prognostic significance. *Int J Colorectal Dis*. 2017 Jul;32(7):991-998. doi: 10.1007/s00384-017-2778-8. Epub 2017 Feb 16. PMID: 28210855; PMCID: PMC5486641.
8. Brown G, Radcliffe AG, Newcombe RG, et al. Preoperative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. *Br J Surg*. 2003 Mar;90(3):355-64. doi: 10.1002/bjs.4034. PMID: 12594673.
9. Betge J, Pollheimer MJ, Lindtner RA, et al. Intramural and extramural vascular invasion in colorectal cancer: prognostic significance and quality of pathology reporting. *Cancer*. 2012 Feb 1;118(3):628-38. doi: 10.1002/cncr.26310. Epub 2011 Jul 12. PMID: 21751188.
10. Smith NJ, Barbachano Y, Norman AR, et al. Prognostic significance of magnetic resonance imaging-detected extramural vascular invasion in rectal cancer. *Br J Surg*. 2008 Feb;95(2):229-36. doi: 10.1002/bjs.5917. PMID: 17932879.
11. Horvat N, Carlos Tavares Rocha C, Clemente Oliveira B, et al. MRI of Rectal Cancer: Tumor Staging, Imaging Techniques, and Management. *Radiographics*. 2019 Mar-Apr;39(2):367-387. doi: 10.1148/rg.2019180114. Epub 2019 Feb 15. PMID: 30768361; PMCID: PMC6438362.
12. Hötker AM, Tarlinton L, Mazaheri Y, et al. Multiparametric MRI in the assessment of response of rectal cancer to neoadjuvant chemoradiotherapy: A comparison of morphological, volumetric and functional MRI parameters. *Eur Radiol*. 2016 Dec;26(12):4303-4312. doi: 10.1007/s00330-016-4283-9. Epub 2016 Mar 5. PMID: 26945761; PMCID: PMC5203699.
13. Petrillo, A., Fusco, R., Petrillo, M. *et al.* DCE-MRI time–intensity curve visual inspection to assess pathological response after neoadjuvant therapy in locally advanced rectal cancer. *Jpn J Radiol* **36,** 611–621 (2018). https://doi.org/10.1007/s11604-018-0760-1
14. Barbaro B, Vitale R, Leccisotti L, et al. Restaging locally advanced rectal cancer with MR imaging after chemoradiation therapy. *Radiographics*. 2010 May;30(3):699-716. doi: 10.1148/rg.303095085. PMID: 20462989.
15. van der Paardt MP, Zagers MB, Beets-Tan RG, et al. Patients who undergo preoperative chemoradiotherapy for locally advanced rectal cancer restaged by using diagnostic MR imaging: a systematic review and meta-analysis. *Radiology*. 2013 Oct;269(1):101-12. doi: 10.1148/radiol.13122833. Epub 2013 Jun 25. PMID: 23801777.
16. Gollub, M.J., Lall, C., Lalwani, N. *et al.* Current controversy, confusion, and imprecision in the use and interpretation of rectal MRI. *Abdom Radiol* **44,** 3549–3558 (2019). https://doi.org/10.1007/s00261-019-01996-3
17. Chen, S, Li, N, Tang, Y. *et al.* The prognostic value of MRI-detected extramural vascular invasion (mrEMVI) for rectal cancer patients treated with neoadjuvant therapy: a meta-analysis. *Eur Radiol* **31,** 8827–8837 (2021). https://doi.org/10.1007/s00330-021-07981-z
18. Pangarkar, S., Mistry, K., Choudhari, A. *et al.* Accuracy of MRI for nodal restaging in rectal cancer: a retrospective study of 166 cases. *Abdom Radiol* **46,** 498–505 (2021). https://doi.org/10.1007/s00261-020-02708-y