Accuracy of 3T MRI for local staging and extramural vascular invasion assessment in rectal cancer with pathological correlation

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Aims and objectives

Accordingly to the data of Kazakh Scientific Research Institute of Oncology and Radiology, in Kazakhstan rectal carcinoma (RC) keeps the 8th position in cancer morbidity rate (4.5% or 8.2 cases per 100,000 of population), and the 8th position in cancer-related mortality rate as well (4.7%) [1]. Despite the fact that these indexes are lower comparing with the similar data from developed countries (the forth most frequently diagnosed cancer, and the second leading cause of cancer-related death [2,3]), growing morbidity rate, especially in population younger than 50 years old, requires thorough management approach. The role of high-resolution magnetic resonance imaging (MRI) in RC management has evolved greatly, due to its ability to accurately evaluate the depth of tumor invasion, mesorectal fascia and sphincter involvement. Up to the current moment, there are a lot of international scientific papers were published, reporting accuracy rates for 3 tesla MRI systems in rectal cancer staging [4-8]. As tumor epidemiology, phenotype, frequency of different pathology subtypes can vary in different parts of the world, we tried to summarize diagnostic accuracy and predictive value of 3T MRI in RC staging on Central Asia patients population.

The purposes of this study are (i) MR-imaging staging of rectal carcinoma and correlation with pathology results; (ii) assessment of the diagnostic accuracy and predictive power of 3 tesla MRI for extramural vascular invasion in RC.
Methods and materials

Patients

This study included 86 patients (46 men, 40 women, mean age 61.7±12.9 years) with a new diagnosis of rectal carcinoma established on site at the Kazakh State Institution of Oncology and Radiology, between January 2015 and June 2018. The study was approved by the institutional review board. The inclusion criterion was a new diagnosis of path-proved rectal carcinoma below the sacral promontorium with no gender or age predilection.

MRI technique

MRI was performed using a 3.0-T system pre-operatively (GE Discovery MR750w, USA), utilizing a pelvic phased-array surface coil (Gem body coil 8ch.). T2-weighted turbo-spin echo (TSE) sequences in sagittal, paracoronal, and para-axial planes were used. Slice thickness was 3 mm without gap, field of view 26 cm, matrix 320x320.

Image analysis

The MRI data were assessed by two radiologists with 5 and 15 years of experience in oncology imaging respectively. MRI reporting criteria for T staging of rectal carcinoma were listed as standard and described elsewhere [5,6]. Briefly, the tumor confined to only to submucosa is considered as T1, with involvement of muscular layer but sparing perirectal fat (PF) as T2, with PR invasion as T3, and extension to other pelvic organs or distant metastases as T4. Images were assessed for infiltration of the rectal wall layers, perirectal fat and pelvic structures, and for the evidence of extramural vascular invasion. The mesorectal fascia was regarded as intact at a distance from the tumor margin or involved mesorectal lymph nodes> 2 mm; a possible invasion of 1-2 mm, and is considered as an involved in the process at a distance #1 mm [10,11]. Extramural vascular invasion was assessed as the part of the standard MR protocol [12-16]. EMVI was divided as the involvement of large vessels (more than 3 mm) and small vessels (less than 3 mm in diameter).

Histopathology evaluation

All patients underwent surgery; 71 out of total 86 patients underwent preoperative neoadjuvant therapy consisting of radiotherapy and/or chemotherapy. In all 86 patients, histological examination and pathological staging was performed on the surgical specimens through conventional pathology examination. Pathological staging was
carried out according to TNM criteria [3,4]. The pathologist with 20 years' experience examined the specimen blinded to the preoperative radiological staging.

**Statistical analysis**

Correlative analysis of MRI and histopathological findings was performed. The sensitivity, specificity, and accuracy were calculated [17,18]. The MRI data were assessed by two radiologists with 5 and 15 years of experience in oncology imaging respectively. Interobserver agreement was assessed using Cohen's Kappa coefficient. Agreement was defined as substantial (0.78) for T staging, and for extramural vascular invasion assessment (0.63).
Results

Evaluation of tumor staging according to MRI data in comparison with histopathological data

The results of preoperative MRI staging and postoperative pathology T-staging are presented in Table 1.

The discrepancy between the MR and pathological staging was noted by us in 16 cases out of 86. An analysis of the discrepancy between the results is shown in Table 2.

There were following cases of overdiagnosis (reassessment of the stage) of the process according to MRI (see table 2):

- In one case, on the pathomorphological data, the Tis stage was registered - villus adenoma with intramucosal foci of adenocarcinoma; on MRI there were diagnosed polypoid lesion of the lower ampullar rectus, T2 st.

This case can be considered as a casuistry, rarely observed in everyday practice; the recognition of the Tis stage lies outside the diagnostic capabilities of the MRI. In its turn, when visualizing polypoid lesion, it is difficult to judge only on the basis of MRI data about the benign or malignant nature of a tumor. Rather, this case illustrates that the polypoid and infiltrative tumors of the rectum should be considered as stages of one process, and preferably all polypoid formations are considered as potentially malignant.

- In five cases, MRI overestimated the involvement of adjacent pelvic organs with fibrosis after neoadjuvant therapy, pathomorphology excluded the invasion of adjacent organs (T4 stage lowered to T3).

This problem is often mentioned in similar studies and is mentioned in all similar studies we examined [5,6, 19-20]. Post-radiation fibrosis, as a rule, is present in patients with a primary verified T3 stage, makes it difficult to determine the exact boundaries of the tumor process and pre-operative re-staging. A possible solution to this problem is the use of DWI with a sufficiently high b-factor [21, 22], application of additional contrast series [4, 11], as well as the use of additional to the standard protocol thin-cutting (1-2 mm) 3D T2-series [20].

Underestimation (hypodiagnosis) of the tumor stage:

- According to the MRI data, we concluded T1 stage, while pathomorphology revealed the focus of invasion in the muscle layer and T2 stage has been verified - 2 cases;

- The cT2 stage is verified as pT3a (pathologically verified spread beyond the intestinal wall by 1-2 mm) - 3 cases;
The cT3 stage was considered in pathomorphology as pT4 (4 cases) - in patients after neoadjuvant CRT.

Difficulties in recognizing the T1-T2 stage are often mentioned in the literature, especially in early studies based on 1.5 T MRT data [10,11]. Although most researchers do not notice significant differences in the sensitivity and specificity of the 1.5T and 3T MRI in the staging of rectal cancer, for 3T MRI, a higher sensitivity in the differentiation of the submucosal layer and the muscular wall was established, and consequently, recognition of the T1 and T2 stages of the process [20, 23, 24]. In our study, for T1 and T2 stages, sensitivity and specificity for the T1 stage, 100% and 97.5%, respectively (table 3).

Sensitivity, specificity and diagnostic accuracy [17, 18], 3T MRI for different T-stages of colorectal cancer obtained in our work are presented in Table 3.

Mistakes in the separation of T2 and T3a stages (limited spread beyond the limits of muscularis propria plate to mesorectal tissue) due to desmoplastic reaction and postradiation fibrosis, are also often mentioned in publications, constituting one of the main reasons for the decrease in the sensitivity and specificity of MRI for these stages of the process [4,6, 8, 11, 20]. In this case, the sensitivity for the T3 stage in these sources varies from 71 to 83%, and the specificity is 20-76%. In our study, the sensitivity and specificity for T3 was 87.1% and 92.1%, respectively, for the T2 stage - 81.3% and 94.5% (table 3).

Despite the generally recognized limitations of MRI in the separation of T2 and T3a, a small clinical significance of this fact is noted, due to the of the same therapeutic approach to these patients adopted in the most countries (a short neoadjuvant dose of radiotherapy and surgical intervention, the type of which is determined by the tumor localization).

**Extramural vascular invasion (EMVI)**

EMVI was identified in 14 patients (16.2%) out of 86, Fig. 1-2. Estimated diagnostic accuracy for EMVI as compared with tumor endovascular emboli evidence on pathology was 93%.

8 (57%) of patients with pathology verified EMVI were diagnosed local T3 stage by MRI (with or without mesorectal fascia involvement). 5 (35.7%) were proved to have T4 stage. Only one (7.3 %) - had no evidence of perirectal fat involvement.

Thus, according to our data, EMVI was diagnosed in 20,5% cases of MRI- evidence of local T3 stage (8 out of 39 cases). During further short time follow-up (within two weeks after primary MRI), distant liver metastases were detected in 6 out of 8 patients with EMVI and local T3 stage on MRI (75%). To compare, among the rest 31 patients with MRI proved local T3 without evidence of EMVI only 4 had distant metastases (12,9%).
Previously, extramural vascular invasion was assessed only with a pathomorphological study [12]. Currently, MRI makes it possible to clearly differentiate EMVI as a proven important risk factor for early recurrence, tumor aggressiveness, its sensitivity to neoadjuvant chemoradiotherapy [12, 13]. EMVI is associated with poor prognosis of the course of the disease and as a result - low overall survival of patients [12, 15-16].

The sensitivity and specificity of MRI detection of EMVI reported by Smith NJ et al. in 94 patients undergoing primary surgery were 62 and 88 per cent respectively [12]. Thus, MR-EMVI can be used as a potential biomarker that facilitates the choice of a method of treatment [12,13]. Sohn B et al. showed that EMVI detected by MRI serves as an independent risk factor for the detection of distant synchronous metastases in a primary examination of the patients, therewith the involvement of large vessels (more than 3 mm) is associated with a higher risk in comparison with small vessels (less than 3 mm in diameter) [13]. Similarly, Barbaro B et al. showed the relationship of EMVI and risk of synchronous metastases in patients with a non-mucinous form of adenocarcinoma [15].
Table 1: Correlation of MRI and pathology staging

<table>
<thead>
<tr>
<th>Pat</th>
<th>Tis</th>
<th>T2</th>
<th>MRI T3</th>
<th>T4</th>
<th>FN</th>
<th>Total Pat</th>
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<tr>
<td>Tis</td>
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<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>T1</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
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<td>2</td>
<td>13</td>
<td>1</td>
<td>-</td>
<td>16</td>
</tr>
<tr>
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<td>-</td>
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<td>5</td>
<td>42</td>
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<td>TN</td>
<td>81</td>
<td>69</td>
<td>47</td>
<td>61</td>
<td>-</td>
<td>86</td>
</tr>
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</table>

MRI-stage according to 3T MRI, Pat – pathomorphology data
TN - true negative
FN – false negative, FP – false positive

Table 2: The analysis of the discrepancy between the MRI and pathology staging

<table>
<thead>
<tr>
<th>3T MRI</th>
<th>Pathomorphology</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overstaging</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>Tis</td>
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</tr>
<tr>
<td>T4</td>
<td>T3</td>
<td>5</td>
</tr>
<tr>
<td>T3</td>
<td>T2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Understaging</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>T2</td>
<td>2</td>
</tr>
<tr>
<td>T2</td>
<td>T3</td>
<td>3</td>
</tr>
<tr>
<td>T3</td>
<td>T4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>16</td>
</tr>
</tbody>
</table>

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Table 3: Sensitivity, specificity and diagnostic accuracy of 3T MRI for different T-stages of colorectal cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
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<tbody>
<tr>
<td>T1</td>
<td>100%</td>
<td>97.5%</td>
<td>97.6%</td>
</tr>
<tr>
<td>T2</td>
<td>81.3%</td>
<td>94.5%</td>
<td>92.1%</td>
</tr>
<tr>
<td>T3</td>
<td>87.1%</td>
<td>92.1%</td>
<td>89%</td>
</tr>
<tr>
<td>T4</td>
<td>83.3%</td>
<td>92.4%</td>
<td>90%</td>
</tr>
<tr>
<td>Average value</td>
<td>87.9%</td>
<td>94.1%</td>
<td>92.2%</td>
</tr>
</tbody>
</table>
Fig. 1: Patient S., 63 years old, adenocarcinoma of the lower ampullar rectus, T3a with extramural vascular invasion

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Fig. 2: Patient A., 50 years old, adenocarcinoma of the mid-rectum, pathology verified non-mucinous adenocarcinoma G2, stage T3a. Extramural vascular invasion with small vessels (less than 3 mm diameter) involvement.

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Conclusion

3T MRI imaging enables to achieve high levels of diagnostic accuracy in local rectal cancer staging, including assessment of mesorectal fascia infiltration. The reasons over- or underestimation of all the stages were analyzed and compared with the results of similar studies. High-resolution MRI can clearly differentiate EMVI-status with high accuracy as well, evaluating this important risk factor for early recurrence and tumor aggressiveness.
References


