THE VALUE OF MAGNETIC RESONANCE IMAGING IN ASSESSING THE CIRCUMFERENTIAL RESECTION MARGIN OF RECTAL CANCER

Pham Hoang Ha[1,2,✉], Nguyen Minh Trong[3]
Nguyen Xuan Hung[4], Pham Quang Thai[1,2]
[1]Viet Duc University Hospital
[2]University of Medicine and Pharmacy, Vietnam National University
[3]National hospital for tropical diseases
[4]Hong Ngoc Hospital

This study evaluated the value of magnetic resonance imaging (MRI) in assessing the circumferential resection margin (CRM) and lymph node metastasis in rectal cancer. This cross-sectional study, conducted at Viet Duc University Hospital between October 2016 and May 2019, involved 109 rectal cancer patients, who underwent rectal resection after receiving pre-operative MRI staging. The correlation between preoperative MRI and postoperative histological analysis was evaluated regarding CRM invasion, the distance from the tumor or metastatic lymph node to the mesorectal fascia, the tumor stages (≤ T3, > T3), and lymph node metastasis. MRI had an accuracy of 86.2% in predicting invasive CRM with a sensitivity of 65.0%, a specificity of 91.0%, a positive diagnostic value of 61.9%, and a negative diagnostic value of 92.1%. Regarding the diagnosis of metastatic lymph nodes, MRI showed an accuracy of 50.5%, a sensitivity of 88.6%, and a specificity of 24.6%, the positive diagnostic value was 44.3%, while the negative diagnostic value was 76.2%. These results indicate a strong correlation between the performance of MRI and pathology for diagnosis of CRM invasion. When detecting metastatic lymph nodes, MRI exhibited higher sensitivity at the expense of lower specificity.

Keywords: Rectal cancer, Circumferential resection margin, Magnetic resonance imaging, Lymph node metastasis.

I. INTRODUCTIONS

Rectal cancer (RC) is the third most frequently diagnosed cancer worldwide, and the status of its circumferential resection margin (CRM) is of paramount significance for treatment strategies and prognosis.[1] With the introduction of new treatment approaches like preoperative radiotherapy and total mesorectal excision, there has been an increasing demand for precise imaging tools to preoperatively identify various rectal cancer patients. In 1986, Quirke first described the concept of the circumferential resection margin (CRM) of the rectum and observed a correlation between local recurrence and lateral invasion of rectal adenocarcinoma tumors.[2]

CRM in rectal cancer is characterized as the non-peritonealized surface of a resected specimen, resulting from the dissection of the subperitoneal aspect during surgery.[3] The minimal distance between the tumor or metastatic lymph node and the CRM was used to assess the tumor invasion.[2] A CRM is

Corresponding author: Pham Hoang Ha
Viet Duc University Hospital
Email: Hadrvd@gmail.com
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considered positive (+) when this distance is equal to or less than 1mm, indicating potential tumor invasion. On MRI, the presence of a positive CRM ranged from 7.3% to 25% and serves as an independent predictor of local recurrence.[3] In a study conducted by Wibe et al. the assessment of CRM was reported for 686 patients undergoing total mesorectal excision surgery. The study found that patients with a positive CRM (+) had a local recurrence rate of 22%, whereas those with a negative CRM (-) had a lower rate of 5%. Numerous other studies have also demonstrated the predictive value of a positive CRM (+) in terms of a higher risk of local recurrence and generally poorer prognosis in rectal cancer patients.[4] For this reason, standardized clinical trials focused on rectal cancer have recognized CRM (+) as an essential prognostic factor.[5] Besides, the presence of lymph node metastasis also has a significant impact in multivariate analysis when assessing the likelihood of local recurrence. While the diagnostic threshold value for lymph node metastasis has been a subject of debate, it remains a valuable parameter for patient prognosis.[6]

Recent research has reached a consensus on the diagnostic capabilities of MRI for the detection of CRM + and lymph node metastases.[7] The objective of this study was to determine a correlation between MRI findings and pathology results in evaluating CRM + and lymph node metastases in patients with rectal cancer.

II. MATERIALS AND METHODS

1. Subjects

Patients: From October 2016 to May 2019, 109 patients diagnosed with rectal carcinoma underwent surgery at Viet Duc University Hospital (Hanoi, Vietnam) and were enrolled in this study. The patient cohort included 73 male and 36 female, with an average age of 63.5 ± 12.2 years old (ranging from 26 to 90). The average duration from the onset of symptoms to diagnosis was about 3.7 months with the primary symptom being the presence of blood in the feces (82.6%).

All patients diagnosed with rectal cancer based on colo-rectal endoscopy and confirmed by adenocarcinoma biopsy underwent surgery as the recommended treatment approach. Preoperative MRI was conducted on all patients, followed by postoperative histological examination. Additionally, computed tomography (CT) screening of the lung, abdomen, and pelvis confirmed the absence of distant metastasis in all patients.

2. Methods

Study design: a cross-sectional research.

The MRI assessment, using the Siemens Magnetom Avanto 1.5T, followed a standardized procedure to ensure consistency as follows:

Sequences include T1-weighted, T2-weighted, Diffusion-weighted imaging (DWI) and post-contrast fat-saturated axial T1-weighted images, as these are typically essential in rectal cancer staging. For slice thickness, T2-weighted (T2W) high-resolution sequences in three planes: sagittal, coronal, and axial (perpendicular to the affected rectal segment), with a slice thickness of 3mm. DWI with b = 0 and b = 800 to assess cellularity and tumor characterization. T1 fatsat post-contrast with a slice thickness of 3mm in at least two planes (sagittal, axial), ensuring that the imaging captures both tumor characteristics and involvement of surrounding structures.

The measurement of the minimum distance between the tumor or metastatic lymph node and the mesorectal fascia was conducted using the MRI ruler tool. The distance, measured in

millimeters, determined whether the CRM was diagnosed as (+). If the distance was equal to or less than 1mm, CMR was classified as (+).

The evaluation of lymph node metastasis involved analyzing the diameter and the shape of the lymph node.[8]

• Lymph nodes measuring less than 5mm are considered metastatic if they exhibit three specific criteria: indistinct margins, heterogeneous signal, and a round shape.

• Lymph nodes ranging from 5 to 9mm are considered metastatic if they meet at least two of the above-mentioned three criteria, which include indistinct margins, heterogeneous signal, and a round shape.

• Lymph nodes that measure 9mm or larger are always classified as metastatic, regardless of the presence or absence of specific criteria.

- The evaluation of tumor stage involved classifying the depth of tumor invasion into the layers of the rectal wall. The tumor stage (T) was divided into 2 groups: ≥ T3 and < T3.

MRI results are reviewed by the radiologist who interprets the images and by other experts with more than 5 years of experience to ensure accuracy. This dual review system ensures the reliability of the results.

The MRI variables are determined by standardized protocols, which include considerations for tumor staging, lymph node metastasis, and CRM involvement. The evaluation is primarily based on high-resolution T2-W. DWI sequences help assess the tumor and lymph node involvement, providing insight into cellularity and the presence of potential metastases. Post-contrast fatsat T1-weighted sequences are used to assess the enhancement characteristics of the lesions, particularly in cases following treatments such as chemotherapy or radiotherapy, allowing for better differentiation between viable tumor tissue and treatment effects.

The assessment of pathology involved total mesorectal excision and systematic lymphadenectomy in all patients. The histologic examination of tumor specimens and lymph nodes was performed according to the guideline outlined in the WHO Classification of Tumours.[9] Postoperative staging of rectal cancer was determined using the pTNM based on the AJCC 2010 standards.

The histologic examination was grouped based on the following factors:

- Distance of the tumor or metastatic lymph node to the CRM, measured in mm; CRM invasion (+) margins indicated tumor-free resection margins of 1 mm or less).

- Presence of lymph node metastasis, along with the average number of dissected lymph nodes.

- Tumor stage classification (≤ T3, > T3).

MRI images and pathological assessments were initially reviewed by radiologists, anatomopathologist and further evaluated by others with more than 5 years of working experience, focusing on research variables.

Data analysis aimed at evaluating a correlation between preoperative MRI and postoperative histological analysis in the assessment of CRM invasion, measuring the distance in millimeters from the tumor or metastatic lymph node to the mesorectal fascia, determining the tumor stages (≤ T3, > T3) and lymph nodes metastasis.

Statistical analysis included the calculation of sensitivity, specificity, accuracy, positive predictive value, negative predictive value, and odd ratios (OR) with 95% confidence intervals for the T stage, N stage, and CRM involvement. Statistical significance was determined at $p < 0.05$. The data analysis was conducted using SPSS 25.0 64-bit for Windows, developed by

IBM Corporation, USA.

3. Research ethics

Collected data was used for research. We will present honest research results, even if they are unexpected. We will also ensure the confidentiality of this study's patients' personal information.

Limitations: Bias of MRI report and pathology report.

Although the MRI and pathology interpreting procedures are generally the same for colorectal cancer patients, potential inaccuracies still exist due to variation in interpreting by different interpreters. To address these inaccuracies, we invited experienced doctors to review both MRI imaging and pathological findings.

III. RESULTS

From October 2016 to May 2019, a total of 109 eligible patients were enrolled in this study and the findings are as follows.

Colorectal endoscopy was performed to measure the distance from the tumor to the anal margin could, leading to the categorization of patients into three groups: the upper (23 patients, 21.2%), the middle (42 patients, 38.5%), the lower (44 patients, 40.3%). Endoscopic biopsies were used to confirm the diagnosis of adenocarcinoma. On average, a total of 10.4 ± 5.4 lymph nodes were dissected during the surgical procedure.

Table 1. Average distance from the tumor or metastatic lymph node to the CRM measured by both MRI and pathology

Distance	MRI	Pathology	p
Distance from the tumor to the CRM (n = 109) (mm)	4.3 ± 3.9 (0 – 15)	4.2 ± 3.1 (0 – 14)	0.794
Distance from the nearest metastatic node to the CRM (n = 44) (mm)	2.9 ± 1.5 (1 – 10)	2.5 ± 1.7 (0,5 – 8)	0.073

Table 2. Correlation between MRI and pathology in the diagnosis of CRM +

Evaluating CRM		MRI		Total
		CRM (+)	CRM (-)	
Pathology	CRM (+)	13	7	20
	CRM (-)	8	81	89
Total		21	88	109

The correlation between MRI and pathology in the diagnosis of CRM + is described in Table 2: the odds ratio (OR) was found to be 18.804 (95% confidence interval of 5.824 – 60.662), p < 0.001. The diagnostic performance of MRI in this regard is as follows: a sensitivity of 65.0%, a specificity 91.0%, an accuracy of 86.2%, a positive diagnostic value of 61.9% and a negative diagnostic value of 92.1%.

Table 3. Correlation between MRI and pathology in the diagnosis of lymph node metastasis

Pathology \ MRI	Lymph node +	Lymph node -	Total
Lymph node +	39	5	44
Lymph node -	49	16	65
Total	88	21	109

The correlation between MRI and pathology in the diagnosis of lymph node metastasis is described in Table 3: OR = 2.549 (95% confidence interval of 0.857 - 7.565), p = 0.085. The diagnostic performance of MRI has a sensitivity of 88.6%, a specificity of 24.6%, an accuracy of (39 + 16)/109 = 50.5%, a positive diagnostic value: 44.3%, and a negative diagnostic value: 76.2%.

Table 4. Correlation between MRI and Pathology in the diagnosis of tumor staging

Evaluation of tumor staging	MRI (≥ T3)	MRI (< T3)	Total
Pathology (≥ T3)	79	4	83
Pathology (< T3)	12	14	26
Total	91	18	109

The correlation between MRI and Pathology in the diagnosis of tumor staging is described in Table 4: OR = 20.75 (95% confidence interval of 5.96 - 72.22). The diagnostic performance of MRI in this regard is as follows: a sensitivity of 95.1%, a specificity of 53.8%, an accuracy of 85.3%, a positive diagnostic value of 86.8%, and a negative diagnostic value of 77.8%.

IV. DISCUSSION

Distance from the tumor or metastatic lymph node to the mesorectal fascia measured using MRI

In 1982, Heald and colleagues introduced the concept of “total mesorectal excision of the rectum” as a more effective therapeutic approach for colorectal cancer, especially in cases of local recurrence. It is important to note the excellent results of a 5% local recurrence rate without adjuvant therapy.[10] The study by Hugen. et al showed that the rate of local recurrence and distant metastasis was related to the nature of CRM involvement, with the lowest rate for lymph node metastasis and the highest rate for multiple factors.[11]

In our study, the average distance from tumors to CRM, as evaluated by MRI and pathological examination, was 4.3mm and 4.2mm, respectively. There was no significant difference observed between the two methods (p = 0.794). Similarly, the average distance from the metastatic lymph node to the CRM, as measured by MRI and pathology, was 2.9mm and 2.5mm, respectively. Again, there was no statistically significant difference between the measurements (p = 0.073) (refer to Table 1).

Comparison between MRI and histopathological CRM predictions showed that using a threshold of less than 1mm is currently practiced, with a prospective study also showing that a 1mm threshold on MRI predicts clear margins in 96.7% of cases.[12] In

a multicenter observational prospective study, the minimal distance of the tumor from the mesorectal fascia was investigated using a cutoff of equal to or less than 1mm to predict CRM involvement. The study observed an 82% agreement (266 out of 325 cases; 95% confidence interval [CI], 77% – 85%) between MRI and histopathologic assessment of CRM status, where CRM involvement was defined as tumor with a 1mm or less extension into the mesorectal fascia.

Evaluating MRI in the diagonsis of CRM+

CRM involvement was reported to occur in approximately 7.3 to 25.0% of all cases of colorectal adenocarcinoma.[3] Some studies have highlighted the significance of CRM + as a prognostic indicator for local recurrence and distant metastasis. As a result, CRM + has gained importance as a critical factor in colorectal cancer clinical trials.[4,5]

MRI has emerged as a valuable tool in diagnosing rectal cancer by assessing the relationship between tumors, metastatic lymph nodes, and mesorectal fascia. Karatag et al.[13] demonstrated that MRI had an accuracy of 95.8% in evaluating the extent of CRM involvement and a negative diagnostic value of 100%. In cases where CRM involvement is detected, patients often undergo concomitant chemoradiotherapy as a preoperative treatment approach. Subsequently, if the down-staged disease is confirmed by MRI, total mesorectal excision (TME) would be performed to improve the therapeutic efficacy in patients with colorectal cancer.[9]

Our research enrolled a total of 109 patients with colorectal cancer MRI-diagnosed to evaluate the extent of CRM involvement. The diagnostic performance of MRI was found to be accurate (86.2%), sensitive (65.0%), and specific (91.0%) in the diagnosis of CRM+. A detailed comparison of the MRI and pathological data are displayed in Table 2.

A recent meta-analysis conducted by Al-Sukhni et al. examined 21 independent studies and provided valuable insights into the diagnostic accuracy of MRI in detecting CRM positivity.[14] It revealed a specificity of 94% (with a 95% confidence interval of 88% to 97%) for MRI in diagnosing CRM positivity. Importantly, the correlation between MRI findings and pathological data was found to vary depending on the location of the tumor. It emphasizes the importance of considering tumor location when interpreting MRI data to assess CRM involvement. Peschaud et al. made a comparison between MRI and pathology diagnosis in different locations within the rectum.[15] Specifically, MRI was found to be comparable to pathological assessment in 22% of patients with tumors in the anterior wall of the lower rectum, 83% of patients with tumors in the posterior wall of the lower rectum, and 100% of patients with tumors in the middle rectum. When patients with tumors in the anterior wall of the lower rectum were excluded from the analysis, the diagnostic accuracy of MRI improved, with an overall accuracy of 90%. The sensitivity of MRI reached 100% in detecting CRM involvement, while the specificity was 86%. These findings also suggest that the accuracy and reliability of MRI in assessing CRM involvement may vary depending on the location of the tumor within the rectum.

Evaluating MRI in the diagnosis of lymph node metastasis

In the past, the classification of node metastasis staging relied on the nodal size on MRI images. Nevertheless, recent evidence has demonstrated the inaccuracy of this approach. Instead, the more reliable criteria should be a combination of lymph node margin, nodal size,

and signal intensity.[8] Based on MRI images, 88 cases of metastatic lymph nodes were detected (Table 3). On the other hand, pathological examination confirmed 44 cases, resulting in an accuracy of 50.5%. The sensitivity of MRI in detecting lymph node metastasis was 88.6%, while the negative diagnostic value was 76.2% (as shown in Table 4). The average number of lymph nodes resected and pathologically confirmed was 10.4 ± 5.4 (ranging from 3 to 27 nodes). It is evident from our results that MRI is not highly accurate in diagnosing lymph node metastasis.

Bipat et al. reported in a meta-analysis, inclusive of 90 scientific studies, that the diagnostic performance of MRI for metastatic lymph nodes could have an accuracy in the range of 39 - 95%, a sensitivity of 66% (95% CI: 54% to 76%), a specificity of 76% (95% CI: 59% to 87%).[16] Thus, the combination of endorectal coil and pelvic phased-array coil MRI was recommended for better accuracy in detecting metastatic lymph nodes. According to Felipe Aluja Jaramillo et al., the size of lymph nodes is of limited value for determination of whether metastasis is present.[17] As is well known, there can be microscopic metastasis in normal sized lymph nodes. A diameter of 5 mm implies a sensitivity of 68% and specificity of 78% for differentiation of malignant from benign lymph nodes.

In our study, the specificity of MRI diagnosis for lymph node involvement was only 24.6% (Table 4). The average number of dissected lymph nodes was 10.4 ± 5.4 nodes, which falls below the recommended standard. According to most authorities, the examination of a minimum of 12 lymph nodes is advisable, although the evidence supporting this guideline is not robust. One potential reason for the lower number of dissected lymph nodes could be the lack of systematic utilization of endorectal coil MRI for patients in our study.

Recently, there has been increasing interest in the use of ultra-small superparamagnetic iron oxide (USPIO) as a promising approach to strengthen the applicability of MRI in diagnosing metastatic lymph nodes. To fully explore the benefits and implications of incorporating USPIO into MRI protocols for the diagnosis of lymph node metastasis, research data has been reported. For instance, Koh et al. diagnosed 25 rectal cancer patients with an accuracy of 65% and a specificity of 93%.[18] This finding suggests that it is worth studying USPIO for the detection of mesolectal fascia nodes.

V. CONCLUSIONS

The study shows a strong correlation between the performance of MRI and pathology for CRM diagnosis. It provides accurate imaging for identifying patients at high risk of local recurrence before surgery. It plays a crucial role in the preoperative assessment of CRM invasion, tumor-CRM distance, and the depth of rectal wall invasion. However, it should be noted that MRI still has limitations in assessing lymph node metastasis, and additional diagnostic modalities may be necessary for a comprehensive evaluation in such cases.

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Conflict of interest: None

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