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Role of diffusion-weighted magnetic resonance imaging in detection of lymph node metastasis in rectal cancer

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Abstract

Background Rectal cancer is the most prevalent gastrointestinal tumor. Early diagnosis, accurate staging as well as early treatment are the keys for improving the five-year survival rate. The objective of this research is to assess the effectiveness of diffusion-weighted MRI (DWI) in identifying lymph nodes and distinguishing between benign and metastatic nodes throughout the first stage of primary rectal cancer.

Results The study showed that mean ADC value was significantly higher in mucinous carcinoma ($1.72 \pm 0.36 \times 10^{-3}$ mm^2/sec) than that in non-mucinous carcinoma ($0.981 \pm 0.276 \times 10^{-3}$ mm^2/sec) with a cutoff value of (1.3×10^{-3}) mm^2/s which was the precise value to produce high sensitivity, specificity and accuracy of 93%, 94%, and 94%, respectively. ADC analysis showed either intermediate or low signal in 49 (70%) and high signal in 21 (30%) L.Ns. Mean ADC value showed a significant reduction in malignant L.Ns ($1.01 \pm 0.54 \times 10^{-3}$ mm^2/sec) compared to benign L.Ns ($1.51 \pm 0.51 \times 10^{-3}$ mm^2/sec), AUC of 0.674 ($P = 0.008$) and a cutoff value of 0.987×10^{-3} mm^2/s with sensitivity, specificity and accuracy of 44.4%, 91.2% and 67.5%, respectively. The mean L.N /tumor ratio was 1.65 ± 0.73 in benign L.Ns and 1.06 ± 0.37 in malignant L.Ns.

Conclusions In rectal cancer, there was a significant difference between benign and malignant L.Ns regarding diffusion result, L.Ns size, shape, and margin. The study demonstrated the effectiveness of DWI in diagnosing lymph node metastasis in colorectal cancer; true diffusion restriction was significantly noted in malignant L.Ns compared to benign L.Ns. Mean ADC value showed a significant reduction in malignant L.Ns compared to benign L.Ns. L.N/tumor ratio showed a significant reduction in malignant L.Ns compared to benign L.Ns.

Keywords Diffusion-weighted Images, Lymph Node metastasis, Rectal cancer

Background

Colorectal cancer is the most prevalent gastrointestinal tumor. Early detection, precise determination of the stage, and prompt treatment of rectal cancer are crucial for enhancing the five-year survival rate [1].

Rectal MRI is essential for assessing rectal cancer as it offers many prognostic indicators and imaging characteristics that assist in appropriate patient care [2].

The recommendations of the European Society for Medical Oncology suggest that MRI should be used as the first imaging test due to its ability to comprehensively assess both the internal and external areas of the mesorectum. MRI has exceptional contrast resolution in soft tissue and possesses outstanding multiplanar imaging capabilities, making it a very effective technique that is often used for the first assessment of rectal cancer [3].

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Preoperative chemoradiotherapy and complete mesorectal excision are the established therapies for locally advanced rectal cancer in order to select the optimal therapeutic approach. It is necessary to assess the state of the lymph nodes, the stage of the tumor, and the involvement of the mesorectal fascia [4].

Multiple researches have concentrated on determining the practicality of forecasting the spread of cancer to nearby lymph nodes by imaging procedures conducted before surgery [5]. The assessment of lymph node metastases in rectal cancer using computed tomography (CT) mostly relies on size-related and morphological characteristics. Typically, in CT imaging, lymph nodes that have a diameter more than 10 mm are considered to be indicative of malignancy. Furthermore, the quantitative characteristics of density, area, and heterogeneity of the lesions may be used to enhance the identification of metastatic lymph nodes in rectal cancer [6].

The objective of this research is to assess the efficacy of diffusion-weighted MRI (DWI) in identifying lymph nodes and distinguishing among benign and metastatic nodes in the first stage of primary rectal cancer.

Methods

This study was done between March 2021 and August 2022 At Ain Shams University Hospitals, Radiodiagnosis department including 35 patients; 29 patients with histopathologically proven rectal carcinoma underwent surgical resection at Ain Shams University Hospitals, and 6 cases potentially free of cancer considered as control.

Inclusion criteria

Patients with histopathologically proven rectal carcinoma, with no age or gender consideration undergoing surgical resection with available pathological report.

Exclusion criteria

Patients with certain medical conditions should not undergo magnetic resonance imaging (MRI). This includes those with implanted devices that rely on electrical, magnetic, or mechanical stimulation, such as cardiac pacemakers or automated cardioverter defibrillators since the aforementioned materials may interact with these devices. Patients who have contraindications for MRI contrast agents, such as a glomerular filtration rate (GFR) < 30 mL/min/1.73 m^2 or a past severe allergic response, and have been pathologically confirmed to not have rectal cancer.

Methods/Techniques of study

Every patient underwent comprehensive history taking. Patients diagnosed with rectal cancer were scheduled to have a contrast-enhanced MR imaging of the pelvis before surgical removal. All patients were examined by 1.5 Tesla MRI machine (Philips Achieva and Intera 16 channels) using external phased-array surface coil.

MRI protocol

1. Initial three plane localizer views covering the entire pelvis.
2. Pre and post fat sat axial high-resolution T2 WIs
3. Sagittal, coronal T2 WIs, axial T1 WIs.
4. Post contrast axial, sagittal and coronal T1 WIs.
5. Diffusion-weighted imaging performed in the transverse plane with tri-directional diffusion gradients by using b values of 0, 400 & 800 s/mm^2. Mean ADC of each visible node is taken by drawing an oval-shaped region of interest, including as much of the nodal parenchyma as possible.

Histopathology

After the surgical excision, the specimens were evaluated with regard to histopathology and matched with the MRI image analysis.

Statistical analysis

A combination of Microsoft Excel 2016, the statistical tool SPSS (Statistical tool for the Social Sciences), and the MedCalC program software version 19.1 will be used to collect, organize, and analyze the data. The researchers used the mean ± SD (standard deviation), the minimum and maximum values of the range to perform descriptive statistics on numerical parametric data. The median, the first and third inter-quartile range were used for numerical nonparametric data. The number and percentage were used to assess the categorical data.

Results

This prospective study was carried out on 35 patients; 29 patients with histopathologically proven rectal carcinoma underwent surgical resection at Ain Shams University Hospitals, Radiodiagnosis Department, and 6 cases potentially free of cancer considered as control.

Out of 35 patients, there were 15 males (42.9%) and 20 females (57.1%) with a male to female ratio of 0.75:1. The mean age of patients was 46.31 ± 16.13 years and ranged from 21 to 82 years**.** The mean age of males was 49.93 ± 17.27 years and that of females was 43.60 ± 15.09.

According to pathological results, more than half of the cases (54.3%) had adenocarcinoma grade 2, 17.1% of them had mucinous adenocarcinoma, 5.7% of them had signet ring adenocarcinoma and 2.9% had undifferentiated carcinoma**.**

Figure 1 shows: Diffusion and ADC value of the rectum in the studied patients.

Regarding the relation between types of pathology of rectal carcinoma and diffusion results, it is declared in Fig. 2.

Table 1 summarizes DWI and ADC value of lymph nodes in the studied patients. The 800 b-value DWI images showed high signal in 63 (90%) and either intermediate or low signal in 7 (10%) L.Ns. ADC analysis showed either intermediate or low signal in 49 (70%) and

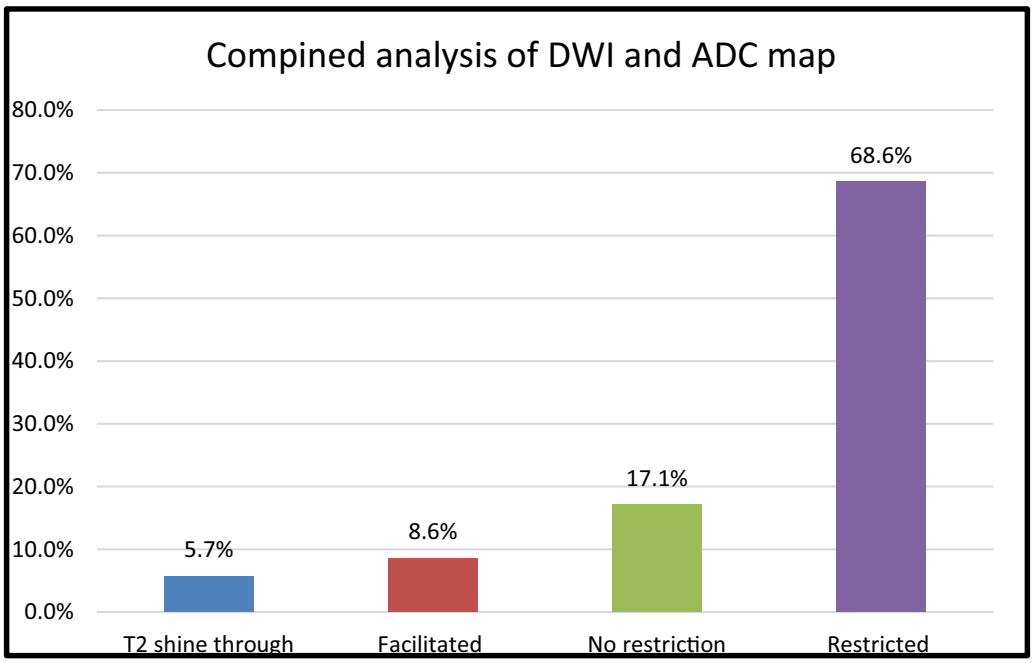

Fig. 1 Distribution of the studied cases as regard DWI and ADC map result

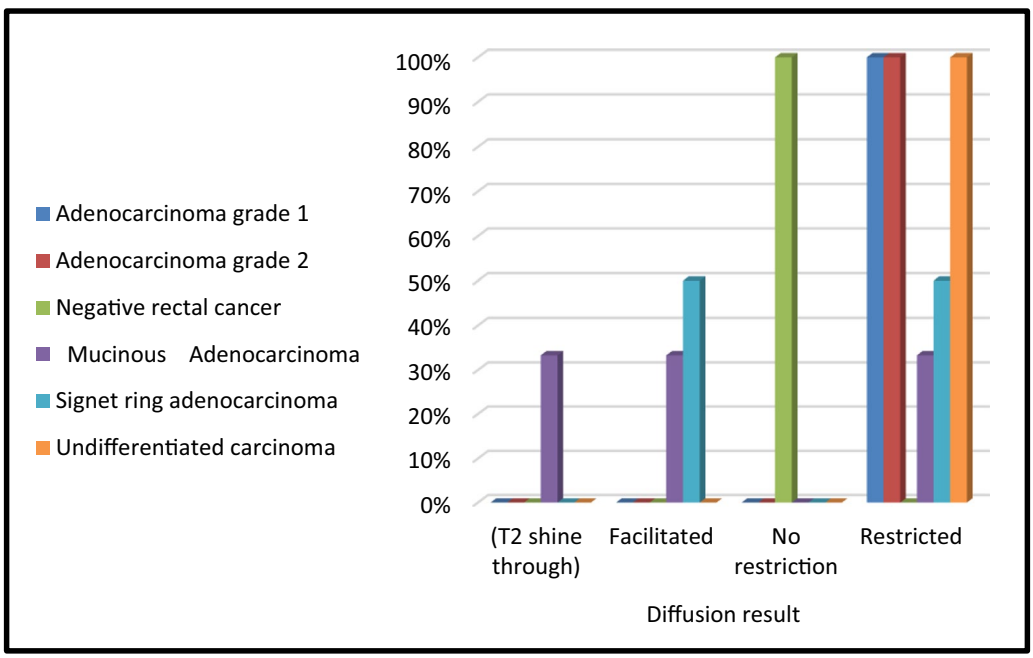

Fig. 2 Relation between types of pathology of rectal carcinoma and diffusion result

Table 1 DWI and ADC Value of lymph nodes in the studied patients

Parameters		**Studied L.N (N = 70)**	
		N	**%**
Diffusion of lymph nodes			
DWI	High	63	90.0
	Intermediate or Low	7	10.0
ADC map	High	21	30.0
	Intermediate or Low	49	70.0
Diffusion result	(T2 shine through)	3	4.3
	Facilitated	18	25.7
	No restriction	7	10.0
	Restricted	42	60.0

ADC Value of lymph nodes ($\times 10^{-3}$ mm^2/sec)

	Mean	**SD**	**Median**	**IQR**		**Range**	
Mean	1.35	.54	1.27	.98	1.69	.39	2.75
Max	1.49	.52	1.47	1.10	1.78	.51	2.94
Min	1.16	0.56	1.09	.78	1.57	.0.2	2.65

high signal in 21 (30%) L.Ns. The mean ADC value of the assessed L.Ns was 1.35 ± 0.54. Combined analysis of the DWI and ADC maps revealed true diffusion restriction in 42 (60%) L.Ns, no restriction in 7 (10%), diffusion facilitation in 18 (25.7%) and T2 shine through in 3 (4.3%) L.Ns.

Table 2 summarizes the comparison between the presence and absence of rectal masses (case versus control) regarding diffusion and ADC value. There was a significant difference between positive and negative cases of rectal masses regarding diffusion result ($p < 0.001$). Mean ADC value showed a significant decrease in positive rectal masses compared to negative rectal masses ($p = 0.003$). Table 2, Fig. 3.

Out of 70 lymph nodes, 34 (48.6%) L.Ns were benign and 36 (51.4%) L.Ns were malignant. The mean L.N size was 0.69 ± 0.41 cm. with more than half of which (n = 40, 57.1%) had oval shape, and half had irregular margin with the other half with smooth margin. On the T2-weighted images, a total of 50 (71.4%) displayed isointense, 8 (11.4%) were hyperintense, and 12 (17.1%) were hypointense in signal. Significant enhancement was observed in 44 (62.9%) cases. 28 (40%) L.Ns had suspicious criteria by MRI.

For histopathologically proven benign L.Ns**,** the mean size was 0.40 ± 0.17 cm. where most benign L.Ns 24 (70.6%) had oval shape and 10 (29.4%) had rounded shape. All appeared having smooth margin. On the other hands, the pathologically proven malignant L.Ns in our study, the mean size was 0.97 ± 0.37 cm. More than half L.Ns 20 (55.6%) had rounded shape and 16 (44.4%) had oval shape. Irregular margin was depicted in 35 (97.2%) L.Ns and smooth margin in 1(2.8%) Table 3.

Regarding the prognostic performance for morphological criteria of the examined lymph nodes in predicting metastasis**,** we found that ROC curve of the rounded shape L.N had sensitivity of 55.6% & specificity of 70.6% and that of irregular L.N margin, the sensitivity and specificity were 97.2% and 100%, respectively.

Table 2 Comparison between positive and negative rectal masses (case and control) regarding Diffusion and ADC Value

Variable		**Control (negative rectal masses) (N = 6)**		**Case (positive rectal masses) (N = 29)**		***P* value**	**Sig**
		No	**%**	**No**	**%**		
DWI result	Facilitated	0	0.0%	5	17.3%	< 0.001	HS
	No restriction	6	100%	0	0.0%		
	Restricted	0	0.0%	24	82.7%		
Mean ADC value ($\times 10^{-3}$ mm^2/sec)	Mean ± SD	1.14 ± 0.09		1.074 ± 0.026		0.703	NS

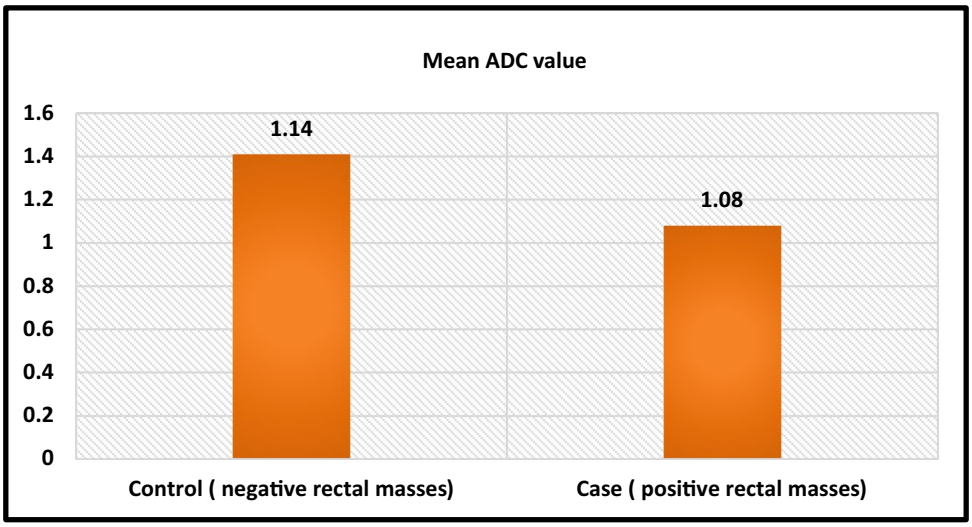

Fig. 3 Comparison between positive and negative rectal masses regarding ADC Value

Table 3 Distribution of size, shape & margin in malignant L.N

Variable		Malignant (N = 36)	
		No	%
Size	Mean ± SD	0.97 ± 0.37	
	Median (IQR)	0.93 (0.70–1.1)	
	Range	0.4–2.0	
Shape	Oval	16	44.4
	Rounded	20	55.6
Margin	Irregular	35	97.2
	Smooth	1	2.8

High DWI and low ADC map were significantly higher in malignant L.Ns compared to benign L.Ns. Mean ADC value showed significant reduction in malignant L.Ns ($1.01 \pm 0.54 \times 10^{-3}$ mm^2/sec) compared to benign L.Ns ($1.51 \pm 0.51 \times 10^{-3}$ mm^2/sec). In addition, there was statistically significant difference between benign and malignant L.Ns regarding Diffusion result, L.Ns size, shape, and margin. Also, there was significant difference between them regarding T2 Signal, Enhancement as well as suspicious criteria by MRI as shown in Table 4.

ROC curve analysis for the evaluation of L.N size as an *indicator* of L.N. metastasis:

Showed an AUC of 0.955 ($P < 0.001$) and a cutoff value of 0.5 cm with sensitivity, specificity and accuracy of 88.2%, 94.4% and 96%, respectively (Fig. 4).

ROC curve analysis for the evaluation of ADC Value of L.N. as an *indicator* for L.N. metastasis

Showed an AUC of 0.674 ($P = 0.008$) and a cutoff value of 0.987×10^{-3} mm^2/s with sensitivity, specificity and accuracy of 44.4%, 91.2% and 67.5%, respectively (Figs. 5,6).

Evaluation of the ratio of L.N. ADC value to primary tumor ADC value (L.N /T ratio)

The mean L.N/tumor ratio was 1.65 ± 0.73 in benign L.Ns and 1.06 ± 0.37 in malignant L.Ns. L.N/tumor ratio showed a significant reduction in malignant L.Ns compared to benign L.Ns ($p = 0.001$).

Discussion

Colorectal cancer prevalence is considerably higher in more developed countries. However, mortality rates in more developed countries is reduced, reflecting increased screening and advancements in the diagnosis, staging, and treatment of rectal cancer [7].

Nodal metastasis is considered an important prognostic marker for local recurrence as well as disease-free survival rates. Therefore, it is important to accurately predict the need for neoadjuvant chemotherapy and radiation prior to surgery [8].

The objective of this research is to assess the efficacy of diffusion-weighted MRI (DWI) in identifying lymph nodes and distinguishing among benign and metastatic nodes in the first stage of primary rectal cancer.

The incidence rates of malignant and benign lymphadenopathy in the investigation aligned with the findings of Rutegård et al. [9], who found that preoperative MRI

Table 4 Comparison between benign and malignant L.N regarding different parameters

Variable		Benign (N = 34)		Malignant (N = 36)		Test value	P value	Sig
		No	%	No	%			
DWI	high	27	79.4	36	100.0	$X^2 = 8.235$	0.004	HS
	low	7	20.6	0	0.0			
ADC map	high	15	44.1	6	16.7	$X^2 = 6.275$	0.012	S
	low	19	55.9	30	83.3			
Diffusion result	(T2 shine through)	0	0.0	3	8.3	$X^2 = 25.68$	< 0.001	HS
	facilitated	15	44.1	3	8.3			
	no restriction	7	20.6	0	0.0			
	restricted	12	35.3	30	83.3			
Mean ADC value ($\times 10^{-3}$ mm^2/sec)	Mean ± SD	1.51 ± 0.51		1.01 ± 0.54		$Z_{MWU} = 2.51$	0.012	S
	Median (IQR)	1.47 (1.1–1.75)		1.05 (0.81–1.41)				
	Range	0.52–2.75		0.39–1.68				
Size	Mean ± SD	0.40 ± 0.17		0.97 ± 0.37		$Z_{MWU} = 6.57$	< 0.001	HS
	Median (IQR)	0.35 (0.3–0.5)		0.93 (0.70–1.1)				
	Range	0.2–1.10		0.4–2.0				
Shape	oval	24	70.6	16	44.4	$X^2 = 4.88$	0.027	S
	rounded	10	29.4	20	55.6			
Margin	Irregular	0	0.0	35	97.2	$X^2 = 66.11$	< 0.001	HS
	smooth	34	100.0	1	2.8			
T2 Signal	High	0	0.0	8	22.2	$X^2 = 26.44$	< 0.001	HS
	Iso	34	100.0	16	44.4			
	Low	0	0.0	12	33.3			
Enhancement	No significant enhancement	26	76.5	0	0.0	$X^2 = 43.8$	< 0.001	HS
	Significant enhancement	8	23.5	36	100.0			
Suspicious criteria by MRI	No	33	97.1	9	25.0	$X^2 = 37.8$	< 0.001	HS
	Yes	1	2.9	27	75.0			

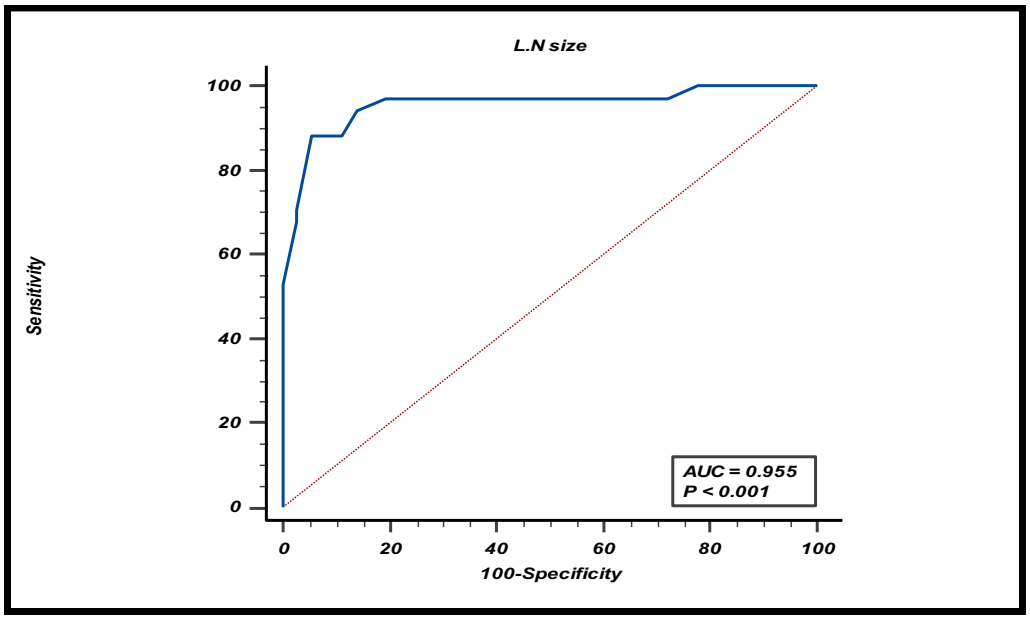

Fig. 4 ROC curve for the performance of L.N size in predicting malignancy

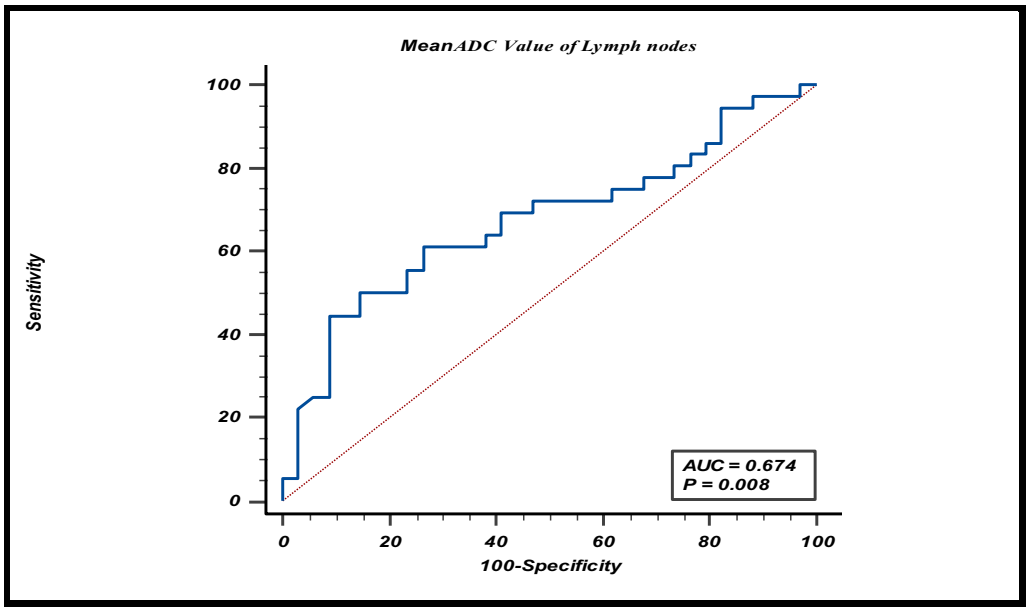

Fig. 5 ROC curve for the performance of ADC Value of Lymph nodes in predicting malignant L.N

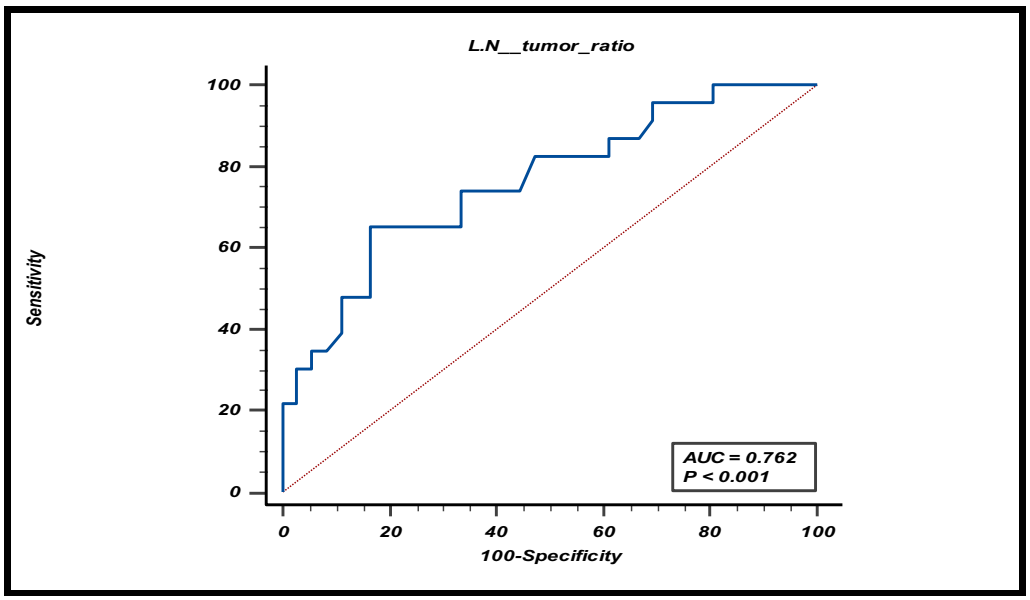

Fig. 6 ROC curve for the performance of L.N/ T ratio in predicting malignant rectal mass

detected 197 mesorectal nodal formations of which 92 (47%) could be physically correlated with histology.

The prevalence rates of malignant and benign lymphadenopathy in this study agreed with the findings published by Zhuang et al. [10], who documented similar rates. In total, 346 mesorectal lymph nodes were identified during imaging assessment. Out of them, 313 were verified after histological examination; while, 33 were not matched. The approach had a success rate of 90.5%. A detailed investigation of each individual node showed that 280 (89%) of them were benign; whereas, 33 (10.5%) were determined to be cancerous. They found that the median short-axis diameters of mesorectal lymph nodes, which were histopathologically matched, were 4.0 mm (range 2.0–9.0 mm) for negative nodules and 5.6 mm (range 2.5–11.8 mm) for positive nodules, as shown using MRI.

The MRI data on the appearance criteria of LNs yielded compatible findings to the research conducted by Miao et al. [11], which examined a total of 794 LNs for size, margins, and morphology. Based on the histological findings, it was found that 27.3% (217 out of 794) of the lymph nodes (LNs) examined were positive for metastasis (LN+). Lymph nodes (LNs) that had an oval form with a well-preserved central hilum, or those that had an oblong shape, were more likely to be negative for metastasis (LN-). On the other hand, LNs that were lobulated and irregular in shape were more likely to be positive for metastasis (LN+). There were notable disparities between benign and malignant lymph nodes in terms of diffusion results, lymph node size, shape, and margin.

The study conducted by Zhuang et al. [10] provides support for the current research. They found that the median short-axis diameters of mesorectal lymph nodes, which were matched with histological data, were 4.0 mm (range 2.0–9.0 mm) for negative nodules and 5.6 mm (range 2.5–11.8 mm) for positive nodules, as determined by MRI.

The ROC curve analysis revealed that the area under the curve (AUC) for predicting lymph node (L.N.) metastasis based on L.N. size was 0.955 ($P > 0.001$). The cutoff value for L.N. size was determined to be 0.5cm, with corresponding sensitivity, specificity, and accuracy values of 88.2%, 94.4%, and 96%, respectively.

The findings of Abd El Samei et al. [12] corroborated the results of this study, as they indicated that the sensitivity, specificity, and accuracy were 88.89%, 94.74%, and 91.89%, respectively.

Miao et al. [11] found that 27.3% (217/794) of lymph nodes (LNs) were determined to be metastatic (LN+) based on histopathological data. Furthermore, lymph nodes larger than 10 mm showed a sensitivity of 47.0%, specificity of 80.9%, positive predictive value (PPV) of 48.1%, and negative predictive value (NPV) of 80.2%. The odds ratio (OR) was 3.77 with a 95% confidence interval (CI) ranging from 2.69 to 5.28.

Fowler et al. [13] reported that MRI has a high sensitivity in identifying enlarged lymph nodes, but it lacks specificity in distinguishing between benign and malignant nodes with accuracies ranging from 59 to 83%.

Surov et al. [14] found that ADC values were recorded for a total of 1376 lymph nodes, with 623 (45.3%) being metastatic and 754 (54.7%) being non-metastatic. The mean apparent diffusion coefficient (ADC) value of the metastatic lymph node was determined to be 1.05×10^{-3} mm^2/s with a range from 0.94 to 1.15. The mean apparent diffusion coefficient (ADC) value of the non-metastatic lymph node (LN) was estimated to be 1.17 (1.01, 1.33). The sensitivity and specificity values obtained were 81% and 67%, respectively.

The findings of Ge et al. [15] corroborated the results of this study as they found that a total of 67 lymph nodes were subjected to histological investigation with 24 in the non-metastatic group and 43 in the metastatic group. The average ADC values for metastatic lymph nodes were $1.17 \pm 0.16 \times 10^{-3}$ mm^2/s, which were substantially lower compared to the average ADC values of benign lymph nodes, which were $1.29 \pm 0.15 \times 10^{-3}$ mm^2/s.

Heijnen et al. [16], reported that the use of the ADC of the nodes in relation to the main rectal tumor yielded an AUC of 0.67, with a sensitivity of 75%, specificity of 61%, PPV of 20%, and NPV of 95%.

Our present study had few limitations where individual node-to-node matching between imaging and histopathology was not attempted. Mismatch can occur when multiple lymph nodes detected by MRI and then resected, since multiple enlarged lymph nodes are commonly found around area of rectal cancer. Although we done our effort to track lymph nodes, complete matching could not be possible.

Conclusions

In rectal cancer, there was a significant difference between benign and malignant L.Ns regarding diffusion result, L.Ns size, shape, and margin. This study demonstrated the effectiveness of DWI in diagnosing lymph node metastasis in colorectal cancer; true diffusion restriction was significantly noted in malignant L.Ns compared to benign L.Ns. Mean ADC value showed a significant reduction in malignant L.Ns compared to benign L.Ns. L.N /tumor ratio showed a significant reduction in malignant L.Ns compared to benign L.Ns.

Abbreviations

ADC	Apparent diffusion coefficient
DWIs	Diffusion-weighted images
MRI	Magnetic resonance imaging
LNs	Lymph nodes
ROI	Region of interest

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43055-024-01324-w.

Additional file 1.

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Not applicable.

Author contributions

Rehab M shimy collected the patient data and participated in its design. Asmaa Monir Aly responsible for the correspondence to the journal. Samer Ali Elshishtawy wrote the manuscript. Mona H Hassan contributed to the image processing and collection of the patient's images. Shimaa H.I Desouky participated in the design of the study, performed the statistical analysis. Amir Hanna participated in its design and coordination, and helped to draft the manuscript. All authors have read and approved the final manuscript.

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Availability of data and materials
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the ethical committee of the radiology department of faculty of medicine Ain Shams University. An informed written consent was taken from all patients.

Consent for publication
An informed written consent was taken from all subjects.

Competing interests
The authors declare that they have no competing interests.

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