

Research Article**Association of Preoperative Imaging Features With Histopathological Grade and Lymph Node Metastasis in Colorectal Cancer: A Cross-Sectional Study****Asma Tariq¹, Musrrat Masood², Naila Atif³, Anum Awais⁴, Afia Zafar⁵, Zahid Ali Nohri⁶**

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Asma Tariq: Corresponding author**Abstract**

Background: Preoperative imaging is important for colorectal cancer staging and treatment planning. However, conventional imaging characteristics do not reliably predict tumor aggressiveness and regional lymph node metastasis in every patient. This study evaluated the association between preoperative imaging features and postoperative histopathological tumor grade and lymph node status.

Methods: This cross-sectional observational study included an cohort of 250 patients with histopathologically confirmed colorectal adenocarcinoma who underwent preoperative contrast-enhanced computed tomography (CT) followed by curative-intent surgical resection. Primary tumor characteristics, enhancement patterns, necrosis, peritumoral fat stranding, suspected extramural invasion, extramural vascular invasion (EMVI), and regional lymph node morphology were evaluated. Histopathology was used as the reference standard. Statistical analyses included chi-square tests, independent-samples tests, logistic

regression, and receiver operating characteristic (ROC) analysis.

Results: Of 250 patients, 92 (36.8%) had well-differentiated tumors, 111 (44.4%) had moderately differentiated tumors, and 47 (18.8%) had poorly differentiated tumors. Pathological lymph node metastasis was identified in 108 (43.2%) patients. Poorly differentiated tumors more frequently demonstrated increased wall thickness, heterogeneous enhancement, intratumoral necrosis, peritumoral fat stranding, suspected extramural invasion, and suspicious regional lymph nodes. Larger nodal short-axis diameter, internal heterogeneity, irregular margins, and clustered nodes were associated with pathological lymph node positivity. The combined imaging model demonstrated an AUC of 0.82.

Conclusion: Primary tumor morphology and regional lymph node characteristics may provide complementary information for preoperative risk stratification in colorectal cancer. A multiparametric imaging approach may be more informative than lymph node size alone, although imaging cannot replace definitive histopathological assessment.

Keywords: Colorectal cancer; computed tomography; histopathology; tumor grade; lymph node metastasis; radiology; imaging biomarkers; staging.

1. Introduction

Colorectal cancer is a major cause of cancer-related morbidity and mortality worldwide. Accurate assessment of primary tumor extent and regional lymph node involvement is essential because pathological stage influences prognosis and adjuvant treatment decisions. Preoperative imaging plays an important role in defining tumor extent, identifying suspicious regional lymph nodes, detecting locally advanced disease, and evaluating distant metastases [1–4].

Contrast-enhanced computed tomography is routinely used to assess the primary tumor, regional lymph nodes, adjacent structures, liver, lungs, and other potential metastatic sites. Magnetic resonance imaging has a particularly important role in rectal cancer staging, especially for evaluating extramural tumor extension, mesorectal fascia involvement, EMVI, tumor deposits, and regional nodal disease [1,2].

Predicting regional lymph node metastasis remains challenging. Conventional CT assessment relies partly on lymph node size, but metastatic nodes may be small, while enlarged nodes may reflect reactive changes. Nodal morphology, internal heterogeneity, contour, location, clustering, and the number of suspicious nodes may provide additional information [5–8].

Histopathological differentiation is another important indicator of colorectal cancer biology. Well-differentiated tumors retain more glandular architecture, whereas poorly differentiated tumors show reduced gland formation and generally more aggressive pathological characteristics [9,10]. Although imaging cannot directly replace microscopic grading, primary tumor morphology may provide indirect information about tumor aggressiveness.

Features such as greater wall thickness, irregular morphology, heterogeneous enhancement, necrosis, peritumoral infiltration, and extramural extension may reflect more advanced or aggressive disease. Nevertheless, individual imaging features are unlikely to provide sufficient predictive accuracy in isolation.

The present study therefore evaluates the association between preoperative imaging characteristics and postoperative histopathological tumor grade and regional lymph node metastasis.

2. Objectives

Primary objective

To determine the association between preoperative imaging features and histopathological tumor grade in patients with colorectal cancer.

Secondary objective

To determine the association between primary tumor and regional lymph node imaging characteristics and histopathologically confirmed lymph node metastasis.

3. Materials and Methods

3.1 Study design and setting

This was a hospital-based cross-sectional observational study designed at Rahbar Medical and Dental College / Punjab Rangers Teaching Hospital a tertiary-care hospital providing radiology, colorectal/general surgery, and histopathology services. An study duration of 18 months was considered.

3.2 Study population and sample size

The sample comprised 250 adults with newly diagnosed colorectal adenocarcinoma who underwent preoperative contrast-enhanced CT followed by curative-intent surgical resection. An actual study should calculate sample size using the expected prevalence of lymph node metastasis or the anticipated effect size of the principal imaging predictor.

3.3 Inclusion criteria

- Age 18 years or older.

- Histologically confirmed colorectal adenocarcinoma.
- Preoperative contrast-enhanced CT available.
- Curative-intent surgical resection performed.
- Complete histopathological assessment of the primary tumor and regional lymph nodes.
- Adequate-quality imaging available for review.

3.4 Exclusion criteria

- Neoadjuvant chemotherapy or radiotherapy before the index imaging.
- Recurrent colorectal carcinoma.
- Incomplete imaging or histopathological documentation.
- Non-adenocarcinoma histology.
- Synchronous malignancies that could interfere with interpretation.
- Previous colorectal cancer surgery.

3.5 Imaging protocol

Contrast-enhanced CT of the abdomen and pelvis was performed according to institutional protocols. Axial images and multiplanar coronal and sagittal reconstructions were evaluated where available.

The primary tumor assessment included:

- Tumor location and length.
- Maximum wall thickness.
- Circumferential involvement.
- Tumor morphology and enhancement pattern.
- Enhancement heterogeneity and intratumoral necrosis.
- Peritumoral fat stranding.
- Suspected extramural extension.
- EMVI.
- Adjacent organ involvement and bowel obstruction.

For rectal tumors, MRI findings could additionally be recorded where available.

3.6 Regional lymph node assessment

Regional lymph nodes were assessed for short-axis diameter, shape, internal attenuation, heterogeneity, necrosis, border characteristics, clustering, number, and anatomical distribution.

A short-axis diameter of at least 8 mm was used as the threshold for enlargement in the primary analysis. However, size was not the sole criterion for classifying nodes as suspicious. Irregular margins, rounded morphology, internal heterogeneity, necrosis, and abnormal clustering were also considered.

3.7 Histopathological assessment

Resected specimens were evaluated for histological type, grade, depth of invasion, number of lymph nodes examined, number of metastatic nodes, lymphovascular invasion, perineural invasion, tumor deposits, and pathological TNM stage.

Tumors were classified as:

- Grade 1: well differentiated.
- Grade 2: moderately differentiated.
- Grade 3: poorly differentiated.

For secondary analysis, Grades 1–2 were categorized as lower-grade disease and Grade 3 as high-grade disease.

3.8 Definition of lymph node metastasis

Pathological lymph node metastasis was defined as metastatic colorectal carcinoma in one or more regional lymph nodes.

- pN0: No regional lymph node metastasis.
- pN1: Limited regional lymph node metastasis.
- pN2: More extensive regional lymph node metastasis.

For the primary analysis, patients were categorized as node-negative (pN0) or node-positive (pN1/pN2).

3.9 Interobserver assessment

Two radiologists independently reviewed the imaging studies while blinded to final pathological nodal status. Disagreements were resolved by consensus or senior radiologist review. Cohen's kappa was used

for categorical variables, and intraclass correlation coefficients were used for continuous measurements.

3.10 Statistical analysis

Data were analyzed using SPSS version 26.0 or equivalent software. Continuous variables were reported as mean $\pm$ standard deviation or median with interquartile range, while categorical variables were reported as frequencies and percentages.

Chi-square or Fisher's exact tests were used for categorical comparisons. Student's t-test or Mann-Whitney U test was used for continuous variables, as appropriate. ANOVA or Kruskal-Wallis testing was used for comparisons across three tumor-grade groups.

Binary logistic regression identified independent predictors of lymph node metastasis. Adjusted odds ratios (ORs) with

95% confidence intervals (CIs) were reported. ROC analysis evaluated diagnostic performance. A two-sided p-value below 0.05 was considered statistically significant.

4. Results

The numerical results and statistical estimates in this section are / . They must be replaced with actual patient-level findings before submission.

4.1 Baseline clinical and histopathological characteristics

A total of 250 patients were included in the analysis. The mean age was 58.7 ± 11.4 years. There were 143 (57.2%) males and 107 (42.8%) females. Histopathology identified 92 well-differentiated, 111 moderately differentiated, and 47 poorly differentiated tumors. Pathological lymph node metastasis was present in 108 (43.2%) patients.

Table 1. Baseline Clinical and Histopathological Characteristics

Variable	Value, n (%) or mean $\pm$ SD
Total patients	250 (100%)
Age, years	58.7 ± 11.4
Male sex	143 (57.2%)
Female sex	107 (42.8%)
Colon tumor	178 (71.2%)
Rectal tumor	72 (28.8%)
Well-differentiated tumor	92 (36.8%)
Moderately differentiated tumor	111 (44.4%)
Poorly differentiated tumor	47 (18.8%)
Lymph node negative	142 (56.8%)
Lymph node positive	108 (43.2%)
Lymphovascular invasion	83 (33.2%)

Perineural invasion	57 (22.8%)
Pathological T3/T4 disease	157 (62.8%)

4.2 Association between primary tumor imaging features and histopathological grade

Poorly differentiated tumors more frequently demonstrated increased maximum wall thickness, heterogeneous enhancement, intratumoral necrosis, peritumoral fat stranding, suspected extramural extension, and suspected EMVI.

Table 2. Association of Primary Tumor Imaging Features With Histopathological Grade

Imaging feature	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	p-value
Tumor length ≥ 5 cm	29 (31.5%)	48 (43.2%)	25 (53.2%)	0.036
Wall thickness ≥ 15 mm	18 (19.6%)	35 (31.5%)	24 (51.1%)	0.001
Circumferential involvement	34 (37.0%)	52 (46.8%)	29 (61.7%)	0.019
Heterogeneous enhancement	24 (26.1%)	43 (38.7%)	28 (59.6%)	0.001
Intratumoral necrosis	13 (14.1%)	26 (23.4%)	21 (44.7%)	0.001
Peritumoral fat stranding	21 (22.8%)	37 (33.3%)	25 (53.2%)	0.002
Suspected extramural extension	25 (27.2%)	45 (40.5%)	28 (59.6%)	0.001
Suspected EMVI	10 (10.9%)	21 (18.9%)	17 (36.2%)	0.001

EMVI = extramural vascular invasion.

4.3 Association between lymph node imaging features and pathological nodal status

Patients with pathological lymph node metastasis demonstrated larger nodal short-axis diameters, more frequent rounded morphology, irregular margins, internal heterogeneity, necrosis, and clustered nodes.

Table 3. Preoperative Lymph Node Imaging Characteristics According to Pathological Nodal Status

Imaging feature	pN0 (n=142)	pN+ (n=108)	p-value
Largest node short axis ≥ 8 mm	35 (24.6%)	65 (60.2%)	Less than 0.001
Mean largest nodal short axis, mm	6.3 $\pm$ 2.1	9.2 $\pm$ 3.4	Less than 0.001
Rounded nodal morphology	29 (20.4%)	54 (50.0%)	Less than 0.001

Irregular nodal margin	19 (13.4%)	48 (44.4%)	Less than 0.001
Internal heterogeneity	16 (11.3%)	43 (39.8%)	Less than 0.001
Nodal necrosis	8 (5.6%)	24 (22.2%)	Less than 0.001
Clustered nodes	22 (15.5%)	49 (45.4%)	Less than 0.001
At least 3 suspicious regional nodes	28 (19.7%)	62 (57.4%)	Less than 0.001

4.4 Multivariable predictors of lymph node metastasis

In the multivariable logistic regression analysis, tumor thickness, intratumoral necrosis, suspected EMVI, nodal short-axis diameter, nodal heterogeneity, irregular nodal margins, and clustered nodes remained independently associated with pathological lymph node positivity.

Table 4. Multivariable Logistic Regression Analysis of Imaging Predictors of Pathological Lymph Node Metastasis

Predictor	Adjusted OR	95% CI	p-value
Tumor thickness ≥ 15 mm	1.91	1.08–3.39	0.026
Intratumoral necrosis	2.08	1.08–4.01	0.028
Suspected EMVI	2.54	1.27–5.08	0.008
Largest node ≥ 8 mm	3.41	1.91–6.08	Less than 0.001
Nodal heterogeneity	2.67	1.42–5.02	0.002
Irregular nodal margin	2.31	1.20–4.45	0.012
Clustered regional nodes	2.46	1.33–4.54	0.004

EMVI = extramural vascular invasion; OR = odds ratio; CI = confidence interval.

4.5 Diagnostic performance of selected imaging variables

The largest nodal short-axis diameter demonstrated moderate discriminatory ability. Combining nodal size and morphology improved the diagnostic performance.

Table 5. Diagnostic Performance of Selected Imaging Variables

Imaging parameter	AUC	Sensitivity	Specificity
Nodal short-axis diameter	0.73	63.9%	76.1%
Nodal heterogeneity	0.69	39.8%	88.7%

Irregular nodal margin	0.67	44.4%	86.6%
Clustered nodes	0.71	57.4%	84.5%
Size + morphology	0.80	72.2%	79.6%
Combined imaging model	0.82	75.9%	80.3%

AUC = area under the receiver operating characteristic curve. The AUC values are and require validation using actual patient data.

5. Discussion

This study examined the association between preoperative imaging features and two clinically important pathological characteristics of colorectal cancer: histological grade and regional lymph node metastasis.

The findings suggest that primary tumor morphology and lymph node characteristics may provide complementary information regarding pathological disease severity. Greater tumor thickness, heterogeneous enhancement, necrosis, peritumoral fat stranding, and suspected extramural extension were more frequent among poorly differentiated tumors. Enlarged nodes, internal heterogeneity, irregular margins, and clustered regional nodes were associated with pathological nodal positivity.

5.1 Imaging features and histological grade

Greater tumor wall thickness, heterogeneous enhancement, necrosis, peritumoral fat stranding, and suspected extramural extension were more common in higher-grade tumors in the analysis.

These associations are biologically plausible because aggressive tumors may exhibit disorganized growth, abnormal vascularity, necrosis, and invasive extension. However, imaging cannot directly replace histopathological grading, which depends on microscopic assessment of tumor differentiation and gland formation.

The findings should therefore be interpreted as potential preoperative risk indicators

rather than evidence that CT can definitively establish tumor grade.

5.2 Lymph node size and metastasis

Larger nodal short-axis diameter was associated with pathological lymph node metastasis. However, nodal size alone has important limitations: small nodes can contain metastatic deposits, while enlarged nodes can be reactive.

The findings support combining size with morphology to improve the assessment of regional nodal disease [5–8].

5.3 Importance of nodal morphology

Internal heterogeneity and irregular margins were associated with pathological nodal positivity. Previous imaging research has also investigated nodal enhancement, contour, and internal architecture as potential indicators of metastatic disease [6,7].

These features may improve specificity, but they should not be regarded as definitive evidence of metastasis without histopathological confirmation.

5.4 Number and clustering of lymph nodes

The number and distribution of suspicious nodes may provide additional information beyond the diameter of the largest node. Multiple abnormal nodes clustered around the primary tumor or along regional lymphatic pathways may reflect more extensive lymphatic involvement [8].

Nevertheless, the diagnostic contribution of these features requires validation across different patient populations, CT protocols, and radiologist experience levels.

5.5 Extramural vascular invasion

Suspected EMVI was independently associated with nodal metastasis in the model. EMVI is an important imaging feature, particularly in rectal cancer, where MRI is used to assess local tumor extension and other high-risk characteristics [1,2]. Because CT and MRI differ in their ability to evaluate local tumor structures, EMVI assessment should be interpreted in the context of the imaging modality and tumor location.

5.6 Clinical implications

A structured imaging report may provide a more comprehensive preoperative risk profile by including:

- Tumor location and length.
- Maximum wall thickness and circumferential involvement.
- Enhancement pattern and necrosis.
- Extramural extension and EMVI.
- Largest nodal short-axis diameter.
- Nodal shape, margins, and internal heterogeneity.
- Number and clustering of suspicious regional nodes.

This approach may improve communication between radiologists, surgeons, oncologists, and pathologists. It should complement, rather than replace, definitive pathological staging.

5.7 Strengths

The study framework correlates preoperative imaging with postoperative histopathological findings. It assesses both primary tumor and lymph node characteristics, considers morphology in addition to size, and incorporates multivariable analysis.

5.8 Limitations

The cross-sectional hospital-based design may limit generalizability. Conventional CT cannot reliably identify all microscopic lymph node metastases. Imaging interpretation may vary between radiologists, and tumor grading itself can involve classification and interobserver challenges.

The analysis also excludes advanced radiomics, artificial intelligence-derived imaging features, and molecular biomarkers such as mismatch repair status, KRAS, NRAS, BRAF, and microsatellite instability. Most importantly, the numerical findings are and cannot be treated as actual clinical evidence or validated diagnostic performance.

6. Conclusion

Preoperative imaging characteristics may be associated with histopathological tumor grade and regional lymph node metastasis in colorectal cancer. Greater tumor thickness, heterogeneous enhancement, intratumoral necrosis, suspected EMVI, enlarged nodes, irregular nodal margins, internal heterogeneity, and clustered regional nodes may help identify patients at increased risk of aggressive pathological disease.

A multiparametric approach combining primary tumor morphology and lymph node characteristics may be more informative than nodal size alone. Nevertheless, imaging should complement rather than replace histopathological assessment for definitive tumor grading and confirmation of lymph node metastasis.

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