Section: Pathology

Original Research Article

HISTOPATHOLOGICAL FEATURES OF COLORECTAL CANCER: A COMPARATIVE STUDY OF DIFFERENT STAGING METHODS

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Received *: 28/02/2026*
Received in revised form *: 18/04/2026*
Accepted *: 05/05/2026*

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DOI:10.70034/ijmedph.2026.2.300

Source of Support: Nil,
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2026; 16 (2); 1803-1808

ABSTRACT

Background: Colorectal cancer is one of the leading causes of cancer-related morbidity and mortality worldwide. Histopathological evaluation and accurate staging are essential for determining prognosis and guiding treatment. Various staging systems, including TNM and Dukes staging, are used to assess disease extent and outcome. Aim: To evaluate histopathological features of colorectal cancer and compare the effectiveness of different staging methods.

Methods: This hospital-based cross-sectional comparative study included 160 histopathologically confirmed cases of colorectal cancer. Surgical specimens were examined for tumor type, grade, size, depth of invasion, lymph node involvement, lymphovascular invasion, perineural invasion, tumor budding, and margin status. Staging was performed using TNM and Dukes systems. Statistical analysis was carried out using appropriate tests, and associations were evaluated with a significance level of $p<0.05$.

Results: The mean age was 56.84±11.72 years, with a male predominance (58.1%). Adenocarcinoma was the most common histological type (85.6%), and moderately differentiated tumors were predominant (51.9%). Most cases presented in advanced stages, with TNM Stage III (45.0%) and Dukes Stage C (44.4%) being the most frequent. Significant associations were observed between advanced-stage disease and adverse histopathological features such as lymphovascular invasion, perineural invasion, high tumor budding, poor differentiation, margin involvement, and larger tumor size ($p<0.05$). Strong concordance (94.7%) was observed between TNM and Dukes staging systems.

Conclusion: Colorectal cancer commonly presents at advanced stages and is associated with multiple adverse histopathological features. TNM staging provides more detailed and accurate stratification compared to Dukes staging, although both systems show strong correlation. Comprehensive histopathological assessment combined with appropriate staging is essential for prognosis and management.

Keywords: Colorectal cancer, Histopathology, TNM staging.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies worldwide and represents a significant cause of cancer-related morbidity and mortality. It ranks among the top three cancers in terms of incidence and mortality globally, with increasing trends noted in developing countries due to changing lifestyle factors such as diet, obesity, sedentary habits, and aging populations. In India, CRC incidence is rising steadily, especially in urban populations, highlighting the need for improved diagnostic, staging, and management strategies. Histopathological evaluation remains the cornerstone for diagnosis and prognostication of

colorectal cancer, as it provides essential information regarding tumor type, grade, depth of invasion, lymph node involvement, and other prognostic indicators.[1]

Accurate staging of colorectal cancer is critical for determining prognosis, guiding treatment decisions, and predicting survival outcomes. Various staging systems have been developed over time, with the Tumor-Node-Metastasis (TNM) staging system by the American Joint Committee on Cancer being the most widely used. This system incorporates the depth of tumor invasion, regional lymph node involvement, and presence of distant metastasis. Another commonly used system is the Dukes staging system, which, although older, still provides a simplified approach to staging based on tumor spread. Histopathological examination plays a vital role in accurately assigning stages in these systems, as it directly evaluates tumor invasion and nodal status.[2]

Apart from staging, several histopathological features such as tumor differentiation, lymphovascular invasion, perineural invasion, tumor budding, and margin status have been identified as important prognostic factors. These features help in risk stratification and may influence decisions regarding adjuvant therapy. For instance, poorly differentiated tumors and those exhibiting lymphovascular invasion are associated with a higher risk of recurrence and poorer outcomes. Therefore, a comprehensive histopathological assessment is essential not only for staging but also for predicting disease behavior.[3]

Comparative evaluation of different staging methods is important to understand their clinical applicability, accuracy, and prognostic value. While the TNM system provides detailed stratification, simpler systems like Dukes staging may still be useful in resource-limited settings. Assessing the correlation between histopathological findings and staging systems can help identify the most reliable and practical method for clinical use. Moreover, such comparative studies contribute to improving diagnostic accuracy and optimizing patient management protocols.[4]

Aim

To evaluate histopathological features of colorectal cancer and compare the effectiveness of different staging methods.

Objectives

1. To assess the various histopathological features of colorectal cancer specimens.
2. To compare different staging systems and correlate them with histopathological findings.

MATERIALS AND METHODS

Source of Data

The data for the present study were obtained from patients diagnosed with colorectal cancer whose surgical resection specimens were received in the Department of Pathology of the tertiary care hospital. Relevant clinical details were collected from patient records and histopathology requisition forms.

Study Design

The study was conducted as a hospital-based cross-sectional comparative study.

Study Location

The study was carried out in the Department of Pathology in collaboration with the Department of General Surgery at a tertiary care teaching hospital.

Study Duration

The study was conducted over a period of 12 months.

Sample Size

A total of 160 histopathologically confirmed cases of colorectal cancer were included in the study.

Inclusion Criteria

- All patients with histopathologically confirmed colorectal carcinoma.
- Surgical resection specimens (colectomy, hemicolectomy, abdominoperineal resection).
- Adequate clinical and pathological data available.

Exclusion Criteria

- Biopsy specimens without definitive resection.
- Recurrent colorectal cancer cases.
- Inadequate or poorly preserved specimens.
- Patients who received neoadjuvant therapy prior to surgery (to avoid staging bias).

Procedure and Methodology

All specimens were received in 10% formalin and subjected to gross examination. Relevant details such as tumor size, location, morphology, extent of invasion, and lymph node status were noted. Sections were taken from representative areas including tumor margins, deepest point of invasion, adjacent mucosa, and lymph nodes. Histopathological examination was performed using Hematoxylin and Eosin staining.

Tumors were classified based on histological type and grade of differentiation. Staging was performed according to the TNM classification system recommended by the American Joint Committee on Cancer. Dukes staging system was also applied for comparison. Histopathological parameters such as lymphovascular invasion, perineural invasion, tumor budding, and margin involvement were assessed.

Sample Processing

Tissue specimens were fixed in 10% buffered formalin, processed using standard paraffin embedding techniques, and sectioned at 3–5 microns thickness. Sections were stained with Hematoxylin and Eosin and examined under light microscopy. Special stains were used wherever required.

Statistical Methods

Data were entered in Microsoft Excel and analyzed using statistical software (SPSS version 25.0).

Descriptive statistics such as mean, standard deviation, frequency, and percentage were used. Chi-square test was applied to assess the association between staging systems and histopathological parameters. A p-value of <0.05 was considered statistically significant.

Data Collection

Data were collected using a predesigned structured proforma including demographic details, clinical findings, histopathological features, and staging parameters. All relevant variables were systematically recorded and analyzed for correlation between staging methods and histopathological findings.

RESULTS

Table 1: Overall Clinicopathological Profile and Staging Distribution of Colorectal Cancer Cases (n=160)

Variable	Category / Value	n (%) / Mean ± SD	Test value	95% CI	p-value
Age	Mean age	56.84 ± 11.72 years	t=61.29	55.01–58.67	<0.001
Sex	Male	93 (58.1%)	χ^2=4.23	50.4–65.5%	0.040
	Female	67 (41.9%)		34.5–49.6%	
Tumor location	Colon	91 (56.9%)	χ^2=3.03	49.1–64.3%	0.082
	Rectum	69 (43.1%)		35.7–50.9%	
Histological type	Adenocarcinoma	137 (85.6%)	χ^2=81.22	79.2–90.4%	<0.001
	Mucinous carcinoma	19 (11.9%)		7.7–17.8%	
	Signet ring carcinoma	4 (2.5%)		0.9–6.2%	
Tumor grade	Well differentiated	38 (23.8%)	χ^2=19.86	17.8–30.9%	<0.001
	Moderately differentiated	83 (51.9%)		44.2–59.5%	
	Poorly differentiated	39 (24.4%)		18.3–31.5%	
TNM stage	Stage I	18 (11.3%)	χ^2=46.95	7.2–17.1%	<0.001
	Stage II	47 (29.4%)		22.8–36.9%	
	Stage III	72 (45.0%)		37.5–52.7%	
	Stage IV	23 (14.4%)		9.8–20.6%	
Dukes stage	A	17 (10.6%)	χ^2=48.73	6.7–16.3%	<0.001
	B	49 (30.6%)		24.0–38.2%	
	C	71 (44.4%)		36.9–52.1%	
	D	23 (14.4%)		9.8–20.6%	

The present study included 160 cases of colorectal cancer with a mean age of 56.84 ± 11.72 years, which was statistically significant (p<0.001), indicating that the disease predominantly affected middle-aged to elderly individuals. Males constituted a higher proportion of cases (58.1%) compared to females (41.9%), and this difference was statistically significant (p=0.040), suggesting a male predominance. Regarding tumor location, the colon was more commonly involved (56.9%) than the rectum (43.1%); however, this difference was not statistically significant (p=0.082).

Histologically, adenocarcinoma was the most common subtype, accounting for 85.6% of cases, followed by mucinous carcinoma (11.9%) and signet ring carcinoma (2.5%), with a highly significant distribution (p<0.001). In terms of tumor differentiation, moderately differentiated tumors were most frequent (51.9%), followed by poorly differentiated (24.4%) and well-differentiated tumors (23.8%), which was statistically significant (p<0.001).

According to TNM staging, the majority of patients presented in Stage III (45.0%), followed by Stage II (29.4%), Stage IV (14.4%), and Stage I (11.3%), indicating late presentation in a significant proportion of cases (p<0.001). Similarly, Dukes staging showed that most cases were in Stage C (44.4%), followed by Stage B (30.6%), Stage D (14.4%), and Stage A (10.6%), with a statistically significant distribution (p<0.001).

Table 2: Histopathological Features of Colorectal Cancer Specimens (n=160)

Histopathological Feature	Category	n (%) / Mean ± SD	Test value	95% CI	p-value
Tumor size	Mean size	4.82 ± 1.63 cm	t=37.39	4.57–5.07	<0.001
Depth of invasion	T1	11 (6.9%)	χ^2=69.84	3.8–12.0%	<0.001
	T2	26 (16.3%)		11.3–22.7%	
	T3	88 (55.0%)		47.3–62.5%	
	T4	35 (21.9%)		16.1–28.9%	
Lymph node metastasis	Present	83 (51.9%)	χ^2=0.23	44.2–59.5%	0.637
	Absent	77 (48.1%)		40.5–55.8%	
Lymphovascular invasion	Present	61 (38.1%)	χ^2=9.03	31.0–45.9%	0.003
	Absent	99 (61.9%)		54.1–69.0%	
Perineural invasion	Present	49 (30.6%)	χ^2=24.03	24.0–38.2%	<0.001
	Absent	111 (69.4%)		61.8–76.0%	
Tumor budding	Low	59 (36.9%)	χ^2=10.94	29.8–44.6%	0.004
	Intermediate	64 (40.0%)		32.7–47.7%	
	High	37 (23.1%)		17.2–30.3%	
Resection margin	Involved	14 (8.8%)	χ^2=108.90	5.3–14.2%	<0.001

	Free	146 (91.3%)		85.8–94.7%	
Necrosis	Present	73 (45.6%)	χ^2=1.23	38.1–53.4%	0.267
	Absent	87 (54.4%)		46.6–61.9%	

The mean tumor size in the study was 4.82 ± 1.63 cm, which was statistically significant (p<0.001), indicating relatively large tumor burden at presentation. The depth of invasion showed that most tumors were classified as T3 (55.0%), followed by T4 (21.9%), T2 (16.3%), and T1 (6.9%), with a highly significant distribution (p<0.001), suggesting that the majority of tumors had invaded beyond the muscularis propria.

Lymph node metastasis was present in 51.9% of cases and absent in 48.1%, but this difference was not statistically significant (p=0.637), indicating a relatively balanced distribution. Lymphovascular invasion was observed in 38.1% of cases and was statistically significant (p=0.003), highlighting its importance as a prognostic factor. Perineural invasion was present in 30.6% of cases and was also highly significant (p<0.001), suggesting aggressive tumor behavior in a subset of patients.

Tumor budding was categorized as intermediate in 40.0% of cases, low in 36.9%, and high in 23.1%, with a statistically significant distribution (p=0.004), reflecting variability in tumor aggressiveness. Resection margins were free in the majority of cases (91.3%), while margin involvement was seen in 8.8%, which was highly significant (p<0.001). Tumor necrosis was present in 45.6% of cases and absent in 54.4%, but this difference was not statistically significant (p=0.267).

Table 3: Comparison of TNM and Dukes Staging with Histopathological Risk Features (n=160)

Parameter	Early stage TNM I–II n=65	Advanced stage TNM III–IV n=95	Test value	95% CI / OR	p-value
Poor differentiation	9 (13.8%)	30 (31.6%)	χ^2=6.61	OR=2.87; 1.24–6.64	0.010
Lymphovascular invasion	13 (20.0%)	48 (50.5%)	χ^2=15.01	OR=4.09; 1.96–8.54	<0.001
Perineural invasion	10 (15.4%)	39 (41.1%)	χ^2=12.07	OR=3.83; 1.73–8.48	0.001
High tumor budding	8 (12.3%)	29 (30.5%)	χ^2=7.15	OR=3.13; 1.31–7.49	0.007
Margin involvement	2 (3.1%)	12 (12.6%)	χ^2=4.30	OR=4.55; 0.98–21.12	0.038
Mean tumor size	4.21 ± 1.38 cm	5.24 ± 1.66 cm	t=4.12	Mean difference=1.03; 0.54–1.52	<0.001
Dukes C/D correlation with TNM III/IV	94.7% concordance		κ=0.91	0.86–0.96	<0.001

The comparison between early-stage (TNM I–II) and advanced-stage (TNM III–IV) colorectal cancer revealed significant associations with adverse histopathological features. Poor differentiation was more common in advanced-stage tumors (31.6%) compared to early-stage tumors (13.8%), with a statistically significant association (p=0.010; OR=2.87), indicating higher odds of poor differentiation in advanced disease.

Lymphovascular invasion was significantly higher in advanced-stage tumors (50.5%) compared to early-stage tumors (20.0%), with a strong association (p<0.001; OR=4.09), suggesting its role as an important marker of tumor progression. Similarly, perineural invasion was observed more frequently in advanced-stage cases (41.1%) than early-stage cases (15.4%), showing statistical significance (p=0.001; OR=3.83).

High tumor budding was also significantly associated with advanced-stage disease (30.5% vs 12.3%, p=0.007; OR=3.13), indicating increased tumor aggressiveness. Margin involvement was more frequent in advanced-stage tumors (12.6%) compared to early-stage tumors (3.1%), with borderline statistical significance (p=0.038; OR=4.55). Additionally, the mean tumor size was significantly larger in advanced-stage cases (5.24 ± 1.66 cm) compared to early-stage cases (4.21 ± 1.38 cm), with a significant mean difference of 1.03 cm (p<0.001).

Furthermore, Dukes staging showed excellent concordance with TNM staging, with 94.7% agreement and a kappa value of 0.91 (p<0.001), indicating strong reliability between the two staging systems. Overall, advanced-stage colorectal cancer was strongly associated with multiple adverse histopathological features, emphasizing their prognostic significance.

DISCUSSION

In the present study, the mean age of patients with colorectal cancer was 56.84±11.72 years, showing that most cases occurred in middle-aged and elderly patients. This finding was comparable with Singla et al. (2017),[1] who reported a mean age of 57.31±15.31 years in patients with colorectal carcinoma. Male predominance was observed in the present study, with males forming 58.1% of cases, similar to the findings of Barresi et al. (2016),[2] who also reported colorectal cancer to be more frequent among males. Colon involvement was slightly higher than rectal involvement in the present study, although the difference was not statistically significant. This supports the observation that colorectal carcinoma may involve both colonic and rectal segments with variable distribution depending on geographical and demographic factors.

Adenocarcinoma was the commonest histological type in the present study, accounting for 85.6% of

cases, followed by mucinous carcinoma and signet ring carcinoma. Similar findings were reported by Wu et al. (2019),[3] who described conventional adenocarcinoma as the predominant histological type of colorectal cancer. In the present study, moderately differentiated tumors were most frequent, followed by poorly differentiated and well-differentiated tumors. This pattern was consistent with Khalil et al. (2018),[4] who emphasized that tumor grade is an important histopathological prognostic factor in colorectal carcinoma.

In the present study, most cases were diagnosed at advanced stages, with TNM Stage III being the most common stage, followed by Stage II. Similarly, Dukes C was the commonest Dukes stage. These findings were comparable with Malik et al. (2019),[5] who reported that many colorectal cancer patients presented with advanced-stage disease. Davri et al. (2022),[6] also observed that TNM and modified Dukes staging were useful in assessing disease extent and prognosis in colorectal carcinoma. The predominance of Stage III/Dukes C disease in the present study suggests delayed presentation and highlights the need for early screening and timely diagnosis.

The mean tumor size in the present study was 4.82±1.63 cm. Most tumors showed T3 invasion, followed by T4, indicating that the majority had extended beyond the muscularis propria. Similar observations were made by Falih Soliman et al. (2022),[7] who stated that depth of tumor invasion is a key component of TNM staging and has direct prognostic relevance. Lymph node metastasis was present in 51.9% of cases in the present study, which was slightly higher than that reported by Araujo et al. (2015),[8] where lymph node metastasis was observed in 43.6% of cases. This difference may be due to variation in case selection, stage at presentation, and adequacy of lymph node retrieval.

Lymphovascular invasion was present in 38.1% of cases and perineural invasion in 30.6% of cases in the present study. Both were significantly associated with adverse pathological features. Hsu et al. (2019),[9] reported that lymphovascular invasion, perineural invasion, and tumor budding were important prognostic factors in colon cancer. Konishi et al. (2018),[10] also observed that lymphovascular and perineural invasion were associated with poorer outcomes in locally advanced colorectal cancer. Thus, the present findings support the role of these parameters as important markers of aggressive tumor behavior.

Tumor budding was observed as low, intermediate, and high in 36.9%, 40.0%, and 23.1% of cases respectively, and showed statistically significant distribution. High tumor budding was significantly more common in advanced TNM stages. This was in accordance with Bahnassy et al. (2019),[11] who noted that histopathological features such as tumor budding and differentiation may be associated with lymph node metastasis and disease progression. Tumor budding is now increasingly recognized as an important marker of epithelial-mesenchymal transition and tumor invasiveness.

In the comparison between early-stage and advanced-stage disease, poor differentiation, lymphovascular invasion, perineural invasion, high tumor budding, margin involvement, and larger tumor size were significantly more frequent in advanced-stage tumors. These findings indicate that advanced TNM stage was strongly associated with adverse histopathological risk factors. The odds of lymphovascular invasion and perineural invasion were notably higher in advanced-stage disease, supporting their role in tumor progression and metastatic potential.

The present study also showed excellent concordance between Dukes C/D and TNM III/IV staging, with 94.7% agreement and a kappa value of 0.91. This indicates that although Dukes staging remains simple and practical, TNM staging provides more detailed pathological stratification. Similar conclusions were drawn by Morino et al. (2015),[12] and Peng et al. (2018),[13] who observed that TNM and Dukes staging systems are useful for prognostication, but TNM allows better subclassification of disease extent.

CONCLUSION

The present study demonstrated that colorectal cancer predominantly affects middle-aged and elderly individuals, with a slight male predominance. Histopathologically, adenocarcinoma was the most common subtype, with moderately differentiated tumors forming the majority. A significant proportion of cases presented at advanced stages, as evidenced by the predominance of TNM Stage III and Dukes Stage C disease, indicating delayed diagnosis and the need for improved screening strategies.

Detailed histopathological evaluation revealed that adverse prognostic features such as lymphovascular invasion, perineural invasion, high tumor budding, poor differentiation, margin involvement, and larger tumor size were significantly associated with advanced-stage disease. These parameters reflect aggressive tumor biology and play a crucial role in predicting disease progression and outcomes.

The study also established a strong correlation between TNM and Dukes staging systems, with excellent concordance observed between advanced stages in both systems. However, TNM staging provided more comprehensive and precise stratification of tumor extent, nodal involvement, and metastasis, making it a superior and more informative staging system in modern clinical practice.

Limitations of the study

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings.
2. The sample size, although adequate, may not fully represent the broader population.
3. Being a cross-sectional study, long-term follow-up and survival outcomes could not be assessed.
4. Molecular and genetic markers of colorectal cancer were not evaluated.
5. Interobserver variability in histopathological interpretation was not assessed.
6. The study excluded patients who received neoadjuvant therapy, which may limit applicability in such cases.
7. Limited evaluation of rare histological subtypes due to small numbers.
8. Environmental and lifestyle risk factors were not analyzed in correlation with histopathological findings.
9. Imaging correlation with staging was not included.
10. Lack of comparison with newer prognostic scoring systems beyond TNM and Dukes staging.

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