



## RESEARCH ARTICLE

## Clinicopathological Profile and Tnm Stage Distribution of Colorectal Adenocarcinoma

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### ABSTRACT

**Background:** Colorectal cancer (CRC) stands as a formidable global health challenge, representing the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide. From a histopathological perspective, the landscape of CRC is dominated by adenocarcinoma. The clinical impact of colorectal adenocarcinoma is intrinsically linked to the stage at which the disease is detected. Accurate pathological staging and identification of adverse histopathological features are therefore essential for prognosis and treatment planning.

**Methods:** This prospective observational study included 50 consecutive patients with a new, histologically confirmed diagnosis of colorectal adenocarcinoma at a tertiary care hospital. Demographic and clinical characteristics, tumor localization, histological grade, lymphovascular invasion (LVI), perineural invasion (PNI), and TNM stage were evaluated. Patients were stratified into three age groups: <40 years, 40-59 years, and ≥60 years. Pathological staging was performed according to the eighth edition of the AJCC/UICC TNM staging system. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

**Results:** The mean age of the study cohort was  $57.8 \pm 12.1$  years, with 46.0% of patients aged ≥60 years. Males constituted 64.0% of the cohort. Rectal bleeding was the most common presenting symptom (62.0%), followed by altered bowel habits (56.0%) and abdominal pain (44.0%). The rectum was the most common primary tumor site (42.0%), followed by the left colon (36.0%) and right colon (22.0%). Moderately differentiated adenocarcinoma was the predominant histological grade (64.0%), while poorly differentiated tumors accounted for 22.0%. LVI was present in 48.0% and PNI in 28.0% of patients. Stage III was the most common stage group (38.0%), followed by Stage II (26.0%), Stage IV (24.0%), and Stage I (12.0%). Overall, 62.0% of patients presented with Stage III/IV disease. Advanced stage was significantly associated with older age ( $p=0.04$ ), poor tumor differentiation ( $p<0.01$ ), lymph node positivity ( $p<0.001$ ), and LVI ( $p<0.001$ ).

**Conclusion:** Colorectal adenocarcinoma in the studied population predominantly presented at an advanced stage, particularly among older male adults. Rectal and left-sided tumors were the most frequent, while poor differentiation, lymph node positivity, and LVI were strongly associated with advanced disease. These findings emphasize the importance of structured early detection and screening programs and meticulous histopathological evaluation for appropriate stage-based management.

**Keywords:** colorectal adenocarcinoma; colorectal cancer; TNM staging; histopathology; lymphovascular invasion

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### INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide [1]. Although historically more common in developed countries, its incidence is increasingly rising among younger populations, highlighting its evolving epidemiology [1,2].

Colorectal adenocarcinoma accounts for over 90% of CRC cases and arises from the glandular epithelium of the colorectal mucosa, commonly through the adenoma-carcinoma sequence [3-5]. Prognosis is strongly influenced by the stage at diagnosis. While Stage I/II disease may be curable with surgical resection, Stage III and IV disease requires multimodal treatment and is associated with

poorer outcomes [6,3]. Delayed presentation remains a major concern, particularly in settings without established screening programs, where patients may present with rectal bleeding, altered bowel habits, obstruction, or weight loss [7,3,8].

The TNM staging system provides a standardized assessment of tumor extent based on primary tumor invasion (T), regional lymph node involvement (N), and distant metastasis (M) [9]. In addition to TNM stage, histopathological parameters including tumor differentiation, lymphovascular invasion (LVI), and perineural invasion (PNI) provide important prognostic information [5,9]. Molecular characteristics such as microsatellite instability and KRAS/BRAF status further

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contribute to understanding tumor biology and treatment selection [10].

Tumor location also influences clinical presentation and biological behavior, with right-sided, left-sided, and rectal tumors demonstrating distinct clinicopathological characteristics [1,2]. Regional studies have reported variations in demographic profile, clinical presentation, and stage distribution, emphasizing the importance of institution-specific data [7].

Therefore, evaluation of the clinicopathological profile and TNM stage distribution of colorectal adenocarcinoma is important for identifying patterns of presentation, recognizing adverse pathological features, and strengthening strategies for early diagnosis and Appropriate Management.

## **MATERIALS AND METHODS**

This was a prospective observational study conducted over a period of 12 months in the Department of Pathology, in collaboration with the Department of General Surgery, Index Medical College Hospital & Research Centre, Indore. The study was designed to evaluate the clinicopathological profile and stage at presentation of patients with histologically confirmed colorectal adenocarcinoma.

The study cohort comprised 50 consecutive patients with a new, histologically confirmed diagnosis of colorectal adenocarcinoma during the study period. Patients were included irrespective of age, gender, or clinical stage.

### **Inclusion Criteria**

Patients with a new, histologically confirmed diagnosis of colorectal adenocarcinoma during the study period were included in the study.

### **Exclusion Criteria**

The following patients were excluded from the study:

- Patients with other histological types of colorectal malignancy, such as neuroendocrine tumors, gastrointestinal stromal tumors, and lymphomas.
- Patients with recurrent colorectal adenocarcinoma.
- Cases where the primary tumor site was ambiguous or where insufficient tissue was available for complete histopathological evaluation.

## **METHODOLOGY**

After obtaining informed consent, detailed demographic and clinical data were recorded for each participant using a standardized proforma. Collected data included:

- Demographics: Age, gender.
- Clinical Presentation: Primary presenting symptoms (e.g., rectal bleeding, altered bowel habits, abdominal pain, weight loss, obstruction) and their duration.
- Tumor Localization: The anatomical location of the primary tumor was categorized based on endoscopic and surgical findings as: right colon (cecum, ascending colon, hepatic flexure, transverse colon), left colon (splenic flexure, descending colon, sigmoid colon), and rectum.
- Age Cohorts: For analytical purposes, patients were stratified into three age groups: young adults (<40 years), middle-aged adults (40–59 years), and older adults (≥60 years).

### **Pathological Evaluation**

All histopathological assessments were performed on formalin-fixed, paraffin-embedded tissue specimens obtained from either endoscopic biopsies or surgical resections. The definitive assessment was based on the examination of the surgical resection specimen whenever available. The evaluation was conducted by experienced pathologists blinded to the patient's clinical details (except for tumor location). The following parameters were systematically recorded:

- **Histological Type and Grade:** Tumors were classified according to the World Health Organization (WHO) classification. Adenocarcinomas were subtyped (e.g., conventional, mucinous, signet-ring cell, etc.). Tumor differentiation was graded as well (G1), moderately (G2), or poorly differentiated (G3) based on the extent of gland formation.
- **Pathological Prognostic Markers:** The presence or absence of lymphovascular invasion (LVI) and perineural invasion (PNI) was specifically evaluated and documented.
- **TNM Staging:** Pathological staging (pTNM) was performed for resection specimens according to the 8th edition of the AJCC/UICC TNM staging system for colorectal cancer. The depth of tumor invasion (pT), number of regional lymph nodes examined and number involved (pN), and presence of distant metastasis (pM) were recorded. For biopsy-only cases (e.g., inoperable metastatic disease), clinical and radiological staging (cTNM) was used and clearly noted. The integrated stage groups (I, II, III, IV) were derived from the TNM components.

### Statistical Analysis

Data were compiled and analyzed using statistical software SPSS version 26. Descriptive statistics were expressed as mean  $\pm$  standard deviation for continuous variables (like age) and as frequencies and percentages for categorical variables (like gender, tumor location, grade, stage). Associations between categorical variables, such as age cohorts and clinicopathological parameters (tumor grade, stage, LVI, PNI), were assessed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

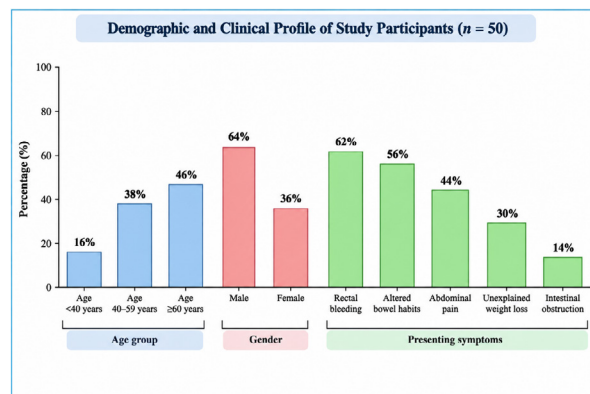
### Demographic and Clinical Profile

The cohort had a mean age of 57.8 years, with nearly half of the patients belonging to the  $\geq 60$  years age group. A clear male predominance (64%) was observed. Among the presenting symptoms, rectal bleeding (62%) and altered bowel habits (56%) were the most common and frequently occurred together. Abdominal pain and unexplained weight loss were also reported, although less frequently. Overall, these findings describe the demographic profile and major symptomatic presentations leading to clinical evaluation in the study population. [Table 1, Graph 2]

**Table 1:** Demographic and Clinical Profile of the Study Cohort (n=50)

| Variable                   | Category                | Number of Patients (n) | Percentage (%) |
|----------------------------|-------------------------|------------------------|----------------|
| Age (Years)                | Mean $\pm$ SD           | 57.8 $\pm$ 12.1        | --             |
|                            | <40                     | 8                      | 16.0           |
|                            | 40-59                   | 19                     | 38.0           |
|                            | $\geq 60$               | 23                     | 46.0           |
| Gender                     | Male                    | 32                     | 64.0           |
|                            | Female                  | 18                     | 36.0           |
| Primary Presenting Symptom | Rectal Bleeding         | 31                     | 62.0           |
|                            | Altered Bowel Habits    | 28                     | 56.0           |
|                            | Abdominal Pain          | 22                     | 44.0           |
|                            | Unexplained Weight Loss | 15                     | 30.0           |
|                            | Intestinal Obstruction  | 7                      | 14.0           |
|                            |                         |                        |                |

\*Patients often presented with more than one symptom.



**Graph 1:** Demographic and Clinical Profile of the Study Cohort (n=50)

### Tumor Location and Histopathological Grade

The rectum was the most common primary tumor site (42%), followed by the left colon (36%), while the right colon was involved in 22% of cases. Histologically, moderately differentiated tumors (Grade 2) predominated (64%), representing the most frequent histological grade. Poorly differentiated tumors (Grade 3) accounted for 22% of cases and represent a subset with more aggressive pathological characteristics. Overall, the findings demonstrate the

**Table 2:** Tumor Location and Histopathological Grade (n=50)

| Characteristic     | Category                          | Number of Patients (n) | Percentage (%) |
|--------------------|-----------------------------------|------------------------|----------------|
| Primary Tumor Site | Rectum                            | 21                     | 42.0           |
|                    | Left Colon (Sigmoid, Descending)  | 18                     | 36.0           |
|                    | Right Colon (Cecum to Transverse) | 11                     | 22.0           |
| Histological Grade | Well Differentiated (G1)          | 7                      | 14.0           |
|                    | Moderately Differentiated (G2)    | 32                     | 64.0           |
|                    | Poorly Differentiated (G3)        | 11                     | 22.0           |

anatomical distribution and histological grade of colorectal adenocarcinoma in the study population. [Table 2, Graph 2]

### Pathological Prognostic Markers

Lymphovascular invasion (LVI) was present in 48% of cases, while perineural invasion (PNI) was identified in 28% of patients. Notably, 18% of patients demonstrated both LVI and PNI concurrently, indicating the presence of adverse pathological features in a subset of tumors. These findings highlight the importance of assessing LVI and PNI as part of the histopathological evaluation, as their presence provides additional prognostic information beyond TNM staging. [Table 3, Graph 3]

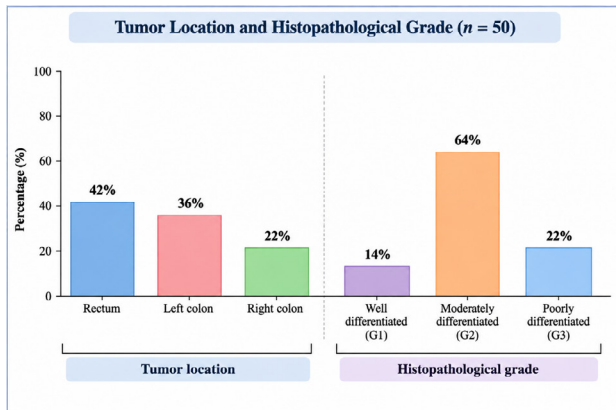
### Pathological TNM Stage Distribution

Only 38% of patients presented with early-stage disease (Stage I/II), whereas 62% were diagnosed at an advanced

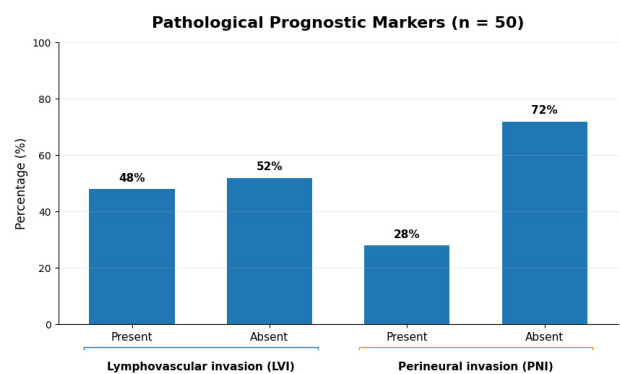
stage (Stage III/IV). Stage III was the most common stage (38%), followed by Stage IV (24%). Furthermore, 52% of patients had lymph node metastasis (N+) at diagnosis. These findings indicate a high burden of advanced disease and emphasize the importance of early detection and accurate pathological staging in colorectal adenocarcinoma. [Table 4, Graph 4]

### Association of Advanced Stage (III/IV) With Age Cohort and Pathological Features

Advanced-stage disease showed a significant association with increasing age, with the proportion of Stage III/IV disease rising from 37.5% in patients aged <40 years to 63.2% in those aged 40-59 years and 69.6% in those aged ≥60 years (p=0.04). A strong association was also observed with tumor grade, as 90.9% of poorly differentiated (G3) tumors were diagnosed at Stage III/IV compared with



**Graph 2:** Tumor Location and Histopathological Grade (n=50)



**Graph 3:** Key Pathological Prognostic Markers (n=50)

**Table 3:** Key Pathological Prognostic Markers (n=50)

| Pathological marker           | Present (n) | Percentage (%) | Absent (n) | Percentage (%) |
|-------------------------------|-------------|----------------|------------|----------------|
| Lymphovascular Invasion (LVI) | 24          | 48.0           | 26         | 52.0           |
| Perineural Invasion (PNI)     | 14          | 28.0           | 36         | 72.0           |

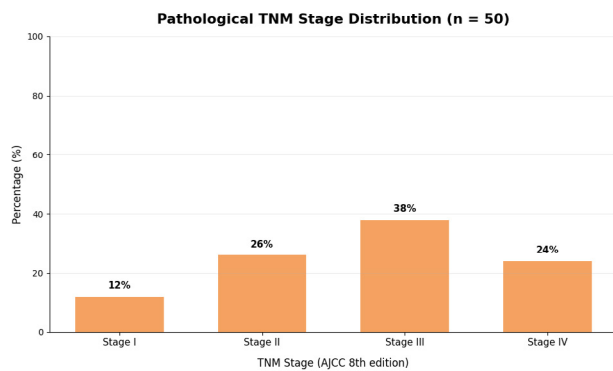
Note: 9 patients (18%) had both LVI and PNI present concurrently.

**Table 4:** Pathological TNM Stage Distribution (n=50)

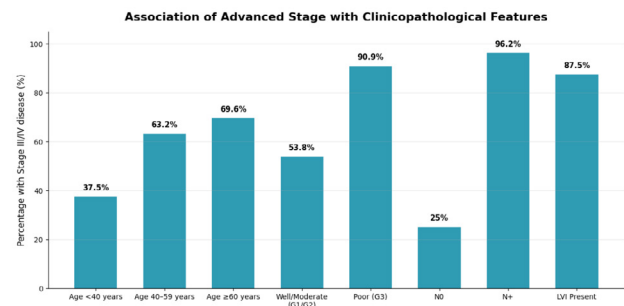
| Stage Group (AJCC 8th Ed.)     | TNM Classification | Number of Patients (n) | Percentage (%) |
|--------------------------------|--------------------|------------------------|----------------|
| Stage I                        | T1-T2, N0, M0      | 6                      | 12.0           |
| Stage II                       | T3-T4, N0, M0      | 13                     | 26.0           |
| Stage III                      | Any T, N1-N2, M0   | 19                     | 38.0           |
| Stage IV                       | Any T, Any N, M1   | 12                     | 24.0           |
| Lymph Node Status (All Stages) | Node Positive (N+) | 26                     | 52.0           |
|                                | Node Negative (N0) | 24                     | 48.0           |

53.8% of well/moderately differentiated tumors ( $p<0.01$ ). Lymph node status demonstrated the strongest association, with 96.2% of N+ cases presenting with Stage III/IV disease compared with 25.0% of N0 cases ( $p<0.001$ ). Similarly, 87.5% of patients with LVI had advanced-stage disease.

These findings demonstrate that advanced-stage colorectal adenocarcinoma is closely associated with adverse clinicopathological features, particularly lymph node positivity, poor differentiation, and LVI. [Table 5, Graph 5]



**Graph 4:** Pathological TNM Stage Distribution (n=50)



**Graph 5:** Association of Advanced Stage (III/IV) with Age Cohort and Pathological Features

**Table 5:** Association of Advanced Stage (III/IV) with Age Cohort and Pathological Features

| Variable              | Stage I/II (n=19)   | Stage III/IV (n=31)  | p-value |
|-----------------------|---------------------|----------------------|---------|
| Age Cohort            |                     |                      | 0.04    |
| <40 years             | 5 (62.5% of cohort) | 3 (37.5% of cohort)  |         |
| 40-59 years           | 7 (36.8% of cohort) | 12 (63.2% of cohort) |         |
| ≥60 years             | 7 (30.4% of cohort) | 16 (69.6% of cohort) |         |
| Tumor Grade           |                     |                      | <0.01   |
| Well/Moderate (G1/G2) | 18 (46.2% of G1/G2) | 21 (53.8% of G1/G2)  |         |
| Poor (G3)             | 1 (9.1% of G3)      | 10 (90.9% of G3)     |         |
| Lymph Node Status     |                     |                      | <0.001  |
| N0                    | 18 (75.0% of N0)    | 6 (25.0% of N0)      |         |
| N+                    | 1 (3.8% of N+)      | 25 (96.2% of N+)     |         |
| LVI Present           | 3 (12.5% of LVI+)   | 21 (87.5% of LVI+)   | <0.001  |

Chi-square test;  $p < 0.05$  considered significant.

## DISCUSSION

The present study demonstrates a substantial burden of advanced colorectal adenocarcinoma at diagnosis. In our cohort of 50 patients, 62% presented with Stage III/IV disease, while only 38% had Stage I/II disease. This pattern highlights the continuing problem of delayed diagnosis, particularly in settings where organized screening and early detection remain limited [3,4,11]. Advanced colorectal cancer may involve regional lymph nodes or distant organs and often requires multimodal treatment, resulting in greater therapeutic complexity and poorer outcomes [1,4].

A male predominance (64%) was observed, while 46% of patients were aged  $\geq 60$  years. Increasing age was significantly associated with advanced disease ( $p=0.04$ ), with 69.6% of patients aged  $\geq 60$  years presenting with Stage III/IV disease. This finding is consistent with the established age-related increase in colorectal cancer incidence [3,12]. At the same time, the increasing occurrence of colorectal cancer among younger individuals emphasizes the changing epidemiological profile of the disease [3,12].

Rectal bleeding was the most common presenting symptom (62%), followed by altered bowel habits (56%) and abdominal pain (44%). The predominance of rectal and left-sided tumors in our cohort may partly account for the frequent occurrence of rectal bleeding and bowel habit changes. Clinical presentation varies according to tumor location, with left-sided and rectal lesions more commonly producing bleeding and obstructive symptoms [3,12]. In our study, the rectum was the most common tumor site (42%), followed by the left colon (36%) and right colon (22%). Similar regional variations have been reported in tertiary-care populations, emphasizing the value of institution-specific data [11].

Histologically, moderately differentiated adenocarcinoma was predominant (64%), whereas 22% of tumors were poorly differentiated. Poor differentiation was significantly associated with advanced disease ( $p<0.01$ ), with 90.9% of poorly differentiated tumors occurring in Stage III/IV disease. Histological grade reflects tumor differentiation and provides important prognostic information in addition to anatomical staging [2,8]. Other histological variants may also demonstrate distinct biological behavior. Rare forms such as adenocarcinoma with enteroblastic differentiation present specific diagnostic challenges, while mixed histological subtypes may demonstrate differences in clinical behavior and survival [13].

Lymphovascular invasion (LVI) was present in 48% of patients and showed a highly significant association

with advanced stage ( $p<0.001$ ). Among patients with LVI, 87.5% had Stage III/IV disease. LVI represents an important marker of aggressive tumor biology and potential metastatic spread [8]. Perineural invasion (PNI) was present in 28% of patients, and 18% demonstrated both LVI and PNI. These findings reinforce the importance of comprehensive pathological assessment, as both features provide additional prognostic information beyond TNM stage [8].

Lymph node involvement was identified in 52% of patients and demonstrated the strongest association with advanced disease ( $p<0.001$ ). Among node-positive patients, 96.2% had Stage III/IV disease. This finding emphasizes the importance of accurate assessment of regional lymph nodes in colorectal cancer staging [8]. The TNM system provides a standardized framework for describing primary tumor extent, nodal involvement, and distant metastasis and remains fundamental to clinical decision-making [5].

The biological heterogeneity of colorectal adenocarcinoma further influences its clinical behavior. Specific variants, including micropapillary adenocarcinoma, have been associated with increased lymphovascular invasion and lymph node metastasis [14]. Colorectal cancer may also present with unusual patterns of metastatic spread, including isolated skeletal involvement, although such presentations are uncommon [10]. These observations emphasize that anatomical stage should be interpreted together with histological characteristics and other pathological findings.

Molecular characterization has further expanded understanding of colorectal cancer. Microsatellite instability and alterations involving genes such as KRAS and BRAF contribute to differences in tumor biology and treatment response [14]. Although molecular parameters were not assessed in the present study, their incorporation into future investigations could provide additional information regarding tumor heterogeneity and individualized treatment.

The findings should be interpreted in light of certain limitations. The relatively small sample size and single-center study design may limit generalizability. In addition, molecular characteristics were not evaluated. Nevertheless, the study provides useful institution-specific information regarding demographic characteristics, clinical presentation, tumor location, histological grade, adverse pathological features, and TNM stage distribution.

Overall, the high proportion of Stage III/IV disease (62%), together with the significant associations of advanced stage with older age, poor differentiation, lymph node positivity, and LVI, emphasizes the importance of early detection and comprehensive pathological

evaluation. Accurate staging, careful assessment of adverse histopathological features, and appropriate integration of clinical and pathological information remain essential for effective multidisciplinary management of colorectal adenocarcinoma.

## CONCLUSION

In conclusion, this clinicopathological study confirms that colorectal adenocarcinoma in our setting predominantly presents at an advanced stage, with a significant burden falling on older male adults. The disease frequently originates in the rectum and left colon, and its advanced stage is strongly correlated with adverse histopathological features, including poor differentiation and the presence of lymphovascular invasion. These findings collectively emphasize the urgent need for the implementation and promotion of structured early detection and screening programs, particularly targeted at high-risk older populations.

Furthermore, they underscore the indispensable role of meticulous histopathological evaluation in identifying high-risk features that guide personalized, stage-appropriate management. A multidisciplinary approach, grounded in precise staging and comprehensive pathological reporting, remains fundamental to improving outcomes for patients with colorectal adenocarcinoma.

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