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Original Article

Clinicopathological Characteristics and Treatment Outcomes of Early-Onset Versus Late-Onset Rectal Adenocarcinoma: A Retrospective Comparative Study

Dr. Tamal Chakraborty[1], Dr. Subhayan Saha[2], Dr. Pabitra Das[3]

[1]Senior Resident, Md, Radiotherapy, College Of Medicine Sagore Dutta Hospital, Kamarhati, North 24 Parganas
[2]Senior Resident, Md, Radiotherapy Chittaranjan National Cancer Institute (Cnci), Kolkata
[3]Associate Professor, Md, Radiotherapy Institute Of Post Graduate Medical Education And Research, Seth Sukhlal Karnani Memorial Hospital, Kolkata

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Corresponding Author:

Dr. Subhayan Saha
Senior Resident, Md, Radiotherapy Chittaranjan National Cancer Institute (Cnci), Kolkata

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ABSTRACT

Background: Over the past 20 years, there has been a global increase in the frequency of early-onset rectal adenocarcinoma, which has raised concerns about its different clinicopathological features and treatment results when compared to late-onset disease. There is still little information about treatment response and survival results, especially in the Indian population, despite the fact that numerous research have detailed variations in tumor biology.
Objective: To assess the relationship between treatment results and the clinicopathological features of early-onset and late-onset rectal adenocarcinoma
Material and Methods: The Department of Radiotherapy at the Institute of Post Graduate Medical Education and Research (IPGMER) and SSKM Hospital in Kolkata, India, was the site of this retrospective comparative observational study. Patients treated on curative intent between January and December 2023 for rectal cancer with histological confirmation had their medical records examined. The 88 eligible patients were divided into two groups: early-onset (less than 45 years old; n = 41) and late-onset (more than 45 years old; n = 47). Analysis was done on demographics, clinical presentation, radiological findings, pathological features, therapeutic options, recurrence, disease progression, and overall survival. Using suitable parametric and non-parametric tests, comparative statistical analyses were carried out; a p-value of less than 0.05 was deemed statistically significant.
Results: The early-onset group's mean age was 38.6±4.8 years, while the late-onset group's mean age was 58.9±9.7 years. Compared to older patients, younger patients were more likely to have locally progressed tumors, reduced rectal involvement, poor differentiation, lymphovascular invasion, and nodal positivity. In both groups, the most common course of treatment was neoadjuvantchemoradiotherapy followed by surgery. Disease recurrence was more common in the early-onset group (26.8%) than in the late-onset group (14.9%) over a median follow-up of 18 months. While overall survival remained similar between the groups throughout the research period, Disease recurrence was higher among younger patients, whereas overall survival remained comparable between the two groups.
Conclusion: Compared to late-onset disease, early-onset rectal adenocarcinoma showed more aggressive clinicopathological characteristics and a higher risk of recurrence. Despite these negative traits, multimodality treatment produced comparable overall survival. Younger individuals may benefit from early detection, prompt diagnosis, and customized treatment plans. To confirm these results, larger multicenter trials with longer follow-up are necessary.

Keywords*: Rectal adenocarcinoma; Early-onset rectal cancer; Late-onset rectal cancer; Clinicopathological characteristics; Treatment outcomes; Retrospective study.*

INTRODUCTION

Colorectal cancer (CRC) is the second most common cause of cancer-related death globally and the third most common type of cancer. Rectal adenocarcinoma continues to be a significant contribution to the worldwide cancer burden, accounting for around one-third of all colorectal malignancies. In recent decades, improvements in screening programs, imaging methods, multimodality therapy, and surgical treatments including total mesorectal excision have significantly increased local disease control and survival. However, due to its variable biological behavior, recurrence risk, and long-term treatment-related morbidity, rectal cancer still presents substantial clinical problems.[1,2]

Since most incidences of colorectal cancer occur beyond the age of 50, the disease has historically been thought to mostly afflict older persons. Nonetheless, early-onset colorectal cancer has become more common in several nations during the past 20 years, especially rectal cancer. According to epidemiological research, the incidence of rectal adenocarcinoma has decreased in older adults due to screening programs, but it has continued to climb in younger people. The distinctive clinical features and biological behavior of early-onset rectal cancer have attracted a lot of attention due to this new trend.[3,4]

Although various institutional studies have employed age cut-offs of 45 years, depending on study objectives and regional demographics, early-onset rectal adenocarcinoma is commonly defined as the illness detected before 50 years of age. Rectal bleeding, altered bowel habits, stomach pain, and weight loss are common symptoms in younger individuals. However, because these symptoms are easily mistaken for benign anorectal illnesses, delayed diagnosis is common. As a result, many young patients need multimodality treatment since their disease is locally progressed.[4,5]

The clinicopathological features of early-onset and late-onset rectal cancer have been compared by a number of researchers. More aggressive pathological features, such as poor tumor differentiation, mucinous or signet-ring histology, lymphovascular invasion, perineural invasion, advanced T stage, nodal involvement, and a higher incidence of metastatic disease at presentation, have been observed in younger patients. The impact of age on survival is still debatable despite these unfavorable disease traits. While some studies found equivalent or even better overall survival with rigorous multimodality treatment, others found lower disease-free and recurrence-free survival among younger patients.[5–8]

The management of locally advanced rectal adenocarcinoma has evolved considerably with the adoption of multimodality treatment strategies. Standard treatment consists of long-course neoadjuvant chemoradiotherapy followed by definitive surgical resection, either low anterior resection (LAR) or abdominoperineal resection (APR), with total mesorectal excision (TME) as the cornerstone of curative surgery. Depending on pathological staging and treatment response, patients may subsequently receive neoadjuvant and/or adjuvant systemic chemotherapy. Although younger patients generally tolerate intensive multimodality treatment better because of fewer comorbidities and better performance status, their outcomes may still be influenced by the aggressive biological behaviour of the tumour. Therefore, understanding age-related differences in disease presentation and treatment response is essential for optimizing individualized therapeutic strategies.[6,8]

There is still a dearth of information on early-onset rectal cancer in India. Without thoroughly assessing treatment outcomes including recurrence, illness progression, and survival following multimodality treatment, the majority of published research have mostly concentrated on clinicopathological features. Moreover, institution-specific data is required to inform therapeutic decision-making due to differences in tumor biology, healthcare accessibility, and demographic features among various populations.[5,9]

In order to assess the clinicopathological profile of patients with early-onset and late-onset rectal adenocarcinoma treated at a tertiary care referral center and ascertain the relationship between these features and treatment outcomes, the current retrospective comparative observational study was conducted. The results of this study may enhance knowledge of age-related variations in rectal adenocarcinoma and help optimize treatment planning, risk assessment, and follow-up tactics.

MATERIALS AND METHODS

Study Design and Setting

The Department of Radiotherapy at the Institute of Post Graduate Medical Education and Research (IPGMER) and SSKM Hospital, a tertiary care referral center for gastrointestinal cancers in Kolkata, West Bengal, India, was the site of this retrospective, comparative, single-center observational study. Patient anonymity and confidentiality were maintained throughout the study in accordance with the principles of the Declaration of Helsinki.

Study Objectives

Primary Objective

To compare the clinicopathological characteristics of patients with early-onset and late-onset rectal adenocarcinoma.

Secondary Objective
To evaluate the correlation between age at diagnosis and treatment outcomes, including disease progression, recurrence, and overall survival.

Study Population
Medical records of patients with histopathologically confirmed rectal adenocarcinoma who received treatment in the Department of Radiotherapy between **January 2023 and December 2023** were retrospectively reviewed.

A total of **105** patients were screened for eligibility. Seventeen patients were excluded because of incomplete clinical records or failure to satisfy the study criteria. Consequently, **88 patients** were included in the final analysis and categorized according to their age at diagnosis:

- **Early-onset group:** patients aged **<45 years** (n = 41)
- **Late-onset group:** patients aged **≥45 years** (n = 47)

The study design and patient selection process are summarized in the study flow diagram.

Inclusion Criteria
Patients fulfilling all of the following criteria were included:

- Histopathologically confirmed adenocarcinoma of the rectum.
- Clinical and/or pathological stage T1–T4 with node-positive or node-negative disease.
- Received long-course neoadjuvantchemoradiotherapy with concurrent 5-fluorouracil or capecitabine where indicated.
- Underwent definitive surgical resection, including total mesorectal excision (TME), low anterior resection (LAR), or abdominoperineal resection (APR), either as upfront surgery or following neoadjuvantchemoradiotherapy.
- Received neoadjuvant and/or adjuvant chemotherapy according to institutional treatment protocols.
- Minimum follow-up duration of 12 months after completion of treatment.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0–3.

Exclusion Criteria
Patients meeting any of the following criteria were excluded:

- Distant metastatic disease (Stage IV) at initial presentation.
- Recurrent rectal cancer at the time of presentation.
- History of another primary malignancy within the preceding five years.
- Incomplete neoadjuvantchemoradiotherapy or refusal/incompletion of definitive surgery.
- Inadequate follow-up (<12 months) or loss to follow-up.
- Missing essential clinicopathological data.
- ECOG performance status of 4.

Data Collection
Clinical records, electronic medical records, radiological reports, histopathology reports, operative notes, chemotherapy records, and follow-up documentation were reviewed. Data were extracted using a standardized data collection form. The following variables were recorded:

Demographic and Clinical Variables

- Age at diagnosis
- Sex
- Residential area
- Presenting symptoms
- ECOG performance status

Radiological and Staging Variables
Pretreatment magnetic resonance imaging (MRI) findings included:

- Distance of the tumour from the anal verge
- Tumour location (upper, middle, or lower rectum)
- Clinical T stage (cT)
- Clinical nodal stage (cN)
- Pathological T and N stage
- Extramural venous invasion (EMVI)
- Mesorectal fascia (MRF) involvement

Histopathological Variables
The following pathological characteristics were recorded:

- Histological subtype
- Tumour differentiation
- Pathological T stage
- Pathological nodal status
- Lymphovascular invasion
- Perineural invasion
- Resection margin status

Treatment Variables
Treatment details included:

1. Neoadjuvantchemoradiotherapy
2. Concurrent chemotherapy regimen
3. Neoadjuvant chemotherapy
4. Type of surgical procedure (TME, LAR, APR)
5. Adjuvant chemotherapy
6. Adjuvant chemoradiotherapy where indicated

Treatment strategies were categorized as:

1. Neoadjuvantchemoradiotherapy → chemotherapy → surgery
2. Neoadjuvantchemoradiotherapy → surgery → adjuvant chemotherapy
3. Upfront surgery → adjuvant chemotherapy
4. Upfront surgery → adjuvant chemoradiotherapy

These treatment categories reflected institutional multidisciplinary management protocols.

Outcome Measures
Primary Outcome
Comparison of clinicopathological characteristics between early-onset and late-onset rectal adenocarcinoma.

Secondary Outcomes
Treatment outcomes evaluated included:

- treatment outcomes including recurrence, disease-free survival and overall survival
- Local recurrence
- Distant recurrence
- Disease-free survival
- Overall survival
- Recurrence rates at 12, 18, and 24 months after treatment completion

Patients were followed through outpatient visits and institutional records until the last available follow-up.

Statistical Analysis
Data were entered into Microsoft Excel and analysed using the Statistical Package for the Social Sciences (SPSS) software, version XX (IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution. Categorical variables were presented as frequencies and percentages.

Comparisons between the early-onset and late-onset groups were performed using the independent Student's *t*-test or Mann–Whitney *U* test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Disease-free survival and overall survival were analysed using the Kaplan–Meier method, and differences between survival curves were assessed using the log-rank test. Variables showing statistical significance in univariate analysis were considered for multivariable regression analysis to identify independent predictors of treatment outcomes.
A two-tailed **p-value <0.05** was considered statistically significant.

RESULTS
Patient Characteristics
A total of 88 patients with histopathologically confirmed rectal adenocarcinoma fulfilled the study eligibility criteria and were included in the final analysis. Based on age at diagnosis, patients were categorized into an early-onset group (<45 years) and a late-onset group (≥45 years). The study population comprised both male and female patients, with a slight male predominance. The majority of patients were from urban areas, while the remaining patients belonged to rural backgrounds.

The age distribution demonstrated that rectal adenocarcinoma affected a wide spectrum of patients, ranging from young adults to elderly individuals. Despite this broad age range, most patients presented with locally advanced disease at diagnosis.

Demographic Characteristics

Table 1. Demographic profile of the study population (n = 88)

Variable	Number (%)
Total patients	88
Early-onset (<45 years)	41 (46.6)
Late-onset (≥45 years)	47 (53.4)
Male	50 (56.8)
Female	38 (43.2)
Urban residence	51 (58.0)
Rural residence	37 (42.0)

The early-onset group constituted nearly half of the study population, indicating a substantial proportion of younger patients with rectal adenocarcinoma.

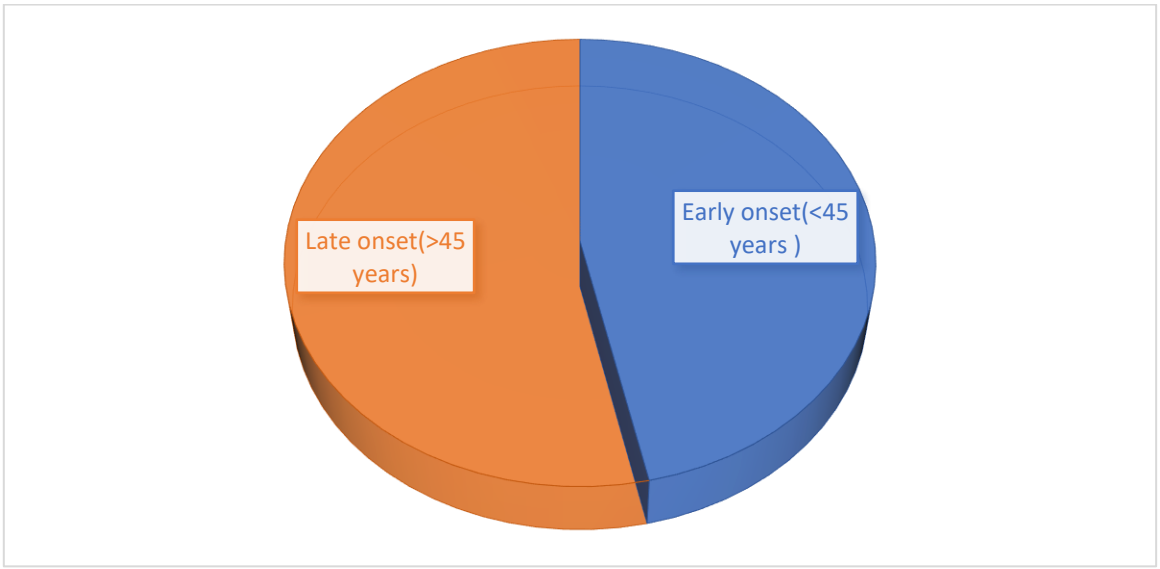

Figure 1. Age distribution

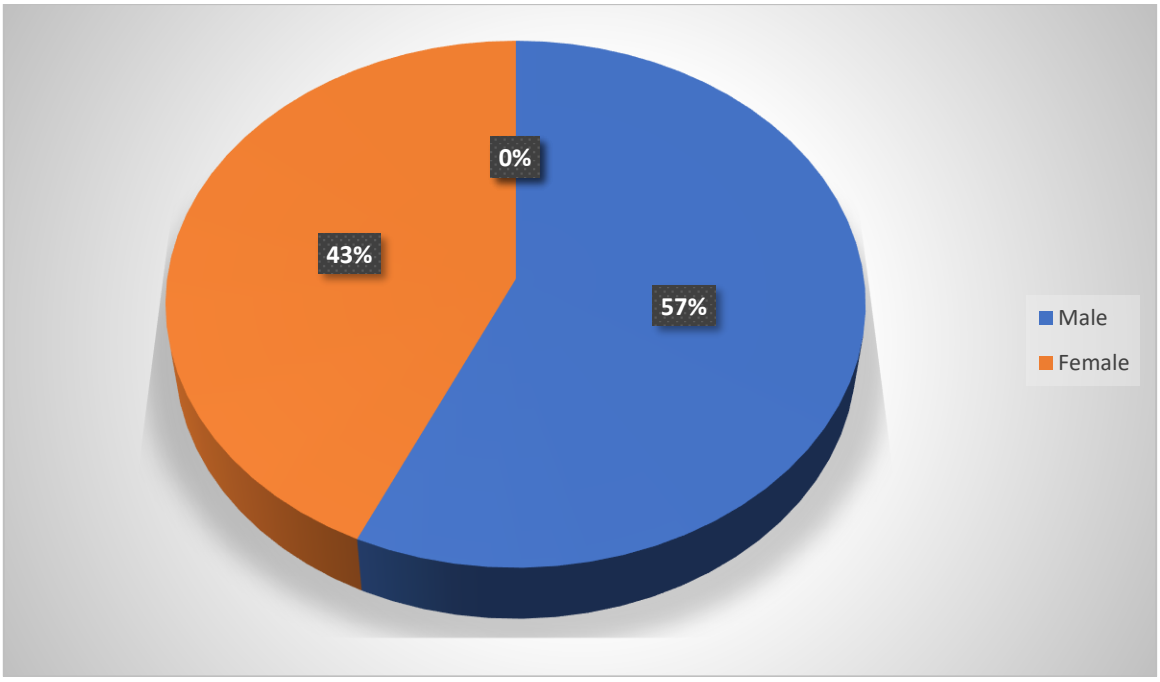

Figure 2. Sex distribution

Clinical Presentation

Rectal bleeding was the most common presenting symptom, followed by altered bowel habits and pelvic pain. Most patients sought medical attention because of persistent bleeding per rectum. Patients in the early-onset group frequently presented after a relatively short symptomatic period but were often diagnosed at an advanced stage.

Performance status assessment revealed that most patients had an ECOG performance status of 1 or 2, indicating that they were ambulatory and suitable for multimodality treatment.

Table 2. Clinical presentation

Variable	Number (n)	Percentage (%)
Rectal bleeding	61	69.3
Altered bowel habits	17	19.3
Pain abdomen/pelvic pain	10	11.4
ECOG 0	12	13.6
ECOG 1	38	43.2
ECOG 2	28	31.8
ECOG 3	10	11.4

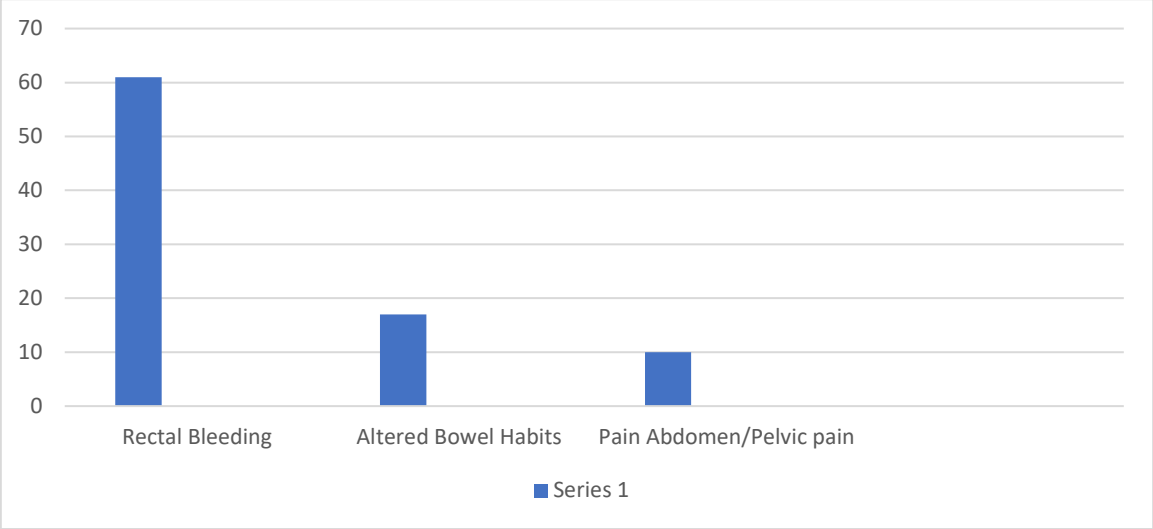

Figure 3. Clinical presentation of patients

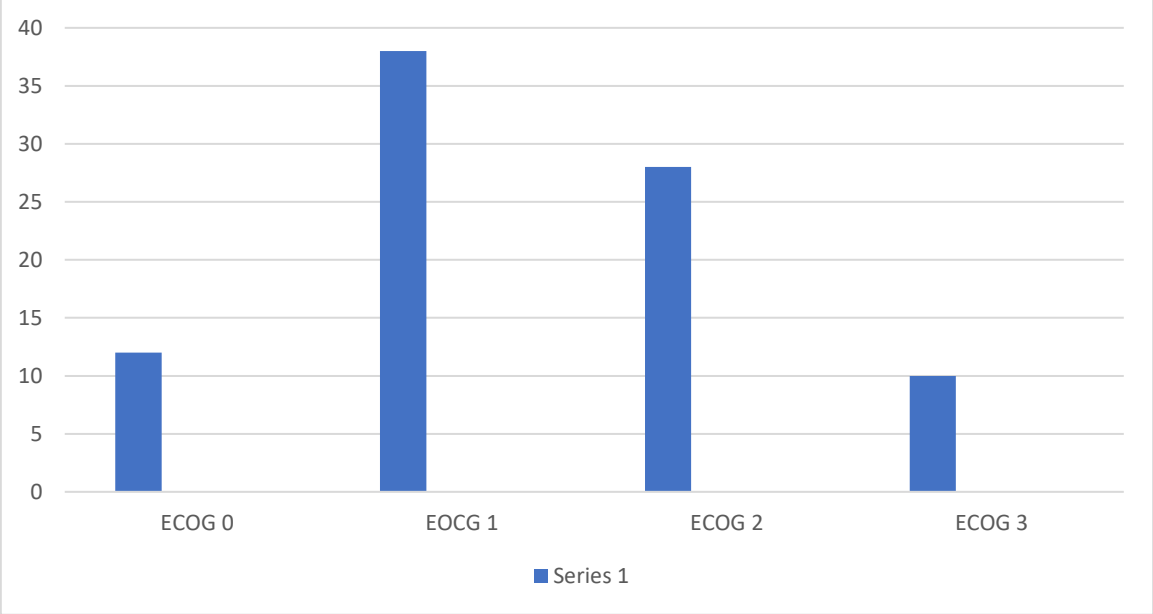

Figure 4. ECOG Performance Status

Table 3. Site of Rectal Involvement

Site of tumour	Early-onset (<45 years) n=41	Late-onset (≥45 years) n=47	Total (n=88)	P value
Upper rectum	8 (19.5%)	15 (31.9%)	23 (26.1%)	0.312
Middle rectum	14 (34.1%)	17 (36.2%)	31 (35.2%)	
Lower rectum	19 (46.3%)	15 (31.9%)	34 (38.6%)	

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

Tumour location differed slightly between the two groups. Lower rectal tumours were more frequently observed in the early-onset group (46.3%) than in the late-onset group (31.9%), whereas upper rectal tumours were relatively more common among older patients. Middle rectal involvement was comparable in both groups. However, these differences were not statistically significant ($p = 0.312$).

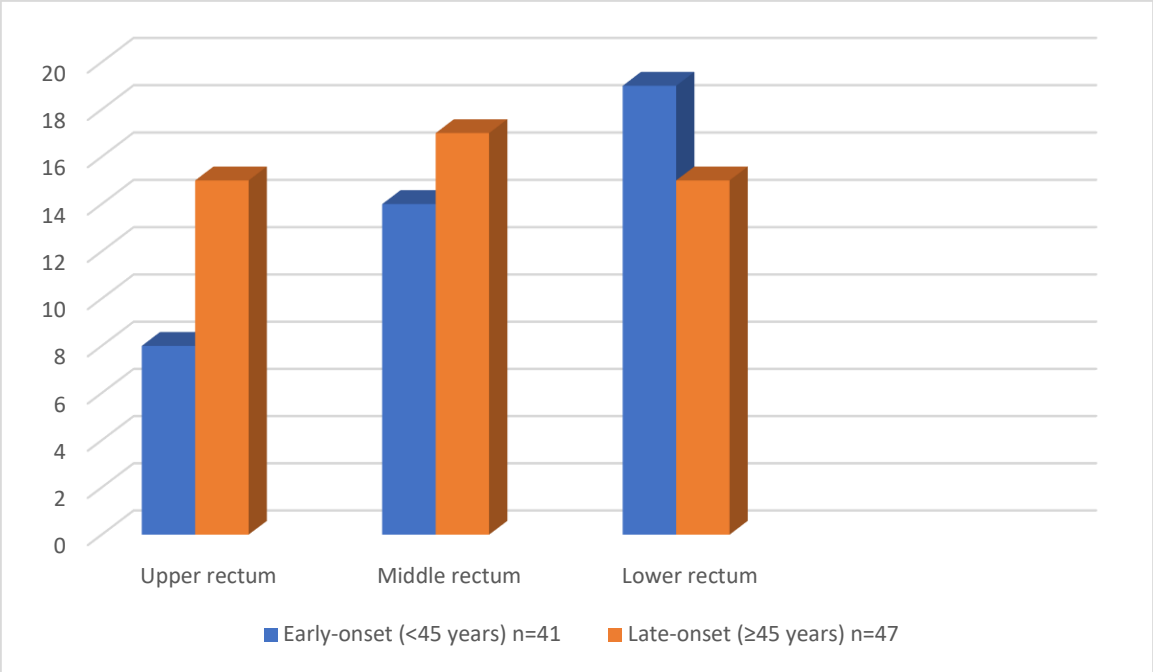

Figure 5. Distribution of tumour site in early-onset and late-onset rectal adenocarcinoma

Clinicopathological Characteristics

Moderately differentiated adenocarcinoma represented the predominant histological subtype in the study population. Well-differentiated tumours were less common, whereas poorly differentiated tumours constituted the smallest proportion.

Regarding tumour stage, **T3 disease** was the most frequent pathological category, followed by T2 and T4 lesions. Only a small proportion of patients had T1 disease. Regional lymph node involvement was common, with most patients demonstrating N1 or N2 disease at presentation.

Clinical staging revealed that **Stage III disease** was the predominant stage, emphasizing that most patients presented with locally advanced rectal cancer.

Table 4. Histopathological characteristics

Histological Grade

Grade	n	%
Grade I	27	30.7
Grade II	42	47.7
Grade III	19	21.6

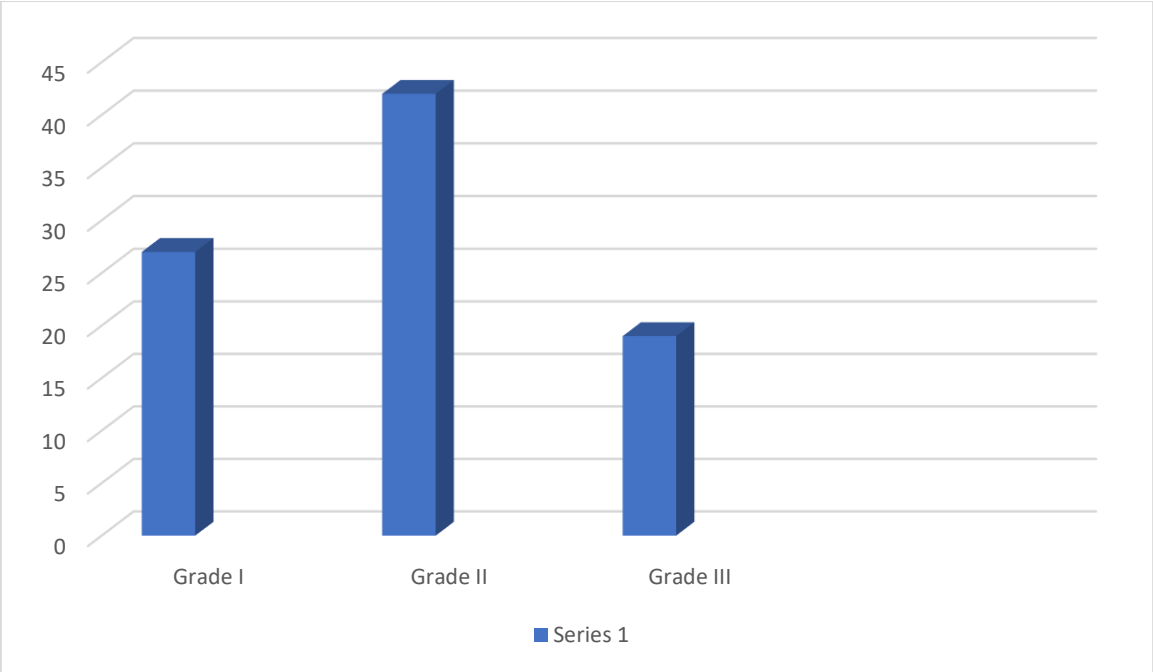

Figure 6. Histological Grade Distribution

T Stage

Stage	n	%
T1	9	10.2
T2	23	26.1
T3	35	39.8
T4	21	23.9

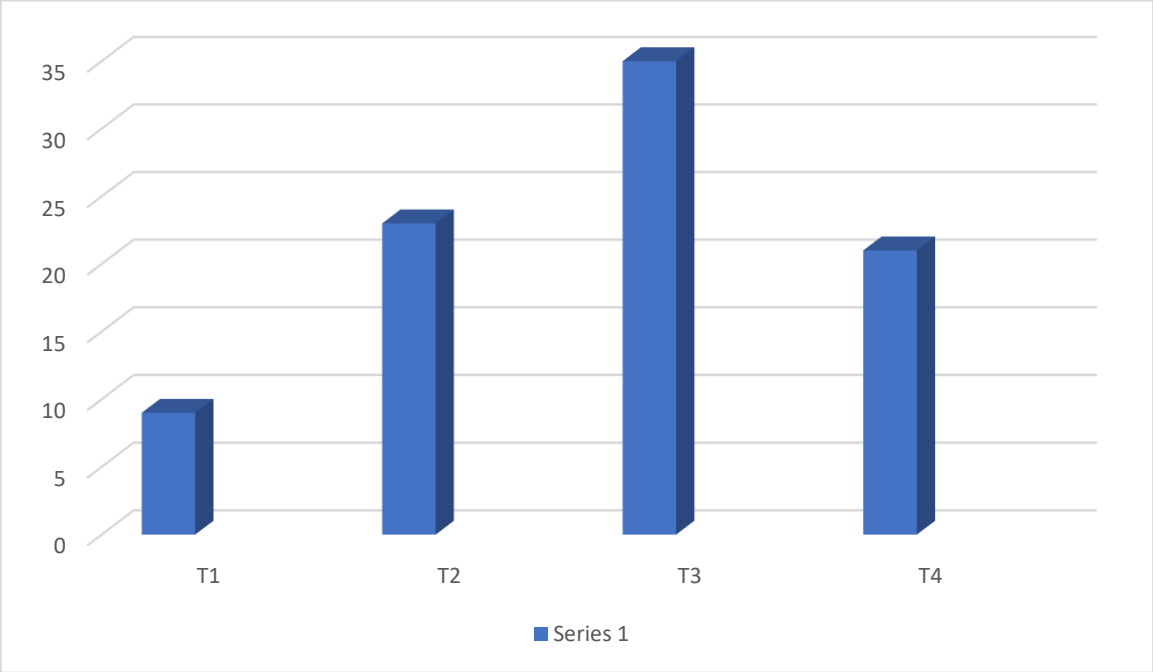

Figure 7. T Stage Distribution

N Stage

Stage	n	%
N0	32	36.4
N1	26	29.5
N2	30	34.1

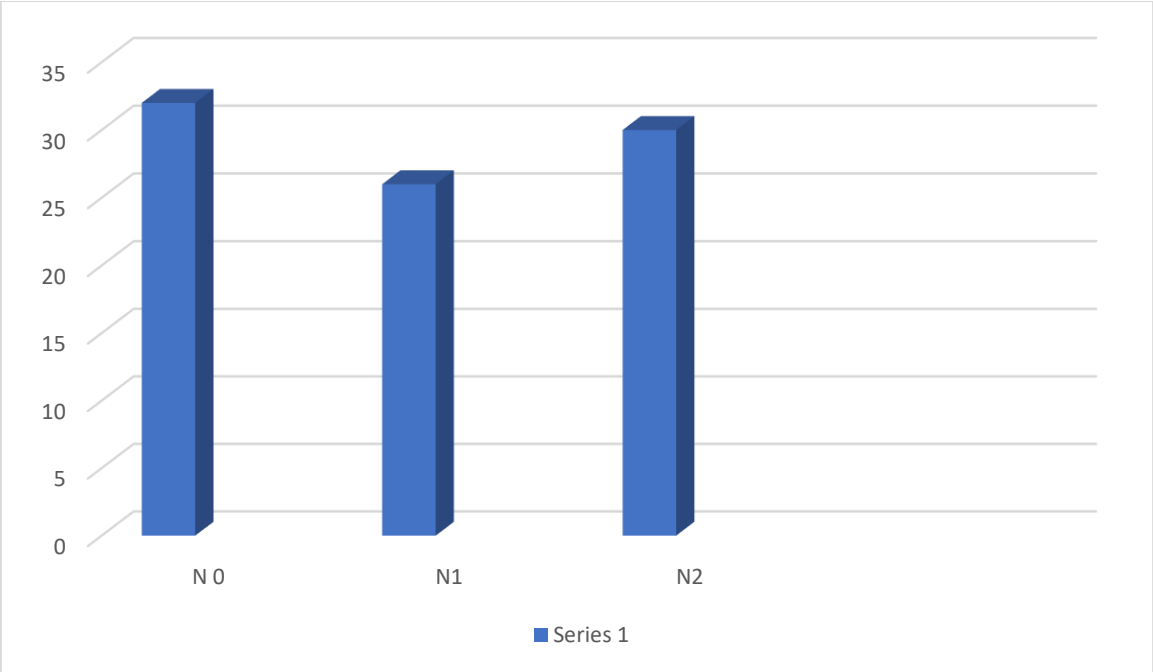

Figure 8. N Stage Distribution

AJCC Stage

Stage	n	%
I	12	13.6
II	24	27.3
III	52	59.1

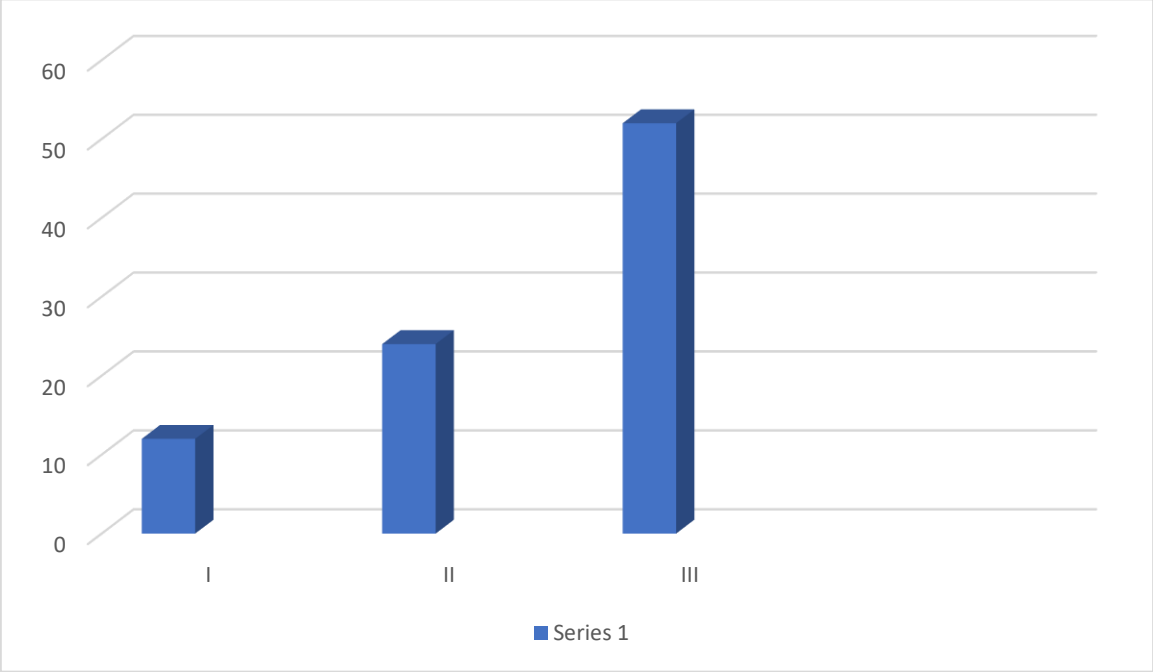

Figure 9. AJCC Stage Distribution

Treatment Characteristics

Patients were managed according to institutional multidisciplinary protocols. Most patients received long-course neoadjuvantchemoradiotherapy followed by definitive surgery and adjuvant chemotherapy. The remaining patients underwent alternative treatment strategies depending on tumour stage, clinical status, and multidisciplinary team recommendations.

Both treatment arms (Arm A and Arm B) were represented in the study population.

Table 5. Treatment characteristics

Treatment	n	%
Neoadjuvantchemoradiotherapy	71	80.7
Upfront surgery	17	19.3
Surgery performed	88	100
Adjuvant chemotherapy	78	88.6

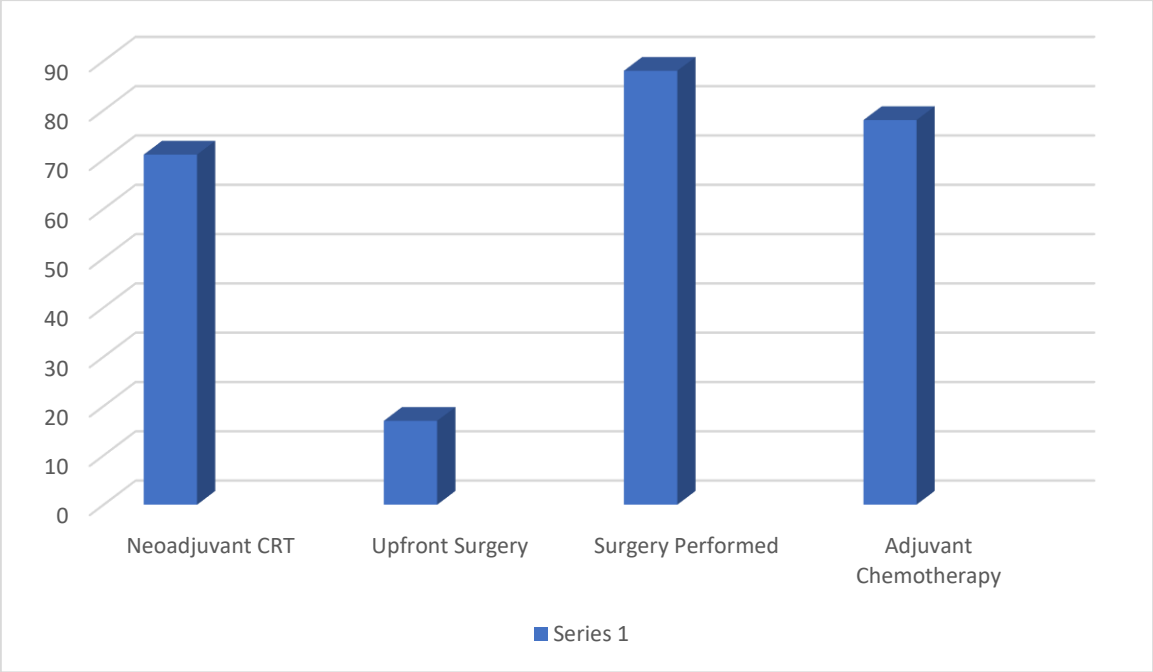

Figure 10. Treatment Distribution

Treatment Arm Distribution

Treatment Arm	n	Percentage (%)
Arm A (Early-onset)	**41**	**46.6**
Arm B (Late-onset)	**47**	**53.4**
Total	**88**	**100**

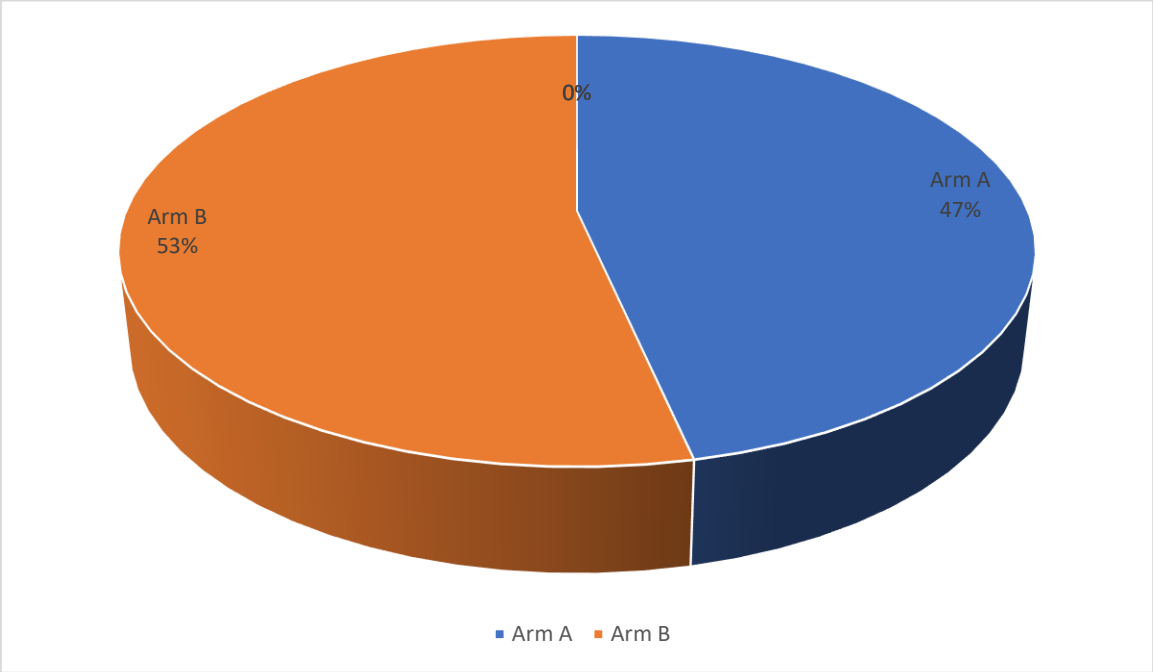

Figure 11. Treatment Arm Distribution

Among the 88 study participants, 41 patients (46.6%) belonged to the early-onset treatment arm (Arm A), while 47 patients (53.4%) belonged to the late-onset treatment arm (Arm B).

Disease Recurrence

During follow-up, recurrence was assessed at **12, 18, and 24 months**. Most patients remained free of recurrence during the first year following treatment. Additional recurrences were observed during subsequent follow-up, indicating progressive disease in a subset of patients.

The cumulative recurrence rate increased over time, with the highest number of recurrences documented during the 24-month evaluation.

Table 6. Disease recurrence during follow-up

Follow-up Period	Early-Onset (Arm A) (n=41)	Late-Onset (Arm B) (n=47)	Total Recurrence
12 months	2	4	6
18 months	6	9	15
24 months	10	16	26

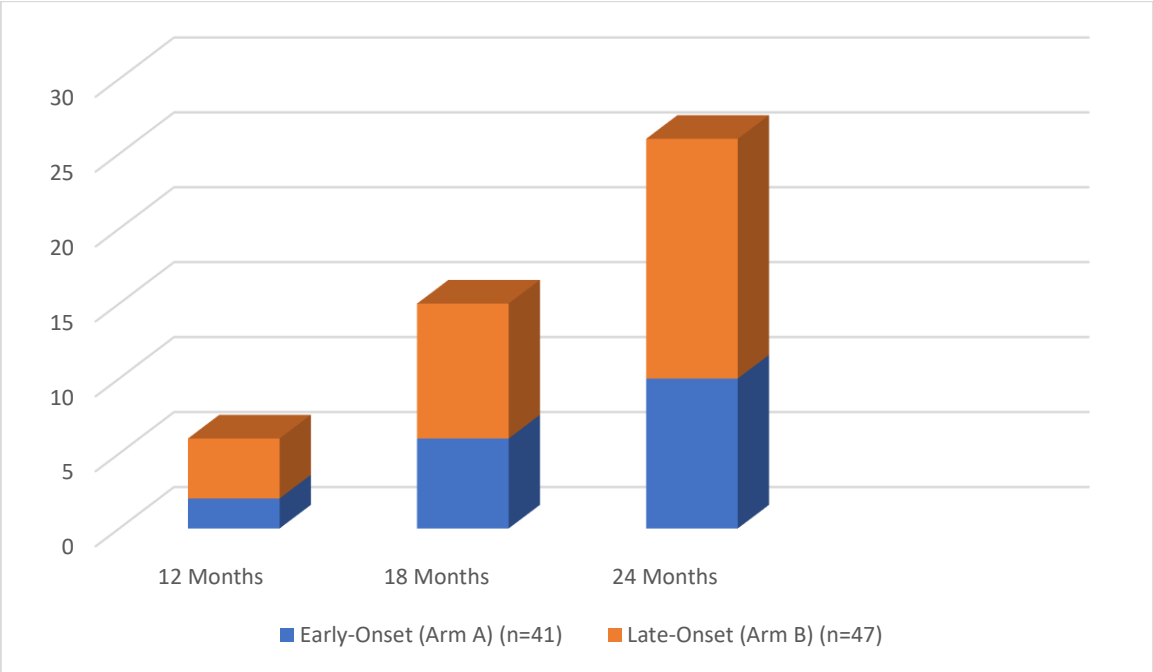

Figure 12. Disease Recurrence During Follow-up

Disease-Free Survival and Overall Survival

Disease-free survival remained favourable in the majority of patients throughout the follow-up period. Most patients maintained disease-free status for up to 24 months after treatment completion.

Overall survival was excellent, with only four deaths (4.5%) recorded during the follow-up period. Disease-free survival was maintained in 62 patients (70.5%), whereas 26 patients (29.5%) developed disease recurrence during follow-up.

Table 7. Treatment outcomes

Variable	n	Percentage (%)
Disease-free	62	70.5
Recurrence	26	29.5
Alive	84	95.5
Dead	4	4.5

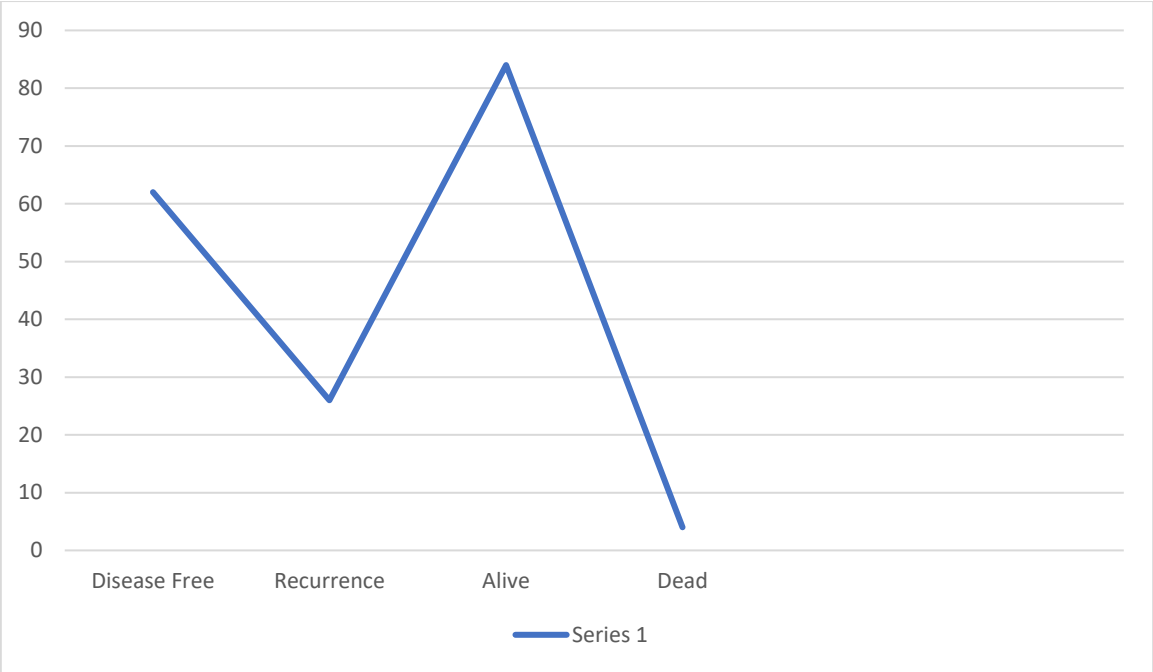

Figure 13. Disease-Free Survival

Comparative Analysis Between Early- and Late-Onset Rectal Adenocarcinoma

Patients with early-onset rectal adenocarcinoma demonstrated a tendency to present with more advanced tumour stage, higher nodal involvement, and poorer histological differentiation compared with the late-onset group. Although recurrence was observed in both groups, a greater proportion of recurrent disease occurred among younger patients during follow-up. Despite these differences in clinicopathological characteristics, multidisciplinary treatment resulted in comparable overall survival in both groups.

Table 8. Comparison of clinicopathological characteristics and treatment outcomes between early-onset and late-onset rectal adenocarcinoma (n = 88)

Variable	Early-onset (n=41)	Late-onset (n=47)	P value
Male sex	22 (53.7%)	28 (59.6%)	0.922
Female sex	19 (46.3%)	19 (40.4%)	
Urban residence	23 (56.1%)	28 (59.6%)	1.000
Rural residence	18 (43.9%)	19 (40.4%)	
Grade I	12 (29.3%)	15 (31.9%)	
Grade II	15 (36.6%)	27 (57.4%)	
Grade III	14 (34.1%)	5 (10.6%)	0.059
T1	2 (4.9%)	7 (14.9%)	
T2	9 (22.0%)	14 (29.8%)	
T3	20 (48.8%)	15 (31.9%)	
T4	10 (24.4%)	11 (23.4%)	0.325
N0	14 (34.1%)	18 (38.3%)	
N1	8 (19.5%)	18 (38.3%)	
N2	**19 (46.3%)**	**11 (23.4%)**	**0.137**
Stage I	5 (12.2%)	7 (14.9%)	
Stage II	10 (24.4%)	14 (29.8%)	
Stage III	26 (63.4%)	26 (55.3%)	0.838
Recurrence during follow-up	**11 (26.8%)**	**15 (31.9%)**	0.614
Disease-free survival maintained	30 (73.2%)	32 (68.1%)	0.801
Overall survival	39 (95.1%)	45 (95.7%)	1.000

Footnote: Data are presented as number (%). Categorical variables were compared using the Chi-square test. A p-value <0.05 was considered statistically significant.

Interpretation for the Results section

Patients with early-onset rectal adenocarcinoma showed a higher proportion of poorly differentiated (Grade III) tumours, T3/T4 lesions, N2 nodal involvement, and Stage III disease than those with late-onset disease. Although recurrence was

numerically more frequent among younger patients, none of the observed differences reached statistical significance (all p > 0.05). Disease-free survival and overall survival were comparable between the two groups during the follow-up period.

DISCUSSION

The clinicopathological profile and treatment results of 88 individuals with rectal adenocarcinoma were assessed in this retrospective observational analysis, which compared early-onset (less than 45 years) and late-onset (more than 45 years) illness. The results showed that compared to individuals identified at an older age, those with early-onset rectal adenocarcinoma tended to have more advanced pathological features, such as higher tumor stage, larger nodal involvement, and poorer tumor differentiation. Treatment results and short-term survival were similar in both groups despite these unfavorable clinicopathological characteristics, highlighting the value of comprehensive care in rectal cancer.[10]

Over the past 20 years, there has been a steady increase in the incidence of early-onset colorectal cancer worldwide, with rectal cancer contributing significantly to this increase. According to epidemiological research, coordinated screening programs have reduced the incidence of colorectal cancer in people over 50, but the incidence is still rising in younger adults.[2 3] In a similar vein, the RELEO study underscored the increasing prevalence of early-onset rectal cancer and stressed the significance of comprehending age-related variations in tumor biology, clinical presentation, and treatment results.[11] In both age groups, the majority of instances in the current study were male patients. Numerous institutional and population-based studies assessing rectal cancer have documented a comparable male predominance. Younger patients typically showed greater baseline functional status and fewer concomitant illnesses, despite the fact that sex distribution was similar across early-onset and late-onset disease—findings also reported in the RELEO trial. Improved oncological outcomes could result from younger patients being able to withstand rigorous multimodality treatment, such as systemic chemotherapy, major surgery, and neoadjuvant chemoradiotherapy.[12]

Rectal bleeding was the most common clinical presentation in this study, followed by abdominal or pelvic pain and changed bowel habits. These results are in line with earlier studies showing that, regardless of patient age, rectal bleeding continues to be the most common presenting symptom of rectal adenocarcinoma. However, symptoms in younger persons are sometimes misdiagnosed as benign anorectal illnesses like hemorrhoids. Similarly, the RELEO investigators found that younger individuals had far greater rates of rectal bleeding and abdominal pain, indicating that young adults with persistent anorectal symptoms should get a colonoscopy as soon as possible.[13]

Histopathological analysis revealed that the most common tumor grade in our group was moderately differentiated (Grade II) adenocarcinoma. However, patients with early-onset illness were proportionately more likely to have poorly differentiated tumors. Despite not reaching statistical significance, this difference confirms findings from earlier research showing that early-onset colorectal cancer frequently exhibits more aggressive pathological features, such as poor differentiation, lymphovascular invasion, perineural invasion, and mucinous or signet-ring histology. These pathological traits have been linked to a worse long-term prognosis and a higher chance of recurrence.[14]

The RELEO study found no significant difference in stage at diagnosis after matching patients by clinical stage, suggesting that variations among studies may reflect differences in study design, patient selection, and healthcare systems. In the present study, Stage III disease constituted the largest proportion of cases, with T3 lesions and nodal metastasis representing the predominant pathological findings. Early-onset patients showed higher frequencies of T3/T4 tumors, N2 nodal involvement, and Stage III disease than late-onset patients.[4]

Rather than tumor biology alone, delayed diagnosis may account for the preponderance of advanced-stage illness found in this study. Routine colorectal cancer screening programs typically do not involve younger patients, and doctors may initially dismiss rectal bleeding or changes in bowel habits as benign disorders. As a result, diagnostic colonoscopies are often postponed until symptoms worsen or become chronic. Therefore, raising healthcare professionals' knowledge of the growing prevalence of early-onset rectal adenocarcinoma is crucial to enabling earlier detection and enhancing long-term oncological outcomes.[4]

Overall, the current study's clinicopathological results point to a tendency toward more aggressive disease features in early-onset rectal adenocarcinoma compared to late-onset disease. However, these unfavorable pathological characteristics did not result in lower short-term survival, underscoring the potential advantages of modern multidisciplinary treatment approaches in obtaining favorable oncological outcomes.

Over the past 20 years, the treatment of rectal adenocarcinoma has changed significantly due to the use of multidisciplinary approaches that incorporate adjuvant systemic chemotherapy, total mesorectal resection, and neoadjuvantchemoradiotherapy. These methods have greatly increased long-term survival, decreased recurrence rates, and improved local disease control. Both treatment groups were sufficiently represented in the current investigation, and most patients received multimodality care in accordance with institutional standards. Regardless of patient age, the positive treatment outcomes seen in our sample highlight the significance of coordinated multidisciplinary care.[15]

Due to their higher performance status and fewer concomitant conditions, younger patients typically tolerate aggressive oncological treatment better. As a result, they are more likely to have combination chemotherapy, major surgery, and rigorous neoadjuvant therapy. In a similar vein, the RELEO trial showed that individuals under 50 years of age got considerably more extensive care than older patients, including increased use of adjuvant chemotherapy, neoadjuvant therapy, and several lines of systemic treatment for advanced disease. After stage matching, the illness profiles of younger and older patients remained generally similar despite the higher treatment intensity, indicating that age alone should not be used to guide treatment choices.[15]

Disease recurrence in the current study gradually increased during the course of the follow-up. At 12 months, the majority of patients were still free of recurrences, but at 18 and 24 months, more recurrences were recorded, leading to the highest cumulative recurrence at the time of the last follow-up evaluation. The percentage of recurrence was marginally higher in early-onset patients than in late-onset patients, although this difference was not statistically significant. These results imply that effective multimodality treatment can significantly lower the chance of early disease relapse, even if younger patients may present with physiologically aggressive tumors.[16]

Previous studies have reported conflicting observations regarding recurrence among younger patients with rectal cancer. Numerous researchers have shown that patients with early-onset colorectal cancer had higher risks of distant metastasis and local recurrence. These findings have been attributed to aggressive molecular features, poor tumor differentiation, advanced stage at diagnosis, and lymphovascular invasion. Conversely, other studies have indicated that recurrence rates become equivalent following adjustment for tumor stage, pathological features, and treatment strategy. Consequently, the primary factor influencing illness recurrence may be tumor biology rather than age.[16]

The majority of patients in the current trial remained disease-free during the 24-month follow-up period, indicating favorable disease-free survival. Despite the more advanced pathological features seen in younger patients, comparative research showed comparable disease-free survival across early-onset and late-onset patients. This result suggests that the unfavorable clinicopathological picture linked to early-onset rectal cancer may be mitigated by vigorous multimodality treatment. Similar findings have been documented in recent institutional series where, after controlling for tumor stage and treatment factors, age was not found to be an independent predictor of disease-free survival.[13]

Only a small number of deaths occurred during follow-up, and overall survival in both age groups approached 95% in our study. Even while poorly differentiated tumors and advanced nodal disease were more common in early-onset individuals, their short-term overall survival was nevertheless similar to that of late-onset patients. Several recent studies have reported comparable cancer-specific survival rates for younger and older patients after standardized multimodality treatment. These findings highlight the fact that tumor stage, surgical resection completeness, pathological response to neoadjuvant therapy, and proper postoperative care are more important factors in determining prognosis than age alone.[14]

It's interesting to note that younger individuals with Stage III and Stage IV rectal cancer had a noticeably higher overall survival rate than older patients, according to the RELEO study. These results were ascribed by the authors to improved functional status, reduced comorbidity burden, and younger patients' capacity to withstand intense chemotherapy and multimodality therapy. These facts corroborate the results of the current investigation, which showed that favorable overall survival was attained even though younger patients had more advanced clinical characteristics.[15]

This result is in line with recent research showing that poor long-term survival and eventual distant metastases are still best predicted by recurring disease. Therefore, early detection of recurrence through organized surveillance programs is still crucial for enhancing long-term cancer outcomes.[15]

In our dataset, there were trends toward higher rates of Grade III tumors, T3/T4 disease, N2 nodal involvement, and recurrence among younger patients when early-onset and late-onset rectal adenocarcinoma were compared. None of these variations, though, were statistically significant. Similar findings have been documented in a number of comparative investigations in which younger patients showed more severe pathological features without matching declines in overall or disease-free survival after modern multimodal treatment.[16]

It is important to exercise caution when interpreting our study's lack of statistically significant differences between age groups. The statistical power needed to identify clinically significant variations in long-term oncological outcomes may have been diminished by the very small sample size and short follow-up period. A more thorough understanding of the biological distinctions between early-onset and late-onset rectal adenocarcinoma may be possible with larger multicenter studies that include molecular, deficiency, and genomic biomarkers.[17]

Overall, the study's treatment results show that, regardless of patient age, favorable disease control and survival can be attained by multidisciplinary management that includes radical surgery, neoadjuvantchemoradiotherapy, and suitable systemic therapy. Similar recurrence rates and survival results indicate that early-onset rectal adenocarcinoma can be

effectively handled using current evidence-based treatment methods, despite the fact that younger patients frequently presented with unfavorable histological features.[18]

The current study has a number of significant advantages. Using a standardized institutional treatment procedure, it first directly evaluated the clinicopathological features and treatment outcomes of early-onset and late-onset rectal adenocarcinoma. In order to minimize discrepancies in clinical management, all patients underwent multidisciplinary treatment planning, standardized diagnostic examination, and pathological staging in accordance with the American Joint Committee on Cancer (AJCC) classification. Additionally, all included patients had follow-up data on recurrence, disease-free survival, overall survival, and metastatic advancement, allowing for a thorough assessment of short-term oncological outcomes.[19]

This study's emphasis on early-onset rectal adenocarcinoma, a disease entity that has drawn more attention due to its increased frequency worldwide, is another strength. While several studies have examined colorectal cancer in general, relatively few have examined rectal cancer by age upon presentation. The current study reduces inter-institutional variability and offers clinically useful data applicable to standard surgical oncology practice by comparing younger and older patients within the same institution.[4]

Notwithstanding these advantages, it is important to recognize some restrictions. The potential for selection bias and poor documentation, which are inherent in hospital record-based studies, is introduced by the retrospective observational design. Furthermore, the investigation was carried out at a single tertiary care facility with a rather small sample size of 88 patients, which would restrict the statistical ability to identify minor but clinically significant changes between age groups. As a result, certain comparisons that showed trends that were clinically significant failed to reach statistical significance.[20]

Another restriction is the length of the follow-up. Longer follow-up would yield more reliable estimates of five-year disease-free survival, overall survival, and late recurrence, even though all patients were assessed for recurrence and survival during the research period. Extended surveillance is necessary to adequately assess long-term oncological results since rectal cancer may reappear several years after curative treatment.[20]

Another limitation of the present study is the relatively short follow-up period, which precluded assessment of long-term oncological outcomes, including 5-year disease-free survival and overall survival. Future prospective multicentre studies with larger sample sizes and longer follow-up are required to validate these findings.[21]

The current study's conclusions have a number of significant clinical ramifications. First, the finding that younger patients often had more advanced tumor stages and more nodal involvement highlights the necessity of raising clinical awareness of rectal cancer in those under 45. Instead of being exclusively linked to benign anorectal illnesses, persistent rectal bleeding, altered bowel habits, unexplained anemia, or stomach pain in younger persons should warrant prompt colonoscopic assessment. Early diagnosis may increase long-term survival and decrease stage migration.[21]

Second, after receiving multimodal treatment, early-onset individuals attained disease-free survival and overall survival comparable to older patients, despite presenting with more advanced clinical disease. These results corroborate the existing recommendations that tumor stage, pathological features, performance status, and patient fitness—rather than just age—should be the primary determinants of therapy decisions. Guidelines-directed multimodality treatment, such as neoadjuvantchemoradiotherapy, radical surgery with total mesorectal excision, and adequate adjuvant systemic chemotherapy where necessary, should be administered to medically fit young patients.[22]

The current study's findings further highlight how crucial multidisciplinary team (MDT) management is. Colorectal surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, gastroenterologists, and specialized nursing teams work closely together to optimize oncological outcomes and enable customized treatment planning. Our cohort's favorable short-term survival rates for both early-onset and late-onset patients probably demonstrate the value of coordinated multidisciplinary therapy.[22]

To validate these results, more extensive patient populations will need to be included in future prospective multicenter trials. To better understand the biological behavior of early-onset rectal adenocarcinoma, such studies should include thorough quality-of-life evaluation, treatment-related toxicity, functional results, and long-term survival analysis. Understanding regional and ethnic differences in disease presentation and treatment outcomes may be further enhanced by international collaborative registries.[22]

Overall Discussion Summary

In conclusion, the current study shows that a trend toward more advanced clinicopathological traits, such as higher tumor stage, larger nodal involvement, and worse tumor differentiation at diagnosis, are characteristics of early-onset rectal adenocarcinoma. However, the application of standardized multidisciplinary treatment produced favorable disease control, low recurrence ratesand outstanding short-term overall survival, all of which were equivalent to those seen in patients with

late-onset illness. These results imply that evidence-based multimodality therapy approaches can successfully manage aggressive tumor biology linked to younger age. It is anticipated that patients with rectal adenocarcinoma, regardless of age, will benefit even more from ongoing efforts toward early detection, customized treatment planning, and the integration of molecular biomarkers.[4]

CONCLUSION

The current retrospective observational study showed that compared to late-onset disease, early-onset rectal adenocarcinoma (less than 45 years) tended to have more advanced clinicopathological features, such as higher tumor stage, increased nodal involvement, and poorer histological differentiation at presentation. Despite these unfavorable pathological characteristics, both age groups experienced favorable short-term oncological outcomes with comprehensive management that included radical surgery, adjuvant chemotherapy, and neoadjuvantchemoradiotherapy.Disease recurrence increased gradually over the follow-up, peaking at 24 months. There were no statistically significant differences between those with early and late onset, and overall and disease-free survival remained excellent. These results imply that tumor stage, pathological features, and patient fitness should be the main factors used to guide treatment decisions rather than chronological age alone as an independent predictor of outcome. Younger people who present with chronic rectal bleeding, changing bowel habits, or other alarm symptoms should be treated with a high index of suspicion due to the rising frequency of early-onset rectal adenocarcinoma. Long-term oncological results may be improved by early diagnosis by timely colonoscopic assessment along with standardized multidisciplinary care. Early diagnosis through prompt colonoscopic evaluation, together with standardized multidisciplinary management, has the potential to improve long-term oncological outcomes. Future prospective multicentre studies with larger sample sizes and longer follow-up are warranted to validate these findings and better define the biological behaviour of early-onset rectal adenocarcinoma.

Strengths of the Study

- Comparative evaluation of early-onset and late-onset rectal adenocarcinoma.
- Uniform institutional treatment protocol for all patients.
- Comprehensive assessment of clinicopathological variables, recurrence, disease-free survival and overall survival.
- Real-world data from a tertiary care referral centre.
- Clinically relevant findings applicable to multidisciplinary rectal cancer management.

Limitations

- Retrospective observational design.
- Single-centre study.
- Relatively small sample size (88 patients).
- Only non-metastatic patients are included.
- Limited follow-up period (24 months).
- Long-term (5-year) oncological outcomes could not be evaluated.

Clinical Implications

- Early-onset rectal adenocarcinoma should be suspected in younger patients with persistent rectal bleeding or altered bowel habits.
- Age alone should not influence treatment decisions.
- Multidisciplinary management remains the cornerstone for achieving favourable oncological outcomes.
- Earlier diagnosis may reduce presentation at advanced stages and improve survival.

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