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ORIGINAL ARTICLE

Concurrent Chemotherapy and Radiotherapy Improves Sphincter Preservation without Significant Toxicity in Low Rectal Disease

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ABSTRACT

Background: *Rectal cancer is an important cause of cancer-related morbidity and mortality. Low rectal tumors often create major challenges in achieving sphincter preservation. Preoperative concurrent chemoradiotherapy may downstage Stage II rectal adenocarcinoma, improve respectability, and reduce the need for permanent colostomy, but local evidence from Bangladesh remains limited.* ***Aim of the study:*** *This study compared preoperative concurrent chemoradiotherapy followed by surgery with immediate surgery alone in patients with Stage II low rectal adenocarcinoma, focusing on sphincter preservation and treatment-related toxicity.* ***Methods & Materials:*** *This comparative interventional study was conducted from July 2011 to January 2017 at BSMMU, NICRH, and DMCH, Dhaka. A total of 60 patients with Stage II low rectal adenocarcinoma were enrolled purposively and divided into two groups: Group I received preoperative concurrent chemoradiotherapy followed by surgery, while Group II underwent immediate surgery. Treatment response, sphincter preservation, Karnofsky performance status, and treatment-related toxicities were assessed. Data were analyzed using SPSS version 26.0, and p<0.05 was considered statistically significant.* ***Results:*** *Among 60 patients, the mean age was 42.3 ± 10.17 years in Group I and 44.0 ± 10.47 years in Group II, with male predominance in both groups. Per rectal bleeding, complete response was observed in Group I, while alteration of bowel habit improved more in Group I than in Group II, 60.0% versus 52.0%, p<0.05. Karnofsky performance score also improved more in Group I. Sphincter-sparing surgery was significantly higher in Group I than Group II, 22 (73.3%) versus 14 (46.7%), p=0.032. Non-hematological toxicities were comparable between groups, and grade I neutropenia in Group I did not interrupt treatment.* ***Conclusion:*** *Preoperative concurrent chemoradiotherapy followed by surgery significantly improved sphincter preservation and functional outcome in selected patients with Stage II low rectal adenocarcinoma. It was well tolerated, with no significant increase in major non-hematological toxicity.*

Keywords: *Rectal adenocarcinoma, Concurrent chemoradiotherapy, Sphincter preservation, Neoadjuvant therapy, and Low rectal cancer*

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INTRODUCTION

Rectal cancer is a major component of colorectal cancer and remains an important cause of cancer-related morbidity and mortality worldwide. Colorectal cancer is the third most commonly diagnosed cancer globally and the second leading cause of cancer-related death, with more than 1.9 million new cases and about 904,000 deaths estimated in 2022 [1]. The global burden is expected to rise further because of population aging, urbanization, westernized dietary patterns, obesity, physical inactivity, smoking, and delayed diagnosis [2–4]. Although colorectal cancer has historically been more common in high-income countries, Asian countries now contribute a large share of global cases, and the burden is increasing in many low- and middle-income settings [5].

In South Asia, including Bangladesh, colorectal and rectal cancers are increasingly encountered in routine oncology and surgical practice. Hospital-based Bangladeshi studies have shown that rectal cancer forms a substantial proportion of colorectal malignancies, often affecting middle-aged and elderly patients, with male predominance and adenocarcinoma as the commonest histological type [6,7]. However, population-based data remain limited, and many patients present after a prolonged symptomatic period with per rectal bleeding, altered bowel habit, tenesmus, anemia, or mucous discharge. This late or symptomatic presentation is clinically important because tumor level and stage strongly influence resectability, sphincter preservation, need for permanent stoma, postoperative function, and quality of life.

The management of rectal cancer has changed significantly over recent decades. Total mesorectal excision improved local control, but surgery alone may be insufficient for tumors with transmural extension or threatened local control. For Stage II rectal adenocarcinoma, particularly cT3–T4, N0, M0 disease, preoperative concurrent chemoradiotherapy has been used to downstage tumors, improve resectability, reduce local recurrence, and increase the possibility of sphincter-saving surgery [8-10]. This approach is especially relevant for low rectal tumors, where abdominoperineal resection and permanent colostomy can have major physical, psychological, social, and economic consequences.

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Neoadjuvant chemoradiotherapy may improve tumor regression and facilitate anus preservation, but its use must be balanced against acute and late toxicities, including gastrointestinal, genitourinary, dermatologic, and hematologic adverse effects [10-12]. In resource-limited settings, clinicians also need locally generated evidence on feasibility, toxicity, and surgical benefit, because outcomes from high-income countries may not fully reflect patient characteristics, diagnostic delay, nutritional status, treatment compliance, and institutional capacity in Bangladesh.

Despite growing international evidence, there is limited local evidence evaluating whether preoperative concurrent chemoradiotherapy improves sphincter preservation without adding significant toxicity among patients with Stage II low rectal adenocarcinoma. This study was therefore designed to compare preoperative concurrent chemoradiotherapy followed by surgery with immediate surgery alone in patients with Stage II rectal adenocarcinoma. The aim was to determine whether neoadjuvant concurrent chemoradiotherapy improves sphincter preservation while maintaining acceptable treatment-related toxicity.

METHODS & MATERIALS

This comparative interventional study was conducted from July 2011 to January 2017 at three tertiary oncology centers in Bangladesh: The Department of Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), the Department of Radiation Oncology, National Institute of Cancer Research and Hospital (NICRH), and the Department of Radiotherapy, Dhaka Medical College Hospital (DMCH).

A total of 60 patients were enrolled using a purposive, non-probability sampling technique according to predefined eligibility criteria. Patients aged 18–70 years with histologically confirmed rectal adenocarcinoma located within 10 cm of the anal verge were included. Eligible patients had clinical Stage II disease, defined as cT3–T4, N0, M0, with ECOG performance status ≤2 and adequate hematologic, renal, and hepatic function. Patients with distant metastasis, previous pelvic radiotherapy, severe cardiomyopathy, hypersensitivity to fluoropyrimidines, or any condition making them unsuitable for surgery or chemoradiotherapy were excluded.

Patients were divided into two treatment groups. Group I (n=30) received preoperative concurrent chemoradiotherapy followed by surgery, while Group II (n=30) underwent immediate surgery without neoadjuvant treatment. Pretreatment evaluation included clinical history, physical examination, digital rectal examination, histopathological confirmation, routine hematological and biochemical investigations, imaging for staging, and assessment of performance status. Tumor location, presenting symptoms, treatment response, operative procedure, sphincter preservation, and treatment-related toxicities were recorded.

The primary outcome was the rate of sphincter-sparing surgery. Secondary outcomes included clinical symptom response, change in Karnofsky performance status, and hematological and non-hematological toxicities. Toxicities were assessed during and after treatment according to standard clinical grading. Data were analyzed using appropriate statistical methods in SPSS (V 26.0). Categorical variables were expressed as frequency and percentage, while continuous variables were expressed as mean ± standard deviation. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Boards of BSMMU, NICRH, and DMCH. Written informed consent was obtained from all participants before enrollment. Confidentiality of patient information was maintained throughout the study.

RESULTS

Table I shows the baseline demographic characteristics of the study patients. The highest proportion of patients was in the 41–50 years age group, 12 (40.0%) in Group I and 11 (36.7%) in Group II. The mean age was 42.3 ± 10.17 years in Group I and 44.0 ± 10.47 years in Group II. Male patients were predominant in both groups, 17 (56.7%) in Group I and 18 (60.0%) in Group II.

Table I: Baseline demographic characteristics of the patients

Variables	Group I (n=30)	Group II (n=30)	Total (n=60)
Age group (years)			
21–30	3 (10.0)	4 (13.3)	7 (11.7)
31–40	4 (13.3)	6 (20.0)	10 (16.7)
41–50	12 (40.0)	11 (36.7)	23 (38.3)
51–60	9 (30.0)	6 (20.0)	15 (25.0)
61–70	2 (6.7)	3 (10.0)	5 (8.3)
Mean ± SD	42.3 ± 10.17	44.0 ± 10.47	43.15 ± 10.24
Sex			
Male	17 (56.7)	18 (60.0)	35 (58.3)
Female	13 (43.3)	12 (40.0)	25 (41.7)

Smoking was common in both groups, observed in 18 (60.0%) patients in Group I and 16 (53.3%) in Group II. A positive family history was present in 2 (6.7%) patients in Group I and 3 (10.0%) in Group II (*Table II)*.

Table II: Distribution of patients according to risk factors

Risk factors	Group I (n=30)	Group II (n=30)	Total (n=60)
Smoker	18 (60.0)	16 (53.3)	34 (56.7)
Non-smoker	12 (40.0)	14 (46.7)	26 (43.3)
Positive family history	2 (6.7)	3 (10.0)	5 (8.3)
No family history	28 (93.3)	27 (90.0)	55 (91.7)

Per rectal bleeding, complete response in Group I increased from 26 (86.7%) before treatment to 0 (0.0%) after treatment, compared with 92.9% in Group II. Alteration of bowel habit also improved more in Group I (60.0%) than in Group II

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(52.0%). These two differences were statistically significant (p<0.05) (*Table III*)

Table III: Comparison of clinical response according to presenting symptoms

Clinical symptom	Group	Pre-treatment n (%)	Post-treatment n (%)	Response (%)	p-value
Per rectal bleeding	Group I	26 (86.7)	0 (0.0)	100	<0.05
	Group II	28 (93.3)	2 (6.7)	92.9	
Alteration of bowel habit	Group I	25 (83.3)	10 (33.3)	60	<0.05
	Group II	25 (83.3)	12 (40.0)	52	
Tenesmus	Group I	17 (56.7)	4 (13.3)	76.5	>0.1
	Group II	15 (50.0)	6 (20.0)	60	
Mucoid discharge	Group I	15 (50.0)	3 (10.0)	80	>0.1
	Group II	16 (53.3)	5 (16.7)	68.8	
Anaemia	Group I	8 (26.7)	4 (13.3)	50	>0.1
	Group II	10 (33.3)	6 (20.0)	40	

In Group I, patients with Karnofsky performance score 90 increased from 4 (13.3%) before treatment to 17 (56.7%) after treatment. In Group II, the increase was from 4 (13.3%) to 8 (26.7%). This indicates better post-treatment functional improvement in Group I (*Table IV*).

Table IV: Distribution of patients according to Karnofsky performance status

Karnofsky performance score	Group I		Group II	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
	n (%)			
90	4 (13.3)	17 (56.7)	4 (13.3)	8 (26.7)
80	21 (70.0)	12 (40.0)	20 (66.7)	21 (70.0)
70	5 (16.7)	1 (3.3)	6 (20.0)	1 (3.3)

Sphincter-sparing surgery was performed in 22 (73.3%) patients in Group I compared with 14 (46.7%) patients in Group II. This difference was statistically significant (p=0.032), indicating greater sphincter preservation after preoperative chemoradiotherapy (*Table V*).

Table V: Comparison of surgical outcome between the two groups

Surgical outcome	Group I (n=30)	Group II (n=30)	Total (n=60)	p-value
Sphincter-sparing surgery	22 (73.3)	14 (46.7)	36 (60.0)	0.032
Abdominoperineal resection and others	8 (26.7)	16 (53.3)	24 (40.0)	
Total	30 (100.0)	30 (100.0)	60 (100.0)	

Nausea, vomiting, diarrhea, proctitis, and genitourinary toxicity were observed in both groups, but none showed a statistically significant difference. The p-values for nausea, vomiting, diarrhea, proctitis, and genitourinary toxicity were 0.321, 0.118, 0.669, 0.484, and 0.987, respectively (*Table VI*)

Table VI: Distribution of non-hematological toxicity between the two groups

Toxicity	Grade	Group I (n=30)	Group II (n=30)	p-value
Nausea	Grade I	8 (26.7)	11 (36.7)	0.321
	Grade II	18 (60.0)	18 (60.0)	
	Grade III	4 (13.3)	1 (3.3)	
Vomiting	Grade I	14 (46.7)	10 (33.3)	0.118
	Grade II	15 (50.0)	17 (56.7)	
	Grade III	1 (3.3)	0 (0.0)	
Diarrhoea	Grade I	8 (26.7)	5 (16.7)	0.669
	Grade II	9 (30.0)	8 (26.7)	
	Grade III	3 (10.0)	3 (10.0)	
Proctitis	Grade 0	14 (46.7)	10 (33.3)	0.484
	Grade I	9 (30.0)	14 (46.7)	
	Grade II	5 (16.7)	3 (10.0)	
	Grade III	2 (6.7)	3 (10.0)	
Genitourinary toxicity	Grade I	5 (16.7)	4 (13.3)	0.987
	Grade II	5 (16.7)	5 (16.7)	
	Grade III	2 (6.7)	2 (6.7)	

Grade I anemia was observed in 21 (70.0%) patients in Group I and 25 (83.3%) in Group II, while Grade II anemia was found in 9 (30.0%) and 5 (16.7%) patients, respectively. Grade I neutropenia was reported in 5 (16.7%) patients in Group I, but it did not interrupt treatment (*Table VII*).

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Table VII: Distribution of hematological toxicity between the two groups

Hematological toxicity	Grade	Group I (n=30)	Group II (n=30)
Anaemia	Grade I	21 (70.0)	25 (83.3)
Anaemia	Grade II	9 (30.0)	5 (16.7)
Neutropenia	Grade I	5 (16.7)	Not reported

DISCUSSION

The study demonstrated that preoperative concurrent chemoradiotherapy followed by surgery was associated with improved sphincter preservation among patients with Stage II low rectal adenocarcinoma. Sphincter-sparing surgery was performed in 22 (73.3%) patients in the chemoradiotherapy group, compared with 14 (46.7%) in the immediate surgery group; the difference was statistically significant (p=0.032). The finding is clinically important because permanent colostomy after abdominoperineal resection remains a major concern for patients with low rectal cancer. Symptomatic response was also better in the chemoradiotherapy group, particularly for per rectal bleeding (100% versus 92.9%) and alteration of bowel habit (60.0% versus 52.0%), both of which were statistically significant. Functional status improved more in Group I, where Karnofsky performance score 90 increased from 4 (13.3%) to 17 (56.7%), compared with 4 (13.3%) to 8 (26.7%) in Group II.

These findings are consistent with the evolving global concept that rectal cancer treatment should not focus only on tumor clearance, but also on organ preservation and quality of life. Colorectal cancer remains a major global cancer burden, with more than 1.9 million new cases and about 904,000 deaths estimated in 2022 [1]. Asian countries are also experiencing a growing colorectal cancer burden, influenced by urbanization, diet, smoking, obesity, and variable screening coverage [5,8]. In this context, sphincter preservation is particularly relevant for low-resource settings, where stoma care may impose substantial physical, psychological, and financial burden.

The sphincter preservation rate of 73.3% in the present study is higher than the 43.3% reported by Simson et al. in a prospective study of neoadjuvant chemoradiotherapy, in which the pathological complete response rate was 32.6% [13]. The difference may be explained by variation in tumor height, surgical expertise, radiation technique, and patient selection. Similarly, Tey et al. reported that intensified preoperative chemoradiotherapy achieved meaningful tumor downstaging in locally advanced rectal cancer, supporting the role of neoadjuvant treatment in improving respectability [14]. Li et al. also reported that capecitabine-based neoadjuvant chemoradiotherapy achieved high sphincter preservation with acceptable toxicity, consistent with the present findings [15]. Reviews by Li et al., Yamashita et al., and Yoo also emphasized that preoperative chemoradiotherapy can reduce tumor volume, increase downstaging, and support sphincter-preserving surgery in selected patients with rectal cancer [9,10,11].

The benefit observed in this study is also consistent with major neoadjuvant treatment trials, although many of those included patients with Stage II–III or locally advanced rectal cancer, whereas the present study was restricted to Stage II disease. Garcia-Aguilar et al. showed that adding consolidation mFOLFOX6 after chemoradiotherapy increased tumor response and might expand the range of less invasive treatment options [16]. The CAO/ARO/AIO-12 trial reported higher pathological complete response rates with chemoradiotherapy followed by consolidation chemotherapy (25% versus 17%), and later long-term results showed that this sequencing did not compromise disease-free survival, toxicity, quality of life, or stool incontinence [17,18]. The RAPIDO trial and PRODIGE-23 trial further confirmed that intensified neoadjuvant strategies can improve response and disease-related outcomes, although these regimens are generally more intensive than the approach used in the present study [19,20]. The PROSPECT trial showed a 5-year disease-free survival of 80.8% with selective FOLFOX-based treatment versus 78.6% with chemoradiotherapy, suggesting that treatment may be individualized in selected patients, but low rectal tumors still often require careful consideration of sphincter preservation [21].

The toxicity profile in the present study was acceptable. Non-hematological toxicities, including nausea, vomiting, diarrhea, proctitis, and genitourinary toxicity, did not differ significantly between groups. Grade III diarrhea was equal in both groups (3; 10.0% each), and grade III genitourinary toxicity was also equal (2; 6.7% each). Grade I neutropenia occurred in 5 (16.7%) patients in Group I and did not interrupt treatment. This is comparable with Simson et al., who reported grade ≥3 acute toxicities mainly as radiation dermatitis and diarrhea, and with Li et al., who described capecitabine-based chemoradiotherapy as tolerable [13,15]. The absence of major excess toxicity in the present study may reflect careful patient selection, inclusion of patients with ECOG performance status ≤2, and exclusion of patients with severe comorbidity or organ dysfunction.

Recent organ-preservation studies further support the clinical importance of response after neoadjuvant treatment. In the OPRA trial, organ preservation was achievable in about half of patients treated with total neoadjuvant therapy [12]. A secondary OPRA analysis showed that 3-year organ preservation was 77% among patients with clinical complete response and 40% among those with near-complete response [22]. Watch-and-wait studies, including the OnCoRe project and pooled analyses, also suggest that selected complete responders may avoid immediate radical surgery without clear survival disadvantage, although careful surveillance is mandatory [23,24]. These findings strengthen the implication that improving response before surgery may reduce permanent stoma rates and improve long-term quality of life.

LIMITATIONS

The sample size was small, and patients were selected by purposive non-probability sampling, which may limit generalizability. The study was conducted only in selected tertiary hospitals. Long-term outcomes, including local recurrence, disease-free survival, overall survival, stoma-free survival, and quality of life, were not evaluated. Pathological response and late treatment-related toxicity were also not fully assessed.

CONCLUSION

Preoperative concurrent chemoradiotherapy followed by surgery significantly improved sphincter preservation in patients with Stage II low rectal adenocarcinoma compared with immediate surgery alone. It also produced better symptomatic improvement and functional status, without a significant increase in major non-hematological toxicity. Therefore, preoperative concurrent chemoradiotherapy

appears to be a tolerable treatment approach for improving sphincter preservation in selected patients with Stage II low rectal cancer.

RECOMMENDATIONS

Preoperative concurrent chemoradiotherapy is recommended for selected Stage II low rectal adenocarcinoma patients to improve sphincter preservation. Multidisciplinary evaluation, proper staging, toxicity monitoring, and further large-scale studies with long-term follow-up are recommended. Future multicenter studies with standardized MRI staging, pathological response assessment, longer follow-up, and quality-of-life evaluation are needed to confirm these findings.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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