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Neoadjuvant Chemoradiation Improves Sphincter Preservation without Significant Toxicity in Stage II Rectal Cancer

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ABSTRACT

Background: Rectal cancer management increasingly emphasises sphincter preservation alongside oncological control. Neoadjuvant chemoradiation (nCRT) has emerged as an important approach in rectal cancer; however, its impact on sphincter preservation and toxicity remains variable, particularly in resource-limited settings. This study aimed to evaluate whether neoadjuvant chemoradiation improves sphincter preservation without significant toxicity in Stage II rectal cancer. **Methods & Materials:** This prospective comparative study was conducted from July 2011 to January 2017 at BSMMU, NICRH, and DMCH, Dhaka. A total of 60 patients with Stage II rectal adenocarcinoma were enrolled using purposive sampling and divided equally into two groups. Outcomes included sphincter-sparing surgery (SSS) rates and treatment-related toxicity. Data were analysed using SPSS version 26, with $p<0.05$ considered significant. **Results:** Most patients were aged 41-50 years (38.3%), with male predominance (58.3%). Sphincter-sparing surgery rates were higher in Group I (36.7%) compared to Group II (23.3%), while abdominoperineal resection rates were lower in Group I (13.3% vs 26.7%; p=0.032). Grade II nausea was most common (60% in both groups), with higher Grade III nausea in Group I (13.3% vs 3.3%). Vomiting and diarrhoea were predominantly Grade I–II with similar distributions. Proctitis and genitourinary toxicities were minimal, and haematological toxicity was mild with no Grade III/IV events. **Conclusion:** Neoadjuvant chemoradiation followed by surgery (Group I) demonstrated better sphincter preservation compared to surgery alone (Group II) without a significant increase in severe toxicity. These findings support the use of neoadjuvant chemoradiation as a safe and effective treatment strategy for patients with Stage II rectal cancer, particularly in resource-limited settings like Bangladesh.

Keywords: *Rectal Cancer, Neoadjuvant Chemoradiation, Sphincter Preservation, Treatment Toxicity.*

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INTRODUCTION

The rectum is the final 12-15 cm of the large bowel, extending from the sigmoid colon to the anus, and is enclosed within the mesorectum, which includes the lymphatic and vascular systems that allow for the spread of the cancer cells [1]. The proximity of the rectum to the anal sphincters is important for continence, and thus preserving the sphincters is a major factor in the treatment of rectal cancer [2]. Tumours located near the anal sphincters often compromise their integrity, sometimes requiring a more aggressive surgery such as abdominoperineal resection if tumour downstaging cannot be accomplished [3]. It ranks as the third most common type of cancer, where there were an estimated 1.9 million new cases and more than 930,000 deaths in 2020, thus ranking as the second biggest killer of cancer [4]. One-third of these cases are rectal cancers. The rate has been rising in Asia due to various factors, including urbanisation, dietary changes, and increased physical inactivity [5]. For the South Asian population, which includes Bangladesh, the condition often presents itself in the locally advanced stages because of the lack of screening [6]. This regional burden highlights the need for effective preoperative strategies to improve resectability and preserve organ function. Neoadjuvant chemoradiotherapy (nCRT) has emerged as the standard of treatment in locally advanced rectal cancer cases, especially in mid- and low-rectum cancers [7]. The incorporation of radiotherapy and chemotherapy, including fluoropyrimidine-based chemotherapy, facilitates tumour regression, renders the tumour more resectable, and decreases the incidence of local recurrences. Rates of pathological complete response (pCR) in classical nCRT have ranged between 10-20%, while new methods such as TNT offer better pCR rates and survival outcomes [8,9]. The benefit that nCRT provides is its capacity to enhance sphincter-sparing procedures. Sphincter-sparing surgery is enhanced by nCRT through shrinking the tumour and limiting tumour growth distally; this makes sphincter-sparing surgery possible, thus enhancing the quality of life postoperatively [10]. Nevertheless, results from different clinical settings indicate variability with regard to this benefit, as there are studies that indicate improvement, while other studies have shown no significant benefit [11]. Toxicity due to treatment is still a very significant issue. It has been noted that acute toxicity grade 3-4, including both gastrointestinal and haematological complications, is noted in around 10%-25% of cases receiving nCRT [12]. However, preoperative chemoradiotherapy is relatively well-tolerated compared with postoperative treatment, and it is less associated with morbidity [3]. While there has been a lot of investigation in developed countries, no complete data is available from developing countries like Bangladesh. Patient characteristics, health care facilities, and compliance may all play a role in clinical outcomes. In addition, past researches have concentrated more on survival and local tumour control rather than sphincter conservation and toxicity management. This study aims to evaluate whether the neoadjuvant chemoradiation improves sphincter preservation without significant toxicity.

METHODS & MATERIALS

This prospective comparative study was conducted from July 2011 to January 2017 at three tertiary care centers in Bangladesh: the Department of Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka; the Department of Radiation Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka; and the Department of Radiotherapy, Dhaka Medical College Hospital (DMCH), Dhaka. The study specifically included patients with Stage II rectal adenocarcinoma, and all sections of the manuscript were aligned accordingly to

avoid misclassification as locally advanced (stage II–III) disease. A total of 60 patients (N=60) were enrolled using a purposive (non-probability) sampling technique based on predefined eligibility criteria. Patients aged 18–70 years with histologically confirmed rectal adenocarcinoma located within 10 cm of the anal verge, clinical stage II disease (cT3–T4, N0, M0), ECOG performance status ≤2, and adequate hematologic, renal, and hepatic function were included. Patients with metastatic disease, prior pelvic radiotherapy, severe cardiomyopathy, or hypersensitivity to fluoropyrimidines were excluded. Treatment allocation was non-randomised and determined through a multidisciplinary tumour board (MDT) decision, considering tumour characteristics (size, location, resectability), patient clinical condition, institutional logistics, and patient preference. Based on this, patients were assigned into two groups: Group I (n=30) received neoadjuvant chemoradiation followed by surgery, and Group II (n=30) underwent upfront surgery. Baseline evaluation included detailed clinical assessment, digital rectal examination, colonoscopy with biopsy, pelvic magnetic resonance imaging (MRI), and contrast-enhanced computed tomography (CT) scan of the abdomen and chest. Variables collected included sociodemographic data (age, sex, education, tobacco use), clinical features (per rectal bleeding, alteration of bowel habit, tenesmus, mucoid discharge, anaemia, weight loss), and tumour-related parameters (tumour size, distance from anal verge, clinical T stage, and nodal status). Group I received neoadjuvant chemoradiation consisting of external beam radiotherapy (45-50 Gy in 25 fractions over 5 weeks) with concurrent oral Capecitabine (825 mg/m² twice daily during radiotherapy). Patients were reassessed clinically and radiologically after 4-8 weeks for operability. Surgical management in both groups consisted of Total Mesorectal Excision (TME), with attempts at sphincter-sparing surgery (SSS) whenever feasible based on tumour location and response. Data collection was performed prospectively using a structured case record form. Patients were followed from enrollment through treatment and the early postoperative period. The primary outcome variable was the rate of sphincter-sparing surgery. Secondary outcome variables included clinical symptom response, treatment-related toxicity (if available), and performance status assessed using the Karnofsky Performance Score (KPS). Statistical analysis was conducted using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using the independent sample t-test. Categorical variables were presented as frequencies and percentages and analysed using the Chi-square test or Fisher's exact test where appropriate. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Boards (IRB) of BSMMU, NICRH, and DMCH. Written informed consent was obtained from all participants before enrollment. Confidentiality of patient data was strictly maintained, and all procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

RESULTS

Table I shows that the participants in this study were mainly aged 41-50 years old (38.3%) and 51-60 years old (25%). There were more male participants (58.3%) than female participants (41.7%). In terms of educational attainment, 27.1% were uneducated, while 6.8% attained an educational level beyond college. The prevalence of smoking among the participants was at 56.7%.

Table I
Sociodemographic characteristics of the study population.

Variables	Category	Group I (n=30)	Group II (n=30)	Total (N=60)
Age (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%)
Sex	Male	17 (56.7%)	18 (60.0%)	35 (58.3%)
	Female	13 (43.3%)	12 (40.0%)	25 (41.7%)
Education	Illiterate	9 (30.0%)	7 (23.3%)	16 (27.1%)
	Primary	7 (23.3%)	8 (26.7%)	15 (25.4%)
	SSC	6 (20.0%)	5 (16.7%)	11 (18.6%)
	HSC	7 (23.3%)	6 (20.7%)	13 (22.0%)
	Graduate+	1 (3.3%)	3 (10.0%)	4 (6.8%)
Tobacco Use	Smoker	18 (60.0%)	16 (53.3%)	34 (56.7%)
	Non-smoker	12 (40.0%)	14 (46.7%)	26 (43.3%)

Table II reveals that an increased number of sphincter-sparing surgeries (Group I: 36.7%, Group II: 23.3%), whereas abdominoperineal resection (Group I: 13.3%, Group II: 26.7%; p = 0.032) is more common.

Table II
Distribution by rates of sphincter sparing surgery (*n*=60**).**

Surgical Variable	Group I (n, %)	Group II (n, %)	P-value
Abdominoperineal Resection (APR) & Others	8 (26.7%)	16 (53.3%)	0.032
Sphincter Sparing Surgery (SSS)	22 (73.3%)	14 (46.7%)	

Table III presents that Grade II nausea was observed in the majority of both groups at 60%. In comparison, Group I had significantly higher occurrences of Grade III nausea compared to Group II at 13.3% and 3.3%, respectively (p=0.321). In addition, vomiting Grade II was found to affect 50% of Group I participants versus 56.7% of Group II (p=0.118).

Table III
Distribution of patients according to toxicity profile (*n*=60**).**

Toxicity & Grade	Group I (n, %)	Group II (n, %)	P-value
Nausea			
Grade I	8 (26.7%)	11 (36.7%)	>0.05
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%)	>0.05
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%)	>0.05
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%)	>0.05
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			
Grade I	5 (16.7%)	4 (13.3%)	>0.05
Grade II	5 (16.7%)	5 (16.7%)	
Grade III	2 (6.7%)	2 (6.7%)	

Table IV demonstrates that the adverse effects on the blood system were relatively minor for both cohorts. Anaemia at grade I developed in 70.0% of Group I subjects and 83.3% of Group II participants, while anaemia at grade II affected 30.0% of Group I subjects and 16.7% of Group II participants.

Table IV
Distribution of patients by haematological toxicities (*n*=60**).**

	Group I / (n, %)	Group II / (n, %)
Variables	Anaemia	
Grade I	21 (70.0%)	25 (83.3%)
Grade II	9 (30.0%)	5 (16.7%)

DISCUSSION

In this study, the sociodemographic profile showed that the highest proportion of patients belonged to the 41-50 years age group (38.3%), followed by 51-60 years (25.0%), indicating a relatively younger disease burden. This aligns with recent Asian data demonstrating a rising incidence of early-onset colorectal cancer, as reported by Sung et al. and other regional analyses [4,5]. A male predominance (58.3%) was observed, which is consistent with global epidemiological trends [13]. The high proportion of illiterate patients (27.1%) and low representation of higher education (6.8%) reflect limited awareness and delayed healthcare access, which are common challenges in Bangladesh and similar low-resource settings [6]. Additionally, the high prevalence of smoking (56.7%) supports its established association with colorectal carcinogenesis [14]. From a comparative perspective, the key finding of this study was the higher rate of sphincter-sparing surgery (SSS) in patients receiving neoadjuvant chemoradiation (36.7%) compared to those undergoing immediate surgery (23.3%). Conversely, abdominoperineal resection (APR) was notably lower in the neoadjuvant group (13.3% vs 26.7%; p=0.032). These findings indicate a clear advantage of neoadjuvant chemoradiation in facilitating organ preservation. This comparative benefit is consistent with the meta-analysis by Petrelli et al., which demonstrated improved sphincter preservation rates with preoperative chemoradiotherapy [10]. Similarly, Kasi et al. reported better surgical outcomes and increased resectability following neoadjuvant treatment [9]. However, some studies have reported no significant difference in sphincter preservation despite tumour downstaging, suggesting that anatomical factors and tumour location also influence surgical decisions [11]. In comparison to these studies, the present findings reinforce that even in Stage II disease, neoadjuvant therapy can significantly impact surgical outcomes. Regarding toxicity, a comparative analysis between the two groups demonstrated that most adverse events were mild to moderate (Grade I-II) and comparable across both treatment strategies. Grade II nausea was the most frequent toxicity in both groups (60.0%), while Grade III nausea was higher in the neoadjuvant group (13.3% vs 3.3%), although this difference was not statistically significant ($p > 0.05$). Similarly, Grade II vomiting was observed in 50.0% of Group I and 56.7% of Group II patients, without significant variation. Diarrhoea was predominantly Grade I-II, with equal proportions of Grade III toxicity (10.0%) in both groups. Proctitis was mostly mild, with Grade 0 observed in 46.7% of Group I compared to 33.3% of Group II, while severe cases (Grade III) remained low and comparable (6.7% vs 10.0%). Genitourinary toxicity was minimal, with identical rates of Grade III events (6.7%) in both groups. These findings suggest that neoadjuvant chemoradiation does not significantly increase severe toxicity compared to surgery alone. Comparable toxicity profiles have been reported in previous studies evaluating capecitabine-based regimens, which demonstrated acceptable safety and tolerability [15,16]. Hematologic toxicity in this study was also mild, with no Grade III or IV events observed. Although Grade II anaemia was somewhat higher in the neoadjuvant group (30.0% vs 16.7%), the absence of severe toxicity further supports the safety of this treatment approach. This is in agreement with existing literature highlighting the favourable toxicity profile of capecitabine-based chemoradiation [15]. The clinical implications of these findings

are particularly important in resource-limited settings like Bangladesh. The improved rate of sphincter preservation with neoadjuvant chemoradiation translates into better quality of life by avoiding permanent colostomy, which has significant psychological, social, and economic impacts. Moreover, the comparable toxicity profile ensures that this benefit is achieved without compromising patient safety. Therefore, neoadjuvant chemoradiation can be considered a feasible and beneficial strategy even in Stage II rectal cancer patients where organ preservation is a priority. Overall, this study demonstrates that neoadjuvant chemoradiation provides superior short-term clinical outcomes compared to surgery alone in Stage II rectal cancer, particularly in terms of sphincter preservation, without increasing treatment-related toxicity, supporting its integration into standard management in appropriate clinical settings.

LIMITATIONS

This study has several limitations, including a small sample size and a non-randomised design, which may introduce selection bias. The use of purposive sampling limits generalizability. Short-term outcomes were assessed without long-term follow-up for survival or recurrence. Additionally, single-country data may not reflect broader population variability.

CONCLUSION

Neoadjuvant chemoradiation followed by surgery demonstrates superior short-term clinical outcomes compared to surgery alone in Stage II rectal cancer, particularly by significantly increasing sphincter preservation rates. Importantly, this benefit is achieved without a significant rise in treatment-related toxicity. These findings support the incorporation of neoadjuvant chemoradiation as an effective and safe strategy, especially in resource-limited settings where quality of life and organ preservation are critical considerations.

RECOMMENDATIONS

Neoadjuvant chemoradiation might be routinely considered for locally advanced rectal cancer to enhance sphincter preservation. Further large-scale, multicenter studies with long-term follow-up are recommended to evaluate survival, recurrence, and functional outcomes, ensuring optimal patient-centred care.

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