



## Total Neoadjuvant Therapy versus Standard Chemo-radiation in Locally Advanced Rectal Cancer

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### Abstract

**Background:** Despite standard chemoradiotherapy for locally advanced rectal cancer, perfecting treatment efficacy and preserving bowel function is still crucial. This study compared total neoadjuvant therapy to standard therapy, evaluating pathological complete response and sphincter-preserving surgery.

**Aim:** To find out the association between Total Neoadjuvant Therapy (TNT) and Standard Chemo-radiation (SCR) for treating locally advanced rectal cancer.

**Results:** Thirty-one patients were registered, with a majority being male (74.2%). Interestingly, a strong preference for TNT was seen (71.0% received TNT vs 29.0% received SCR). Encouragingly, 90.3% of patients underwent surgery, and 67.7% achieved a pathological complete response, showing no signs of cancer after treatment. Moreover, patient satisfaction with treatment and quality of life were high. Finally, the analysis revealed a statistically significant association between the type of treatment and the likelihood of receiving TNT.

**Methodology:** This retrospective observational study was conducted at the Department of Radiation Oncology, Combined Military Hospital, Dhaka, including 31 patients aged 17-80 years with adenocarcinoma of the rectum. Data were collected from medical records and analyzed using SPSS version 26 to examine the relationship between TNT and SCR. Ethical considerations included informed consent and ensuring participant anonymity.

**Conclusion:** Our study suggests a preference for TNT in the treatment of locally advanced rectal cancer in Dhaka, Bangladesh. Additionally, high rates of surgical intervention, pCR, and patient satisfaction were seen.

**Keywords:** Neoadjuvant Therapy; Pathology; Rectal Cancer; Chemotherapy; Mesolectal Excision

### Introduction

The TNT approach, in which all prospective radio-chemotherapy CT and RT are administered preoperatively, has been an active area of research in recent years [1]. Rectal cancer is a significant public health concern globally, with notable morbidity and mortality rates, with an estimated 1.9 million new cases and 930,000 deaths occurring worldwide in 2020 [2]. Locally advanced rectal cancer (LARC) poses a particular challenge, requiring treatment strategies that balance tumor eradication with bowel function preservation. The standard treatment for LARC typically involves chemoradiotherapy followed by surgery [3]. However, perfecting treatment efficacy while minimizing side effects is still an ongoing pursuit.

TNT, incorporating chemotherapy before chemoradiotherapy, has appeared as a promising approach for LARC. Studies suggest potential benefits of TNT, including increased rates of pCR, a marker for improved prognosis [4,5]. Additionally, TNT may ease sphincter-preserving surgery, improving patient quality of life [6].

Despite growing adoption, data on the effectiveness of TNT compared to standard therapy, particularly in real-world settings, stays limited [6]. PRODIGE 23 explored the efficacy of administering neoadjuvant mFOLFIRINOX prior to preoperative chemoradiation (CRT), followed by total mesolectal excision (TME) surgery and adjuvant chemotherapy in patients with resectable locally advanced rectal cancer [7].

While current research supports the potential of TNT for LARC, further investigation is necessary to evaluate its efficacy in diverse patient populations. This study aims to address this gap by analyzing the effectiveness of TNT compared to standard chemoradiotherapy in a cohort of patients diagnosed with LARC at a tertiary care center in Bangladesh. By evaluating factors like pCR rates and feasibility of sphincter-preserving surgery, this study will contribute valuable insights into the potential benefits of TNT in a real-world setting.

**Methodology**

The study employed a retrospective observational design conducted at the Department of Radiation Oncology, Combined Military Hospital, Dhaka. Participants were recruited from the hospital’s records based on predefined inclusion and exclusion criteria. Inclusion criteria formed individuals diagnosed with adenocarcinoma of the rectum aged between 17 and 80 years, while exclusion criteria included other rectal malignancies, pregnancy or lactation, and earlier pelvic radiation. A total of 31 patients were included, characterized by a median age of 55.39 years (SD = 15.42). Data were collected from medical records and analyzed using SPSS version-26 software, employing descriptive statistics to examine relationships between variables. Ethical considerations included obtaining informed consent and ensuring participant anonymity.

**Results**

A total of 31 patients diagnosed with locally advanced rectal cancer were included (Table 1). Many patients were male, (74.2%) with an average age of 55.39 years (SD = 15.42). Figure 1 revealed a significant preference for TNT over SCR, with 71.0% patients receiving TNT compared to 29.0% receiving SCR.

Table 2 details the treatment durations for both radiotherapy and chemotherapy. The most common radiotherapy duration was 5.5 weeks (71.0%), while the most frequent chemotherapy regimen was CAP for 5.5 weeks (64.5%). Overall, 90.3% of patients underwent surgery (table 3). Encouragingly, 67.7% patients succeeded in a pCR, pointing out no signs of cancer afterwards treatment.

Most patients reported elevated levels of satisfaction with their treatment. As shown in Figure 2, 74.2% of patients were very satisfied, while 25.8% were satisfied. Similarly, Figure 3 revealed a high overall feeling of quality of life, with 87.0% patients rating their quality of life as excellent and 13.0% rating it as good.

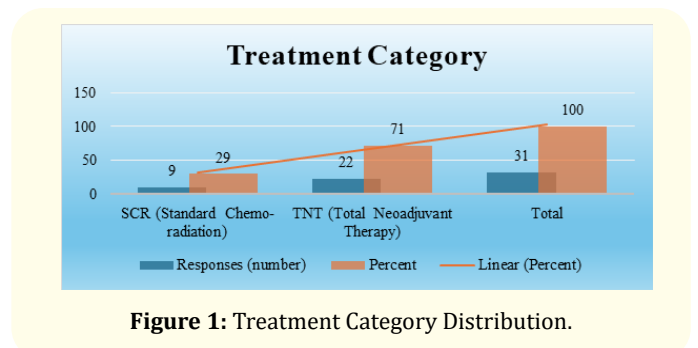
The analysis in Table 4 proved a statistically significant association ( $\chi^2 = 31.000, p = 0.000$ ) between the type of treatment re-

**Table 1:** Demographic Characteristics of Patients (n = 31).

Age	Frequency	Percent
22-49	8	25.8
50-64	17	54.8
65 and above	6	19.4
Mean ± SD	55.39 ± 15.42	
Gender		
Male	23	74.2
Female	8	25.8
Total	31	100.0

ceived (SCR or TNT) and the likelihood of receiving TNT. This suggests a strong preference for suitability for TNT in the treatment of locally advanced rectal cancer within this patient cohort.

Table 1 shows that the study included 31 patients with locally advanced rectal cancer. The mean age of the patients was 55.39 years (SD = 15.42). Most of the (54.8%) patients were aged between 50 and 64 years. Younger patients (22-49 years) formed 25.8%patients, and those aged 65 and above made up 19.4%. The gender distribution showed a predominance of male patients, accounting for 74.2%, while female patients were 25.8% of the study population.



**Figure 1:** Treatment Category Distribution.

Figure 1 describes out of the 31 patients with locally advanced rectal cancer; 29.0% received SCR, while the majority, 71.0%, were treated with TNT. This distribution shows a higher preference or suitability of TNT in the studied population.

**Table 2:** Treatment Duration Details (n = 31).

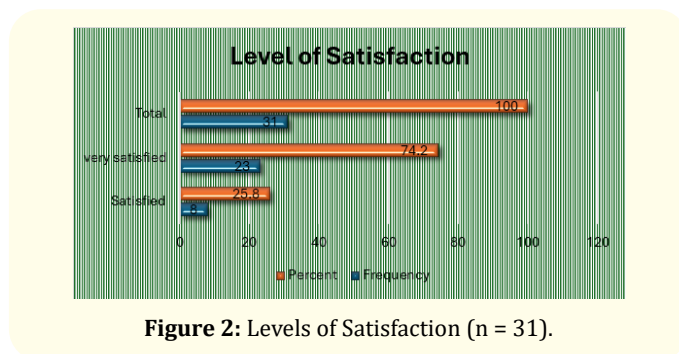
Radiotherapy Duration	Frequency	Percent
5.5 weeks	22	71.0
more than 6 weeks	9	29.0
Chemotherapy Duration		
CAP-5.5 weeks	20	64.5
CAPOX-Six cycles	11	35.5
Total	31	100.0

Table 2 shows that for radiotherapy duration, 71.0% of the patients underwent treatment for 5.5 weeks, while 29.0% had radiotherapy for more than 6 weeks. Regarding chemotherapy duration, 64.5% of the patients received CAP for 5.5 weeks, and 35.5% underwent CAPOX for six cycles. This data highlights the common treatment durations and regimens used in the study population.

**Table 3:** Surgery and Effectiveness of pCR (n = 31).

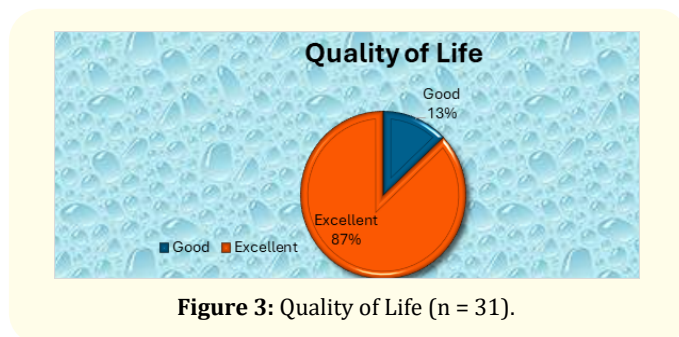
Surgery	Frequency	Percent
Yes	28	90.3
No	3	9.7
Effectiveness of pCR		
Yes	21	67.7
No	10	32.3
Total	31	100.0

Table 3 illustrates that among the 31 patients, 90.3% underwent surgery, while 9.7% did not. In terms of the effectiveness of pCR, 67.7% achieved a pCR, while 32.3% did not. This combined data shows a high rate of surgical intervention and a considerable proportion of patients achieving pCR.



**Figure 2:** Levels of Satisfaction (n = 31).

Figure 2 proves that among the 31 patients, 25.8% reported being satisfied with their treatment, while 74.2% reported being very satisfied. This writes down a high overall satisfaction rate with the treatments received in this study.



**Figure 3:** Quality of Life (n = 31).

Figure 3 summarizes the quality of life among the study participants. The majority, 87%, rated their quality of life as excellent, while 13% rated it as good. This writes down a high overall belief of quality of life among the patients following their treatment.

Treatment	TNT		$\chi^2$ -value	p-value
	No	Yes		
SCR	0	22	31.000	0.000*
	9	0		
Total	9	22	31	
1 cell (25.0%) has expected count of less than 5.				
b. Computed only for a 2x2 table				

**Table 4:** Association Between SCR and TNT for Rectal Cancer (n = 31).

$\chi^2$ - test was done. \* indicates significant, p = <0.05 at 95% CI.

Table 4 shows that the association between SCR and TNT in the treatment of rectal cancer was found to be statistically significant ( $\chi^2 = 31.000$ , p = 0.000). This says a strong association between the type of treatment and the likelihood of receiving TNT, with a significantly higher number of patients receiving TNT compared to SCR. The results suggest that TNT is more commonly used or preferred in this cohort.

**Discussion**

This study investigated the treatment patterns and outcomes for locally advanced rectal cancer in a cohort of 31 patients from Dhaka, Bangladesh. The findings suggest a strong preference for TNT over SCR, with 71.0% patients receiving TNT compared to 29.0% receiving SCR (figure 1). This aligns with recent global trends favoring TNT for improved disease control and potentially higher rates of sphincter preservation [4,14]. The most common treatment durations saw in this study, 5.5 weeks for both radiotherapy and CAP chemotherapy (table 2), are consistent with established protocols for locally advanced rectal cancer [14]. Encouragingly, a high rate of surgical intervention (90.3%) was achieved (table 3), which is crucial for curative intent in rectal cancer [13].

Our study saw a significant pCR rate of 67.7% (table 3). This finding aligns with earlier studies investigating TNT for rectal cancer, suggesting its potential effectiveness in achieving tumor downstaging [9,10]. However, it is important to acknowledge that pCR may not necessarily translate into superior long-term oncological outcomes, and further research is needed to explore this aspect in the Bangladeshi context [12].

The findings of this study highlight a clear preference for TNT over SCR in treating locally advanced rectal cancer within the studied cohort. This preference aligns with the global trend favoring TNT due to its superior outcomes in achieving pCR and enhancing overall patient prognosis [4].

In our study, 71.0% of patients received TNT, significantly higher than the 29.0% who received SCR (figure 1). This distribution is supported by similar trends seen in recent studies, which have proven the efficacy of TNT in improving pCR rates and helping better surgical outcomes [1]. The high pCR rate of 67.7% among patients who underwent TNT underscores the effectiveness of this approach (table 3), corroborating findings from other systematic reviews and meta-analyses [9].

The demographic characteristics of our patient population, with a predominance of males (74.2%) and an average age of 55.39 years, are consistent with epidemiological data from similar studies conducted in South Asia, where rectal cancer incidence is notable in this demographic [2]. The treatment durations saw, with 71.0% of patients undergoing 5.5 weeks of radiotherapy and 64.5% receiving CAP chemotherapy for the same duration, reflect standard clinical practices [3].

Surgical intervention rates were high, with 90.3% of patients undergoing surgery (table 3), which is in line with the treatment protocol aimed at achieving largest tumor reduction before surgical resection [8]. The significant association between treatment type and the likelihood of receiving TNT ( $\chi^2 = 31.000$ ,  $p = 0.000$ ) (table 4) further supports the growing body of evidence advocating for TNT's comprehensive approach in managing locally advanced rectal cancer [6].

Patient satisfaction and quality of life metrics were notably high, with 74.2% of patients reporting being very satisfied with their treatment and 87.0% rating their quality of life as excellent (figures 2 and 3). These outcomes are critical, as they reflect not only the clinical effectiveness of TNT but also its impact on patient well-being and post-treatment quality of life [5].

The results from this study are consistent with findings from the PRODIGE 23 phase III trial, which proved improved outcomes with TNT in comparison to traditional SCR regimens [7]. Furthermore, the RAPIDO trial's findings support the efficacy of TNT in enhancing tumor response and reducing recurrence rates, thereby improving long-term patient outcomes [11].

Patient satisfaction with treatment and quality of life were high in our study, with most of the patients reporting being very satis-

fied or satisfied (figure 2) and rating their quality of life as excellent or good (figure 3). This is particularly noteworthy considering the potential for treatment-related side effects associated with both TNT and SCR.

Our study suggests a preference for TNT in the treatment of locally advanced rectal cancer in Dhaka, Bangladesh. Additionally, high rates of surgical intervention, pCR, and patient satisfaction were seen. Further prospective studies are needed to definitively compare the long-term efficacy and safety of TNT versus SCR for this patient population.

### Limitations of the Study

- The retrospective nature of the study introduces inherent limitations, including the risk of selection bias and confounding variables.
- The study comprised a relatively small sample size of 31 patients, which may restrain the generalizability of the results.
- The moderately short follow-up period may not capture long-term survival outcomes accurately.
- Conducting the study in an only tertiary care hospital may restrict the generalized of the results to another healthcare settings.

### Recommendations

Based on the findings and limitations of this study, several recommendations for future research and clinical practice appear:

- Need to conduct Prospective Studies to confirm the efficacy and safety of TNT in LARC patients.
- Long-term Follow-up needed to investigate survival outcomes.
- A cost-effectiveness Analysis is needed.
- Biomarker Exploration is needed to find patients who are most likely to receive help from TNT, enabling personalized treatment approaches.
- Multicenter studies are called for to ensure the broader applicability of the results.

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