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ORIGINAL ARTICLE

Multidisciplinary Perspectives on Total Neoadjuvant Therapy in Locally Advanced Rectal Cancer: Results of a National Survey

Rahmi Atıl AKSOY,[1,2] Sema YILMAZ RAKICI,[1] Özgür ALTMIŞDÖRTOĞLU,[1] Tahsin Gökhan TELATAR[3]

[1]Department of Radiation Oncology, Recep Tayyip Erdoğan University Faculty of Medicine, Rize-*Türkiye*
[2]Department of Radiation Oncology, İzmir City Hospital, Ministry of Health, İzmir-*Türkiye*
[3]Department of Public Health, Recep Tayyip Erdoğan University Faculty of Medicine, Rize-*Türkiye*

OBJECTIVE

Rectal cancer is a leading cause of cancer-related deaths, with total neoadjuvant therapy (TNT) emerging as a key treatment for locally advanced rectal cancer (LARC). However, its clinical application varies due to differing protocols and physician preferences. This study explores physician perspectives on TNT in LARC management.

METHODS

An online survey was conducted among radiation oncologists, medical oncologists, and colorectal surgeons in Türkiye. The questionnaire, consisting of 24 questions, addressed demographics, staging, treatment sequencing, radiotherapy, chemotherapy regimens, and response evaluation. Responses were analyzed using descriptive statistics, with comparisons made between specialties using chi-square or Fisher's exact test.

RESULTS

A total of 103 participants completed the survey, with 68.9% agreeing on the standardization of TNT as the neoadjuvant treatment for LARC. While no statistically significant differences were observed across specialties, medical oncologists more frequently supported TNT as the standard approach (81.8%) compared to colorectal surgeons (70%) and radiation oncologists (60%). Factors influencing treatment choices included tumor staging, with N stage being the most significant determinant (32%). Opinions on treatment sequencing within TNT were split, with a nearly even distribution between chemotherapy-first and radiotherapy-first approaches.

CONCLUSION

This nationwide survey indicates that, while many clinicians support TNT as a neoadjuvant treatment for LARC, there remains considerable heterogeneity in clinical approaches, and full consensus among specialties has not yet been achieved. Strengthening evidence-based guidelines and enhancing multidisciplinary collaboration are needed to reduce practice variability and improve patient care.

Keywords: Current practice; physician perspective; rectal cancer; survey; total neoadjuvant therapy.

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Dr. Sema YILMAZ RAKICI
Recep Tayyip Erdoğan Üniversitesi Tıp Fakültesi,
Radyasyon Onkolojisi Anabilim Dalı,
Rize-Türkiye
E-mail: sema.rakici@erdogan.edu.tr

INTRODUCTION

Rectal cancer poses a substantial global health challenge, contributing significantly to cancer-related mortality worldwide.[1] The landscape of rectal cancer management has been revolutionized by the integration of multimodality treatment strategies, with total neoadjuvant therapy (TNT) emerging as a particularly promising approach for locally advanced rectal cancer (LARC).[2,3] TNT, which involves the administration of chemotherapy and chemoradiotherapy (CRT) prior to surgical resection, has demonstrated significant benefits in improving patient outcomes.[4] Landmark studies, such as the RAPIDO and PRODIGE 23, have highlighted TNT's ability to enhance disease-free survival and increase pathological complete remission (pCR) rates.[5,6] Building on these findings, the OPRA trial further emphasized the value of TNT by demonstrating that these favorable outcomes not only improve oncological control but also expand the potential for organ-sparing strategies. As a result, the watch-and-wait (W&W) approach has become an emerging option in carefully selected patients with a clinical complete response (cCR).[7]

Despite the growing acceptance of TNT, considerable heterogeneity exists in its implementation.[8] Treatment protocols vary significantly with respect to radiotherapy dose, chemotherapy regimens, and the sequence of administration.[9] Furthermore, physician preferences play a crucial role in shaping treatment decisions. Understanding the factors that influence these preferences is essential for optimizing TNT delivery and ensuring equitable access to high-quality care. This study aims to evaluate current clinical practice patterns and determinants of TNT adoption among specialists in Türkiye, with the goal of informing guideline development and fostering multidisciplinary consensus.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Recep Tayyip Erdoğan University (No: 2023/208, Date: 14.09.2023). All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Verbal informed consent was obtained from the participants who agreed to take part in the study. The design, conduct, and reporting of this survey study adhered to the Checklist for Reporting of Survey Studies (CROSS) guidelines to ensure methodological rigor, transparency, and completeness in accordance with established standards for survey-based research.[10]

Study Design and Participants

We conducted a national, cross-sectional survey among specialist physicians involved in the management of LARC across Türkiye. Eligible participants included radiation oncologists, medical oncologists, and colorectal surgeons actively engaged in treatment decision-making for rectal cancer patients. Physicians of all levels of experience and from all institutional settings were eligible to participate.

Sampling Frame and Recruitment

A total of 285 physicians were invited to participate in the survey: 105 Radiation oncologists, 92 medical oncologists, and 88 colorectal surgeons. The invitation list was assembled using professional society directories, hospital department rosters, and institutional networks. The survey link was distributed via personalized email invitations and professional mailing groups. The online questionnaire was administered using Microsoft Forms (https://forms.office.com), a secure and widely accessible platform. The survey was open from November 1, 2023, to June 30, 2024. Of the 285 invited physicians, 103 fully completed the questionnaire, corresponding to a response rate of 36.1%. Only complete responses were included in the final analysis. Because participation was voluntary and fully anonymous, no individual level information was available for physicians who did not respond, and systematic differences between responders and non responders could not be formally assessed.

Questionnaire Development

The 24-item questionnaire was developed by a multidisciplinary panel of experts in rectal cancer care. It was informed by previously published surveys and the evolving landscape of TNT. The draft survey underwent face validation by three independent specialists and was pilot tested with five clinicians to refine clarity, structure, and response options. The finalized version included six thematic domains:

1. Demographics and institutional characteristics (5 items)
2. Staging practices (1 item)
3. TNT selection and sequencing (10 items)
4. Radiotherapy preferences (3 items)
5. Chemotherapy choices (2 items)
6. Treatment response evaluation and surgical planning (3 items).

The full questionnaire is available as an Appendix.

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Data Collection and Anonymity

All data were collected anonymously. Microsoft Forms ensured no identifying metadata (e.g., email addresses, IP logs) were recorded. Responses were stored on secure, password-protected institutional servers accessible only to the study team.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as frequencies and percentages. For items that allowed multiple responses (e.g., imaging modalities and neoadjuvant treatment approaches), each selected option was counted once per respondent and reported as a frequency (n); consequently, the sum of counts across categories can exceed the total number of participants. Comparisons of categorical variables across specialties were performed using Pearson's chi-square or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant. Given the modest sample size and the distribution of respondents across multiple experience, institutional, and patient-volume categories, we did not perform multivariable modelling; analyses were therefore limited to descriptive statistics and unadjusted comparisons between specialties.

Power Analysis

A priori power analysis was conducted using G*Power to determine the minimum required sample size for detecting differences in proportions across three specialty groups using a chi-square test. Assuming a large effect size (Cohen's w=0.55), a two-tailed α of 0.05, and a statistical power of 0.80, the estimated sample size requirement was 32 participants per group (96 in total). Our final sample of 103 respondents exceeds this threshold, indicating that the study is adequately powered to detect large between-group differences. Nevertheless, it may still be underpowered to detect more subtle effects.

RESULTS

Participant Characteristics

A total of 103 participants were included in the study, comprising radiation oncologists (48.5%), medical oncologists (32.0%), and colorectal surgeons (19.5%). The majority had 10–19 years (41.7%) or 1–5 years (35.0%) of experience in rectal cancer management. Regarding annual treatment volume, 45.6% of participants treated 6–20 patients per year, while 32.0% managed 21–50 cases, and 16.6% treated more than 50 patients annually. Most participants (82.5%) reported involvement in a multidisciplinary tumor board. In terms of institutional affiliation, 43.7% worked in training and research hospitals, 36.9% in university hospitals, 10.7% in state hospitals, and 8.7% in private hospitals. Demographic, professional, and institutional characteristics of the participants are summarized in Table 1.

Table 1 Demographic, professional, and institutional characteristics of the participants

Characteristic	n	%
Specialty		
Radiation Oncologist	50	48.5
Medical Oncologist	33	32.0
Colorectal Surgeon	20	19.5
Experience in rectal cancer (years)		
1–5	36	35.0
6–9	15	14.6
10–19	43	41.7
≥20	9	8.7
Average annual number of treatments		
1–5	6	5.8
6–20	47	45.6
21–50	33	32.0
>50	17	16.6
Participation in multidisciplinary tumor board		
Yes	85	82.5
No	18	17.5
Institution		
State Hospital	11	10.7
Training and Research Hospital	45	43.7
Private Hospital	9	8.7
University Hospital	38	36.9

Imaging and Neoadjuvant Treatment Preferences

The imaging modalities used for staging rectal cancer varied among participants, with magnetic resonance imaging (MRI) being the most utilized method. Specifically, 97 participants reported using MRI, 81 used positron emission tomography (PET), and 38 employed computed tomography (CT). Because multiple responses were allowed for this item, these figures represent the number of respondents who routinely use each modality rather than mutually exclusive choices, and the totals exceed the overall sample size. Regarding neoadjuvant treatment approaches for LARC, 68 participants reported using TNT, 53 long-course chemoradiotherapy (LCRT), 12 short-course radiotherapy (SCRT), and 5 chemotherapy alone. As this question also permitted multiple selections, these frequencies

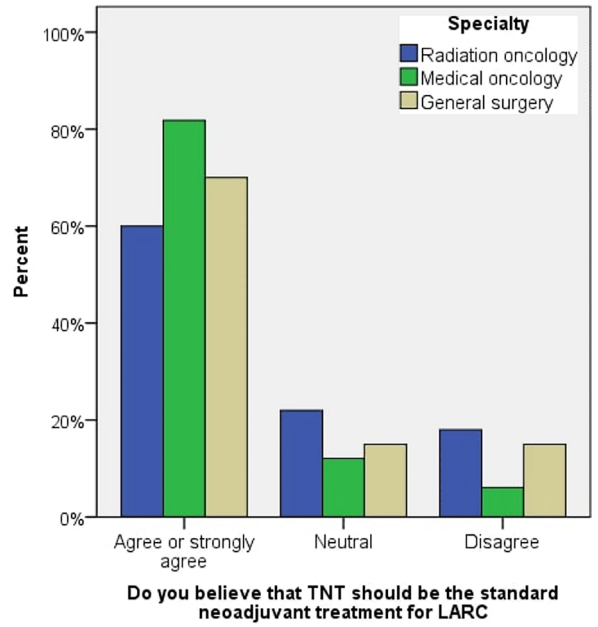

Fig. 1. Specialty-based distribution of opinions on TNT as the standard treatment for LARC.

indicate that many clinicians employ more than one neoadjuvant strategy in different clinical scenarios, reflecting preference diversity in routine practice.

Acceptance of TNT as the Standard Approach

Regarding the adoption of TNT as the standard neoadjuvant approach for LARC, 25.2% of respondents strongly agreed, 43.7% agreed, 17.5% were neutral, and 13.6% disagreed. No statistically significant difference in the level of agreement was detected across specialties (p=0.32). However, because the study was powered to detect only large effect sizes, smaller yet potentially clinically relevant between specialty differences cannot be excluded. Medical oncologists were more likely to support TNT as the standard approach compared to other specialists. The proportion of respondents who either agreed or strongly agreed was highest among medical oncologists (81.8%), followed by colorectal surgeons (70.0%) and radiation oncologists (60.0%). The distribution of responses by specialty is presented in Figure 1.

Factors Influencing Preference for TNT

The primary reason participants preferred TNT over conventional neoadjuvant therapies, such as LCRT or SCRT, was tumor staging. Key factors influencing this preference included N stage (32.0%), T stage (19.4%), and tumor location (17.5%) (Fig. 2). The distribution of these preferences by medical specialty is shown in

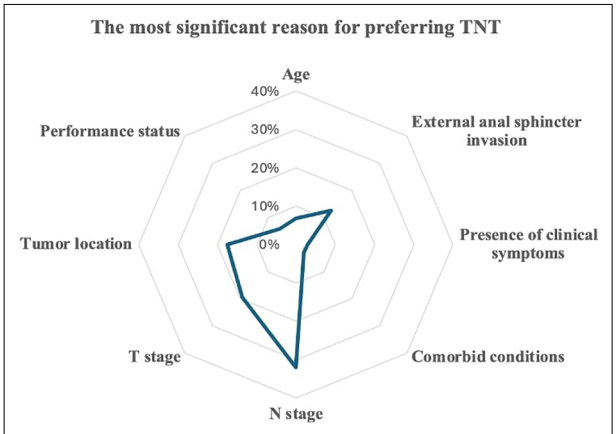

Fig. 2. Radar chart illustrating the distribution of reasons for preferring TNT over conventional neoadjuvant therapy among participants.

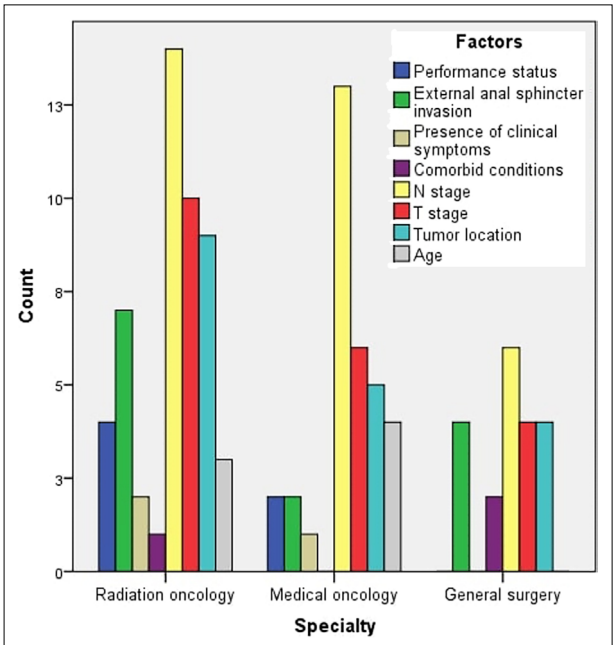

Fig. 3. Specialty-based distribution of factors influencing the preference for TNT over conventional neoadjuvant therapy.

Figure 3. Regarding treatment sequencing within TNT, participants were nearly split, with 49.5% preferring chemotherapy first and 50.5% favoring radiotherapy first. While no statistically significant differences were observed between specialties (p=0.48), trends emerged (Fig. 4). Radiation oncologists tended to prefer initiating treatment with radiotherapy, whereas medical oncologists were more likely to choose chemotherapy first. The factors most influential in sequencing de-

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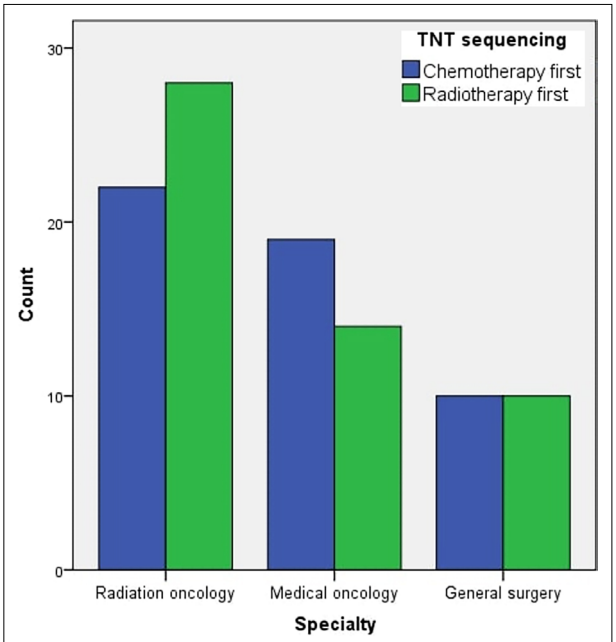

Fig. 4. Specialty-based distribution of preferences regarding TNT sequencing.

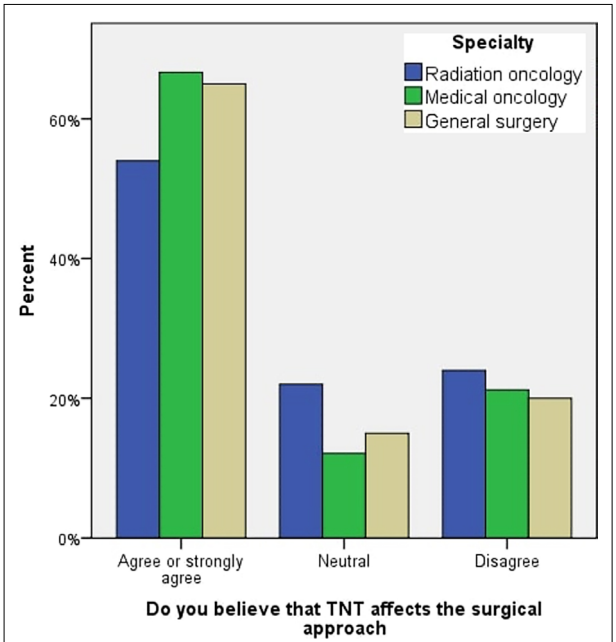

Fig. 5. Specialty-based distribution of perspectives regarding the impact of TNT on the surgical approach.

cisions included clinical symptoms (21.3%), N stage (18.4%), T stage (17.4%), and tumor location (10.6%).

Radiotherapy Strategy and Preferences

In response to the question regarding the most significant factor influencing the decision to use LCRT instead of SCRT in TNT, 21.3% of participants cited the N stage, 18.4% referred to the T stage, 15.5% highlighted tumor location, and 14.5% mentioned external anal sphincter invasion as the primary determinants. On the other hand, when asked about the factors influencing the decision to choose SCRT, 29.1% of participants identified performance status, while 24.2% pointed to comorbid conditions as the most influential factors. In response to the question regarding the appropriate total radiation dose for LCRT, 58.2% of participants indicated 50.4 Gy, while 30% responded as no opinion. The most used radiotherapy device is the linear accelerator (52.4%), while the most frequently employed radiotherapy technique is intensity-modulated radiation therapy (36.8%).

Chemotherapy and Surgical Decision-Making

Regarding the preferred chemotherapy regimen in TNT, 42.7% of participants selected CAPEOX, 22.3% preferred FOLFOX, and 23.3% had no opinion. The primary factors influencing chemotherapy regimen selection were performance status (32.0%) and comorbid conditions (26.2%). The majority of participants (52.4%) recommended evaluating treatment response 8 weeks after TNT. Similarly, 52.4% stated that surgical resection should be performed 8 weeks after TNT. In response to the question of whether TNT affects the surgical approach, 22.3% of participants strongly agreed, 37.9% agreed, 17.5% were neutral, and 22.3% disagreed. There was no statistically significant difference among specialties regarding the belief that TNT affects the surgical approach (p=0.74), although the study may have been underpowered to detect smaller differences. The distribution of responses by specialty is shown in Figure 5.

DISCUSSION

TNT has emerged as a transformative approach in the management of LARC, aiming to improve pCR rates, facilitate organ preservation, and enable non-operative management (NOM) in selected patients.[11–16] To our knowledge, this is the first nationwide survey conducted in Türkiye to evaluate multidisciplinary views on TNT implementation in LARC. Among participating colorectal surgeons, medical oncologists, and radiation oncologists, 25.2% strongly agreed and 43.7% agreed that TNT should be considered the standard neoadjuvant treatment for LARC. This finding reflects a growing shift toward intensified preoperative strategies. It is consistent with evidence from major clinical trials such

as RAPIDO, PRODIGE-23, and OPRA,[5–7] as well as with recent international survey studies reporting similar trends.[17–22] Despite the overall favorable perception of TNT, there remains substantial variability in its clinical application. This variability highlights the need for standardized treatment protocols and improved interdisciplinary collaboration to optimize patient care, but it also reflects the current global uncertainty regarding the optimal TNT paradigm and ongoing efforts to tailor treatment to tumor- and patient-related factors.

Although no statistically significant differences were found between specialties, medical oncologists demonstrated the highest level of agreement with the adoption of TNT. Specifically, 81.8% of medical oncologists agreed or strongly agreed that TNT should be the standard neoadjuvant treatment, compared to 70% of colorectal surgeons and 60% of radiation oncologists. This trend is consistent with the findings of O'Brien et al.,[19] who also reported a greater inclination toward TNT among medical oncologists, likely reflecting their focus on systemic disease control. These differences may reflect variations in clinical training and therapeutic priorities across disciplines. Strengthening multidisciplinary coordination and developing unified treatment algorithms may help bridge these gaps and promote consistent implementation of TNT.[23]

Tumor-specific factors emerged as the most influential elements in treatment selection. N stage (32.0%), T stage (19.4%), and tumor location (17.5%) were most frequently cited as key determinants for preferring TNT over conventional neoadjuvant options. These priorities were consistent across specialties, indicating a shared reliance on oncologic risk factors in decision-making. Our findings align with prior studies identifying nodal involvement, advanced T stage, and mesorectal fascia proximity as major considerations influencing TNT adoption.[17,21] Especially in low rectal tumors, anatomical constraints such as proximity to the sphincter complex further support the preference for TNT.[22] Overall, these results highlight the need for personalized treatment planning based on detailed anatomical and oncological assessment, even in the context of emerging standardization efforts.

Preferences regarding the sequencing of TNT protocols varied considerably among respondents. Approximately half favored induction chemotherapy followed by radiotherapy, while the other half preferred starting with radiotherapy followed by consolidation chemotherapy. This variation reflects the ongoing global uncertainty surrounding optimal sequencing, as previously reported,[17,19] and may also indicate that clinicians are individualizing the order of chemotherapy and radiotherapy according to symptom burden and perceived risk of distant failure. In our study, the most frequently cited factors influencing sequencing decisions were clinical symptoms (21.3%) and nodal stage (18.4%). Radiotherapy was more often selected as the initial modality in patients presenting with symptoms such as rectal pain or bleeding, whereas induction chemotherapy was preferred in cases with a higher risk of systemic dissemination, such as those with nodal metastasis. Although the OPRA trial demonstrated higher rates of organ preservation with consolidation chemotherapy, definitive survival advantages between sequencing strategies remain unclear, which may explain the variability observed in clinical practice.[7,16] Initiating TNT with radiotherapy may also extend the interval to surgery, potentially allowing greater tumor regression. This prolonged interval has been associated with increased rates of clinical complete response and enhanced feasibility of organ-preserving strategies such as non-operative management.[7,24,25]

In our study, LCRT was preferred in cases with advanced N stage, high T stage, low tumor location, or external anal sphincter invasion, reflecting a clinical emphasis on achieving optimal local control. In contrast, SCRT was more often selected for patients with poor performance status or significant comorbidities, due to its shorter duration and potentially lower toxicity. These practice patterns are supported by findings from major clinical trials. The RAPIDO study showed that SCRT followed by chemotherapy and delayed surgery reduced distant metastases compared to conventional chemoradiotherapy, although it was associated with a slightly increased risk of locoregional recurrence, emphasizing the importance of patient selection.[5] The PRODIGE 23 trial, which implemented intensive induction chemotherapy before LCRT, demonstrated improved disease-free and metastasis-free survival without compromising local control, suggesting an advantage for LCRT-based TNT in high-risk patients.[6] Survey studies similarly report a preference for LCRT in settings where tumor regression and sphincter preservation are prioritized,[17,19] and professional experience may also influence regimen selection.[18] Taken together, both LCRT and SCRT are effective components of TNT, and the choice between them should be guided by tumor characteristics, patient comorbidities, and multidisciplinary evaluation to ensure personalized and effective treatment planning. In addition, real-world implementation of TNT is likely influenced by institutional resources, access to advanced technologies, and reimbursement policies.

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Although these system-level factors were not directly assessed in our survey, they may further affect the feasibility and consistency of TNT delivery and warrant dedicated investigation in future studies.

This study has certain limitations that should be considered when interpreting the results. As participation was voluntary and the overall response rate was modest (36.1%), there is a risk of non response bias; physicians with a greater interest in TNT may have been more likely to participate, which could have led to an overestimation of its acceptance and use in routine practice. As we did not have access to data on non responders, we could not determine whether they differed systematically from respondents in terms of institutional type, specialty mix, or level of interest in TNT; however, such differences are possible and may limit the generalizability of our findings. Moreover, colorectal surgeons accounted for only 19.5% of respondents, despite representing almost one third of the invited sample. This underrepresentation may have restricted our ability to fully capture surgical perspectives and to detect specialty specific differences. In addition, the questionnaire was not subjected to formal psychometric validation (e.g., test–retest reliability or factor analysis), which represents an additional methodological limitation. Nevertheless, the survey reached a broad and diverse sample of physicians involved in LARC management across Türkiye. Responses were based on self-reported practices, which may not always align with actual institutional behaviors, yet they provide valuable insight into current clinical thinking. While findings are largely consistent with international data, they reflect perspectives within a specific national context and should be interpreted accordingly. Although the sample size was sufficient for descriptive analysis, further studies with larger and more balanced specialty representation are needed to validate and expand on these observations.

CONCLUSION

Our findings indicate that, although TNT is regarded as a neoadjuvant strategy by many clinicians in Türkiye, a substantial proportion of respondents remained neutral or disagreed with its designation as the standard approach. This highlights the lack of full consensus across specialties and reflects the persistent heterogeneity in its clinical application. Overall, TNT appears to be increasingly incorporated into LARC management, yet differences in preferences across specialties underscore the complexity of clinical decision-making and the multidisciplinary nature of care. These results emphasize the need for collaborative efforts to develop standardized, evidence-based protocols and decision-making frameworks. Establishing clear national guidelines may help reduce unwarranted practice variation, support optimal treatment sequencing, and ultimately improve patient outcomes. Future prospective studies are warranted to further evaluate the real-world implementation of TNT and its long-term oncologic and functional impacts.

Ethics Committee Approval: The study was approved by the Recep Tayyip Erdoğan University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (no: 2023/208, date: 14/09/2023).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors declare no competing interests.

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APPENDIX

QUESTIONNAIRE

Section 1

1. **What is your primary specialty?**
    - Radiation Oncology
    - Medical Oncology
    - General Surgery
2. **What is the duration of your experience in treating rectal cancer?**
    - 1-5 years
    - 6-9 years
    - 10-19 years
    - 20 years or more
3. **On average, how many rectal cancer cases do you manage annually?**
    - 1-5
    - 6-20
    - 21-50
    - More than 50
4. **Are treatment decisions for rectal cancer patients made within a multidisciplinary tumor board setting?**
    - Yes
    - No
5. **In what type of institution are you primarily affiliated?**
    - State Hospital
    - Training and Research Hospital
    - University Hospital
    - Private Hospital

Section 2

6. **Which imaging modalities do you routinely utilize for staging rectal cancer? (Select all that apply)**

- MRI
- Endorectal Ultrasound (ERUS)
- CT
- PET
- Other (Please specify):

Section 3

7. **What neoadjuvant treatment approaches do you typically employ for the management of LARC? (Select all that apply)**
    - Chemotherapy alone
    - Short-course radiotherapy (SCRT)
    - Long-course chemoradiotherapy (LCCRT)
    - Total neoadjuvant therapy (TNT)
8. **Do you believe that TNT should be the standard neoadjuvant treatment for locally advanced rectal cancer?**
    - Strongly agree
    - Agree
    - Neutral
    - Disagree
9. **What factor most significantly influences your decision to utilize TNT over conventional neoadjuvant therapy (LCCRT or SCRT)?**
    - Age
    - Eastern Cooperative Oncology Group (ECOG) / Karnofsky performance status
    - Comorbidities
    - Presence of clinical symptoms (e.g., tenesmus, bleeding, pain)
    - External anal sphincter invasion
    - Tumor location
    - T stage
    - N stage
10. **How does tumor location influence your preference for TNT?**
    - Proximal
    - Mid

- Distal

11. **How does T stage influence your preference for TNT?**
    - T1
    - T2
    - T3
    - T4
12. **How does N stage influence your preference for TNT?**
    - N0
    - N1
    - N2
13. **In your practice, what is the preferred sequence of TNT administration?**
    - Chemotherapy-first
    - Radiotherapy-first

14. What is the most important factor in determining your selection of TNT sequence?

- Age
- ECOG/Karnofsky performance status
- Comorbidities
- COVID-19 risk
- Presence of clinical symptoms
- External anal sphincter invasion
- Tumor location
- T stage
- N stage

15. What is the most significant factor influencing your decision to use LCCRT instead of SCRT in TNT?

- Age
- ECOG/Karnofsky performance status
- Comorbidities
- Presence of clinical symptoms
- External anal sphincter invasion
- Tumor location
- T stage

- N stage

16. What is the most significant factor influencing your decision to use SCRT in TNT?

- Age
- ECOG/Karnofsky performance status
- Comorbidities
- COVID-19 considerations
- Tumor location
- T stage
- N stage

Section 4

17. **If you utilize LCCRT, what is your preferred total radiotherapy dose?**

- 45 Gy
- 50.4 Gy
- Higher dose
- No preference

18. **For TNT protocols, which radiotherapy technique do you typically employ?**

- 3D-Conformal Radiotherapy (3D-CRT)
- Intensity-Modulated Radiotherapy (IMRT)
- Volumetric Modulated Arc Therapy (VMAT)
- No preference
- Other (Please specify):

19. **What radiotherapy delivery system(s) do you utilize for TNT?**

- LINAC
- Tomotherapy
- MR-LINAC
- No preference
- Other (Please specify):

Section 5

20. **What chemotherapy regimen do you prefer for TNT?**

- CAPEOX

- FOLFOX
- FOLFIRINOX
- No preference
- Other (Please specify):

21. What is the primary factor influencing the selection of your chemotherapy regimen for TNT?

- Age
- ECOG/Karnofsky performance status
- Comorbidities
- Presence of clinical symptoms
- External anal sphincter invasion
- Tumor location
- T stage
- N stage

Section 6

22. **When do you typically assess treatment response after TNT?**

- 5 weeks
- 8 weeks
- 12 weeks
- 16 weeks

23. **What is the typical interval between TNT completion and surgical resection?**

- 2-4 weeks
- 5-6 weeks
- 8 weeks
- 9 weeks or more

24. Do you believe that TNT affects the surgical approach?

- Strongly agree
- Agree
- Neutral
- Disagree