International Surgery Journal
Sripathi S et al. Int Surg J. 2026 Jul;13(7):1182-1186
https://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20261995

Original Research Article

Comparing outcomes of open versus minimally invasive total mesorectal excision after total neoadjuvant therapy in rectal cancer: a national cancer database analysis

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Received: 08 June 2026
Revised: 12 June 2026
Accepted: 16 June 2026

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ABSTRACT

Background: Total neoadjuvant therapy (TNT), in which systemic chemotherapy and pelvic radiation are delivered before surgery, improves pathological complete response, disease-free survival and treatment compliance in locally advanced rectal cancer. Large-scale data comparing open and minimally invasive surgery (MIS) approaches to total mesorectal excision (TME) specifically after TNT are lacking.
Methods: The national cancer database was queried (2010–2020) for adults with clinical stage II–III rectal adenocarcinoma who received chemoradiotherapy and at least two chemotherapeutic agents before TME. Stage I or IV disease, primary resection without neoadjuvant therapy and MIS converted to open were excluded. Univariate analysis and multivariable logistic regression were performed. The primary outcome was inadequate lymph node retrieval (<12 nodes); the secondary outcome was 90-day postoperative mortality.
Results: A total of 5,962 patients were included; 3,111 (52.2%) underwent MIS and 2,851 (47.8%) underwent open TME. Inadequate lymph node retrieval was less frequent with MIS (27.1%) than open surgery (33.2%) (OR 0.80; 95% CI 0.71–0.90; p<0.001). 90-day mortality was lower with MIS (0.8%) than open surgery (2.2%) (OR 2.46 for open; 95% CI 1.51–4.03; p<0.001).
Conclusions: After TNT for rectal cancer, an MIS approach to TME was associated with a higher likelihood of adequate lymph node harvest and lower 90-day mortality than open surgery. These differences may reflect improved pelvic exposure, although selection bias toward more advanced tumors in the open cohort cannot be excluded. Prospective studies are warranted.

Keywords: Lymph node retrieval, Minimally invasive surgery, Rectal cancer, Total neoadjuvant therapy, Total mesorectal excision

INTRODUCTION

Colorectal cancer remains the second leading cause of cancer-related death in the United States, with an estimated 49,990 new cases of rectal cancer projected in 2026.[1] The principles of modern rectal cancer surgery were established by Heald and colleagues in 1982, when TME along the avascular "holy plane" between the mesorectal and parietal pelvic fasciae was shown to dramatically reduce local recurrence.[2,3]

Subsequent multimodality refinements such as neoadjuvant chemoradiotherapy, optimization of the circumferential resection margin (CRM) and adjuvant

systemic therapy, have further improved oncologic outcomes for locally advanced rectal cancer (LARC). Despite these advances, distant metastatic relapse continues to affect roughly one-quarter to one-third of patients with LARC and compliance with postoperative adjuvant chemotherapy has historically been poor. TNT was developed to address these limitations by delivering all chemotherapy and radiation before surgery. Randomized trials including RAPIDO, PRODIGE 23 and OPRA have demonstrated that TNT improves pathological complete response, disease-free survival and treatment compliance and, in selected patients with a clinical complete response, enables organ preservation via a watch-and-wait strategy.[4-6] Adoption of TNT has expanded rapidly across academic and community settings.[7]

In parallel, MIS, including laparoscopic and robotic approaches, has been increasingly applied to TME. The COLOR II8 and COREAN9,10 trials demonstrated equivalent oncologic outcomes between laparoscopic and open TME, whereas the ACOSOG Z6051 and ALaCaRT trials failed to establish non-inferiority of laparoscopy with regard to a composite pathologic outcome (CRM, distal margin and completeness of TME).[11-13] The optimal surgical approach in the specific setting of TNT, where tumor downstaging, fibrosis and altered pelvic anatomy may complicate dissection, has not been examined in large real-world datasets.

Lymph node retrieval is a recognized quality metric in rectal cancer surgery, with a minimum of 12 nodes recommended for accurate staging.[14] Neoadjuvant therapy is well known to decrease nodal yield and the prognostic significance of node count after chemoradiation remains debated.[14-16] In this study, we used the National Cancer Database (NCDB) to compare adequacy of lymph node retrieval and short-term mortality between open and MIS TME in patients who completed TNT for rectal cancer.

METHODS

Type of study and data source

This is a retrospective study. NCDB is a joint program of the American college of surgeons commission on cancer and the American cancer society, which has approximately 70% of all newly diagnosed cancers in the United States. Using the NCDB, we identified cases of rectal adenocarcinoma diagnosed between 2010 and 2020.

Inclusion criteria

Inclusion criteria were adult patients with clinical stage II or III rectal adenocarcinoma, receipt of pelvic radiotherapy and systemic chemotherapy in the neoadjuvant period and administration of two or more chemotherapeutic agents prior to surgery, consistent with a TNT regimen described in contemporary randomized trials.[4,5]

Exclusion criteria

Exclusion criteria were clinical stage I or IV disease, primary resection without neoadjuvant therapy and conversion from MIS to open surgery (to avoid intent-to-treat misclassification).

Exposure and outcomes

The exposure of interest was surgical approach (open versus MIS, the latter comprising laparoscopic and robotic TME). The primary outcome was inadequate lymph node retrieval, defined as fewer than 12 lymph nodes examined in the surgical specimen, consistent with American Joint Committee on Cancer (AJCC) staging recommendations and prior literature.[14] The secondary outcome was 90-day postoperative mortality.

Statistical analysis

Baseline characteristics were compared between groups using chi-square tests for categorical variables and Student t or Wilcoxon rank-sum tests for continuous variables, as appropriate.

Univariable and multivariable logistic regression were performed for each outcome, adjusting for age, sex, race/ethnicity, insurance status, income quartile, urban/rural residence, facility type, Charlson-Deyo comorbidity score, clinical T and N stage, interval from radiation to surgery and interval from diagnosis to chemotherapy initiation. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). A two-sided p value <0.05 was considered statistically significant. All analyses were performed using standard statistical software.

Ethical approval

The study was exempted from informed consent or approval from the Institutional Review Board since de-identified, population-based data was used from the National Cancer Database.

RESULTS

Cohort characteristics

A total of 5,962 patients met inclusion criteria. Of these, 3,111 (52.2%) underwent MIS and 2,851 (47.8%) underwent open TME. Patients in the open cohort were more likely to be younger (with a higher proportion aged <50 years), to have private insurance and to reside in metropolitan areas, while patients in the MIS cohort more often had cT4 disease and Medicaid coverage. Baseline characteristics are summarized in Table 1.

Lymph node retrieval

Inadequate lymph node retrieval (<12 nodes) was observed in 842 patients (27.1%) in the MIS group and 947 patients (33.2%) in the open group. On multivariable analysis, MIS was associated with significantly lower odds of inadequate retrieval (OR 0.80; 95% CI 0.71–0.90; p<0.001) (Table 2).

90-day mortality

90-day postoperative mortality occurred in 24 patients (0.8%) in the MIS group and 62 patients (2.2%) in the open group. Open surgery was associated with a more than two-fold increase in odds of 90-day mortality compared with MIS (OR 2.46; 95% CI 1.51–4.03; p<0.001) (Table 2).

Table 1: Baseline characteristics of patients undergoing open versus MIS TME after TNT.

Characteristic	Open (n=2851)	MIS (n=3111)	P value
Age (in years)			<0.001
<50	911	692	
50–65	1441	1401	
65–80	706	688	
>80	53	70	
Gender			0.75
Male	1934	1761	
Female	1177	1090	
Income quartile			<0.001
Lower quartiles	1349	1414	
Higher quartiles	1762	1437	
Insurance			<0.001
Uninsured	99	181	
Private	1870	1415	
Medicaid	248	321	
Medicare	833	867	
Other	61	67	
Race			0.03
White	2641	2385	
Black	243	280	
Asian	118	84	
American Indian	11	14	
Other	98	88	
Geography			0.002
Rural	37	52	
Urban	369	413	
Metropolitan	2513	2231	
Comorbidity score			0.067
0	2508	2244	
≥1	603	607	
Clinical T stage			<0.001
T1	23	37	
T2	183	135	
T3	2583	2181	
T4	322	498	

Table 2: Primary and secondary outcomes by surgical approach.

Outcome	Open (n=2851)	MIS (n=3111)	P value
Lymph node retrieval			<0.001
<12 nodes (inadequate)	947 (33.2%)	842 (27.1%)	
≥12 nodes (adequate)	1904 (66.8%)	2269 (72.9%)	
90-day mortality	62 (2.2%)	24 (0.8%)	<0.001

DISCUSSION

In this large, contemporary, real-world analysis of patients undergoing TNT for stage II–III rectal cancer, a minimally invasive approach to TME was associated with a higher likelihood of adequate lymph node retrieval and lower 90-day postoperative mortality compared with open surgery. To our knowledge, this is the largest study to compare open and MIS approaches in the specific clinical context of TNT.

The findings are concordant with several randomized trials demonstrating the short-term safety of laparoscopic TME. The COLOR II trial reported equivalent rates of CRM positivity and 3-year local recurrence between laparoscopic and open surgery and the COREAN trial, performed exclusively in patients who had received neoadjuvant chemoradiation, demonstrated equivalent short-term and 10-year oncologic outcomes.[8-10] However, the ACOSOG Z6051 and ALaCaRT trials, both employing a composite pathologic non-inferiority endpoint, failed to demonstrate non-inferiority of laparoscopic surgery, raising concern that MIS may compromise specimen quality.[11,13] Long-term follow-up of ACOSOG Z6051 nonetheless showed no significant difference in 2-year disease-free survival or local recurrence between approaches, suggesting that the pathologic endpoint may not directly translate to inferior oncologic outcomes.[12]

The observed advantage of MIS in lymph node retrieval may reflect the technical benefits of laparoscopic and robotic platforms in the deep pelvis: magnified visualization, articulating instruments and improved exposure of the lateral and posterior dissection planes along Heald's holy plane.[2,3] Conversely, neoadjuvant therapy and particularly the intensified regimens used in TNT, is known to substantially reduce nodal yield through tumor regression and treatment-induced fibrosis. Rullier and colleagues reported a reduction in the median number of lymph nodes retrieved from 12.5 to 7 after chemoradiation, with low nodal yield reflecting tumor sensitivity rather than inadequate resection.[14] Persiani and colleagues similarly found that nodal status, but not absolute count, was an independent predictor of survival after neoadjuvant therapy.[15] Nevertheless, an absolute threshold of 12 nodes remains the standard quality metric and an independent prognostic marker in several large series.[16]

The 2.2% 90-day mortality observed in the open cohort, compared with 0.8% with MIS, mirrors prior comparative effectiveness studies and is plausibly explained by reduced perioperative physiologic stress, lower transfusion requirements, faster recovery of gastrointestinal function and shorter hospital stays observed with MIS in the COLOR II and COREAN trials.[8,9] The accelerated adoption of TNT, with longer intervals between completion of chemoradiation and surgery, may also amplify the perioperative benefits of a less invasive approach in this increasingly multimodal pathway.[4-7]

Several limitations warrant emphasis. First, the retrospective and observational design precludes causal inference and significant selection bias is likely. Surgeons may preferentially select an open approach for more advanced, bulky or post-radiation fibrotic tumors with anticipated technical difficulty, precisely the cases in which both lymph node yield and perioperative mortality may be worse independent of approach.

Second, the NCDB does not capture surgeon volume, technique-specific quality metrics (e.g., completeness of mesorectal envelope, plane of dissection) or detailed perioperative complications. Third, the dataset does not differentiate laparoscopic from robotic MIS and the proportional contribution of robotics has grown substantially over the study period. Fourth, although our inclusion criteria operationalize TNT through receipt of multi-agent chemotherapy plus radiation prior to surgery, the precise sequence (induction versus consolidation chemotherapy) cannot be reliably reconstructed from NCDB variables. Propensity score-matched and subgroup analyses (planned in subsequent work) will further address residual confounding.

CONCLUSION

Rectal cancer management is constantly evolving. In patients undergoing Total Neoadjuvant Therapy for rectal cancer, a Minimally invasive approach is associated with a higher chance of an adequate lymph node harvest and a lower 90-day mortality. This may be explained by the fact that a minimally invasive approach provides better exposure with a more precise dissection, particularly in the deep pelvis. However, it may also be due to a selection bias, as open cases are more likely to be advanced tumors with tumor replacement of the lymph nodes, which would lead to a lower harvest if it is responsive to treatment. Further prospective studies are needed to fully understand the implications of TNT on the operative approach.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sripathi S, Pindicura S, Pacheco F, Kamel M. Comparing outcomes of open versus minimally invasive total mesorectal excision after total neoadjuvant therapy in rectal cancer: a national cancer database analysis. Int Surg J 2026;13:1182-6.