



# Assessment of Textbook Oncologic Outcomes Following Proctectomy for Rectal Cancer

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## Abstract

**Background** Outcomes of rectal adenocarcinoma vary considerably. Composite “textbook oncologic outcome” (TOO) is a single metric that estimates optimal clinical performance for cancer surgery.

**Methods** Patients with stage II/III rectal adenocarcinoma who underwent single-agent neoadjuvant chemoradiation and proctectomy within 5–12 weeks were identified in the National Cancer Database (NCDB). TOO was defined as achievement of negative distal and circumferential resection margin (CRM), retrieval of  $\geq 12$  nodes, no 90-day mortality, and length of stay (LOS)  $< 75$ th percentile of corresponding year’s range. Multivariable logistic regression was used to identify predictors of TOO.

**Results** Among 318,225 patients, 8869 met selection criteria. Median age was 62 years (IQR 54–71), and 5550 (62.6%) were males. Low anterior resection was the most common procedure (LAR, 6,037 (68.1%) and 3084 (34.8%) were treated at a high-volume center ( $\geq 20$  rectal resections/year). TOO was achieved in 3967 patients (44.7%). Several components of TOO were achieved commonly, including negative CRM (87.4%), no 90-day mortality (98.0%), no readmission (93.0%), and no prolonged hospitalization (78.8%). Logistic regression identified increasing age, non-private insurance, low-volume centers, open approach, Black race, Charlson score  $\geq 3$ , and abdominoperineal resection (APR) as predictors of failure to achieve TOO. Over time, TOOs were attained more commonly which correlated with increased minimally invasive surgery (MIS) adoption. TOO achievement was associated with improved survival.

**Conclusions** Rectal adenocarcinoma patients achieve TOO uncommonly. Treatment at high-volume centers and MIS approach were among modifiable factors associated with TOO in this study.

**Keywords** Rectal adenocarcinoma · Textbook outcomes

## Introduction

Incidence of rectal adenocarcinoma has increased in the USA, with  $> 43,000$  cases diagnosed annually.<sup>1</sup> A majority of patients with non-metastatic rectal adenocarcinoma

present with invasive tumors which are not amenable to local excision and require transabdominal approaches, such as low anterior resection (LAR) or abdominoperineal resection (APR). Despite surgery remaining the cornerstone of curative-intent treatment, management has extensively evolved over the past few decades through incorporation of multimodal therapy and improvements in surgical technique.<sup>2,3,4</sup>

Despite significant advances, variation across practices remains in the US, and factors affecting postoperative and oncological outcomes such as center volume and specialization have been studied.<sup>5,6,7,8</sup> Conventionally, assessment of surgical quality for rectal adenocarcinoma has focused on unique outcomes such as perioperative morbidity and mortality, length of stay (LOS), and readmissions.<sup>9,10,11</sup> Similarly, adherence to oncological standards is typically estimated by reporting on unique metrics such as margin status, lymph node (LN) numbers, and long-term survival.<sup>12,13</sup>

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Solitary metrics may be imperfect when studying overall quality variation and are less relevant to stakeholders who may not fully grasp cancer care delivery nuances, including referring providers, administrators, and patients. The composite textbook outcome was introduced as a valuable encompassing measurement which reflects average “best” surgical quality.<sup>14</sup> Indeed, textbook outcomes are particularly suited for gauging oncological quality as performance is typically affected by numerous variables. More recently, textbook oncologic outcomes (TOO) have been studied in the context of colonic, esophagogastric, and pancreatic malignancies.<sup>15,16,17</sup> Importantly, attaining TOO has been shown to be associated with improved long-term outcomes.

The Commission on Cancer (CoC) National Accreditation Program for Rectal Cancer (NAPRC) was developed by the American College of Surgeons (ACS) to optimize RCA outcomes.<sup>18,19</sup> However, to date, TOO's have not been studied in rectal adenocarcinoma at CoC centers. We aimed in this study to describe TOO's among patients undergoing proctectomy for rectal adenocarcinoma and to identify further factors associated with failure to achieve a TOO in this study.

## Methods

### Data Source

The National Cancer Database (NCDB) is a joint project of the American Cancer Society and the American College of Surgeons CoC. NCDB collects data from over 1500 CoC-accredited hospitals and includes over 70% of new cancer diagnoses in the USA.<sup>20,21</sup> This study was granted institutional review board exemption. The Rectal Participant User File was utilized to identify all patients presenting with localized rectal adenocarcinoma (defined as nonmetastatic stage T3/T4 N0 or T-any N+) who underwent proctectomy (APR, LAR or pelvic exenteration) between 2010 and 2017. To reflect existing standards in management of stage II/III rectal adenocarcinoma, only patients who received single-agent neoadjuvant chemoradiation followed by proctectomy within 5–12 weeks of radiotherapy conclusion were included. Patients who received alternative doses, fractions, or radiation to areas other than the pelvis/rectum were excluded. Additional exclusion criteria were patients with different histologies, metastatic disease, multiple malignancies, those who underwent procedures other abdominal proctectomy (such as transanal excision, pull-through proctectomy, or unknown/unclear procedures), and receipt of multi-agent neoadjuvant chemotherapy. Patients with missing information on surgical approach (i.e., open, laparoscopic and robotic-assisted) were not included. Finally, patients with missing pathologic data on resection margin status, postoperative LOS, receipt of systemic

chemotherapy, readmission rates, and 30- and 90-day mortality were excluded.

### Textbook Oncologic Outcome

TOO definition was agreed upon a priori by all coauthors and was made to be consistent with previous studies which focused on malignancies other than rectal adenocarcinoma, and after considering relevant NAPRC standards.<sup>16,22,23,24</sup> Ultimately, included elements were ones associated with optimal surgical and oncological outcomes for rectal cancer. A TOO was achieved when all components were met and was expressed as a percentage. Those were resection to negative margins (proximal, distal (DRM) and circumferential, CRM), American Joint Committee on Cancer (AJCC) compliant LN evaluation ( $\geq 12$  LN), LOS less than or equal to the 75th percentile by treatment year and operative approach, no unplanned 30-day readmission, and no 90-day all-cause mortality.

### Statistical Analysis

Conditional logistic regression was used to compare categorical variables and mixed effect modeling to compare continuous variables between groups. Kaplan–Meier method was utilized to study overall survival (OS), which was calculated from the date of diagnosis to the date of last contact or death. Cox proportional hazards model was utilized to determine the association between clinicopathologic factors, surgical approach, center volume and TOO, and overall survival. High volume centers were those that performed 20 or more proctectomies per year.<sup>25,26,27,28,29</sup> A log-rank test was applied to compare OS between groups. Lastly, a backward stepwise multivariable logistic regression was performed to identify significant predictors of TOO. Conditional entry was set at  $p < 0.05$  and exclusion at  $p \geq 0.05$ . All demographic and clinical variables that are not components of TOO were included in the regression model's first step. Variables which remained in the final model were reported and a Bonferroni correction was applied in order to reduce inflated likelihood of type I error.

SPSS v25 (Armonk, NY) with R essentials plug-in (V3.3.3) was used for statistical analysis. Adjusted odds ratios (ORs) and 95% confidence interval (CIs) were reported, with statistical significance set at  $p < 0.05$  throughout the study.

## Results

### Textbook Oncologic Outcomes

NCDB included 189,849 cases of diagnosed rectal malignancies between 2010 and 2017. After application

of inclusion/exclusion criteria, 8869 patients remained (Fig. 1). Median age was 62 years (IQR 54–71), and 5550 (62.6%) were males. Cases were divided evenly among clinical stage II and stage III (46.6% vs. 53.4%, respectively). The majority of patients had clinical T3 lesions (7763, 86.4%), and 4135 (46.6%) were clinically node-negative (N0). Two-thirds of patients underwent LAR (6037, 68.1%) and 1448 patients (16.3%) had a reported complete pathologic response (pCR). Only one-third of patients ( $N=3084$ , 34.8%) received their procedure at a high-volume center (defined as  $\geq 20$  rectal resections per year). Of note, only 2279 patients (25.7%) of the selected population received adjuvant chemotherapy (AC) postoperatively. Table 1 summarizes demographic and perioperative characteristics of selected patients.

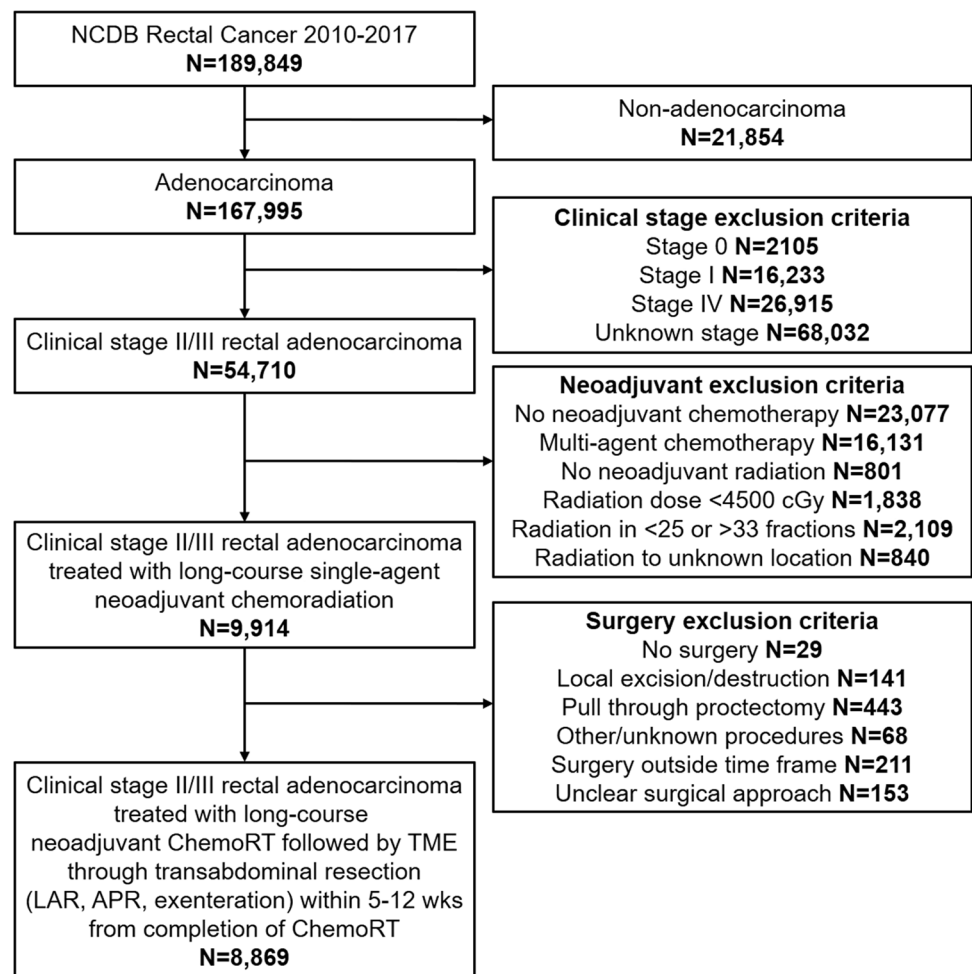
Of 8869 patients, 3967 (44.7%) achieved a TOO. Retrieval of  $\geq 12$  lymph nodes was the least commonly attained component (6257, 70.5%), whereas negative DRM occurred commonly (8583, 96.8%). A negative CRM (defined in NCDB as  $> 1$  mm from tumor) was reported in 7751 patients (87.4%) and overall 90-day mortality was 2.0%. Table 2 summarizes details of TOO in the selected

cohort. Over the study period, an uptrend was observed in incidence of TOO from 36% in 2010 to 51% in 2017.

### Univariable and Multivariable Analysis of Factors Predictive of TOO

Table 3 summarizes final step of multivariable regression analysis of factors associated with TOO achievement. Notably, younger age, female gender, Caucasian race, lower T stage, undergoing LAR, MIS approach, private insurance, and treatment at high volume centers were all among factors associated with achieving a TOO (all  $P < 0.05$ ). To better understand the impact of surgical approach on TOO incidence, chronological trends were plotted over time (Fig. 2). Interestingly, as utilization of robotic surgery increased from 2% in 2010 to 24% in 2017, so did TOO rates in patients approached in that manner. In contrast, incidence of TOO in patients who underwent open resection remained somewhat stable during the study period (range: 11–13%), an effect which mirrored rates of open approach. Finally, while percentage of laparoscopic surgery contribution to TOO increased from 8% in 2010

**Fig. 1** Flow diagram demonstrating the steps of patient selection



**Table 1** Demographic and perioperative characteristics of the selected patients

N		8,869
<b>Age</b>	Mean ± sd, median	61.45 ± 14.96 (62)
<b>Sex</b>	Male	5550 (62.6%)
	Female	3319 (37.4%)
<b>Race/Ethnicity</b>	White	7139 (80.5%)
	Black	670 (7.6%)
	Hispanic	532 (6.0%)
	Other	528 (6.0%)
<b>Charlson Score</b>	0	6772 (76.4%)
	1	1518 (17.1%)
	2	395 (4.5%)
	3+	184 (2.1%)
<b>Insurance</b>	Public	4265 (48.1%)
	Private	4128 (46.5%)
	None	375 (4.2%)
	Not reported	101 (1.1%)
<b>Education</b>	Low < 14%	4127 (46.5%)
	Intermediate 14–21%	2153 (24.3%)
	High > 21%	1292 (14.6%)
	Unknown	1297 (14.6%)
<b>Income</b>	Below poverty	3118 (35.2%)
	Above poverty	4532 (51.1%)
	Unknown	1219 (13.7%)
<b>Area</b>	Metropolitan	7029 (79.3%)
	Urban	1422 (16.0%)
	Rural	220 (2.5%)
	Unknown	198 (2.2%)
<b>Examined nodes</b>	mean ± sd, median	14.96 ± 8.51 (14)
<b>Clinical T stage</b>	T1	62 (0.7%)
	T2	397 (4.5%)
	T3	7663 (86.4%)
	T4	747 (8.4%)
<b>Clinical N stage</b>	N0	4135 (46.6%)
	N1	3951 (4.5%)
	N2	783 (8.8%)
<b>Clinical stage</b>	Stage II	4135 (46.6%)
	Stage III	4734 (53.4%)
<b>CEA</b>	Normal	319 (3.6%)
	Elevated	6416 (72.3%)
	Not reported	2134 (24.1%)
<b>Grade</b>	Well diff	627 (7.1%)
	Moderately diff	6084 (68.6%)
	Poorly diff	815 (9.2%)
	Not reported	1343 (15.1%)
<b>Response</b>	Complete response	1448 (16.3%)
	Partial response	3144 (35.4%)
	No response	4277 (48.2%)
<b>Surgery</b>	LAR	6037 (68.1%)
	APR	2591 (29.2%)
	Exenteration	241 (2.7%)

**Table 1** (continued)

N		8,869
<b>Approach</b>	Open	5006 (56.4%)
	Laparoscopic	2207 (24.9%)
	Robotic	1656 (18.7%)
<b>Weeks from CRT to surgery</b>	5–8 weeks	4006 (45.2%)
	9–12 weeks	4863 (54.8%)
<b>Hospital volume</b>	Low (< 20 rectal surgery/year)	5785 (65.2%)
	High (≥ 20 rectal surgery/year)	3084 (34.8%)

**Table 2** Components of Textbook Surgical Outcome (TOO) in the selected dataset

<b>Circumferential resection margin</b>	Negative	7751 (87.4%)
	Positive	1118 (12.6%)
<b>Distal resection margin</b>	Negative	8583 (96.8%)
	Positive	286 (3.2%)
<b>Retrieved lymph nodes &lt; 12</b>	No	6257 (70.5%)
	Yes	2612 (29.5%)
<b>90-day mortality</b>	No	8696 (98.0%)
	Yes	173 (2.0%)
<b>Hospitalization &lt; 75th percentile</b>	No	6993 (78.8%)
	Yes	1876 (21.2%)
<b>Unplanned 30-day readmission</b>	No	8244 (93.0%)
	Yes	625 (7.0%)
<b>All components of TOO</b>	No	4902 (55.3%)
	Yes	3967 (44.7%)

to 16% by 2014, it plateaued afterwards. Figure 3 demonstrates temporal and fractional relationships between TOO achievement and approach.

To better understand variables associated with attainment of individual TOO components, separate regression analyses were conducted in a similar manner (Supplemental Table 1). Several trends emerged. First, increasing T stage was associated with increased positive CRM and distal margin rates. Second, patients who underwent LAR were less likely to have incomplete lymphadenectomy, have positive margins, increased LOS, or be readmitted. Interestingly, while MIS was associated with higher rates of complete lymphadenectomy, it was linked to higher 30-day readmissions. Finally, White race/ethnicity was among factors protective of prolonged LOS, and 90-day mortality, however did not correlate with readmission rates.

**Table 3** Final step of the backward conditional multivariate regression for predictors of TOO (Entry  $p < 0.05$ , removal  $p \geq 0.05$ ). *APR*, abdominoperineal resection; *CI*, confidence interval; *HR*, hazard ratio; *LAR*, low abdominal resection; *MIS*, minimally invasive surgery. \*Statistically significant

		HR [95% CI]	<i>p</i>
Age		0.992 [0.988–0.996]	< 0.001*
Sex	Males	Referent	
	Females	1.117 [1.023–1.220]	0.014*
Race/Ethnicity	White	Referent	
	Black	0.741 [0.628–0.875]	< 0.001*
	Hispanic	0.812 [0.676–1.011]	0.096
	Other	0.985 [0.823–1.179]	0.869
Charlson score	0	Referent	
	1	0.900 [0.802–1.010]	0.073
	2	0.723 [0.582–0.898]	0.003*
	3+	0.702 [0.514–0.958]	0.026*
Insurance	Public	Referent	
	Private	1.307 [1.179–1.450]	< 0.001*
	None	0.815 [0.647–1.026]	0.082
	Not reported	1.089 [1.065–1.264]	0.678
Clinical T stage	T1	N/A	
	T2	Referent	
	T3	0.844 [0.697–1.022]	0.082
	T4	0.581 [0.455–0.741]	< 0.001*
Surgery	LAR	Referent	
	APR	0.726 [0.660–0.799]	< 0.001*
	Exenteration	0.692 [0.521–0.919]	< 0.001*
Approach	Open	Referent	
	MIS	1.137 [1.039–1.243]	0.005*
Conversion	No	Referent	
	Yes	0.784 [0.641–0.958]	0.017*
Center volume	Low	Referent	
	High	1.205 [1.102–1.318]	< 0.001*

## Survival Analysis

Cox proportional hazards models were then performed to determine impact of TOO on OS (Table 4). Failure to achieve a TOO was associated with decreased OS independent of age, race, Charlson score, clinicopathologic variables, center volume, type of resection, and surgical approach (hazard ratio (HR): 0.590, CI: 0.530–0.656,  $p < 0.001$ ). Conversely, characteristics independently associated improved OS included White race, lower Charlson scores, lower N and T stages, female gender, and receipt of AC (all  $P < 0.05$ ).

To better understand the interplay between receipt of AC and TOO incidence, unadjusted Kaplan–Meier survival functions were computed among various subgroups. As expected, patients who both achieved a TOO and received AC had the highest median survival (94.8 months  $\pm$  1.6 months) whereas patients who neither achieved a TOO nor received AC had

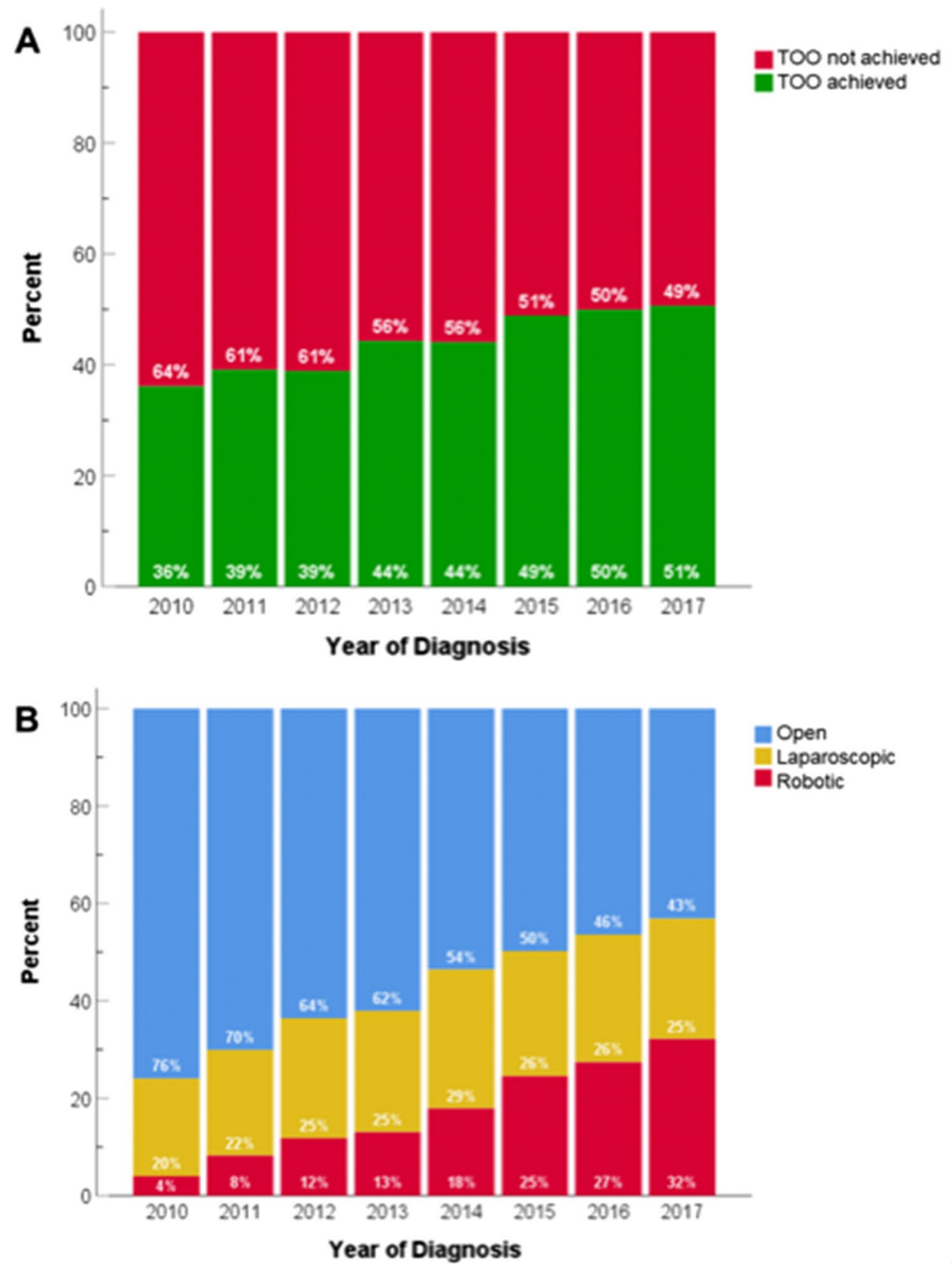
the lowest (median 76.2  $\pm$  0.9 months, Fig. 4). Interestingly, in patients who did not have a TOO, receipt of AC led to comparable survival to those who had a TOO but did not receive AC (89.8  $\pm$  0.9 vs. 86.3  $\pm$  1.3 months).

## Discussion

In this study, which utilized a contemporary national dataset and included over 8000 patients, TOO was achieved in a minority of patients with nonmetastatic rectal adenocarcinoma undergoing proctectomy. TOO was defined as negative proximal, distal, and circumferential margins, regional lymph node counts consistent with national guidelines, no prolonged LOS, no 90-day mortality, and no unplanned 30-day readmission. Notably, increasing age, male gender, Black race, higher Charlson score, public insurance, cT4 lesions, undergoing APR or exenteration as opposed to low anterior resection, open approach and care at low-volume centers were among factors predictive of inability to achieve TOO. Importantly, while a majority of TOO components occurred in most patients, increased adoption of robotic-assisted approach over the study period coincided with increased TOO rates. While a causal relationship between robotic surgery and TOO attainment was not established, it is possible that allowing a larger proportion of patients to undergo MIS translated to improved TOO rates in this study. As expected, achieving a TOO was associated with improved OS in this cohort, even after controlling for potential confounding factors. Finally, optimal OS occurred in patients who both achieved a TOO and had AC, whereas OS was comparable among patients who had AC but failed to achieve TOO and those who did not have AC but did attain a TOO.

In this report, multivariable analysis identified increasing age, male gender, Black race, higher Charlson score, public insurance, cT4 lesions, undergoing APR or exenteration as opposed to LAR, open approach and care at low-volume centers as factors associated with diminished odds of TOO attainment. Those results are consistent with similar studies which examined TOO in other relevant cancers. For example, in a study on colon cancer TOO by Swigert et al., logistic regression identified open cases, older age, Black race, non-private insurance, increased T stage, low volume centers, and the presence of lymphovascular invasion to be associated with decreased odds of achieving TOO.<sup>24</sup> Undergoing APR or exenteration has been linked to inferior short-term outcomes and has been linked to positive CRM and may have further contributed to failure to achieve TOO in this cohort.<sup>30</sup> Collectively, those findings reiterate the importance of establishing standards for rectal adenocarcinoma treatment centers as supported by the ACS and further highlight important disparities.

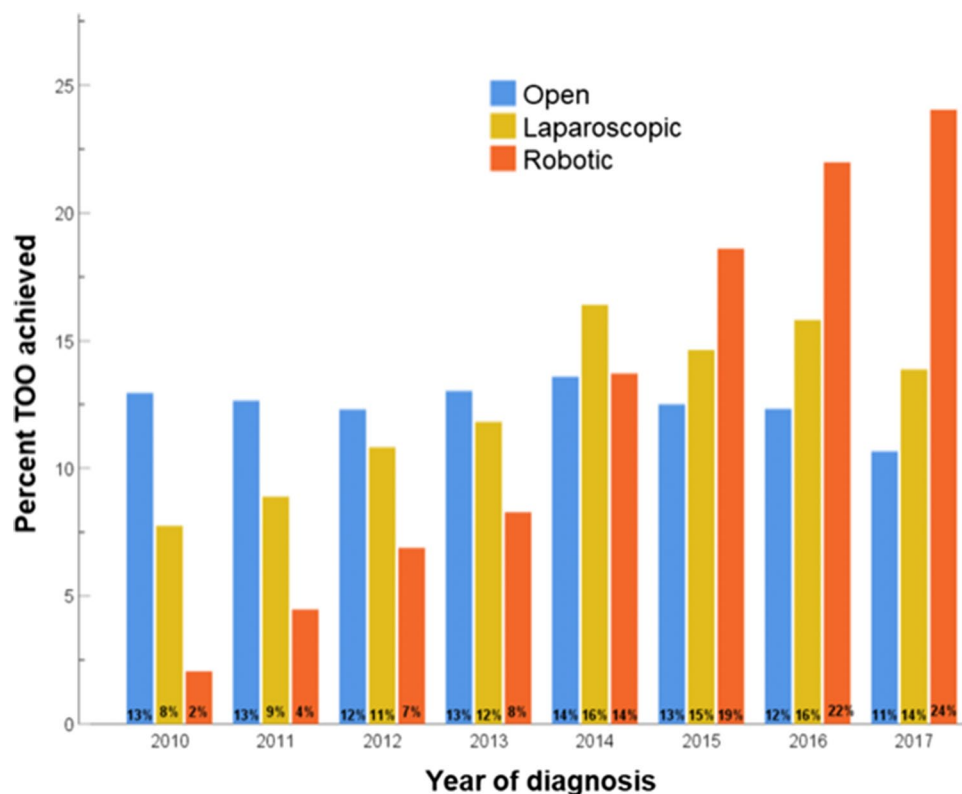
**Fig. 2** Chronological trends of **a** textbook surgical outcome and **b** surgical approach



Guidelines from the National Comprehensive Cancer Network endorse AC for rectal adenocarcinoma patients who qualify for neoadjuvant chemoradiation; however, there remains debate on its value in low-risk tumors.<sup>31,32,33</sup> For example, in a recent analysis of the NCDB, adjuvant chemotherapy did not confer a survival advantage in patients with T3N0M0 rectal adenocarcinoma patients who did not receive neoadjuvant chemoradiation, perhaps indicating a risk of overtreatment in stage II rectal adenocarcinoma. Conversely, another recent analysis of the NCDB found the contrary.<sup>34</sup> While the benefit of postoperative chemotherapy following preoperative

chemoradiotherapy in rectal adenocarcinoma has not been consistently demonstrated in randomized controlled trials,<sup>35</sup> poor compliance to adjuvant systemic treatment is believed to be an essential limitation of those data.<sup>36</sup> In the seminal EORTC trial, only 43% of patients received adjuvant treatment owing to postoperative complications, drug toxicity, disease progression, and patient refusal.<sup>37</sup> This effect has been observed elsewhere.<sup>38</sup> In this study, 2279 patients (25.7%) received AC after surgical resection and an incremental OS advantage was observed in patient subgroups who did. Interestingly, OS was comparable among patients who did not have a TOO and had AC and those

**Fig. 3** Chronological trends of achieved textbook surgical outcome (TOO) by surgical approach during the study period



who had a TOO but did not receive AC, which supports considering AC whenever possible.

Over the study period, a modest but statistically significant increase in rates of TOO attainment was noted which likely reflects improvements in surgical technique and perioperative care. To this extent, a TOO was more commonly achieved in patients who underwent an MIS approach, which also was generally utilized more frequently over time. More specifically, while rates of laparoscopic assisted resections plateaued after 2014, robotic-assisted utilization increased steadily. Those findings suggest that robotic-assisted techniques are more readily adoptable by surgeons, possibly due to a less steep learning curve compared to laparoscopy.<sup>39</sup> MIS's short-term benefits for rectal adenocarcinoma, including decreased pain, LOS, and overall complications, have been established,<sup>40,41</sup> and large retrospective studies have reported incremental oncological advantages with MIS. For example, in a study that utilized NCBD, 6313 patients with nonmetastatic locally advanced rectal adenocarcinoma were included, and approaches (open, laparoscopic, and robotic) were compared.<sup>42</sup> Compared with open surgery, the authors found that MIS was associated with lower positive circumferential margins and improved survival. Indeed, data from randomized trials supports equivalence of MIS and open approaches with respect to perioperative and oncological outcomes. Specifically, COLOR II found similar rates of CRM and comparable survival among MIS and open

groups.<sup>43</sup> Similarly, ACOSOG Z6051 found improved pathologic outcomes (including CRM and completeness of total mesorectal excision) with open surgery compared to MIS, whereas OS was similar.<sup>44</sup> Finally, in AlaCaRT, laparoscopic approach failed to achieve non-inferiority with respect to similar pathologic outcomes.<sup>45</sup> While this was not the case in the present study, it is possible that patients recruited to clinical trials are less susceptible to selection bias and that patients with more favorable clinicopathologic profiles are selected for MIS.

Treatment at high-volume centers (defined in this study as those that perform  $\geq 20$  proctectomies/year) emerged as a critical modifiable independent predictor of achieving a TOO. Low-volume centers were defined as those performing less than 20 proctectomies per year as this cutoff is associated with improved short- and long-term outcomes.<sup>46</sup> Rectal adenocarcinoma's center volume-outcome relationship has been long recognized as outcomes clearly and consistently are superior when rectal adenocarcinoma is treated at experienced institutions.<sup>26,46,47</sup> Certainly, that high-volume centers more commonly achieved a TOO in this study is not unexpected and lends additional evidence regarding the value of center expertise, and is further consistent with the ACS CoC NAPRC's mission.<sup>18,19</sup>

In this report, Black race was among factors predictive of failure to achieve a TOO. Disparities in outcomes for black patients with rectal adenocarcinoma are well established

**Table 4** Cox regression analysis for predictors of overall survival in the selected patient population ( $N=8869$ ). *APR*, abdominoperineal resection; *CEA*, carcinoembryonic antigen; *CI*, confidence interval; *CRT*, chemoradiotherapy; *LAR*, low abdominal resection; *MIS*, minimally invasive surgery; *TOO*, Textbook Surgical Outcome. \*Statistically significant

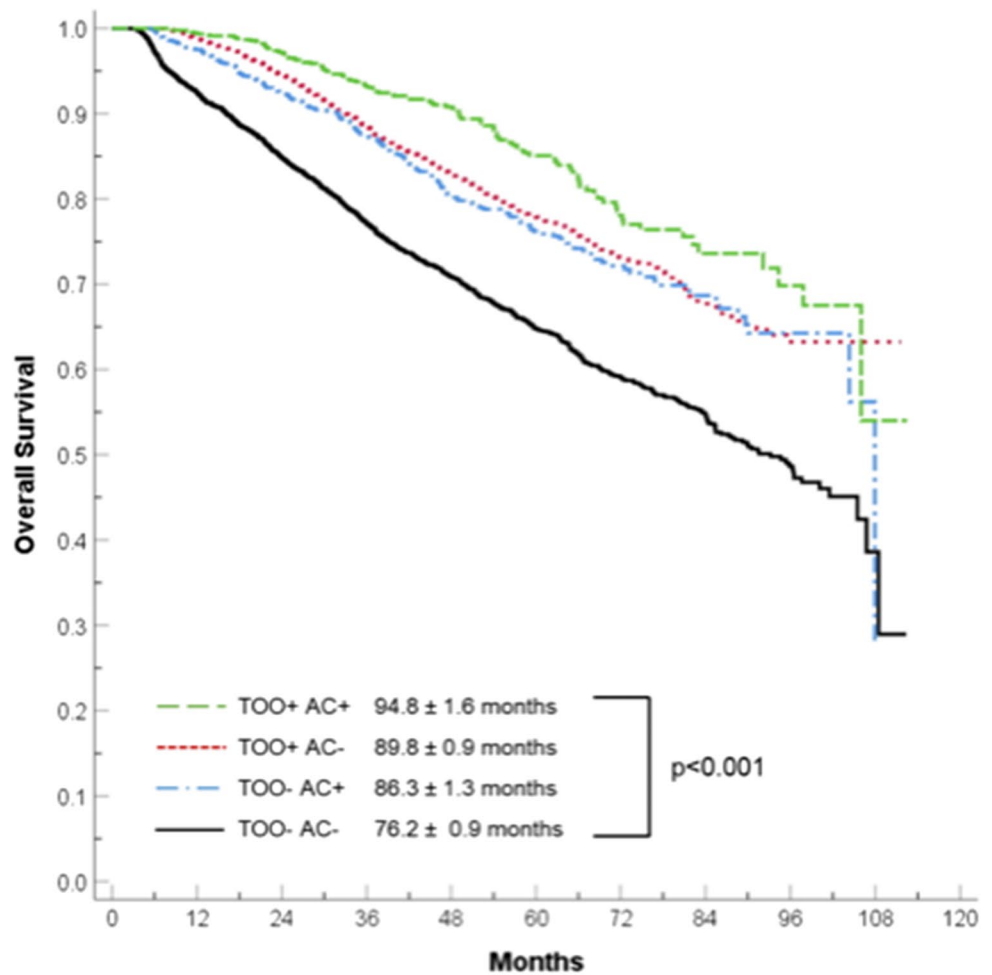
	<u>Univariate analysis</u>		<u>Multivariate analysis</u>	
	<b>Hazard ratio [95% CI]</b>	<b><i>p</i></b>	<b>Hazard ratio [95% CI]</b>	<b><i>p</i></b>
<b>Age</b>	1.036 [1.032–1.040]	<0.001*	1.034 [1.029–1.038]	<0.001*
<b>Sex</b>				
Males	Referent		Referent	
Females	0.825 [0.749–0.909]	<0.001*	0.748 [0.678–0.825]	<0.001*
<b>Race/ethnicity</b>				
White	Referent		Referent	
Black	1.038 [0.875–1.231]	0.670	1.063 [0.895–1.262]	0.489
Hispanic	0.741 [0.591–0.929]	0.009*	0.851 [0.678–1.069]	0.165
Other	0.776 [0.625–0.963]	0.022*	0.853 [0.684–1.057]	0.145
<b>Charlson score</b>				
0	Referent		Referent	
1	1.415 [1.264–1.584]	<0.001*	1.269 [1.132–1.421]	<0.001*
2	1.648 [1.350–2.011]	<0.001*	1.279 [1.046–1.565]	0.016*
3+	3.037 [2.395–3.852]	<0.001*	2.616 [2.059–3.324]	<0.001*
<b>Grade</b>				
Well differentiated	Referent		Referent	
Moderately differentiated	1.009 [0.836–1.218]	0.924	0.950 [0.787–1.148]	0.597
Poorly differentiated	1.917 [1.547–2.376]	<0.001*	1.622 [1.306–2.015]	<0.001*
<b>T stage</b>				
T1	N/A		N/A	
T2	Referent		Referent	
T3	1.460 [1.135–1.878]	0.003*	1.401 [1.087–1.805]	0.009*
T4	2.228 [1.676–2.963]	<0.001*	2.227 [1.657–2.992]	<0.001*
<b>N stage</b>				
N0	Referent		Referent	
N1	1.858 [1.675–2.062]	<0.001*	1.686 [1.512–1.880]	<0.001*
N2	2.700 [2.299–3.172]	<0.001*	2.542 [2.145–3.011]	<0.001*
<b>CEA</b>				
Normal	Referent		Referent	
Elevated	1.551 [1.169–2.057]	0.002*	1.231 [0.926–1.635]	0.152
Missing	1.606 [0.921–2.148]	0.221	1.250 [0.933–1.674]	0.135
<b>Response</b>				
Complete response	Referent		Referent	
Partial response	1.324 [1.119–2.566]	0.001*	1.092 [0.920–1.296]	0.315
No response	2.233 [1.913–2.607]	<0.001*	1.665 [1.416–1.959]	<0.001*
<b>Examined nodes</b>	0.993 [0.988–0.999]	0.016*	1.003 [0.997–1.009]	0.369
<b>Surgery</b>				
LAR	Referent		Referent	
APR	1.321 [1.200–1.456]	<0.001*	1.062 [0.962–1.172]	0.235
Exenteration	1.837 [1.441–2.343]	<0.001*	1.303 [1.004–1.690]	0.047*
<b>Approach</b>				
Open	Referent		Referent	
MIS	0.805 [0.730–0.886]	<0.001*	0.975 [0.793–1.265]	0.228
<b>CRT to surgery</b>				
5–8 weeks	Referent		Referent	
9–12 weeks	1.043 [0.952–1.143]	0.363	1.047 [0.954–1.148]	0.332
<b>Center volume</b>				
Low	Referent		Referent	
High	0.833 [0.755–0.920]	<0.001*	0.938 [0.849–1.037]	0.209



**Table 4** (continued)

	<u>Univariate analysis</u>		<u>Multivariate analysis</u>	
<b>TOO</b>				
Not achieved	Referent		Referent	
Achieved	0.545 [0.493–0.601]	<0.001*	0.590 [0.530–0.656]	<0.001*
<b>Adjuvant chemotherapy</b>				
No	Referent		Referent	
Yes	0.599 [0.530–0.676]	<0.001*	0.649 [0.574–0.733]	<0.001*

**Fig. 4** Kaplan–Meier overall survival analysis for patients divided by achievement of TOO and receipt of adjuvant chemotherapy



<b>TOO+ AC+</b>										
N at risk	916	861	703	493	332	206	111	51	19	2
Survival	0.99	0.97	0.93	0.91	0.85	0.78	0.74	0.71	0.64	0.64
<b>TOO+ AC-</b>										
N at risk	2,385	2,226	1,837	1,341	924	596	332	141	36	2
Survival	0.99	0.95	0.88	0.83	0.78	0.73	0.68	0.64	0.64	0.64
<b>TOO- AC+</b>										
N at risk	997	925	756	553	373	244	141	68	20	1
Survival	0.97	0.92	0.87	0.80	0.76	0.72	0.69	0.64	0.57	0.57
<b>TOO- AC-</b>										
N at risk	3,247	2,863	2,331	1,731	1,230	802	455	223	64	3
Survival	0.92	0.85	0.77	0.71	0.65	0.59	0.55	0.49	0.43	0.28

and are consistently less favorable, even when treatment and stage are accounted for.<sup>48,49</sup> Racial disparities in cancer care delivery are often a consequence of the interaction of a complex set of factors such as access to healthcare, conscious and unconscious bias, and lack of healthcare literacy.<sup>50,51</sup> Findings from the present study are consistent with existing literature on this topic and lends additional evidence on how this group remains disadvantaged. Certainly, targeted interventions on the local and national scale are necessary in order to overcome those barriers.

Limitations of this study should be noted. First, it is a retrospective review of a large national oncology dataset and is therefore susceptible to selection and omitted variable biases. For example, selection bias may plausibly account for the association between TOO and age, which may affect the interpretation of survival outcomes. Second, despite rigorous quality-standard processes, errors in data coding are conceivable. Third, while TOO's definition in this study was both clinically relevant and largely consistent with previous similar reports, it remains subjective as standardized components have not been agreed upon through consensus. Lastly, NCDB lacks granularity on relevant variables such as severity and impact of postoperative complications and type and extent of adjuvant therapy. Moreover, details of rates of diverting ileostomy formation and reasons for readmission are not captured in NCDB. This shortcoming may, in turn, limit interpretability as details on why adjuvant therapy was not pursued are not made clear. Given considerably low compliance rates, there likely were factors other than postoperative morbidity, which may have contributed to that effect. Despite those shortcomings, this study utilizes a robust national dataset to describe TOO's in rectal adenocarcinoma and successfully identifies modifiable factors that may be targeted for future research that aims to improve outcomes in this population.

## Conclusion

A TOO for nonmetastatic rectal adenocarcinoma was outlined in this study. This composite outcome metric may inform stakeholders on the overall quality of cancer care. This data also adds evidence to the significance of delivering comprehensive cancer care as TOO affects survival and only occurs in a minority of rectal adenocarcinoma patients.

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Study design: SN, FD, SK.

Manuscript preparation: FD, SN.

Data acquisition: SN, FD.

Quality control of data algorithm: SK, GS, BW, MA.

Manuscript review: SN, FD, SK, GS.

## Declarations

**Conflict of Interest** The authors declare no competing interests.

**Synopsis** Textbook outcomes of rectal adenocarcinoma in NCDB are achieved uncommonly. MIS and volume are modifiable factors.

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