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ORIGINAL ARTICLE

Facility Variation in Local Staging of Rectal Adenocarcinoma and its Contribution to Underutilization of Neoadjuvant Therapy

Douglas S. Swords[1,2] · Benjamin S. Brooke[1] · David E. Skarda[1,2] · Gregory J. Stoddard[3] · H. Tae Kim[2] · William T. Sause[4] · Courtney L. Scaife[1]

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Abstract

Background Guidelines recommend neoadjuvant therapy (NT) for clinical stage II–III (locally advanced) rectal adenocarcinoma, but utilization remains suboptimal. The causes of NT omission remain poorly understood.

Methods The main outcomes in this study of patients with resected clinically non-metastatic rectal adenocarcinoma in the 2010–2015 National Cancer Database were local staging utilization in patients with non-metastatic tumors (i.e., undocumented clinical stage/pathologic stage I–III) and NT utilization for locally advanced tumors. Multivariable regression was used to examine predictors of these outcomes. Facility-specific risk- and reliability-adjusted local staging and NT rates were calculated. Positive margins and overall survival (OS) were examined as secondary outcomes.

Results Local staging was omitted in 7737/43,819 (17.7%) patients with clinically non-metastatic tumors and NT was omitted in 5199/31,632 (16.4%) patients with locally advanced tumors. NT was utilized in 24,826 (91.1%) locally advanced patients who had local staging vs. 1607 (36.6%) patients who did not; 2785 (53.6%) locally advanced patients with NT omitted also had local staging omitted. Treatment at facilities with lowest quintile local staging rates was associated with NT omission (relative risk 2.41, 95% confidence interval 2.11, 2.75). Adjusted facility local staging rates varied sixfold (16.1–98.0%), facility NT rates varied twofold (43.9–95.9%), and they were correlated ($r = 0.58$; $P < 0.001$). Local staging omission and NT omission were independently associated with positive margins and decreased OS.

Conclusions Local staging omission is a common care process in over half of cases of omitted NT. These data emphasize the need for quality improvement efforts directed at providing facilities feedback about their local staging rates.

Keywords Rectal cancer · Rectal adenocarcinoma · Locally advanced · Local staging · Clinical staging · Neoadjuvant · Facility variation · Underutilization

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✉ Douglas S. Swords
douglas.swords@hsc.utah.edu

[1] Department of Surgery, University of Utah, 30 North 1900 East, Salt Lake City, UT 84132, USA

[2] Surgical Services Clinical Program, Intermountain Healthcare, Salt Lake City, UT, USA

[3] Division of Epidemiology, Department of Internal Medicine, University of Utah, Salt Lake City, UT, USA

[4] Oncology Services Clinical Program, Intermountain Healthcare, Salt Lake City, UT, USA

Introduction

The management of non-metastatic rectal adenocarcinoma is based on the depth of tumor penetration and presence of local lymph node metastases, which are ascertained by pelvic magnetic resonance imaging (MRI) (preferred) or endoscopic ultrasound (EUS) (i.e., local staging procedures). National Comprehensive Cancer Network (NCCN) guidelines recommend upfront surgery for clinical stage I tumors.[1] Conversely, neoadjuvant therapy (NT) is recommended for clinical stage II–III (i.e., locally advanced) tumors because it decreases locoregional recurrences and toxicity.[1–3] NT has been the standard of care for locally advanced rectal cancer since the early 2000s, but utilization of NT in the United States (US) remains suboptimal.[4–8] Two nationwide quality improvement (QI) efforts addressing this issue are underway. First, the Commission on Cancer (CoC) created a rectal cancer quality measure in 2015 stating that patients with locally advanced tumors should receive NT.[9] Second, the CoC and the Optimizing the Surgical Treatment of Rectal Cancer (OSTRICH) consortium have developed standards for a National Accreditation Program for Rectal Cancer (NAPRC), and program applications are currently open.[10–12] NAPRC standards emphasize utilization of pelvic MRI and pre-treatment multidisciplinary discussion, but *do not* include a specific standard addressing NT utilization.

The care processes leading to omission of appropriate NT remain poorly understood. Specifically, it remains unclear whether most cases of omitted NT are the result of failure to perform local staging or whether they are due to failure to deliver NT once a patient is known to have a locally advanced tumor. A systematic failure to perform local staging would imply that QI efforts should focus on increasing access to and knowledge about local staging studies. Conversely, a systemic pattern of omitting NT in patients with locally advanced disease on local staging studies would indicate that QI efforts should instead focus on educating physicians about interpretation of local staging studies. Previous studies of the National Cancer Database (NCDB) either excluded patients with undocumented cTN status[6,7] or recoded clinical stage using pathologic stage in patients with missing clinical stage,[4,5] precluding readers from understanding the role of local staging omission in NT omission. We recently found that 88% of cases of omitted NT occurred after omission of local staging procedures in a study of nine hospitals in Utah.[13] Confirmation of widespread omission of local staging in patients who do not receive appropriate NT would imply that increasing utilization of local staging should be a cornerstone of QI efforts.

We hypothesized that a substantial proportion of cases of omitted NT nationwide are caused by failure to obtain local staging and that facilities with lower local staging rates also tend to have lower NT rates. The objectives of this study were to use the 2010–2015 NCDB to (1) examine factors associated with omission of local staging in non-metastatic patients and NT in locally advanced patients, (2) characterize facility-level variation in utilization of local staging and NT, and (3) examine the associations of local staging and NT omission with positive margins and overall survival (OS) in locally advanced patients.

Methods

Data Source

We used the 2015 participant user file (PUF) of the NCDB, a nationwide, facility-level database managed by the American Cancer Society and the Commission on Cancer (CoC) that includes 70% of malignancies in the US.[14,15] Data elements are collected by trained abstractors using standardized definitions.[16] The University of Utah Institutional Review Board determined that this NCDB study was exempt from review.

Patients and Exclusions

We included patients ages 18–79 years with invasive clinical stage I–III or undocumented clinical stage/pathologic stage I–III rectal adenocarcinoma who underwent proctectomy. We applied the exclusions used by the CoC in determining eligibility for its quality measure (Fig. 1).[9] We also excluded patients whose surgery was not at the reporting facility so that accurate surgical volumes could be calculated.

The first year was 2010 because documentation of clinical stage in the PUF was not mandated until 2008.[14] In a preliminary analysis after applying other exclusions, rates of documented clinical stage increased rapidly in 2008–2009 but were stable in 2010–2015 (Supplemental Fig. 1). Some patients with undocumented clinical stage in earlier years likely underwent local staging procedures but the clinical stage was not recorded in the PUF.

Outcomes and Analytic Cohorts

Figure 1 displays the analysis flowchart. The primary outcome measures were (1) omission of local staging in patients with non-metastatic disease and (2) omission of NT for locally advanced tumors. We examined two secondary outcome measures in locally advanced patients: (1) positive margins (positive proximal/distal margin *or* circumferential radial margin ≤ 1.0 mm) and (2) OS, which was measured from date of diagnosis.

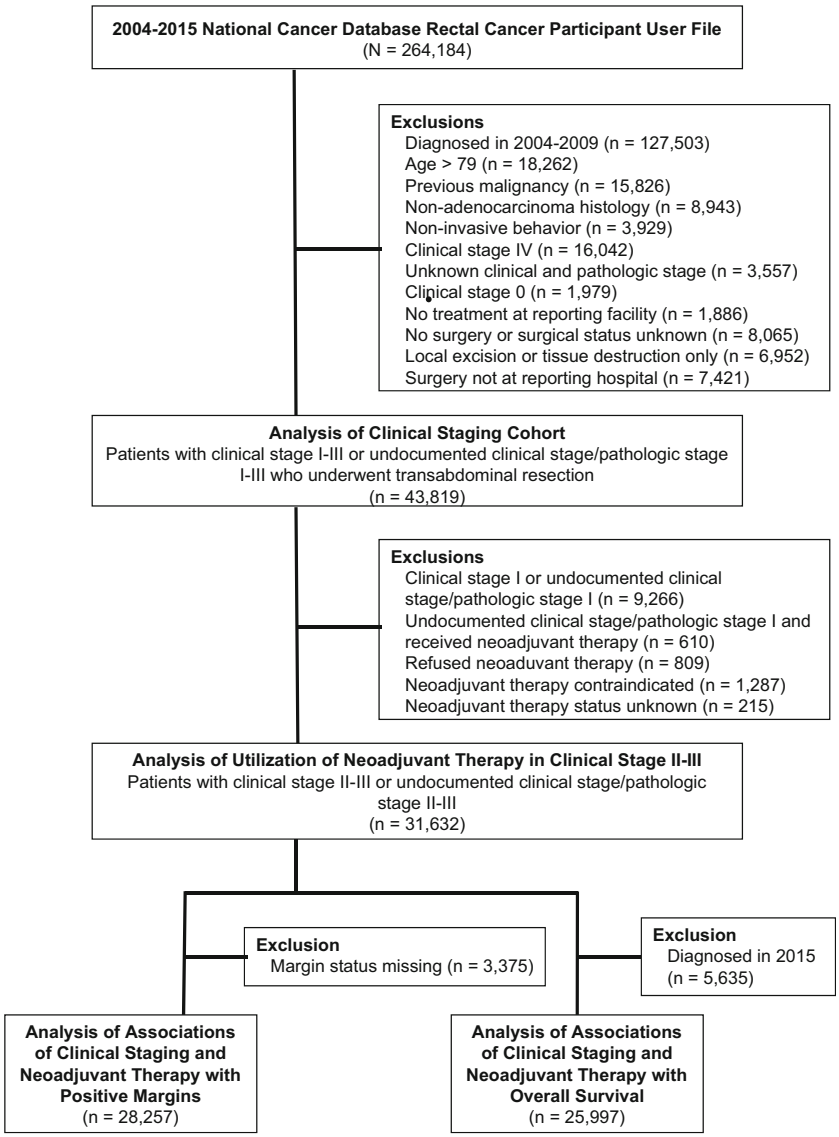

Fig. 1 Flowchart of exclusion criteria and analyses

Local Staging and Clinical Stage

Beginning in 2008, registrars were required to abstract the clinical stage using best available information in the medical record in cases where the clinical stage was not explicitly stated by a clinician.[14,16] We therefore categorized patients with clinically non-metastatic tumors who had undocumented clinical stage group *and* unknown cT and cN statuses as having not undergone local staging studies. We categorized clinical stage using cTNM stage components when available and used the overall clinical stage group if they were missing, as the CoC quality measure does.[9] cT3-T4NXM0 patients were considered to have undergone local staging since NT was indicated by the cT status even though cN status was unknown. Conversely, cT1-2NXM0 patients with missing clinical stage group were considered not to have undergone local staging since the decision about NT depends on nodal status in cT1-2 patients. Patients with missing cM status were excluded (Fig. 1).

Importantly, the NCDB does not include information on which specific local staging studies a patient underwent (i.e., EUS vs. MRI). Rather, we used the presence of a documented clinical stage as a surrogate for having undergone *any* local staging study. It is important to realize that patients who were assigned a clinical stage based on computed tomography (CT) would have been considered as having undergone local staging by this methodology.

Neoadjuvant Therapy

The CoC Quality Measure only gives facilities credit for NT administration if radiation *and* chemotherapy were delivered preoperatively.[9] However, due to randomized clinical trials (RCTs),[17,18] NCCN guidelines consider short-course radiation

an appropriate option for cT3N0M0 and cT1-3N1-2M0 tumors.[1] Furthermore, a phase II trial which treated stage II–III patients with induction chemotherapy followed by radiation only in patients with stable or progressive disease showed promising results,[19] and this strategy is being compared to standard chemoradiation in the ongoing PROSPECT trial.[20] We counted chemoradiation, radiation alone, *and* chemotherapy alone preoperatively as receipt of NT to give facilities credit for these reasonable alternatives. We considered 79 patients with cT4 tumors who received preoperative radiation without chemotherapy to have received NT because the NCCN recommendation against short-course radiation for cT4 tumors was added in 2017.[21]

Covariate Selection

Variables that were available at the time of decisions about local staging and NT were included in multivariable models. Surgical volume was calculated as the mean of each facility's numbers of cases in the year of diagnosis and the previous year. Volume was categorized into quintiles: first quintile ≤ 5 cases/year, second 5.5–9, third 9.5–14, fourth 14.5–21.5, and fifth ≥ 22. Variables related to events taking place after the exposures of interest (local staging and NT) such as readmissions and adjuvant therapy were not analyzed in the survival analysis to avoid over-adjustment bias.[22] Pathologic variables were not included in secondary analyses because adverse features were more common when NT was omitted, likely due to NT's tumoricidal effect (Supplemental Table 1).

Statistical Analyses

Univariate associations between covariates and binary outcomes were examined with chi-square tests. Covariates with a univariate $P < 0.20$ were included in multivariable models. Binary outcomes were analyzed using multivariable logistic regression models that included a clustered sandwich estimator to allow for clustering of observations within facilities. There have been calls for reporting adjusted absolute differences in addition to relative effect measures in observational research,[23,24] and odds ratios are exaggerated estimates of effect size.[25] We therefore calculated adjusted rate differences (ARDs) and adjusted risk ratios (ARRs) using average marginal estimation.[26] Adjusted rates were reported for each covariates referent and ARDs were reported for other values. Omission of NT and secondary outcomes was analyzed using patient-level *and* facility-level models.

Unadjusted 25th percentile OS and 5-year OS were calculated. Adjusted OS was analyzed with multivariable Cox models that adjusted for covariates with a univariate $P < .20$ and accounted for clustering at the facility-level.

Hierarchical mixed-effects logistic regression models were used to quantify how much observed facility-level variation in utilization outcomes was explained by various factors. Model 1 included only the facility identifier, model 2 added patient factors, and model 3 added facility type/volume. A fourth model adding adjusted facility local staging rates was included in the analysis of NT. The relative decrease in variance of facility-level random effects was calculated to determine the effect of measured variables on observed variation.[27]

Small facility sample sizes can cause misclassification of facility outcome rates as spuriously high or low.[28] To overcome this, we calculated risk- and reliability-adjusted facility local staging and NT rates. Reliability-adjustment is a hierarchical modeling technique that shrinks facilities observed rates towards the mean, with the degree of shrinkage being inversely proportional to volume.[29,30] Risk-adjustment was performed by fitting a multivariable logit model adjusted for patient-level covariates with a univariate $P < .20$. The log(odds) of the outcome for each patient were obtained using postestimation prediction. A two-level hierarchical logistic regression model was used to generate risk- and reliability-adjusted rates for each facility.[29] Adjusted facility local staging and NT rates were categorized into quintiles for subsequent analyses. The correlation between adjusted facility local staging and NT rates in locally advanced patients was assessed by calculating a Pearson's correlation coefficient that was weighted for the number of patients treated at each facility. The *P* value for this correlation coefficient was based on the number of facilities, as recommended by Bland and Altman.[31,32] Statistical analyses were performed using STATA 14.2 (StataCorp; College Station, TX). A $P < 0.05$ was considered statistically significant. *P* values represent two-sided comparisons.

Sensitivity Analysis

Studies have suggested that NT can be safely omitted in patients with (variably-defined) "low-risk" locally advanced disease,[33–35] and the safety of this approach is a topic of continued investigation.[36] We recalculated adjusted facility-specific NT rates after excluding clinical stage IIA patients and retested the correlation between facility-specific local staging and NT rates, hypothesizing that facility local staging and NT rates would be more strongly correlated in this subgroup with a more unequivocal indication for NT.

Results

Local Staging Omission

Of 43,819 patients with clinically non-metastatic rectal adenocarcinoma, local staging was omitted in 7737 patients (17.7%). The univariate analysis of factors associated with omission of local staging is shown in Supplemental Table 2.

Table 1 Factors associated with omission of local staging in 43,819 patients with clinically non-metastatic rectal adenocarcinoma

	ARR (95% CI)[a]	ARD (95% CI)[a, b]
Patient-level covariates		
Age, years		
18–39	1.00 (reference)	*14.3* (*12.5–16.0*)
40–49	1.10 (0.97–1.24)	1.4 (−0.4–3.2)
50–59	**1.18 (1.05–1.34)**	**2.6 (0.9–4.4)**
60–69	**1.28 (1.14–1.45)**	**4.0 (2.2–5.8)**
≥70	**1.41 (1.24–1.61)**	**5.9 (3.8–7.9)**
Sex		
Male	1.00 [reference]	*17.4* (*16.4–18.3*)
Female	**1.04 (1.002–1.09)**	**0.8 (0.04–1.5)**
Race/ethnicity		
NH White	1.00 [reference]	*17.5* (*16.6–18.5*)
NH Black	1.04 (0.94–1.15)	0.7 (−1.2–2.5)
Hispanic	0.98 (0.88–1.11)	−0.3 (−2.3–1.7
Asian	1.06 (0.93–1.21)	1.0 (−1.4–3.4)
Other/unk	1.15 (0.99–1.34)	2.7 (−0.3–5.7)
Insurance		
Private	1.00 [reference]	*17.5* (*16.5–18.6*)
Medicare	1.04 (0.98–1.11)	0.8 (−0.3–1.9)
Medicaid	0.98 (0.89–1.07)	−0.4 (−2.0–1.1)
Uninsured	0.90 (0.79–1.03)	−1.7 (−3.8–0.3)
Other gov	1.07 (0.89–1.29)	1.3 (−2.2–4.7)
Unk	0.82 (0.48–1.38)	−3.2 (−10.8–4.3)
CDCC		
0	1.00 [reference]	*17.3* (*16.4–18.3*)
1	1.06 (0.99–1.12)	1.0 (−0.02–2.0)
2	1.11 (0.99–1.23)	1.9 (−0.2–3.9)
≥3	**1.31 (1.14–1.49)**	**5.3 (2.3–8.3)**
Histology		
Adenocarcinoma	1.00 [reference]	*17.5* (*16.6–18.5*)
Mucinous	**1.13 (1.03–1.23)**	**2.2 (0.4–4.0)**
Signet ring cell	1.16 (0.90–1.48)	2.8 (−2.3–8.0)
Median income		
<$38,000	1.00 [reference]	*17.5* (*16.1–19.0*)
$38,000–$47,999	1.00 (0.93–1.07)	0.0 (−1.3–1.2)
$48,000–$62,999	1.01 (0.93–1.10)	0.2 (−1.4–1.7)
≥$63,000	1.02 (0.91–1.14)	0.3 (−1.6–2.3)
Unknown	0.95 (0.41–2.20)	−1.0 (−14.9–13.0)
% without HS degree		
≥21%	**1.20 (1.08–1.34)**	**3.2 (1.3–5.2)**
13–20.9%	**1.10 (1.01–1.20)**	**1.6 (0.2–3.0)**
7–12.9%	**1.08 (1.01–1.16)**	**1.3 (0.2–2.5)**
<7%	1.00 [reference]	*16.2* (*14.9–17.4*)
Unknown	1.74 (0.78–3.86)	11.9 (−10.4–34.3)
Census division		
New England	0.85 (0.63–1.14)	−2.3 (−6.3–1.8)
Mid Atlantic	1.22 (0.95–1.57)	3.3 (−0.8–7.4)
South Atlantic	1.12 (0.89–1.41)	1.8 (−1.8–5.3)
East NC	1.06 (0.83–1.34)	0.9 (−2.7–4.5)
East SC	**1.46 (1.07–1.99)**	**6.9 (1.1–12.7)**
West NC	1.00 [reference]	*14.9* (*11.8–17.9*)
West SC	**1.75 (1.38–2.23)**	**11.2 (6.7–15.7)**
Mountain	1.09 (0.80–1.47)	1.3 (−3.5–6.0)
Pacific	1.08 (0.84–1.38)	1.2 (−2.7–5.0)
Year of diagnosis		
2010	1.00 [reference]	*18.4* (*17.0–19.8*)
2011	0.95 (0.87–1.03)	−1.0 (−2.5–4.4)
2012	1.00 (0.93–1.08)	0.0 (−1.4–1.4)
2013	0.92 (0.85–1.001)	−1.5 (−3.0–0.02)
2014	**0.89 (0.82–0.97)**	**−1.9 (−3.4, −0.5)**
2015	1.00 (0.92–1.10)	0.1 (−1.6–1.7)
Surgical procedure		
Low anterior resection	1.00 [reference]	*19.4* (*18.4–20.4*)
Abdominoperineal resection	**0.67 (0.63–0.71)**	**−6.4 (−7.4, −5.5)**
Surgery NOS	**0.56 (0.36–0.88)**	**−8.5 (−13.3, −3.6)**
Surgery at diagnosing facility		
No	1.00 [reference]	*16.6* (*15.6–17.6*)
Yes	**1.16 (1.10–1.23)**	**2.7 (1.6–3.7)**
Facility-level covariates		
Facility volume		
Quartile 1	1.13 (0.96–1.34)	2.3 (−0.7–5.3)
Quartile 2	1.01 (0.85–1.19)	0.1 (−2.8–3.0)
Quartile 3	1.00 (0.84–1.17)	−0.1 (−2.9–2.8)
Quartile 4	0.97 (0.83–1.14)	−0.5 (−3.2–2.2)
Quartile 5	1.00 [reference]	*17.2* (*14.8–19.7*)
Facility type		
Community	1.02 (0.87–1.18)	0.3 (−2.7–3.4)
Comprehensive Community	1.00 [reference]	*19.8* (*18.3–21.3*)
Academic	**0.72 (0.63–0.83)**	**−5.5 (−7.7, −3.3)**
Integrated network	0.93 (0.79–1.08)	−1.5 (−4.3–1.4)

ARR adjusted risk ratio, *ARD* adjusted risk difference, *CI* confidence interval, *NH* non-Hispanic, *unk* unknown, *gov* government, *CDCC* Charlson-Deyo comorbidity score, *HS* high school, *NC* North Central, *SC* South Central, *NOS* not otherwise specified

[a] Bold values indicate $P < 0.05$

[b] The adjusted predicted probability of the referent value for each variable is shown in italics. Adjusted risk differences in comparison to the referent are shown for other values

Local staging omission was independently associated with age ≥ 50 years, female sex, ≥ 3 comorbidities, mucinous histology, lower graduation rates, certain census divisions, and having surgery at the diagnosing facility (Table 1). Diagnosis in 2014, abdominoperineal resection (APR) and unspecified surgical procedures, and treatment at academic facilities were associated with local staging utilization.

NT Omission for Locally Advanced Tumors

Of 31,632 patients with locally advanced disease, NT was omitted in 5199 patients (16.4%). NT rates were 91.1% in locally staged patients vs. 36.6% in patients without local staging (Table 2). Of 5199 patients in whom NT was omitted, 2785 (53.6%) were not locally staged. The univariate analysis of NT omission is shown in Supplemental Table 3 and the multivariable patient-level and facility-level models are shown in Table 3. Local staging omission was associated with 7.7-fold higher adjusted risk of NT omission (vs. clinical stage III). Likewise, treatment at a facility with lowest quintile local staging rates was associated with 2.4-fold higher adjusted risk of NT omission (vs. highest quintile). In patient- and facility-level models, NT omission was associated with age ≥ 60, female sex, comorbidities, certain census divisions, and surgery at the diagnosing facility. NT utilization was associated with Medicaid insurance, diagnosis in 2011–2014, APR, and surgery at an Integrated Network facility.

Facility Variation in Local Staging and NT

Patient factors explained 7.5% of observed variation in facility local staging rates and facility type/volume collectively explained 60.3%. Adjusted local staging rates varied sixfold from 16.1 to 98.0% (Fig. 2a). Adjusted local staging rates in each quintile were as follows: first 16.1–70.7%, second 70.8–80.1%, third 80.2–86.1%, fourth 86.2–91.3%, and fifth 91.4–98.0%.

Patient factors explained 12.5% of observed variation in facility NT rates, facility type/volume collectively explained 16.6%, and facility local staging rates explained 29.3%. Adjusted NT rates varied twofold from 43.9 to 95.9% (Fig. 2b). Adjusted NT rates in each quintile were as follows: first 43.9–78.7%, second 78.8–84.0%, third 84.1–87.3%, fourth 87.4–90.1%, and fifth 90.2–95.9%.

Adjusted facility local staging and NT rates were moderately correlated ($r = 0.58$; $P < 0.001$; Fig. 2c).

Secondary Outcomes in Locally Advanced Patients

In patient-level models, local staging omission (vs. clinical stage II) and NT omission were both independently associated with positive margins (Table 4). In facility-level models, treatment at facilities with quintile 1–2 local staging rates and quintile 1–4 adjusted NT rates were independently associated with positive margins.

In patient-level models, local staging omission (vs. clinical stage II) and NT omission were independently associated with shorter OS (Table 5). In facility-level models, treatment at facilities with quintile 1 local staging rates and quintiles 1–2 NT rates were independently associated with shorter OS.

Sensitivity Analysis

Among 21,104 patients with clinical stage IIB–III or undocumented clinical stage/pathologic stage II–III tumors, adjusted NT rates ranged from 41.3–96.2% (Supplemental Fig. 2A). Facility local staging and NT rates were more strongly correlated in this subgroup ($r = 0.67$; $P < 0.001$; Supplemental Fig. 2B).

Discussion

In this study of patients undergoing surgery for rectal adenocarcinoma at CoC-accredited facilities in 2010–2015, local staging was omitted in 17.7% of non-metastatic patients and NT was omitted in 16.4% of locally advanced patients. NT rates were 91% in patients who received local staging vs. 37% in patients who did not, and treatment at facilities with the lowest local staging rates was independently associated with 2.4-fold higher risk of NT omission. Patient factors explained less variation in facility local staging and NT rates than facility factors. Risk- and reliability-adjusted facility local staging and NT rates varied sixfold and twofold, respectively, and were correlated. Finally, omission of local staging and NT (and treatment at facilities with low local staging and NT rates) were associated with positive margins and shorter OS.

Previous NCDB studies also reported suboptimal utilization of NT for locally advanced rectal cancer.[4–8] Our exclusions were most similar to those in a study of 2006–2011 data, which found a 74% NT rate.[4] The 83.6% NT rate we observed is likely the result of different exclusions rather than improved utilization, as the rates we report in 2010–2011 (81.7% and 83.0%) are higher than previously observed in those years (74.8% and 75.3%).[4] Our exclusions mirrored those used by the CoC quality measure.[9] The NT rate herein is similar to the rate we observed at nine Utah hospitals in 2010–2016 (82.9%).[13]

Previous NCDB studies similarly found that factors such as older age, female sex, comorbidities, lower clinical stage, LAR (vs. APR), and lower facility volume were associated with NT omission.[4–7] Those studies excluded patients with unknown clinical stage/ pathologic stage II–III tumors[6,7] or reclassified clinical stage by pathologic stage.[4,5] Conversely, we found that 53.6% of cases of omitted NT occurred after omitted local staging. This confirms the generalizability of our previous finding that most cases of omitted NT occurred after omitted local staging procedures.[13]

We observed substantial facility-level variation in NT utilization, as previously reported by Midura et al. in clinical stage III patients.[6] Our study builds upon that finding by showing that facilities also vary in how often they perform

Table 2 Rates of neoadjuvant therapy by clinical stage in 31,632 patients with locally advanced tumors

	Neoadjuvant therapy no. (%)[a]	No neoadjuvant therapy no. (%)[a]
Local staging performed	24,826 (91.1)	2414 (8.9)
Clinical stage II	10,354 (89.5)	1216 (10.5)
Clinical stage III	14,282 (92.4)	1170 (7.6)
Clinical stage T3-T4NXM0	190 (87.2)	28 (12.8)
Local staging not performed (but pathologic stage II–III)	1607 (36.6)	2785 (63.4)

[a] Percentages may not add to 100% because of rounding

Table 3 Patient- and facility-level multivariable models of factors associated with omission of neoadjuvant therapy in 31,632 patients with locally advanced tumors

	Patient-level model[a]		Facility-level model[a]	
	ARR (95% CI)[b]	ARD (95% CI)[b, c]	ARR (95% CI)[b]	ARD (95% CI)[b, c]
Patient-level covariates				
Age, years				
18–39	1.00 [reference]	*15.6 (14.0–17.3)*	1.00 [reference]	*14.3 (12.5–16.1)*
40–49	0.94 (0.83–1.06)	− 1.0 (− 2.8–0.9)	0.98 (0.85–1.31)	− 0.2 (− 2.2–1.8)
50–59	1.04 (0.93–1.17)	0.7 (− 1.1–2.4)	1.11 (0.97–1.27)	1.6 (− 0.4–3.5)
60–69	1.07 (0.96–1.20)	1.1 (− 0.7–2.9)	**1.20 (1.05–1.37)**	**2.8 (0.8–4.8)**
≥ 70	**1.14 (1.003–1.29)**	**2.2 (0.1–4.3)**	**1.32 (1.13–1.54)**	**4.6 (2.2–6.9)**
Sex				
Male	1.00 [reference]	*15.7 (15.2–16.3)*	1.00 [reference]	*15.6 (15.0–16.2)*
Female	**1.12 (1.07–1.17)**	**1.9 (1.1–2.7)**	**1.15 (1.09–1.21)**	**2.3 (1.4–3.2)**
Insurance				
Private	1.00 [reference]	*16.9 (16.2–17.7)*	1.00 [reference]	*16.8 (16.0–17.6)*
Medicare	0.97 (0.91–1.03)	− 0.6 (− 1.6–0.5)	0.98 (0.91–1.05)	−0.4 (−1.6–0.8)
Medicaid	**0.81 (0.74–0.89)**	**− 3.2 (− 4.5, −1.9)**	**0.83 (0.75–0.92)**	**− 2.9 (−4.3, −1.4)**
Uninsured	0.92 (0.82–1.02)	− 1.4 (− 3.1–0.3)	0.94 (0.84–1.06)	− 1.0 (− 2.9–0.9)
Other gov	0.98 (0.80–1.20)	− 0.4 (− 3.7–3.0)	0.96 (0.75–1.24)	− 0.6 (− 4.7–3.4)
Unknown	1.12 (0.96–1.29)	2.0 (− 0.8–4.7)	1.17 (0.97–1.41)	2.8 (− 0.8–6.5)
CDCC				
0	1.00 [reference]	*16.1 (15.6–16.7)*	1.00 [reference]	*15.9 (15.3–16.6)*
1	**1.06 (1.01–1.13)**	**1.0 (0.1–2.0)**	**1.10 (1.03–1.18)**	**1.6 (0.5–2.8)**
2[d]	**1.12 (1.003–1.25)**	1.9 (− 0.001–3.9)	**1.22 (1.08–1.38)**	**3.5 (1.1–5.9)**
≥ 3	**1.28 (1.08–1.50)**	**4.5 (1.1–7.8)**	**1.43 (1.20–1.70)**	**6.8 (2.9–10.8)**
% without HS degree				
≥ 21%	0.96 (0.89–1.04)	− 0.7 (− 1.9–0.6)	1.02 (0.94–1.10)	0.3 (− 1.1–1.6)
13–20.9%	0.96 (0.90–1.03)	− 0.6 (− 1.7–0.4)	1.03 (0.96–1.11)	0.5 (− 0.7–1.7)
7–12.9%	0.99 (0.93–1.05)	− 0.2 (− 1.2–0.8)	1.05 (0.97–1.12)	0.7 (− 0.4–1.9)
< 7%	1.00 [reference]	16.8 (15.9–17.1)	1.00 [reference]	*16.0 (15.0–17.0)*
Unknown	0.75 (0.48–1.19)	− 4.1 (−9.9–1.7)	1.03 (0.66–1.63)	0.5 (− 7.0–8.1)
Census division				
New England	1.09 (0.92–1.29)	1.2 (− 1.2–3.7)	1.09 (0.89–1.33)	1.3 (− 1.6–4.2)
Mid Atlantic	**1.15 (1.01–1.32)**	**2.2 (0.1–4.2)**	1.13 (0.96–1.32)	1.7 (− 0.6–4.1)
South Atlantic	**1.22 (1.07–1.40)**	**3.1 (2.2–5.1)**	**1.23 (1.05–1.43)**	**3.1 (0.9–5.4)**
East NC	**1.16 (1.02–1.33)**	**2.3 (0.4–4.2)**	1.15 (0.98–1.35)	2.1 (− 0.2–4.4)
East SC	**1.28 (1.08–1.52)**	**4.0 (1.1–6.8)**	**1.42 (1.16–1.73)**	**5.8 (2.4–9.3)**
West NC	1.00 [reference]	*14.1 (12.5–15.6)*	1.00 [reference]	*13.8 (12.0–15.6)*
West SC	1.03 (0.88–1.20)	0.4 (− 1.8–2.7)	1.11 (0.94–1.32)	1.6 (− 0.9–4.1)
Mountain	1.19 (0.99–1.44)	2.7 (− 0.2–5.7)	**1.23 (1.01–1.50)**	**3.2 (0.2–6.3)**
Pacific	**1.33 (1.15–1.54)**	**4.7 (2.3–7.0)**	**1.38 (1.17–1.63)**	**5.3 (2.6–7.9)**
Year of diagnosis				
2010	1.00 [reference]	*17.4 (16.3–18.6)*	1.00 [reference]	*18.3 (17.0–19.6)*
2011	0.95 (0.88–1.03)	− 0.8 (− 2.2–0.6)	**0.92 (0.84–0.998)**	**− 1.6 (− 3.1, − 0.03)**
2012	**0.92 (0.85–0.998)**	**− 1.4 (− 2.7, − 0.03)**	**0.89 (0.81–0.97)**	**− 2.1 (− 3.6, − 0.5)**
2013	**0.89 (0.82–0.97)**	**− 1.9 (− 3.3, −0.5)**	**0.83 (0.76–0.91)**	**− 3.1 (− 4.7, − 1.6)**
2014	**0.91 (0.84–0.99)**	**− 1.5 (− 2.9, − 0.09)**	**0.84 (0.76–0.91)**	**− 3.0 (− 4.5, − 1.5)**
2015	0.98 (0.90–1.07)	− 0.3 (− 1.7–1.1)	0.94 (0.86–1.02)	− 1.2 (− 2.8–0.4)
Surgery at diagnosing facility				
No	1.00 [reference]	*13.9 (13.3–14.5)*	1.00 [reference]	*13.5 (12.9–14.2)*
Yes	**1.45 (1.38–1.52)**	**6.3 (5.4–7.1)**	**1.55 (1.46–1.64)**	**7.4 (6.4–8.4)**
Surgical procedure				
Low anterior resection	1.00 [reference]	*17.8 (17.2–18.5)*	1.00 [reference]	*18.6 (17.9–19.3)*
Abdominoperineal resection	**0.70 (0.66–0.74)**	**− 5.4 (− 6.2, − 4.6)**	**0.58 (0.54–0.62)**	**− 7.8 (− 8.7, −6.9)**
Surgery NOS	1.08 (0.92–1.28)	1.5 (− 1.7–4.7)	0.95 (0.79–1.15)	− 0.9 (− 4.2–2.5)
Clinical stage				
II	**1.32 (1.21–1.44)**	**2.5 (1.7–3.4)**	–	–
III	1.00 [reference]	7.9 (7.3–8.5)	–	–
T3-T4NXM0	**1.67 (1.18–2.36)**	**5.3 (0.8–9.8)**	–	–
Local staging omitted	**7.72 (7.09–8.40)**	**53.0 (50.8–55.1)**	–	–
Facility-level covariates				
Adjusted facility local staging rates				
Quartile 1	–	–	**2.41 (2.11–2.75)**	**15.5 (13.4–17.7)**
Quartile 2	–	–	**1.66 (1.45–1.91)**	**7.3 (5.4–9.2)**
Quartile 3	–	–	**1.31 (1.14–1.50)**	**3.4 (1.7–5.1)**

Table 3 (continued)

	Patient-level model[a]		Facility-level model[a]	
	ARR (95% CI)[b]	ARD (95% CI)[b, c]	ARR (95% CI)[b]	ARD (95% CI)[b, c]
Quartile 4	–	–	1.12 (0.95–1.30)	1.3 (−0.6–3.1)
Quartile 5	–	–	1.00 [reference]	*11.0* (*9.7–12.3*)
Facility volume				
Quartile 1	1.20 (1.07–1.35)	3.2 (1.3–5.2)	**1.32 (1.17–1.50)**	**4.9 (2.8–7.0)**
Quartile 2	1.06 (0.95–1.19)	1.0 (−0.8–2.8)	1.13 (0.995–1.27)	1.9 (−0.03–3.8)
Quartile 3	0.98 (0.87–1.10)	−0.4 (−2.2–1.4)	1.01 (0.89–1.15)	0.2 (−1.8–2.1)
Quartile 4	0.91 (0.81–1.01)	−1.5 (−3.1–0.2)	0.90 (0.79–1.03)	−1.5 (−3.4–0.5)
Quartile 5	1.00 [reference]	*15.9* (*14.4–17.3*)	1.00 [reference]	*15.2* (*13.6–16.8*)
Facility type				
Community	1.05 (0.94–1.18)	0.9 (−1.1–2.9)	1.09 (0.96–1.23)	1.5 (−0.7–3.7)
Comprehensive Community	1.00 [reference]	*16.8* (*16.0–17.6*)	1.00 [reference]	*17.0* (*16.1–17.9*)
Academic	0.97 (0.89–1.05)	−0.5 (−1.9–0.8)	0.95 (0.87–1.04)	−0.9 (−2.4–0.7)
Integrated network	**0.85 (0.76–0.96)**	**−2.5 (−4.2, −0.8)**	**0.79 (0.70–0.90)**	**−3.5 (−5.3, −1.7)**

ARR adjusted risk ratio, *ARD* adjusted rate difference, *CI* confidence interval, *NH* non-Hispanic, *unk* unknown, *gov* government, *CDCC* Charlson-Deyo comorbidity score, *HS* high school, *NC* North Central, *SC* South Central, *NOS* not otherwise specified

[a] The patient-level model includes clinical stage as a patient-level variable, whereas the facility-level model instead included quintiles of the adjusted facility rate of local staging

[b] Bold values indicate $P < 0.05$

[c] The adjusted predicted probability of the referent value for each variable is shown in italics. Adjusted risk differences in comparison to the referent are shown for other values

[d] Occasionally, the adjusted risk ratio can be barely significant when the adjusted risk difference is not

local staging, that facility local staging rates explained more variation in facility NT rates than patient- and other facility-level factors, and that facilities with higher local staging rates tended to have higher NT rates.

Local staging was omitted in 1607 of 26,433 (5.1%) patients who received NT for locally advanced tumors (Table 2). Some of the 610 patients with pathologic stage I tumors after receiving NT without local staging likely also had clinical stage I tumors (Fig. 1). We also observed cases of NT without local staging in our multiinstitutional study in Utah.[13] Midura et al. found that 25% of patients with clinical stage I tumors were *overtreated* with NT in 2005–2010.[6] Overtreatment of clinical stage I rectal cancer with NT has received less attention than undertreatment of locally advanced tumors, but it is also a problem. Omission of local staging should be recognized as a contributor to undertreatment *and* overtreatment.

Similar to a previous NCDB study,[7] we found that NT omission was associated with positive margins and shorter OS. We also found that local staging omission was associated with positive margins and shorter OS, as was treatment at facilities with lower local staging and NT rates. Conversely, most RCTs have shown that NT *does not* improve OS.[2,3,37]

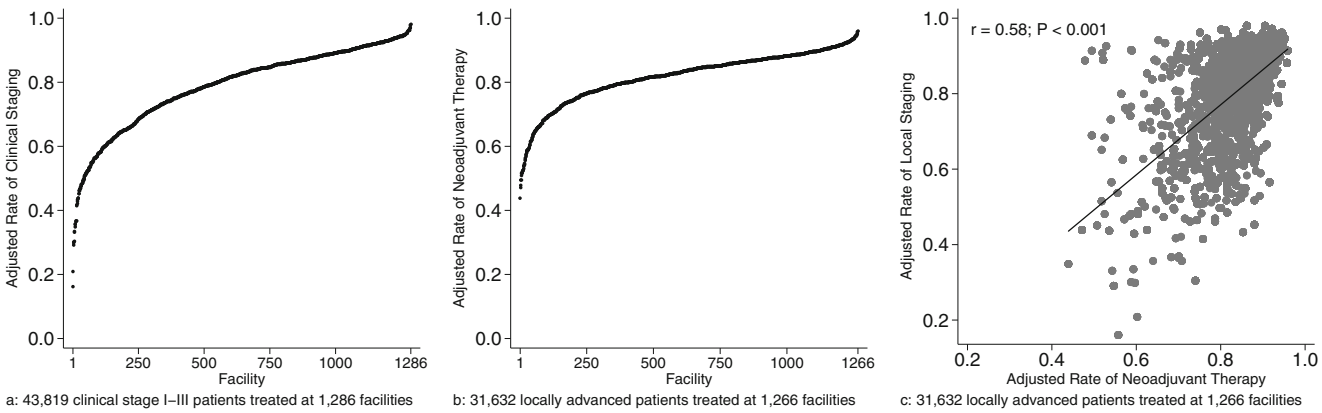

Fig. 2 Risk- and reliability-adjusted facility rates of local staging in patients with clinical stage I–III tumors or undocumented clinical stage but pathologic stage I–III tumors (**a**), neoadjuvant therapy in patients with clinical stage II–III tumors or undocumented clinical stage but pathologic stage II–III tumors (**b**), and the correlation between adjusted facility local staging and neoadjuvant therapy rates (**c**). Each dot represents one facility's adjusted rate

Table 4 Patient- and facility-level models of the relationship between local staging and neoadjuvant therapy and positive margins[a]

	Unadjusted rates	Multivariable results[b]	
	No. with positive margins (%)	ARR (95% CI)[c]	ARD (95% CI)[c, d]
Patient-level models			
Clinical stage			
II	1753 (17.1)	1.00 [reference]	*17.2* (*16.2–18.1*)
III	1753 (19.5)	**1.14 (1.08–1.20)**	**2.4 (1.3–3.4)**
T3-T4NXM0	40 (20.9)	1.16 (0.88–1.53)	2.8 (− 2.7–8.2)
Local staging omitted	1016 (25.6)	**1.49 (1.39–1.60)**	**8.5 (6.9–10.1)**
Neoadjuvant Therapy			
Yes	4379 (18.8)	1.00 [reference]	*18.7* (*17.9–19.5*)
No	1070 (23.2)	**1.27 (1.19–1.35)**	**5.0 (3.6–6.4)**
Facility-level models			
Adjusted facility local staging rate			
Quintile 5 (highest)	949 (17.3)	1.00 [reference]	*17.2* (*15.6–18.8*)
Quintile 4	1082 (19.3)	1.11 (0.98–1.26)	2.0 (− 0.3–4.2)
Quintile 3	1100 (19.2)	1.12 (0.99–1.25)	2.0 (− 0.1–4.1)
Quintile 2	1133 (19.7)	**1.18 (1.03–1.34)**	**3.0 (0.6–5.5)**
Quintile 1 (lowest)	1185 (22.3)	**1.28 (1.14–1.44)**	**4.8 (2.5–7.1)**
Adjusted facility neoadjuvant therapy rate			
Quintile 5 (highest)	906 (16.8)	1.00 [reference]	*16.5* (*15.0–18.1*)
Quintile 4	1057 (18.8)	**1.16 (1.01–1.32)**	**2.6 (0.2–4.9)**
Quintile 3	1098 (19.7)	**1.19 (1.05–1.36)**	**3.2 (0.8–5.6)**
Quintile 2	1197 (21.1)	**1.26 (1.12–1.43)**	**4.4 (2.1–6.6)**
Quintile 1 (lowest)	1191 (21.2)	**1.29 (1.15–1.46)**	**4.9 (2.6–7.1)**

ARR adjusted risk ratio, *ARD* adjusted rate difference, *CI* confidence interval

[a] Positive margins were defined as a positive proximal or distal margin or a circumferential radial margin ≤ 1.0 mm

[b] Multivariable models additionally adjusted for age, race/ethnicity, insurance status, histology, urban/rural status, census division, surgical procedure, whether surgery was at the diagnosing facility, facility type, and facility volume. Other covariates, which had a univariate $P > 0.20$, were not included in these models

[c] Bold values in multivariable results indicate $P < 0.05$

[d] The adjusted predicted probability of the referent value for each variable is shown in italics. Adjusted risk differences in comparison to the referent are shown for other values

These survival differences could be due to unmeasured confounding rather than a true treatment effect of NT. Regardless, these data suggest that local staging and NT are beneficial.

The CoC rectal cancer quality measure takes the somewhat conservative stance that *all* patients with stage II–III disease should receive NT.[9] This may reflect that underutilization of NT has historically been thought of as a bigger problem than overutilization. Nevertheless, a growing body of literature suggests that *selective omission* of NT is safe,[33–36] which may be why the NAPRC standards emphasize utilization of pelvic MRI but *do not* include a standard addressing NT utilization.[10–12] Among the 31,632 patients in this study with locally advanced disease, 2414 (7.6%) underwent local staging but did not receive neoadjuvant therapy. It must be emphasized that this strategy was likely appropriate in many of those patients. In the sensitivity analysis where patients with clinical stage IIA tumors were excluded, a stronger correlation between facility local staging and NT rates was observed. This suggests that omission of local staging may be an even stronger risk factor for NT omission in the patients who need NT the most. While the indications for NT may continue to evolve, local staging is unquestionably an essential component of rectal cancer care.

This study has several other limitations. Most substantially, we lacked specific information about local staging studies (i.e., MRI and EUS). If a complete clinical stage was documented even though local staging was omitted, then we would have incorrectly considered that patient as having undergone local staging, and vice versa. It is possible that a small percentage of patients were assigned a clinical stage based only on CT and were subsequently considered as having undergone local staging procedures in this study. Nevertheless, the rigorous definitions employed by NCDB abstractors and the similarity of findings to our study in which data on utilization of

Table 5 Patient- and facility-level models of the associations between local staging and neoadjuvant therapy and overall survival

	Univariate analysis		Multivariable analysis[a]
	25th percentile OS, months (95% CI)	5-year OS, % (95% CI)	Adjusted hazard ratio (95% CI)[b]
Patient-level models			
Clinical stage			
II	63.8 (60.1–66.5)	76.3 (75.1–77.4)	1.00 [reference]
III	60.5 (58.4–63.7)	75.3 (74.2–76.3)	**1.20 (1.12–1.28)**
T3-T4NXM0	55.1 (33.1–74.9)	72.5 (63.0–80.0)	1.37 (0.97–1.92)
Local staging omitted	49.3 (45.6–52.4)	69.5 (67.5–71.5)	**1.34 (1.23–1.47)**
Neoadjuvant Therapy			
Yes	61.4 (59.8–64.5)	75.7 (74.9–76.5)	1.00 [reference]
No	49.1 (45.2–52.7)	70.4 (68.5–72.1)	**1.31 (1.21–1.42)**
Facility-level models			
Adjusted facility local staging rate			
Quintile 5 (highest)	62.4 (59.9–68.0)	76.5 (64.9–78.1)	1.00 [reference]
Quintile 4	62.1 (59.4–67.6)	76.4 (74.8–77.9)	1.09 (0.98–1.23)
Quintile 3	62.1 (57.2–67.0)	75.5 (73.8–77.1)	0.99 (0.88–1.10)
Quintile 2	57.1 (54.1–60.8)	73.7 (72.0–75.3)	0.99 (0.88–1.11)
Quintile 1 (lowest)	52.0 (49.1–55.0)	71.6 (69.8–73.3)	**1.19 (1.06–1.32)**
Adjusted facility neoadjuvant therapy rate			
Quintile 5 (highest)	67.6 (63.2–73.3)	77.7 (76.1–79.2)	1.00 [reference]
Quintile 4	62.0 (58.4–67.0)	75.8 (74.1–77.3)	1.07 (0.95–1.20)
Quintile 3	63.4 (59.1–67.7)	76.3 (74.7–77.9)	1.04 (0.92–1.19)
Quintile 2	54.6 (51.4–56.8)	72.1 (70.4–73.8)	**1.25 (1.11–1.39)**
Quintile 1 (lowest)	53.1 (50.3–56.9)	72.1 (70.4–73.7)	**1.24 (1.10–1.40)**

OS overall survival, *CI* confidence interval

[a] Multivariable models adjusted for age, race/ethnicity, insurance status, histology, urban/rural status, census division, surgical procedure, whether surgery was at the diagnosing facility, facility type, and facility volume. Other covariates, which had a univariate $P > 0.20$, were not included in these models

[b] Bold values in multivariable models indicate $P < 0.05$

pelvic MRI and EUS *were* available suggest that this was uncommon.[13] Second, we excluded patients who did not undergo surgery at the reporting facility. Although this is necessary in NCDB studies analyzing surgical volume, it could have introduced bias. Third, reliability-adjustment produces conservative estimates of facility variation because low volume facilities are "given the benefit of the doubt" by shrinking observed rates towards the mean.[29,30] Nevertheless, the degree of facility-level variation after reliability-adjustment was substantial. Finally, the NCDB lacks data on tumor distance from the anal verge, which we previously found to be a predictor of local staging and NT omission,[13] and local recurrence, which forms the main rationale for NT.[1–3]

Despite these limitations, these findings have implications for QI efforts aimed at improving rectal cancer care in the US. This study is novel because it implicates a single care process (local staging omission) in over half of cases of omitted NT. It is rare to find a single process that is responsible for such a large proportion of a problem in healthcare, and increasing utilization of local staging is highly actionable. The correlation between facility local staging and NT rates suggests that the NAPRC standard that 95% of patients should undergo pre-treatment pelvic MRI will lead to improvements in utilization of NT.[12] Increasing local staging utilization could also address overtreatment of stage I tumors and will be essential if selective use of NT becomes more widely utilized. The CoC currently provides facilities feedback on NT utilization as part of its rectal quality measure.[9] Additionally providing facilities feedback about their local staging rates could be an easily implementable QI strategy. This could be especially important at CoC-accredited facilities that do not pursue NAPRC-accreditation and would allow each facility to form an individualized QI plan. For example, facilities with low local staging rates and high NT rates would need different QI goals than facilities with

low local staging *and* low NT rates. Nevertheless, the correlation between facility local staging and NT rates was less than 1, indicating that other care processes will also need to be addressed to fully optimize utilization of NT.

Conclusion

Over half of patients who did not receive NT for locally advanced rectal cancer in 2010–2015 did not undergo local staging, and facility local staging and NT rates were correlated. These data emphasize the need for quality improvement efforts directed at providing facilities feedback about their local staging rates. The CoC could consider providing CoC-accredited facilities with their local staging rates as a strategy for improving the quality of rectal cancer care in the US.

Author Contributions All authors have provided substantial contributions to the conception or design of the work or to the acquisition, analysis, or interpretation of the data for the work; drafted the work or revised it critically for important intellectual content; approved the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

NCDB Disclosure The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

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