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Surgeon-Level Variation in Utilization of Local Staging and Neoadjuvant Therapy for Stage II-III Rectal Adenocarcinoma

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Abstract

Introduction Neoadjuvant therapy (NT) is the standard of care for clinical stage II-III rectal adenocarcinoma, but utilization remains suboptimal. We aimed to determine the underlying reasons for omission of local staging and NT.

Methods We conducted a retrospective study of patients with clinical stage II-III or undocumented clinical stage/pathologic stage II-III rectal adenocarcinoma who were treated in 2010–2016 in one of nine Intermountain Healthcare hospitals. The outcomes of *omission* of local staging and NT were examined with multivariable models. Risk- and reliability-adjusted rates of local staging and NT were calculated for surgeons who treated ≥ 3 patients. Pathologic and long-term outcomes were examined after excluding patients who were not resected or who underwent local excision ($N = 11$).

Results Local staging was omitted in 43/240 (17.9%) patients and NT was omitted in 41/240 (17.1%). The strongest risk factors for local staging and NT omission were upper rectal tumors and surgeons who treated ≤ 3 cases/year. Thirty-six of 41 (87.8%) cases of omitted NT had local staging omitted. Adjusted surgeon-specific local staging rates varied 1.6-fold (56.3–92.4%) and NT rates varied 2.8-fold (34.1–97.1%). Surgeon local staging and NT rates were strongly correlated (r = 0.92). NT was associated with lower rates of positive circumferential radial margins (7.9 vs. 20.0%; $P = 0.02$), node positivity (33.3 vs. 55.0%; $P = 0.01$), and local recurrences (7.6 vs. 14.9% at 5 years; $P = 0.0176$).

Conclusions NT omission should be understood as a consequence of surgeon failure to perform local staging in most cases. Quality improvement efforts should focus on improving utilization of local staging.

Keywords Rectal cancer · Locally advanced · Clinical staging · Local staging · Locoregional staging · EUS · MRI · Neoadjuvant treatment · Preoperative · Neoadjuvant chemoradiotherapy · Disparities · Centers of excellence · OSTRICH Consortium · National Accreditation Program for Rectal Cancer

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Introduction

Neoadjuvant chemoradiation has been recommended by National Comprehensive Cancer Network (NCCN) guidelines for clinical stage II-III rectal adenocarcinoma since 2002.[1] The benefits of this approach were confirmed by the landmark 2004 German Trial, which showed that it halved the rate of local recurrences and caused reduced toxicity compared with postoperative chemoradiation.[2] Other putative advantages of neoadjuvant therapy (NT) include the expectation that radiation is more effective in surgery-naïve tissue and avoidance of radiating recent anastomoses and small bowel loops tethered in the pelvis by post-surgical adhesions.[3] Although NT continues to be recommended by NCCN guidelines for all patients with clinical stage II-III rectal adenocarcinoma who are treated with curative-intent,[3] recent studies using the National Cancer Database (NCDB) have shown that rates of NT remain suboptimal.[1, 4–6]

The USA has lagged beyond Europe in adoption of evidence-based approaches to rectal cancer.[7] To that end, two recent initiatives have been undertaken in an effort to improve utilization of evidence-based management in the USA. First, the Optimizing Surgical Treatment of Rectal Cancer (OSTRICH) Consortium has worked with the American College of Surgeons' Commission on Cancer (CoC) to develop standards for a National Accreditation Program for Rectal Cancer (NAPRC),[7–11] and applications for program accreditation are currently open. Second, the CoC implemented a rectal cancer Quality of Care Measure in 2015 stating that patients with clinical II-III rectal adenocarcinoma should receive NT.[12] Despite NCDB studies demonstrating that NT rates are lower than expected,[1, 4–6] the underlying reasons for this failure of evidence-based therapy remain largely unknown, as databases such as the NCDB have limited clinical granularity. One reason for this knowledge gap may be that physicians interested in rectal cancer outcomes research and quality improvement (QI) largely practice in higher-performing centers, and consequently do not have access to detailed clinical data at centers where improvements are needed the most.

Given the limitations of the existing literature, we performed this retrospective study using granular clinical data from Intermountain Healthcare (IH), a 22-hospital system. Both fellowship-trained colorectal surgeons (CRSs) and general surgeons (GSs) perform rectal cancer surgery within IH, and these surgeons have a variety of clinical volumes. Our primary objectives were to (1) examine factors associated with omission of local staging and NT for stage II-III rectal adenocarcinoma, (2) describe the processes of care in cases in which NT was omitted, and (3) describe surgeon-level variation in utilization of local staging and NT. We also examined associations of NT utilization with pathologic and long-term outcomes.

Methods

Data Source and Exclusions

This is a retrospective cohort study of consecutive patients diagnosed with clinical stage II-III rectal adenocarcinoma in 2010–2016 who were treated with initial curative-intent in an IH hospital. IH is the largest healthcare provider in the Intermountain West, and it provides approximately 55% of medical care in Utah. Many patients receive all of their medical care in IH facilities because IH offers integrated managed care under their own insurance brand. We identified patients by cross-referencing the Utah Cancer Registry with data from our electronic medical record system. The initial cohort contained 361 consecutive patients diagnosed in 2010–2016. Patient were excluded for the following reasons: clinical/pathologic stage 0 ($N = 13$), clinical/pathologic stage I ($N = 55$), clinical stage I disease that was upstaged to pathologic stage II-III at surgery ($N = 12$), clinical stage IV disease that was apparent at the time of the decision for NT ($N = 33$), refusal of all treatment ($N = 3$), contraindications to all treatment ($N = 1$), death before a decision about treatment could be made ($N = 1$), and patients who were seen at an IH hospital after having initial treatment decisions made at an outside hospital ($N = 3$). There were thus 240 patients with clinical stage II-III or unknown clinical stage/pathologic stage II-III rectal adenocarcinoma who were analyzed.

Patients who did not undergo resection ($N = 4$) or who underwent local excision instead of transabdominal resection ($N = 7$) were excluded from analysis of pathologic outcomes and long-term outcomes, leaving 229 patients. This study was approved by the IH Institutional Review Board.

Outcomes

The main outcomes were utilization of local staging and NT. NCCN guidelines and the NAPRC standards call for local staging with pelvic MRI instead of EUS.[3, 13] We also counted patients as having received local staging if pre-treatment EUS was performed since EUS was the predominant method of local staging in the earlier years of this study. In some cases, clinical stage II-III disease can be ascertained via physical exam and/or computed tomography (CT), although presence of clinical stage II-III disease cannot be *ruled out* with these modalities. Therefore, if a physician stated in the medical record that a patient was clinical stage II-III based on physical exam and/or CT, we also counted that patient as having received local staging.

The CoC Quality of Care Measure only considers hospitals compliant if both chemotherapy *and* radiation were delivered preoperatively. However, NCCN guidelines also consider short-course radiation as an appropriate alternative for cT3N0M0 and cT1-3N1-2M0 tumors.[3] Additionally, a phase II trial of induction chemotherapy followed by radiation only in patients with stable or progressive disease showed promising results,[14] and this strategy is being compared to standard chemoradiation in the ongoing PROSPECT trial.[15] Therefore, we considered patients to have received NT if they were treated with any of these three strategies.

We also examined univariate associations of NT utilization with surgical, pathologic, and postoperative variables for descriptive purposes. Multivariable models were not performed for these analyses because the number of events was often low, which would introduce issues with model overfitting, and because our main goal was to examine utilization of appropriate care.

The long-term outcomes examined were local recurrence, distant metastasis, disease-specific survival (DSS), and overall survival (OS). Time zero for all long-term outcomes was the diagnosis date. Survival time was right censored at 7 years post-diagnosis. Again, multivariable Cox models were not fitted to avoid overfitting given the low number of events. Local recurrence was defined as tumor within the perineal scar or pelvis.[2, 16]

The NCCN guidelines and the CoC quality metric take the stance that all patients with clinical stage II-III rectal cancer should receive NT.[3, 12] Conversely, some have suggested that NT can safely be omitted for proximal T3N0 tumors, with adjuvant chemotherapy given instead.[3, 17–19] Since we found that more patients who had NT omitted had upper rectal tumors, we presented cross-tabulations of tumor location and pathologic stage in patients who did not receive NT to allow readers to judge whether NT omission was actually a reasonable end result for some of these patients.

Unit of Variation

We examined variation in utilization of local staging and NT at the surgeon-level instead of the hospital-level because the surgeon is more directly responsible for care rendered. While hospital resources and culture may contribute to variation in utilization of appropriate care, our sample size prohibited simultaneous examination of both surgeon- and hospital-level variation. Of the nine hospitals included in this study, two had only one surgeon each that performed these surgeries, one had two surgeons, and one had three surgeons.

Covariate Selection and Definitions

Multivariable models only included variables that would have been available at the time of decisions about local staging and NT to avoid over-adjustment bias.[20] Charlson-Deyo scores were calculated based on clinical documentation.[21] Tumor distance from the anal verge was abstracted using measurements obtained during rigid proctoscopy when it was performed; distance was otherwise abstracted as measured at colonoscopy, digital rectal exam, or surgery. Carcinoembryonic antigen was classified as normal or elevated using the reference level for the lab where the test was performed. "Urgent" presentation was defined as obstruction requiring surgical or endoscopic intervention, symptomatic bleeding, or perforation. The examined surgeon-level factors were CRS fellowship training and annual volume of patients with clinical stage II-III rectal adenocarcinoma. Surgeon volume was calculated by dividing each surgeon's total number of cases by the number of years during the study period that they practiced in an IH hospital. Four CRSs had a low volume of cases in IH hospitals but are known to have very busy colorectal practices in a non-IHC hospital; their volumes were thus also classified as > 3 cases/year. A positive circumferential radial margin (CRM) was defined as ≤ 1 mm.[22]

Statistical Analysis

Univariate comparisons of covariates by whether local staging and NT were utilized were performed using two-sided *t* tests for continuous variables and Chi-squared or Fisher's exact tests, as appropriate, for categorical variables. Covariates with a univariate $P < 0.1$ were entered into multivariable logistic regression models. Odds ratios (ORs) are inflated estimates of effect size, and they are frequently misinterpreted as risk ratios (RRs).[23, 24] Therefore, we used average marginal estimation (i.e., marginal standardization) to compute adjusted RRs using a post-estimation command introduced by Norton et al.[25, 26] Confidence intervals (CIs) for these RRs were based on complex survey design adjusted linearized standard errors.[26] These logistic regression models included a clustered sandwich estimator with surgeon ID as the cluster variable to account for the likelihood of outcome correlation at the surgeon-level.

Three separate models were fitted for the outcome of NT omission. Model A included surgeon type (i.e., CRS vs. GS) and volume. In Model B, clinical stage (local staging omitted vs. II vs. III) was instead included. These two models were fitted separately to present accurate effect sizes because local staging omission was collinear with low-volume surgeons. Finally, Model C included both the surgeon-level variables *and* clinical stage; this model was performed in order to assess the discriminative ability of the model when all predictive variables were included. The discriminative ability of each model was assessed by calculating the area under the receiver operator curve (AUC). The specific care processes in cases where NT was omitted were abstracted. We subjectively graded NT omissions as avoidable, potentially avoidable, and unavoidable.

Small surgeon sample sizes can cause misclassification of surgeon-specific outcomes as spuriously high or low.[27] We used two methods to overcome this. First, we excluded patients treated by surgeons who treated < 3 patients during the study period (14 surgeons/23 patients). Second, we calculated risk- and reliability-adjusted surgeon-specific rates of local staging and NT. Reliability adjustment is a hierarchical modeling technique that shrinks each surgeon's observed rate towards the mean, with the degree of shrinkage being inversely proportional to volume.[28, 29] Risk-adjustment was performed by fitting a multivariable logit model adjusted for patient-level covariates with a univariate $P < 0.10$. The log (odds) of the outcome for each patient was obtained using postestimation prediction. Two-level hierarchical logistic regression models were then used to generate risk- and reliability-adjusted rates and confidence intervals for each surgeon.[28, 29] The correlation between adjusted surgeon local staging and NT rates was assessed by a calculating Pearson's correlation coefficient that was weighted for the number of patients treated by each surgeon. The P value for this correlation coefficient was based on the number of surgeons, as recommended by Bland and Altman.[30, 31]

Long-term outcomes were visualized using the Kaplan-Meier (KM) method, and the log-rank test was used for comparisons. Results of unadjusted Cox proportional hazards models and 5-year survival were reported with KM curves. Statistical analyses were performed in STATA 14.2 (StataCorp; College Station, TX). A $P < 0.05$ was considered statistically significant and reported P values are two-sided.

Results

Pre-treatment patient characteristics stratified by utilization of local staging and NT are shown in Table 1. The median age was 59 years (interquartile range 50, 71), 50.4% of patients were male, and 85.8% were non-Hispanic White. Tumors were located within 6 cm of the anal verge in 55.0%, at 6.01–12 cm in 32.9%, and > 12 cm from the anal verge in 12.1%.

These 240 patients were treated by 35 surgeons at nine hospitals. Nine of the 35 surgeons (25.7%) were fellowship-trained colorectal surgeons; they treated 129/240 (53.8%) patients. Six of the 35 surgeons (17.1%) treated > 3 patients/year during the study period; these six surgeons treated 123/240 patients (51.3%). There was one non-colorectal surgeon who treated > 3 patients/year. Conversely, there were four colorectal surgeons who treated ≤ 3 patients per year. The three highest volume surgeons treated 102/240 patients (42.5%).

Omission of Local Staging

Local staging was omitted in 43/240 patients (17.9%). Of the 197 patients where local staging *was utilized*, 115 (58.4%) were staged with EUS, 46 (23.4%) with MRI, and 36 (18.3%) with a combination of physical exam and CT. Table 2 shows the multivariable model examining associations of baseline factors with omission of local staging. Treatment by a surgeon who treated ≤ 3 cases/year was associated with over 4-fold higher risk of omission of local staging. Omission of local staging was additionally associated with a personal cancer history, tumor location in the upper rectum, and an urgent presentation. The AUC for this model was 0.85.

Omission of Neoadjuvant Therapy

Forty-one of the 240 patients (17.1%) did not receive NT. Of the 199 patients where NT *was utilized*, 186 patients (93.5%) received standard chemoradiation, 11 (5.6%) received short-course radiation, and 1 (0.5%) received chemotherapy alone. Table 2 shows the three multivariable models examining associations of pre-treatment factors with omission of NT. In Model A, surgeon volume ≤ 3 cases/year was associated with over 9-fold higher risk of NT omission while fellowship training was not independently associated with NT omission. Tumor location in the upper rectum was also predictive of NT omission. Female sex, a personal cancer history, and urgent presentations were predictive of NT omission in Model A, whereas they were not in Models B and C. In Model B, omission of local staging was associated with 17-fold higher risk of not receiving NT (vs. clinical stage II). In Model C, surgeon-level variables *and* local stage were included; surgeon volume ≤ 3 cases/year *and* omission of local staging remained significantly associated with omission of NT, but the effect sizes were attenuated due to collinearity of these variables. Tumor location was additionally associated with NT omission in Models B, C. Model C had near-perfect discriminative ability for predicting NT omission (AUC 0.97).

Care Processes in Cases Where Neoadjuvant Therapy Was Omitted

Table 3 shows the processes of care of the 41 patients who did not receive NT. In descending order of frequency, the most common care processes were as follows: surgeons performing upfront surgery without documenting why local staging was not obtained for a tumor *documented preoperatively as being rectal cancer* (43.9%), failure to appreciate that a reported sigmoid cancer was actually a rectal cancer until in the operating room (26.8%), "urgent" presentations (9.8%), and upfront surgery despite local staging demonstrating clinical stage II-III disease with no contraindication to NT (9.8%). Together, these four care processes were present in 37/41 (90.2%) cases of omitted NT. Two cases of omitted NT were judged as unavoidable, and another was judged as potentially avoidable. We considered the remaining 38 cases of omitted NT to have been avoidable.

Surgeon-Level Variation in Utilization of Local Staging and Neoadjuvant Therapy

Twenty-one surgeons treated ≥ 3 patients during the study period; there were 217 patients in this cohort. The rates of both local staging and NT in the 23 patients excluded from this analysis were 73.9%. Risk- and reliability-adjusted surgeon-specific rates of local staging varied 1.6-fold (56.3 to 92.4%) and the average adjusted rate was 83.9% (Fig. 1a). Risk- and reliability-adjusted surgeon-specific rates of NT varied 2.8-fold (34.1 to 97.1%) and the average adjusted rate was 82.9% (Fig. 1b). There was a very strong correlation between adjusted surgeon-specific rates of local staging and NT ($r = 0.92$, Fig. 1c).

Table 1 Univariate associations of pre-treatment factors with utilization of local staging and neoadjuvant therapy

	Outcome 1: local staging		Outcome 2: neoadjuvant therapy	
	Omitted ($N = 43$) N (%)	Utilized ($N = 197$) N (%)	Omitted ($N = 41$) N (%)	Utilized ($N = 199$) N (%)
Patient-level factors				
Sex	$P = 0.06$		$P = 0.02$	
Male	16 (37.2)	105 (53.3)	14 (34.2)	107 (53.8)
Female	27 (62.8)	92 (46.7)	27 (65.9)	92 (46.2)
Age, years	$P = 0.21$		$P = 0.46$	
< 50	10 (23.3)	49 (24.9)	8 (19.5)	51 (25.6)
50–59	8 (18.6)	56 (28.4)	9 (22.0)	55 (27.6)
60–69	8 (18.6)	44 (22.3)	9 (22.0)	43 (21.6)
≥ 70	17 (39.5)	48 (24.4)	15 (36.6)	50 (25.1)
Race/ethnicity	$P = 0.16$		$P = 0.12$	
NHW	34 (79.1)	172 (87.3)	32 (78.1)	174 (87.4)
All others	9 (20.9)	25 (12.7)	9 (22.0)	25 (12.6)
Marital status	$P = 0.33$		$P = 0.60$	
Married	25 (58.1)	130 (66.0)	25 (61.0)	69 (34.7)
Single	18 (41.9)	67 (34.0)	16 (39.0)	130 (65.3)
Insurance status	$P = 0.61$		$P = 0.55$	
Medicare	20 (46.5)	73 (37.1)	17 (41.5)	76 (38.2)
Medicaid	2 (4.7)	18 (9.1)	1 (2.4)	19 (9.6)
Private	19 (44.2)	90 (45.7)	20 (48.8)	89 (44.7)
Uninsured	2 (4.7)	16 (8.1)	3 (7.3)	15 (7.5)
BMI, mean (SD)	$P = 0.25$		$P = 0.16$	
	29.4 (6.4)	28.0 (6.8)	29.6 (6.5)	28.0 (6.7)
Charlson-Deyo score	$P = 0.43$		$P = 0.30$	
0	25 (58.1)	133 (67.5)	23 (56.1)	135 (67.8)
1	10 (23.3)	40 (20.3)	10 (24.4)	40 (20.1)
≥ 2	8 (18.6)	24 (12.2)	8 (19.5)	24 (12.1)
Cancer history	$P = 0.054$		$P = 0.04$	
No	36 (83.7)	183 (92.9)	34 (82.9)	185 (93.0)
Yes	7 (16.3)	14 (7.1)	7 (17.1)	14 (7.0)
CEA	$P = 0.42$		$P = 0.80$	
Normal	16 (37.2)	76 (38.6)	16 (39.0)	76 (38.2)
Elevated	16 (37.2)	87 (44.2)	16 (39.0)	87 (43.7)
Unknown	11 (25.6)	34 (17.3)	9 (22.0)	36 (18.1)
Distance from anal verge, cm	$P < 0.001$		$P < 0.001$	
≤ 6	14 (32.6)	118 (59.9)	11 (26.8)	121 (60.8)
6.01–12	13 (30.2)	66 (33.5)	14 (34.2)	65 (32.7)
> 12	16 (37.2)	13 (6.6)	16 (39.0)	13 (6.5)
Synchronous colon cancer	$P = 0.86$		$P = 0.80$	
No	41 (95.4)	189 (95.9)	39 (95.1)	191 (96.0)
Yes	2 (4.7)	8 (4.1)	2 (4.9)	8 (4.0)
Urgent presentation[a]	$P = 0.02$		$P = 0.01$	
No	38 (88.4)	191 (97.0)	36 (87.8)	193 (97.0)
Yes	5 (11.6)	6 (3.1)	5 (12.2)	6 (3.0)
Clinical stage			$P < 0.001$	
Local staging omitted	–	–	36 (87.8)	7 (3.5)

Table 1 (continued)

	Outcome 1: local staging		Outcome 2: neoadjuvant therapy	
	Omitted ($N = 43$) N (%)	Utilized ($N = 197$) N (%)	Omitted ($N = 41$) N (%)	Utilized ($N = 199$) N (%)
II	–	–	4 (9.8)	109 (54.8)
III	–	–	1 (2.4)	83 (41.7)
Local staging modality[b]	–		$P < 0.001$	
Omitted	43 (100)	0 (0)	36 (87.8)	7 (3.5)
EUS	0 (0)	115 (58.4)	2 (4.9)	113 (56.8)
MRI	0 (0)	46 (23.4)	2 (4.9)	44 (22.1)
Physical exam/CT	0 (0)	36 (18.3)	1 (2.4)	35 (17.6)
Surgeon-level factors				
Colorectal surgeon	$P < 0.001$		$P < 0.001$	
Yes	12 (27.9)	117 (59.4)	10 (24.4)	119 (59.8)
No	31 (72.1)	80 (40.6)	31 (75.6)	80 (40.2)
Surgeon volume	$P < 0.001$		$P < 0.001$	
≤ 3 cases/year	37 (86.1)	80 (40.6)	38 (92.7)	7(39.7)
> 3 cases/year	6 (14.0)	117 (59.4)	3 (7.3)	120 (60.3)

SD standard deviation, *NHW* non-Hispanic White, *HS* high school, *CEA* carcinoembryonic antigen, *EUS* endoscopic ultrasound, *MRI* magnetic resonance imaging, *CT* computed tomography, *CRS* fellowship-trained colorectal surgeon

[a] Urgent presentations were defined as complete/near complete obstruction, symptomatic bleeding, or perforation

[b] Included here for descriptive purposes, but not considered as a candidate for inclusion in subsequent multivariable models because of collinearity with clinical stage

Table 2 Multivariable models of associations of pre-treatment factors with omission of clinical staging and neoadjuvant therapy

	Outcome 1: omission of local staging	Outcome 2: omission of neoadjuvant therapy		
		Model A: includes surgeon factors only	Model B: includes clinical stage only	Model C: includes surgeon factors and clinical stage
AUC	0.85	0.90	0.94	0.97
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Female sex	1.51 (0.88, 2.59)	*1.74 (1.06, 2.87)*	1.23 (0.96, 1.58)	1.28 (0.97, 1.68)
Cancer history	*2.24 (1.32, 3.79)*	*2.34 (1.33, 4.12)*	1.22 (0.68, 2.19)	1.41 (0.77, 2.57)
Distance from anal verge, cm				
≤ 6 cm	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
6.01–13	1.27 (0.67, 2.39)	1.70 (0.80, 3.63)	1.44 (0.97, 2.14)	1.24 (0.89, 1.71)
> 12	*3.68 (2.26, 5.99)*	*4.30 (2.65, 7.00)*	*1.72 (1.23, 2.40)*	*1.51 (1.06, 2.16)*
Urgent presentation[a]	*2.33 (1.13, 4.78)*	*2.40 (1.24, 4.64)*	1.33 (0.93, 1.90)	1.35 (0.92, 1.96)
Non-colorectal surgeon	1.15 (0.64, 2.07)	1.08 (0.60, 1.93)	–	0.91 (0.77, 1.07)
Surgeon volume ≤ 3 cases/year	*4.57 (2.19, 9.53)*	*9.79 (2.93, 32.71)*	–	*2.96 (1.07, 8.16)*
Clinical stage				
Not utilized	–	–	*17.10 (5.62, 52.01)*	*8.98 (3.14, 25.64)*
II	–	–	1.00 (Reference)	1.00 (Reference)
III	–	–	0.34 (0.03, 3.81)	0.29 (0.02, 3.32)

Notes: Values in italics indicate significance at $P < 0.05$

AUC area under the curve, *RR* risk ratio, *CI* confidence interval

[a] Urgent presentations were defined as complete/near complete obstruction, symptomatic bleeding, or perforation

Table 3 Specific care processes in 41 patients where neoadjuvant therapy was omitted

Process of care	Avoidable?	*N* (%)
Local staging omitted		36 (87.8)
Taken directly to surgery without EUS or MRI for a tumor documented as rectal cancer preoperatively; no justification given by surgeon in for why local staging omitted	Avoidable	18 (43.9)
Thought to be sigmoid cancer preoperatively; surgeon did not confirm distance from rectum preoperatively	Avoidable	11 (26.8)
"Urgent" presentation[a]	Avoidable	4 (9.8)
Presented with synchronous obstructing splenic flexure cancer and rectal cancer. Upfront resection of both cancers	Avoidable	1 (2.4)
Thought that patient might not tolerate radiation given synchronous uterine cancer	Possibly avoidable	1 (2.4)
Not thought to be invasive cancer preoperatively due to multiple negative biopsies	Unavoidable	1 (2.4)
Local staging utilized		5 (12.2)
Taken directly to surgery even though clinical stage II-III. No other mention of why NT omitted.	Avoidable	4 (9.8)
Clinical stage IIA on MRI. NT omitted because of concerns over how patient would tolerate given baseline incontinence and malnutrition.	Unavoidable	1 (2.4)

EUS endoscopic ultrasound, *MRI* magnetic resonance imaging, *NT* neoadjuvant therapy

[a] Urgent presentations were defined as complete/near complete obstruction, symptomatic bleeding, or perforation

Pathologic and Postoperative Variables

Supplemental Table 1 shows univariate associations of NT utilization with surgical, pathologic, and postoperative outcomes among patients who underwent transabdominal resection ($N = 229$). Sphincter-sparing surgeries were more common among patients in whom NT was omitted, reflecting that more of these patients had tumors in the upper rectum. Minimally invasive surgery was performed more commonly in patients who received NT.

Upon pathologic review, patients who received NT had smaller tumors (mean 1.9 vs. 4.8 cm, $P < 0.001$), lower rates of CRM involvement (7.9 vs. 20.0%, $P = 0.02$), lower rates of node positivity (33.3 vs. 55.0%, $P = 0.01$), and lower overall pathologic stages (Supplemental Table 1). Rates of postoperative complications and 30-day readmissions and length of stay were not significantly different based upon NT status. Among patients where NT was omitted, 47.1% received postoperative chemoradiation. The overall rate of adjuvant systemic chemotherapy was 67.6%, and it did not vary by NT status.

Long-Term Outcomes

NT was associated with a 72% reduction in the risk of local recurrence compared to cases where NT was omitted (7.6 vs. 14.9% at 5 years, $P = 0.0176$, Fig. 2a). There were no

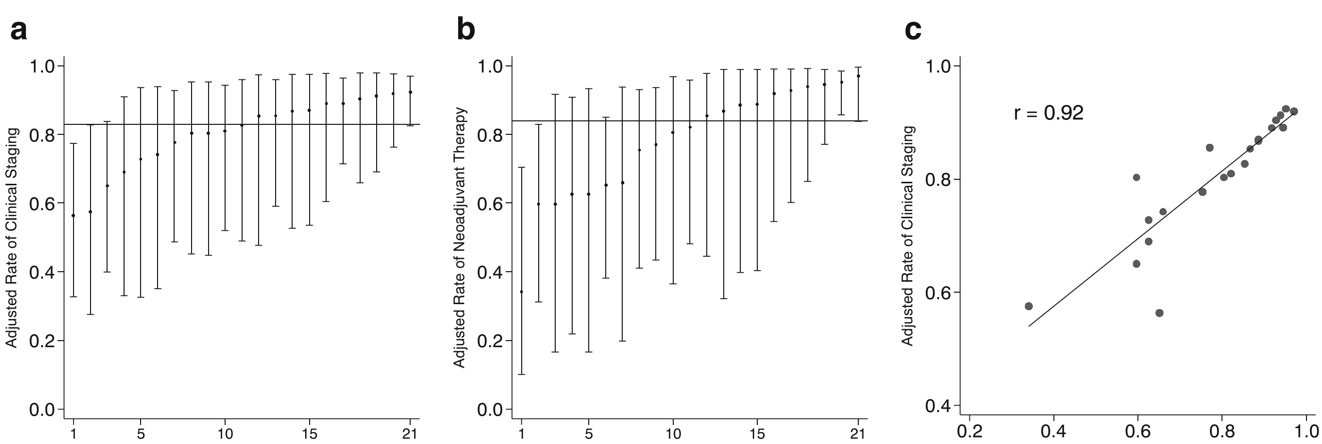

Fig. 1 Risk- and reliability-adjusted surgeon-specific rates of local staging (**a**) and neoadjuvant therapy (**b**) and the correlation between adjusted local staging and neoadjuvant therapy rates (**c**). Notes: These analyses excluded 14 surgeons who treated < 3 patients during the study (23 patients excluded/217 included). For **a** and **b**, dots represent surgeons' risk- and reliability-adjusted rates, and error bars represent 95% confidence intervals. Horizontal lines for **a** and **b** represent mean adjusted rates. Dots in **c** represent the same adjusted rates, and Pearson's correlation coefficient is reported

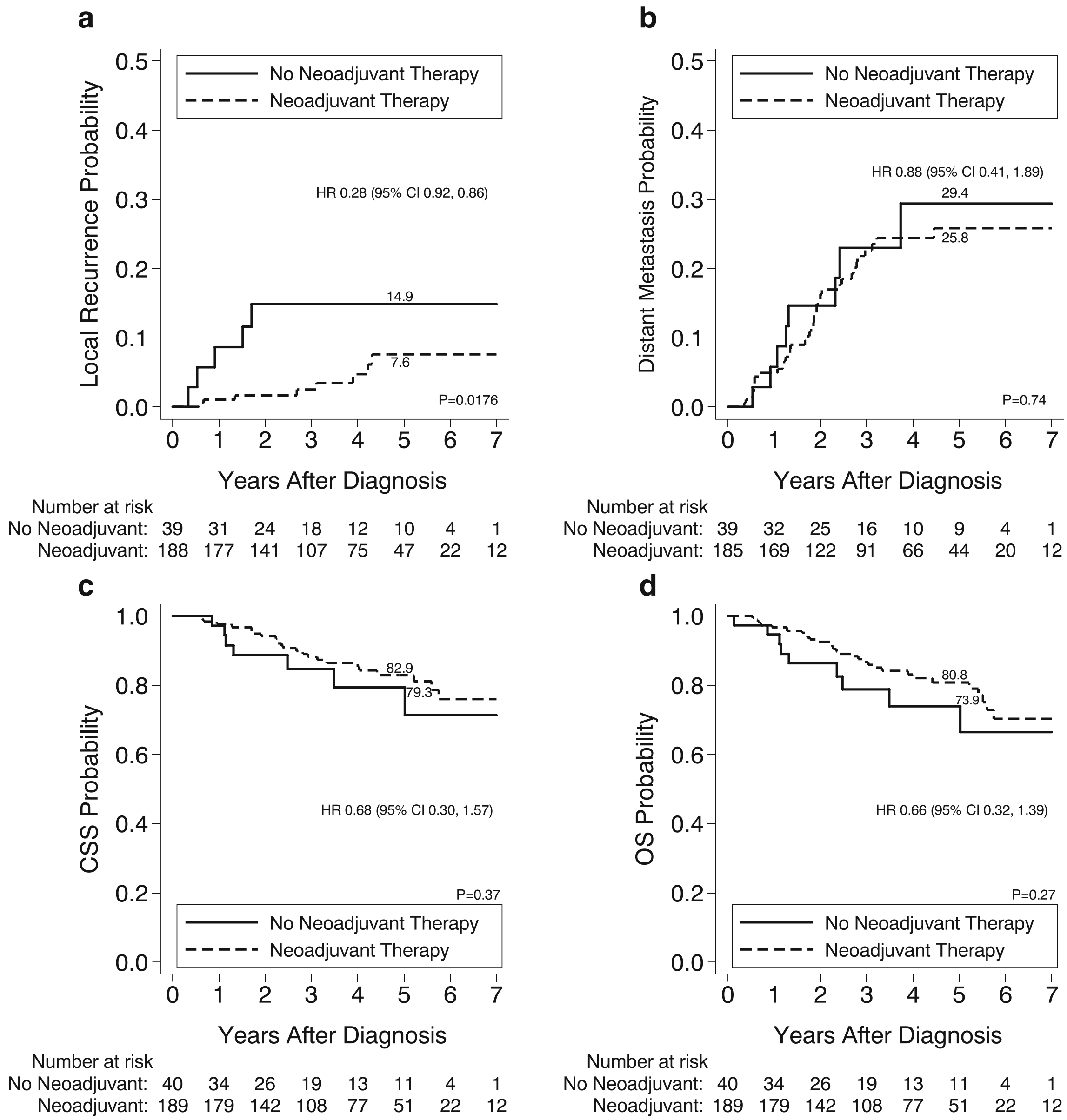

Fig. 2 Local recurrence (**a**), distant metastasis (**b**), disease-specific survival (**c**), and overall survival (**d**) by whether neoadjuvant therapy was utilized. Abbreviations: HR, hazard ratio; CI, confidence interval. Notes: Each plot also displays the results of a univariate Cox proportional hazards model and the outcome rate at 5 years post-diagnosis. Patients with missing data on local recurrences ($N = 2$) and distant metastases ($N = 5$) were excluded from these analyses

significant differences in occurrence of distant metastases (Fig. 2b), DSS (Fig. 2c), or OS (Fig. 2d).

Pathologic Stage and Tumor Location in Cases of Omitted Neoadjuvant Therapy

Supplemental Table 2 shows the cross-tabulation of pathologic stage and tumor location for cases where NT was omitted. Only 7/41 patients (17.1) ended up having a pT3N0 tumor in the upper rectum. Overall, a total of 18/41 (43.9%) patients had pT3N0 tumors, 1 (2.4%) had a pT4N0M0 tumor, and 22 (53.7%) had pathologic stage III tumors.

Discussion

In this study of 240 patients with stage II-III rectal adenocarcinoma, local staging was omitted in 17.9% of patients and NT was omitted in 17.1%. The main risk factors for both local staging omission and NT omission were tumor location in the upper rectum and treatment by a low-volume surgeon. In a model that included clinical stage instead of surgeon-level variables, the process of omission of local staging was associated with *17-fold higher* risk of NT omission. We observed substantial surgeon-level variation in adjusted rates of local staging and NT, and adjusted surgeon rates of these two outcomes were strongly correlated (r = 0.92, Fig. 1c). The most common scenarios in which NT was omitted was that the patient was taken to surgery without any specific mention of why local staging was not pursued for a tumor that was known to be a rectal cancer or that the surgeon realized intra-operatively that a reported sigmoid cancer was actually a rectal cancer. Finally, NT utilization was associated with smaller tumors on pathologic review and lower rates of CRM involvement, node positivity, and local recurrences.

These results uniquely demonstrate that underutilization of NT for stage II-III rectal cancer, which has been reported in several recent NCDB studies,[1,4–6] should be understood as a *logical and inevitable consequence of surgeon failure to perform appropriate local staging*. Although there were a few cases of inappropriate upfront surgery after local staging revealed clinical stage II-III disease, the majority (87.8%) of cases of omitted NT happened after failure to obtain local staging. A series of important studies by Charlton et al. also point to suboptimal utilization of local staging by surgeons as a driver of NT underutilization.[32–34] In a population-based study of 201 stage II-III patients treated in 2003–2005, adjusted rates of NT were 96% in patients who saw a medical oncologist and/or radiation oncologist prior to seeing a surgeon, but only 48% in those who saw a surgeon first.[32] Patients who saw a surgeon first who had a pelvic MRI or EUS prior to surgery had an adjusted NT rate of 74 vs. 40% for those who did not undergo local staging.[32] In a study of 2005–2009 SEER-Medicare data, patients treated at hospitals with National Cancer Institute designation, residency programs, or medical school affiliation had higher utilization of both local staging and NT.[33] Finally, in a survey of 163 surgeons who performed rectal cancer surgery, fellowship-trained CRSs and surgical oncologists reported that they used MRI and EUS for all rectal cancer patients and used NT for clinical stage II-III cases more often than GSs.[34]

The rate of NT in our study (82.9%) was higher than the rate of 74% in a study of 2006–2011 NCDB data with similar inclusions and exclusions.[1] Future NCDB studies should examine nationwide utilization in more recent years. Our finding that treatment by higher volume surgeons was associated with receipt of NT is not surprising given studies that reported associations between higher hospital volume and utilization of appropriate NT.[1, 5] Analyzing the treatment effect of NT was not our main goal, but our results re-demonstrate that NT benefits these patients. For example, our 5-year local recurrence rates in patients where NT was utilized vs. omitted (7.6 vs. 14.9%) are quite similar to the initial report of the German Trial (6 vs. 13%).[2]

Seven patients received NT without local staging. In such cases, it was only by luck that the patient received the correct treatment. Although they were excluded from this analysis, we also reviewed the records of some patients who received NT after omission of local staging and had pathologic stage I disease. Midura et al. similarly reported that nearly 25% of clinical stage I patient in the 2005–2010 NCDB received non-guideline-concordant NT.[5] Omission of local staging should be recognized as a contributor to *overtreatment* of clinical stage I disease in addition to *undertreatment* of stage II-III disease.

There are several limitations of this study that should be considered. Most substantially, the number of patients and surgeons analyzed was relatively small. It is possible that the reasons we identified as driving omission of local staging and NT are different than those in other parts of the country. Second, as discussed previously, we were unable to simultaneously examine the contributions of hospital *and* surgeon factors to underutilization of local staging and NT. Larger studies that could partition the relative influence of these two cluster levels would be valuable. Third, reliability adjustment tends to produce conservative estimates of variation because low-volume surgeons are "given the benefit of the doubt" by shrinking their observed rates towards the mean.[29] In other words, a surgeon is assumed to be average unless there is evidence to the contrary. Therefore, if anything, these estimates of surgeon-level variation may be underestimates. Finally, patient follow-up was not uniform, as in a randomized trial. Patients who were doing well may have been less likely to present for follow-up than those whose cancer recurred. If so, the reported long-term outcomes would be worse than reality.

Despite these limitations, our findings have implications for national QI efforts aimed at improving the quality of rectal cancer care. Most significantly, they *emphasize that appropriate management of non-metastatic rectal cancer is intrinsically linked with performance of appropriate local staging*. The standards that have been set by the NAPRC standards *do not* include utilization of NT for clinical stage II-III disease, but they do include the hospital-level standard that 95% of patients receive local staging with rectal cancer protocol MRI.[10] This is in contrast to the CoC Quality Metric which emphasizes NT delivery, but does not mention clinical staging.[12] This decision to focus on local staging rather than delivery of NT in the NAPRC standards may reflect the fact that recent studies have demonstrated encouraging results with using pre-treatment MRI to select patients who may safely forgo NT.[35–37] Furthermore, the NAPRC standards emphasize treatment planning discussions for all patients prior to initiating treatment,[10] which could be expected to take care of problem of omission of appropriate NT. Regardless of whether selective NT is eventually adopted by NCCN guidelines, our results emphasize that increasing rates of local staging should be seen as a backbone of QI efforts that can be expected to address both *over-* and *underutilization* of NT.

Since finishing the data collection for this report, we have been providing email-based feedback to surgeons in our healthcare system about guideline discordant care. We are also implementing an electronic medical record-based reminder about utilization of local staging and NT when patients are scheduled for rectal cancer surgery. We continue to closely monitor utilization of appropriate local staging and NT, and plan to describe this quality improvement initiative further in a future report.

Conclusion

We found that patients with stage II-III rectal adenocarcinoma who were treated by low-volume surgeons and those with tumors in the upper rectum had lower rates of local staging and NT. Surgeon-specific rates of local staging and NT varied substantially and were strongly correlated with each other. NT was associated with lower rates of node positivity, lower rates of positive CRMs, and lower rates of local recurrences. Future efforts aimed at improving appropriate utilization of NT should be based in the understanding that improving appropriate utilization of local staging (rectal cancer protocol MRI, specifically) is the most promising leverage point. Improving utilization of local staging should also address overtreatment of stage I cases and will be essential if selective use of NT for clinical stage II-III disease becomes more widespread.

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