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High Rate of Positive Circumferential Resection Margins Following Rectal Cancer Surgery: A Call to Action

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Abstract

Objective—To identify predictors of positive circumferential resection margin following rectal cancer resection in the United States.

Background—Positive circumferential resection margin is associated with a high rate of local recurrence and poor morbidity and mortality for rectal cancer patients. Prior study has shown poor compliance with national rectal cancer guidelines, but whether this finding is reflected in patient outcomes has yet to be shown.

Methods—Patients who underwent resection for stage I-III rectal cancer were identified from the 2010-2011 National Cancer Database. The primary outcome was a positive circumferential resection margin. The relationship between patient, hospital, tumor, and treatment-related characteristics was analyzed using bivariate and multivariate analysis.

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Findings—A positive circumferential resection margin was noted in 2,859 (17.2%) of the 16,619 patients included. Facility location, clinical T and N stage, histologic type, tumor size, tumor grade, lymphovascular invasion, perineural invasion, type of operation, and operative approach were significant predictors of positive circumferential resection margin on multivariable analysis. Total proctectomy had nearly a 30% increased risk of positive margin compared to partial proctectomy (OR 1.293, 95%CI 1.185-1.411) and a laparoscopic approach had nearly 22% less risk of a positive circumferential resection margin compared to an open approach (OR 0.882, 95%CI 0.790-0.985).

Interpretation—Despite advances in surgical technique and multimodality therapy, rates of positive circumferential resection margin remain high in the United States. Several tumor and treatment characteristics were identified as independent risk factors, and advances in rectal cancer care are necessary to approach the outcomes seen in other countries.

INTRODUCTION

Recent improvements in both survival and quality of life for rectal cancer patients have been attributed to advances in surgical technique, neoadjuvant chemoradiation therapy (nCRT), preoperative staging techniques, and new adjuvant therapies over the past 30 years. Total mesorectal excision (TME), as first described by Heald and Ryall in 1982, has become the standard for surgical care of rectal cancer.[1-3] Local recurrence rates decreased from as high as 45% using traditional techniques to less than 10% following TME alone, and to less than 6% following TME in conjunction with nCRT.[3-6]

At the same time, circumferential tumor spread was recognized as a necessary pathologic evaluation of rectal resection specimens. In 1986 Quirke *et al.* published their work examining the specimens of 52 rectal cancer excisions. With 14 specimens having positive lateral resection margins and 12 of the 14 going on to have a local recurrence, this early paper clearly emphasized the importance of obtaining a clear CRM.[7] In a large meta-analysis comprised of over 17,000 patients, Nagtegaal and Quirke were able to show that a CRM ≤1mm was a strong predictor of local recurrence (HR 2.7, 95%CI 1.7-4.3), distant recurrence (HR 2.8, 95%CI 1.9-4.3), and survival (HR 1.7, 95%CI 1.3-2.3). Furthermore, positive CRM has an even greater association with local recurrence when nCRT is used (HR 6.3, 95%CI 3.7-16.7).[8]

The integral link between suboptimal surgery, a positive CRM, and poor oncological outcome has been recognized at a national healthcare policy level in many countries, leading to the establishment of quality assurance programs in several northern European countries during the 1990's. These programs focused on improving outcomes by utilizing evidence based techniques such as a standardized TME technique, appropriate deployment of chemotherapy and radiotherapy and standardized pathological assessment of resected specimens. Many of these goals were achieved through the creation of centers of excellence (CoE), where participating centers had to meet a number of agreed standards for ongoing accreditation. These programs have been associated with an increase in the rate of TME's performed, a decrease in local recurrence rates, and an increase in 5-year survival.[9-12] One of the core quality measures of these programs is CRM status.

Large variation still exists in the quality of treatment received in the United States.[13] The majority of rectal cancer patients still receive their care at low volume hospitals with little formal interaction among the providers involved through the medium of multidisciplinary tumor board meetings.[14] There is an increasing recognition of the need to measure and track the national quality of cancer care, with the quality of TME and CRM rates previously shown to represent possible metrics in other healthcare settings.[14-17] Although CRM status following proctectomy is an accepted quality standard internationally, little is known about the national rates of CRM positivity in current clinical practice in the United States. Therefore the aim of this study was to quantify current rates of positive CRM following rectal cancer resection and to identify predictive factors contributing to an increased risk of a positive margin.[18,19]

METHODS

Data Source

This study is a review of data from the National Cancer Data Base (NCDB) participant user file (PUF) for rectal cancer only and does not include cases from the rectosigmoid PUF. The NCDB is a hospital based, nationwide cancer registry program sponsored jointly by the American College of Surgeons, the Commission on Cancer (CoC), and the American Cancer Society. This comprehensive database receives more than one million case reports per year from over 1,500 hospitals, representing approximately 70% of all new invasive cancer diagnoses in the United States.[20]

Study Subjects

Beginning in 2010 the CoC required the reporting of CRM status from all accredited institutions, and at the time of this study the latest data available from the NCDB were cases from 2011. All patients who underwent partial or complete proctectomy (excluding cases of local excision) for histologically confirmed adenocarcinoma, mucinous adenocarcinoma, or signet ring cell carcinoma (identified using international Classification of Disease for Oncology codes) were included. Cases were limited to patients with pathologic stage I-III cancers of the rectum; cases without CRM status were excluded (Fig. 1).

Statistical Analysis

Analysis was performed using patient, hospital, tumor, and treatment-related characteristics. Patient demographic factors examined included age at diagnosis, gender, race, primary payer, average household income, average education, population density of patient residence, and patient comorbidities. Race was defined as white, black, Hispanic or other. Income and education data were defined by the NCDB using national census data for the zip code of the patient's residence. Education is reported as a percentage of residents without a high school diploma. Patient comorbidities are categorized using the Deyo classification of the Charlson Comorbidity Score. The NCDB does not provide a breakdown of individual comorbidities, nor does it provide information on body mass index or waist circumference.[21]

Hospital characteristics provided by the NCDB include hospital type and geographic location. The CoC provides facility accreditation based on facility volume of newly

diagnosed cancer cases, availability of diagnostic and treatment services, participation in clinical research including clinical trials, and the training of resident physicians. Community Cancer Programs see between 100 and 500 newly diagnosed cancer cases per year, whereas Comprehensive Community Cancer Programs and Academic Comprehensive Cancer Programs see greater than 500 newly diagnosed cancer cases per year. Resident physician teaching is optional for Comprehensive Community Cancer Programs and Community Cancer Programs, whereas Academic Comprehensive Cancer Programs must provide postgraduate medical education in at least four program areas, including internal medicine and general surgery. Whether or not Comprehensive Community Cancer Programs and/or Community Cancer Programs provided resident physician education was not provided. Hospital location was identified by US census division of reporting facility and categorized by region (Table 1). Hospital volume was defined by the average annual number of rectal cancer resections for each institution over the two participating years. The average number of rectal cancer resections per year at each institution ranged from 1 case per year to 85.5 cases per year. Those centers with 1-10 cases per year were categorized as low volume, 11-30 cases as moderate volume, and 31-85.5 cases per year as high volume centers.

Tumor-related factors included pathologic stage, clinical tumor and nodal stage, histological type, tumor size, grade, and presence of lymphovascular or perineural invasion. Treatment-related factors included the use of neoadjuvant chemoradiation, type of surgery for the primary site, and operative approach. Tumor size was categorized into 3 groups: <1cm, between 1 and 2cm, and greater than 2cm in concordance with prior papers published on rectal cancer margin status NCDB.[22,23] The NCDB defines type of rectal surgery as a partial or total proctectomy. A partial proctectomy includes but is not limited to an anterior resection, Hartmann's operation, low anterior resection (LAR), or trans sacral rectosigmoidectomy whereas total proctectomy includes abdominoperineal resections (APR), pelvic exenteration, and total proctocolectomy, NOS.

The primary outcome of this study was positive CRM. CRM was reported by the NCDB as a continuous variable by every 0.1mm to the margin. For the purpose of this analysis, a CRM ≤1mm was considered a positive CRM.[24] Variations in positive CRM rates were determined by bivariate analysis using Pearson's Chi-Square test for categorical variables and Student's t-test for continuous variables. Factors associated with positive CRM with a p-value<0.05 were included in a multivariable logistic regression to identify those variables independently associated with a positive CRM. Out of concern that patient outcomes may not be independent data with clustering of outcomes at the hospital level, we performed a sensitivity analysis using a hierarchical model to account for unequal variance amongst hospitals. Further analysis was performed on the unadjusted relationship of nCRT with CRM status by stratifying for clinical T stage as well as type of operation. The unadjusted relationship between type of operation and CRM positivity was also further evaluated by stratification of overall clinical stage to identify the relationship of operation within these tumor subtypes. A two-sided p-value<0.05 was considered statistically significant. All analyses were performed using SAS/STAT® Software, Version 9.3 of the SAS system for Microsoft Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

Bivariate Analysis

During the two years of data collection 16,619 patients met study design criteria with 2,859 (17.2%) patients having a positive CRM. Patient and facility characteristics for the cohort can be found in Table 2, and tumor and treatment characteristics in table 3.

The rate of positive CRM had a statistically significant variation between the geographic regions in the United States from 13.5% in the Middle Atlantic to 18.9% in the West South Central and Pacific regions ($p<0.001$). In contrast, there was no statistically significant difference in the positive CRM rate among facility types ($p=0.222$) or the treatment center volume ($p=0.972$).

All tumor characteristics tested were significantly associated with positive CRM rates (Table 3). While T4 tumors had the highest rate of CRM positivity, they only contributed to 9.5% of positive CRM cases reported. Cases with T3 and T2 tumors still had a high rate of CRM positivity with 17.0% and 13.1% respectively.

The type of operation and the operative approach both had a statistically significant variation in positive CRM rates ($p<0.001$). The positive CRM rate was 20.9% for total proctectomies versus 13.4% for partial proctectomies. When performing a sub analysis of the relationship between operation type and CRM status by clinical stage, the type of operation did not have a statistically significant difference in CRM status for clinical stage I patients, however, there was a significant difference for clinical stage II and III cases (Fig. 2). The use of nCRT was not significantly related to positive CRM ($p=0.190$) for the entire cohort. The overall 30-day mortality was 1.4% but higher in those patients who had a positive CRM at 2.0% versus 1.3% for patients with a negative CRM ($p=0.002$).

Comparing positive margin rates, 6.8% of the entire study group had a positive proximal/distal margin whereas the positive CRM rate was 17.2% (N=2,859). Furthermore, 77.8% of cases with a positive proximal/distal margin had a positive CRM whereas 68.8% of patients with a positive CRM had a negative proximal/distal margin. In other words, out of the 2,859 patients with a positive CRM, only 31% would have been recognized as a positive margin based on proximal/distal margin status alone.

Multivariable Analysis

Facility location, health insurance status, clinical T stage, clinical N stage, histologic type, tumor size, tumor grade, presence of lymphovascular invasion, perineural invasion, type of operation, and surgical approach were all included in the multivariable analysis for positive CRM (Table 4). Health insurance status was the only variable that did not have an independent association with a positive CRM when adjusting for the other factors in the analysis. Applying these same factors to a hierarchical model accounting for variance in CRM status amongst hospitals did not change the results seen in the multivariable logistic regression model.

After adjusting for the patient, facility, tumor, and treatment factors, the type of operation and surgical approach remained statistically significantly associated with a positive CRM. Total proctectomy had nearly a 30% increased risk of a positive CRM compared to partial proctectomy (OR 1.293, 95%CI 1.185-1.411) and a laparoscopic approach had nearly 22% less risk of a positive CRM compared to an open approach (OR 0.882, 95%CI 0.790-0.985). When the use of nCRT was included in the multivariable model it had no independent association with a positive CRM (p=0.875) even after adjusting for clinical T stage, type of operation, and all other factors seen in table 4 (results not shown).

DISCUSSION

A large body of literature has established that CRM status plays a significant role in the long-term outcomes of patients with rectal cancer.[8] TME is widely accepted as the standard surgical technique for achieving a clear CRM and for providing patients with the best opportunity for recurrence free survival. Nonetheless, using recent data from the NCDB, this study has shown that current rates of CRM positive resections within the United States are excessive with one in every six rectal resections having a positive margin. In comparison to the rate of 17% seen in this study, other large population based studies following the adoption of TME have seen rates of positive CRM between 8 and 13%.[8,18,25,26] Multiple tumor-specific characteristics as well as treatment factors were independently predictive of a positive CRM in this large cohort of patients. These factors not only provide prognostic value but may also be recognized as high-risk features that warrant preoperative recognition and potential for alteration to the individual patient's treatment plan.

For example, advanced clinical T and N stage, tumors >2cm, mucinous adenocarcinomas and signet ring cell carcinomas, high grade tumors, and lymphovascular and perineural invasion were identified as features independently associated with a positive CRM. This study is not the first to identify these factors as being associated with a positive margin but rather confirms these results in a large national database across thousands of resections and hundreds of hospitals.[19,22,27,28] These features also remained significantly associated with positive CRM even after adjusting for the use of nCRT and type of surgical technique. These high-risk features, although not necessarily modifiable, are preoperatively identifiable. Location and depth of tumor invasion, nodal involvement, and tumor size should all be recognized with routine preoperative high-resolution pelvic MRI. In the MERCURY Study Group experience, high-resolution pelvic MRI has been proven to be a very successful staging tool for rectal cancer and for identifying patients at high risk for positive CRM.[27] Additionally, preoperative MRI assessment of the CRM has been shown to predict short-term and long-term outcomes.[29] Our findings suggest that current strategies for treatment are inadequate. Wider adoption of dedicated high-resolution rectal MRI may be one approach to help aid in the decision for adjunct therapies like chemoradiation, as well as planning for the most appropriate surgical approach to provide the greatest opportunity for a negative CRM.

While the type of surgery and surgical approach used were found to be independently associated with CRM status on multivariable analysis in our study, these results are subject to potential selection bias and confounders that are not controllable with the variables provided by NCDB. Furthermore, surgical specialty training is also a variable not available

and therefor no analysis could be performed on the relationship between specialists and sphincter sparing operations or CRM status. Nonetheless, these results do emphasize the significance of proper surgical technique in achieving the ideal TME specimen and highlight the potential benefits from increasing rates of sphincter preserving operations and minimally invasive surgery as seen with colorectal surgeons in centers of excellence.[9,12] A growing body of evidence suggests that there is a strong association between the quality of TME surgery and outcomes. Quirke *et al.* undertook a detailed pathological analysis of the mesorectal specimens in 1,156 patients enrolled in the CR07 randomized control trial. The overall CRM positivity rate was 11% and the plane of surgery was defined as good (mesorectal plane) in 52%, intermediate in 34% (intramesorectal), and poor (muscularis propria) in 13%. The CRM positivity rate was significantly associated with plane of surgery (mesorectal plane=9% vs. muscularis propria=19%, $p<0.001$). The quality of surgical plane correlated with subsequent 3-year local recurrence rates which were only 4% for patients with a good plane of dissection compared to 13% for patients with a poor plane of dissection ($p=0.0039$), in accordance with previous studies.[30-32]

In a study using NCDB data from 1998-2007, Russell *et al.* studied predictors of a positive margin following surgery for rectal and rectosigmoid tumors and developed a nomogram for a risk-adjusted pathologic margin positivity rate. In this original work they found that low outliers for a positive resection margin were more commonly high volume and academic centers.[22] The group later went on to publish a paper in which they showed that the same low outliers for positive margin also had improved nodal evaluation, greater nCRT use, performed more sphincter preserving operations, had a lower 30-day mortality, and ultimately a greater 5-year survival compared to high outliers.[23] This would suggest that auditing of outcome measures such as margin status could help identify high and low performing institutions. Circumferential margin status represents an excellent outcome measure as it can be accurately assessed pre-operatively on MRI, is associated with oncological outcomes, and accurately measured following surgical resection. MRI results can be incorporated into the deliberations on the need for neoadjuvant therapy and subsequent surgical decision-making. Subsequent pathological assessment of the CRM provides a valuable feedback loop to both the radiologist and surgeon. These steps are predicated on a standardized patient assessment pathway, which is facilitated by a multidisciplinary tumor board and audit, and forms the basis of the program of Centers of Excellence being proposed by the OSTRiCh Clinical Consortium.[9]

Since our study found no hospital level factors associated with CRM status and largely poor CRM rates across the nation, these results further support the role for surgical improvement and teaching programs proposed and encouraged by the OSTRiCh Clinical Consortium through the CoC.[9] Multidisciplinary programs aimed at improving rectal cancer outcomes in large populations have been proven successful in the past. With the goal of reducing local recurrence rates and improving compliance with evidence-based treatment guidelines, in 2002 British Columbia held educational programs that were attended by approximately 80% of surgeons performing rectal cancer resections in that region. Following these sessions, the Province recognized a significant improvement in patient outcomes. The rate of negative CRM increased from 41.6% in 1996 to 86.9% ($p<0.001$) in 2003/04. Compliance with recommendations for preoperative radiation significantly improved and they experienced a

significant decrease in 2-year pelvic recurrence among patients with stage III cancer from 18.2% to 9.2% (p=0.020).[26,33]

While our study does provide significant power through the large number of patients provided by the NCDB, we do acknowledge several limitations. Several important variables were not available for adjustment in this analysis, including tumor location, distance from the anal verge, surgeon specialty and operative volume, pathologic response to nCRT, diagnostic modality utilized, and information on the plane of surgery. Furthermore, the NCDB has limited data on operative details including a description as to what procedural codes comprise the two major categories for resection, partial and total proctectomy. Similar to other studies using NCDB, this study only includes data from CoC accredited hospitals and may misrepresent the true rates of positive CRM in this country and the relationship of hospital characteristics to non-CoC accredited institutions. However, it is reasonable to suggest that institutions achieving successful CoC accreditation are unlikely to have worse outcomes than non-accredited hospitals. Additionally, racial minorities appear to be under-represented in this cohort of patients as has been seen in other NCDB studies and warrant additional consideration.[22] Lastly, the definition of “center” in the NCDB may include a heterogeneous group of institutions ranging from single site to multiple site facilities.

CONCLUSION

National rates of positive CRM following rectal cancer resection remain high, with one in six patients having an inadequate oncologic resection resulting in high risk for poor long-term outcomes. These rates are higher than those rates reported in contemporaneous International studies. Seen alongside data from the same source relating to apparent failure of guideline adherence, it strongly suggests that the United States is lagging significantly behind other countries in delivery of optimal care for patients with rectal cancer. Whereas many patient- and hospital-level characteristics were not significant predictors of positive CRM rates, multiple tumor-related and treatment-related factors were identified as high-risk factors for a positive CRM. By greater adherence to basic surgical tenets of rectal cancer care such as TME, improved pathologic assessment (grading of TME specimens, notation of CRM status), advanced imaging techniques, devotion to appropriate neoadjuvant therapy, and commitment to a multidisciplinary team approach to rectal cancer care a substantial reduction in CRM positivity and its attendant negative oncological outcomes can be delivered.

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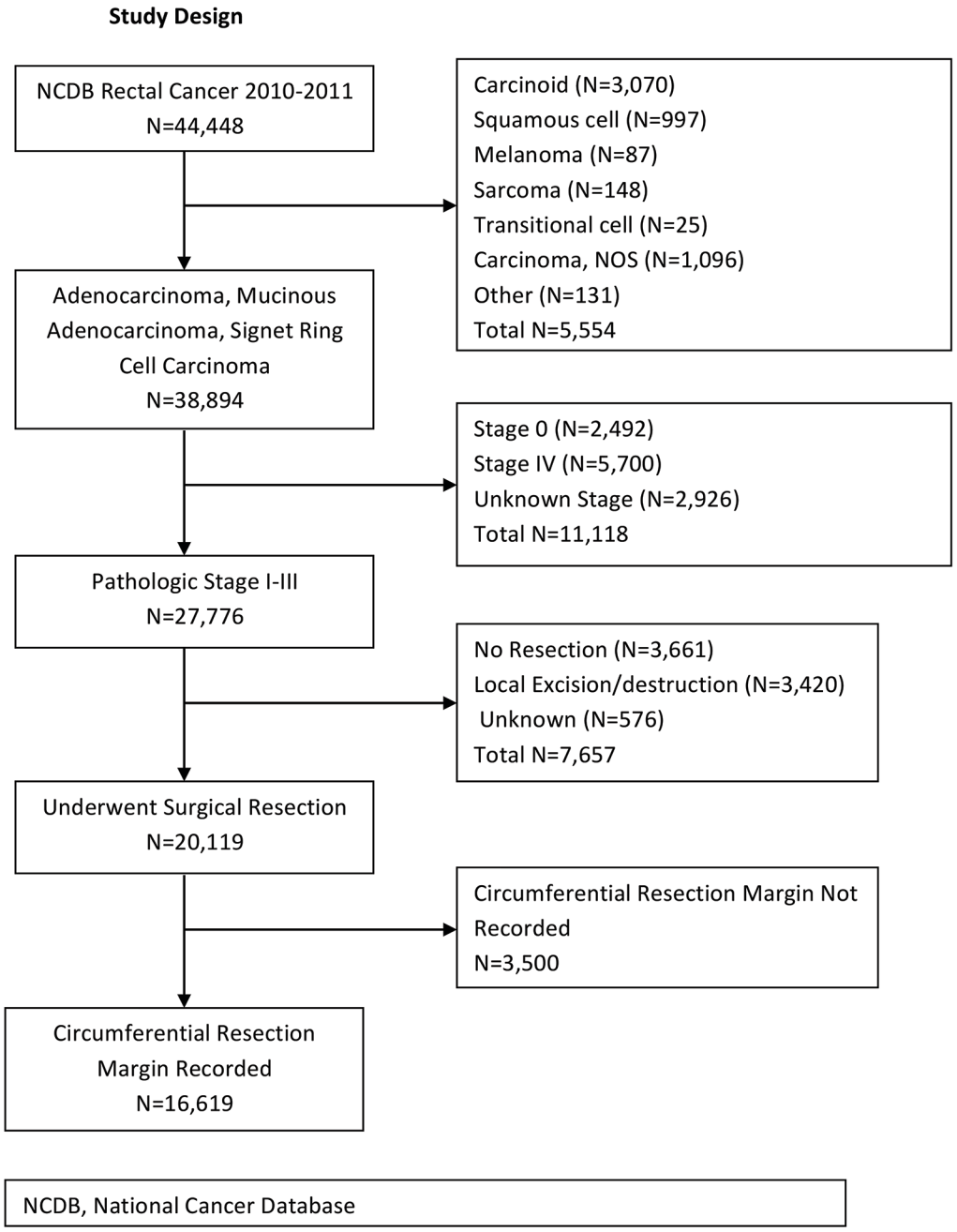

Figure 1.

Flow Chart displaying the breakdown of cases included and excluded from the original 44,448 rectal cancer cases in the National Cancer Database from 2010-2011. Following inclusion and exclusion criteria, 16,619 cases were included in the study.

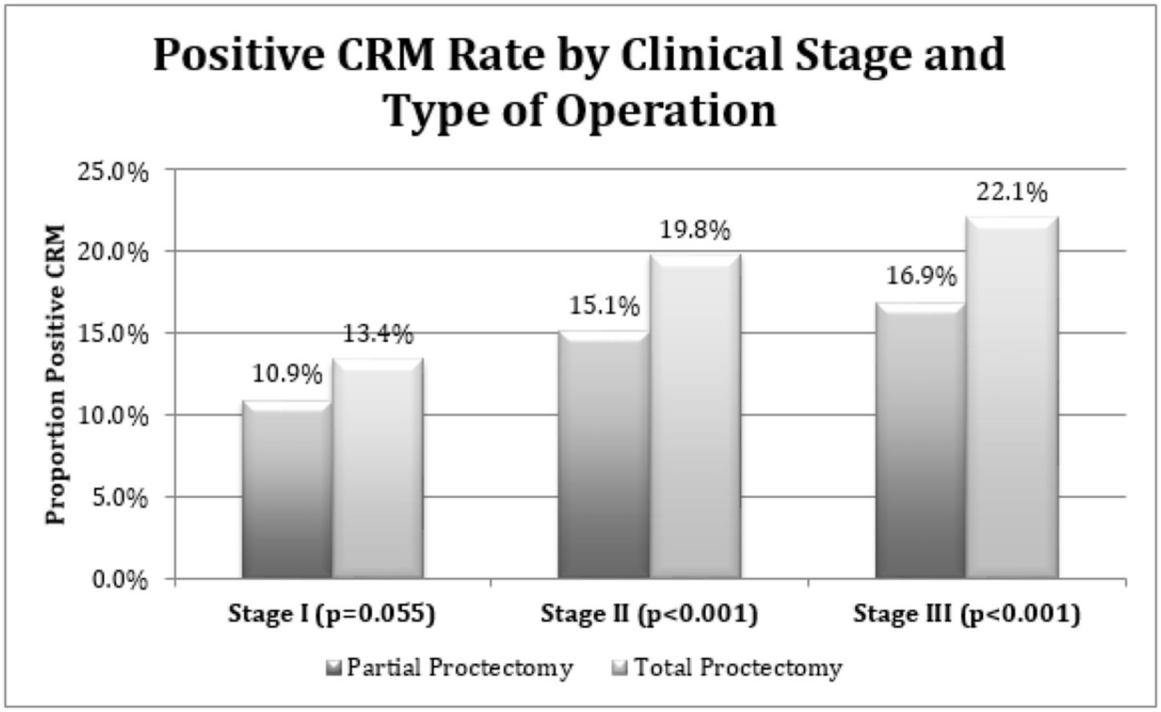

Figure 2.
Comparison of positive circumferential resection margin (CRM) rates by clinical stage for each type of operation.

Table 1

Hospital Location

Region	States
New England	CT, MA, ME, NH, RI, VT
Middle Atlantic	NJ, NY, PA
South Atlantic	DC, DE, FL, GA, MD, NC, SC, VA, WV
East North Central	IL, IN, MI, OH, WI
East South Central	AL, KY, MS, TN
West North Central	IA, KS, MN, MO, ND, NE, SD
West South Central	AR, LA, OK, TX
Mountain	AZ, CO, ID, MT, NM, NV, UT, WY
Pacific	AK, CA, HI, OR, WA
Out of US	All other values

Table 2

Patient and Facility Characteristics

	Patients, N=16,619 (%)	CRM Negative, N=13,760 (%)	CRM Positive, N=2,859 (%)	P-value
Mean Patient Age (SD)	62.5 (±13.0)	62.5 (±12.9)	62.8 (±13.4)	0.158
Sex				0.939
Male	10005 (60.2)	8282 (82.8)	1723 (17.2)	
Female	6614 (39.8)	5478 (82.8)	1136 (17.2)	
Race				0.369
White	13492 (81.2)	11207 (83.1)	2285 (16.9)	
Black	1338 (8.1)	1088 (81.3)	250 (18.7)	
Hispanic	894 (5.4)	736 (82.3)	158 (17.7)	
Other	782 (4.7)	635 (81.2)	147 (18.8)	
Unknown	113 (0.7)	94 (83.2)	19 (16.8)	
Insurance				<0.001
Uninsured	695 (4.2)	551 (79.28)	144 (20.7)	
Government	8013 (48.2)	6545 (81.7)	1468 (18.3)	
Private	7703 (46.4)	6489 (84.2)	1214 (15.8)	
Unknown	208 (1.3)	175 (84.1)	33 (15.9)	
Mean Household Income				0.410
<$30,000	2039 (12.3)	1698 (83.3)	341 (16.7)	
$30,000-$34,999	3043 (18.3)	2485 (81.7)	558 (18.3)	
$35,000-$45,999	4388 (26.4)	3638 (82.9)	750 (17.1)	
>$45,999	6165 (37.1)	5114 (83.0)	1051 (17.1)	
Unknown	984 (5.9)	825 (83.8)	159 (16.2)	
Without High School Degree				0.442
>28.9%	2627 (15.8)	2158 (82.2)	469 (17.9)	
20.0-28.9%	3733 (22.5)	3080 (82.5)	653 (17.5)	
14.0-19.9%	3867 (23.3)	3232 (83.6)	635 (16.4)	
<14.00%	5404 (32.5)	4461 (82.6)	943 (17.5)	
Unknown	988 (6.0)	829 (83.9)	159 (16.1)	
Charlson/Deyo Score				0.930
Score 0	12567 (75.6)	10399 (82.8)	2168 (17.3)	
Score 1	3175 (19.1)	2636 (83.0)	539 (17.0)	
Score 2	877 (5.3)	725 (82.7)	152 (17.3)	
Facility Type				0.223
Community Cancer Program	1703 (10.3)	1405 (82.5)	298 (17.5)	
Comprehensive Community Program	9532 (57.4)	7871 (82.6)	1661 (17.4)	
Academic	5308 (31.9)	4415 (83.2)	893 (16.8)	
Other	76 (0.5)	69 (90.8)	7 (9.2)	

	Patients, N=16,619 (%)	CRM Negative, N=13,760 (%)	CRM Positive, N=2,859 (%)	P-value
Facility Location				<0.001
New England	933 (5.6)	759 (81.4)	174 (18.7)	
Middle Atlantic	2278 (13.7)	1971 (86.5)	307 (13.5)	
South Atlantic	3552 (21.4)	2942 (82.8)	610 (17.2)	
East North Central	3076 (18.5)	2503 (81.4)	573 (18.6)	
East South Central	989 (6.0)	813 (82.2)	176 (17.8)	
West North Central	1542 (9.3)	1325 (85.9)	217 (14.1)	
West South Central	1444 (8.7)	1171 (81.1)	273 (18.9)	
Mountain	851 (5.1)	691 (81.2)	160 (18.8)	
Pacific	1954 (11.8)	1585 (81.1)	369 (18.9)	
Center Volume				0.972
1-10 cases	7721 (46.5)	6387 (82.7)	1334 (17.3)	
11-30 cases	7046 (42.4)	5839 (82.9)	1207 (17.1)	
31-85.5 cases	1852 (11.1)	1534 (82.8)	318 (17.2)	
Distance Traveled				0.558
≤30mi	13166 (79.2)	10879 (82.6)	2287 (17.4)	
30-60mi	1862 (11.2)	1555 (83.5)	307 (16.5)	
60-100mi	830 (5.0)	685 (82.5)	145 (17.5)	
>100mi	761 (4.6)	641 (84.2)	120 (15.8)	
Population Density				0.244
Metro	12284 (73.9)	10128 (82.5)	2156 (17.6)	
Urban	2833 (17.1)	2374 (83.8)	459 (16.2)	
Rural	433 (2.6)	360 (83.1)	73 (16.9)	
Unknown	1069 (6.4)	898 (84.0)	171 (16.0)	

SD, Standard Deviation

Table 3

Tumor and Treatment Characteristics

	Patients, N=16,619 (%)	CRM Negative, N=13,760 (%)	CRM Positive, N=2,859 (%)	P-value
Pathologic Stage				<0.001
Stage I	5403 (32.5)	4864 (90.0)	539 (10.0)	
Stage II	5054 (30.4)	4068 (80.5)	986 (19.5)	
Stage III	6162 (37.1)	4828 (78.4)	1334 (21.7)	
Clinical T Stage				<0.001
cT0	26 (0.2)	21 (80.8)	5 (19.2)	
cTis	91 (0.6)	78 (85.7)	13 (14.3)	
cT1	1683 (10.1)	1517 (90.1)	166 (9.9)	
cT2	2262 (13.6)	1965 (86.9)	297 (13.1)	
cT3	8044 (48.4)	6673 (83.0)	1371 (17.0)	
cT4	773 (4.7)	501 (64.8)	272 (35.2)	
Unknown	3740 (22.5)	3005 (80.4)	735 (19.7)	
Clinical N Stage				<0.001
N0	9717 (58.5)	8198 (84.4)	1519 (15.6)	
N1	4096 (24.7)	3358 (82.0)	738 (18.0)	
N2	759 (4.6)	552 (72.7)	207 (27.3	
Unknown	2047 (12.3)	1652 (80.7)	395 (19.3)	
Histological Type				<0.001
Adenocarcinoma	15569 (93.7)	13012 (83.6)	2557 (16.4)	
Mucinous Adenocarcinoma	945 (5.7)	686 (72.6)	259 (27.4)	
Signet-Ring Cell Carcinoma	105 (0.6)	62 (59.1)	43 (41.0)	
Tumor Size				<0.001
≤10mm	1012 (6.1)	892 (88.1)	120 (11.9)	
11-20mm	2082 (12.5)	1784 (85.7)	298 (14.3)	
>20mm	11336 (68.2)	9148 (80.7)	2188 (19.3)	
Unknown	2189 (13.2)	1936 (88.4)	253 (11.6)	
Tumor Grade				<0.001
Well or Moderately differentiated	13043 (78.5)	10905 (83.6)	2138 (16.4)	
Poorly or Undifferentiated	2100 (12.6)	1594 (75.9)	506 (24.1)	
Unknown	1476 (8.9)	1261 (85.4)	215 (14.6)	
Lymphovascular Invasion				<0.001
No	11381 (68.5)	9575 (84.1)	1806 (15.9)	
Yes	2791 (16.8)	2050 (73.5)	741 (26.6)	
Unknown	2447 (14.7)	2135 (87.3)	312 (12.8)	
Perineural Invasion				<0.001
No	13099 (78.8)	11058 (84.4)	2041 (15.6)	
Yes	1670 (10.1)	1088 (65.2)	582 (34.9)	

	Patients, N=16,619 (%)	CRM Negative, N=13,760 (%)	CRM Positive, N=2,859 (%)	P-value
Unknown	1850 (11.1)	1614 (87.2)	236 (12.8)	
Neoadjuvant Chemoradiation				0.190
No	8034 (48.3)	6663 (82.9)	1371 (17.1)	
Yes	8550 (51.5)	7072 (82.7)	1478 (17.3)	
Unknown	35 (0.2)	25 (71.4)	10 (28.6)	
Operation				<0.001
Partial Proctectomy	10871 (65.4)	9202 (84.7)	1669 (13.4)	
Total Proctectomy	5573 (33.5)	4407 (79.1)	1166 (20.9)	
Proctectomy, NOS	175 (1.1)	151 (86.3)	24 (13.7)	
Surgical Approach				<0.001
Open	10430 (62.8)	8544 (81.9)	1886 (18.1)	
Laparoscopic	3464 (20.8)	2948 (85.1)	516 (14.9)	
Robotic	865 (5.2)	718 (83.0)	147 (17.0)	
Unknown	1860 (11.2)	1550 (83.3)	310 (16.7)	
Proximal/Distal Margins				<0.001
Negative	15419 (92.8)	13453 (87.2)	1966 (12.8)	
Positive	1129 (6.8)	251 (22.2)	878 (77.8)	
Unknown	71 (0.4)	56 (78.9)	15 (21.1)	

NOS, Not Otherwise Specified

Table 4

Multivariable Analysis of Factors Associated With Positive Circumferential Resection Margin

Variable	P-Value	Odds Ratio (95% Confidence Interval)
Facility Location		
New England		Reference
East North Central	0.740	1.034 (0.850, 1.257)
East South Central	0.891	0.983 (0.773, 1.251)
Middle Atlantic	<0.001	0.677 (0.548, 0.837)
Mountain	0.557	1.077 (0.841, 1.379)
Pacific	0.191	1.149 (0.933, 1.414)
South Atlantic	0.588	0.948 (0.781, 1.151)
West North Central	0.009	0.738 (0.589, 0.926)
West South Central	0.742	1.038 (0.832, 1.294)
Insurance		
Uninsured		Reference
Government	0.999	1.000 (0.817, 1.224)
Private	0.168	0.867 (0.707, 1.062)
Unknown	0.342	0.812 (0.528, 1.248)
Clinical T Stage		
cT1		Reference
cT0	0.297	1.741 (0.614, 4.934)
cTis	0.198	1.499 (0.809, 2.777)
cT2	0.066	1.213 (0.987, 1.491)
cT3	<0.001	1.538 (1.285, 1.841)
cT4	<0.001	3.510 (2.787, 4.420)
Unknown	<0.001	1.834 (1.509, 2.228)
Clinical N Stage		
cN0		Reference
cN1	0.223	1.068 (0.961, 1.188)
cN2	<0.001	1.445 (1.203, 1.734)
Unknown	0.807	0.982 (0.846, 1.139)
Operation		
Partial Proctectomy		Reference
Total Proctectomy	<0.001	1.293 (1.185, 1.411)
Proctectomy, NOS	0.566	0.878 (0.562, 1.370)
Surgical Approach		
Open		Reference
Laparoscopic	0.026	0.882 (0.790, 0.985)
Robotic	0.944	0.993 (0.821, 1.202)
Unknown	0.452	0.948 (0.826, 1.089)

Variable	P-Value	Odds Ratio (95% Confidence Interval)
Histologic Type		
Adenocarcinoma		Reference
Mucinous Adenocarcinoma	<0.001	1.705 (1.459, 1.991)
Signet-Ring Cell Carcinoma	<0.001	2.254 (1.473, 3.451)
Tumor Size		
<10mm		Reference
11-20mm	0.343	1.119 (0.887, 1.410)
>20mm	0.004	1.348 (1.100, 1.650)
Unknown	0.330	0.888 (0.700, 1.127)
Tumor Grade		
Well or Moderately Differentiated		Reference
Poorly or Undifferentiated	<0.001	1.260 (1.119, 1.420)
Unknown Differentiation	0.678	0.967 (0.824, 1.134)
Lymphovascular Invasion		
No		Reference
Yes	<0.001	1.375 (1.232, 1.534)
Unknown	0.001	0.790 (0.688, 0.908)
Perineural Invasion		
No		Reference
Yes	<0.001	2.227 (1.971, 2.517)
Unknown	0.050	0.857 (0.735, 1.000)

NOS, Not Otherwise Specified