IMPORTANCE  In colon cancer, radial margin positivity (RMP) is defined as primary disease involvement at the cut edge of the mesentery or nonserosalized portions of the colon. Although extensively studied for rectal malignancies, RMP has unclear prognostic implications for tumors of the colon.

OBJECTIVE  To determine the effect of RMP on perioperative outcomes as well as survival and disease-free survival in colon cancer.

DESIGN, SETTING, AND PARTICIPANTS  A retrospective cohort study including all patients with surgically treated colon cancer at a tertiary care center from January 1, 2004, through December 31, 2011. The cohort was retrospectively extracted from an institutional patient data repository and included in a data repository maintained prospectively starting June 1, 2011, to April 1, 2014. Participants included 984 patients with surgical colon cancer in the given period, excluding patients with intramucosal tumors (n = 47), palliative resections (n = 24), and patients where radial margin status was not assessable (n = 16).

MAIN OUTCOMES AND MEASURES  Surgical characteristics, postoperative staging, and long-term outcomes, including recurrence and disease-free survival.

RESULTS  Of the 984 included cases, 52 (5.3%) had an involved radial margin. Patients with RMP had much higher rates of multivisceral resection (40.4% vs 12.8%; relative risk, 3.16 [95% CI, 2.18-4.58]; P < .001) and conversion (50.0% vs 13.7%; relative risk, 3.78 [95% CI, 1.56-9.18]; P = .01). All patients with RMP had American Joint Committee on Cancer stage II cancer or higher, with higher rates of node positivity (86.5% vs 38.8%; relative risk, 2.23 [95% CI, 1.95-2.55]; P < .001), metastasis (34.6% vs 6.7%; relative risk, 5.20 [95% CI, 3.34-8.11]; P < .001), extramural vascular invasion (76.9% vs 28.4%; relative risk, 2.71 [95% CI, 2.26-3.24]; P < .001), and high-grade tumor (45.1% vs 18.2%; relative risk, 3.01 [95% CI, 2.44-3.88]; P < .001). In patients without baseline metastasis, metastatic disease in follow-up was considerably higher in patients with RMP (37.5% vs 12.5%; relative risk, 3.32 [95% CI, 2.79-3.95]; P < .001), especially peritoneal (18.8% vs 2.6%; relative risk, 7.24 [95% CI, 2.40-21.8]; P < .001) and liver (18.8% vs 6%; relative risk, 3.10 [95% CI, 1.08-8.92]; P = .04) metastasis. In multivariable Cox regression, the hazard ratio for survival adjusted for baseline staging, age, comorbidity, smoking, and neoadjuvant chemotherapy was higher (hazard ratio, 3.39; 95% CI, 2.41-4.77; P < .001) compared with metastasis adjusted for baseline staging, smoking, and neoadjuvant chemotherapy (hazard ratio, 2.03; 95% CI, 1.43-2.89; P < .001). The median follow-up duration for patients alive on April 1, 2014, was 51 months (interquartile range, 33-76 months).

CONCLUSIONS AND RELEVANCE  An involved radial margin leads to high rates of conversion and multivisceral resection. Although occurring infrequently, RMP is an important stage-independent outcome predictor strongly associated with recurrence, risk of death, and shorter survival. Preoperative assessment, especially imaging, could play a key role in the timely identification of potential patients with RMP to take adequate preparatory surgical and therapeutic measures.

Author Affiliations: Division of General Surgery and Gastrointestinal Surgery, Massachusetts General Hospital, Harvard Medical School, Boston.

Corresponding Author: David L. Berger, MD, Division of General Surgery and Gastrointestinal Surgery, Massachusetts General Hospital, 15 Parkman St, 02114 Boston, MA (dberger@mgh.harvard.edu).
The primary goal of surgical resection for malignant solid tumors is to perform a negative or radial margin resection, the cardinal factor in preventing recurrence. Negative margins are the hallmark of a successful oncologic resection. Conversely, a microscopic disease at the margin resection or macroscopic disease at the margin resection are universally poor prognostic factors. However, the magnitude of this effect is variable depending on the disease, its characteristics, and whether a specific margin or margins are found to be positive. Colorectal cancer is not an exception to these variations. In rectal cancer, radial margin positivity (RMP), the circumferential margin of the disease, has been demonstrated to be a very strong predictor of recurrence and eventual outcomes. However, for primary tumors in the colon, research on surgical margins has largely concentrated on proximal and distal margins. The colon has both retroperitoneal and intraperitoneal components and, for this partially free-floating segment of the gastrointestinal tract, circumferential disease involvement may be expected to have less evident effects. The mesenteric attachment point of the colon along with the cut edge of the nonserosalized (retroperitoneal) segments forms the radial margin during colonic resection. Research on the effect of this margin on prognosis and recurrence patterns of colon cancer is lacking.

This study aimed to evaluate the effect of RMP in colon cancer. Our a priori hypothesis was that RMP is associated with higher risk of metastasis, recurrence, and, eventually, death. Therefore, the primary objective was to evaluate the association of RMP with pathological tumor characteristics and outcomes, including recurrence and survival. We also verified whether the effect of RMP on outcomes was independent of baseline staging or any other significant predictors that may have acted as confounders.

Methods

A cohort including all patients with surgically treated colon cancer at Massachusetts General Hospital from January 1, 2004, through December 31, 2011, was retrospectively extracted from the Massachusetts General Hospital cancer registry and included in a data repository using data from the research patient data repository complemented by patient records. Data collection on follow-up and survival status started June 1, 2011, and was regularly updated. Data on long-term outcomes were periodically updated by reviewing follow-up records and the social security death index. The last status review of survival and follow-up was on April 1, 2014. Institutional review board approval was provided by Partners HealthCare. Participant consent was not required owing to the retrospective nature of the study.

Data were reviewed to include all cases where surgical margins were relevant and part of the pathological assessment. Margins were not explicitly assessed when received specimens were flagged as part of a purely palliative resection where a cure was no longer a realistic prospect, if the tumor was revealed to be intramucosal (carcinoma in situ), or in rare cases where the radial margin was not assessable owing to ulcerative disease and/or perforations, which occurred most often in emergency procedures. Of the 1071 patients operated on for colon cancer in the 2004 to 2011 period, 984 were included for subsequent analysis. The 87 exclusions consisted of 24 patients with palliative resections, 47 patients with carcinoma in situ, and 16 cases where the radial margin was not assessed. Figure 1 shows an inclusion flowchart including the loss to follow-up rates.

In the included population, data collected had the following baseline characteristics on presentation: age, body mass,
index (BMI; calculated as weight in kilograms divided by height in meters squared), Charlson comorbidity score excluding colon cancer, reported weight loss greater than 10% in the previous 6 months, rates of smoking, alcohol abuse, history of polyposis, colorectal cancer and hereditary nonpolyposis colon cancer, and emergency and screening presentation. Meta-invasive presentation was also assessed and defined as any suspicion of distant metastasis confirmed within 30 days of the index admission by imaging or surgical pathology.

All procedures performed aimed to be en bloc resections of the primary tumor along with all mesentry containing the primary blood supply, lymphatics of the involved colonic segment, and any involved adjacent organs. In a subsequent pathologic analysis, a team of 6 gastrointestinal pathologists paired with specifically trained physician assistants processed and prepared the surgical oncological specimens according to the American Joint Committee on Cancer (AJCC) TNM staging system with assessment of completeness of the resection. The radial margin represents the adventitial soft tissue margin of the colon, which can be either partially peritonealized (in the ascending, descending, and rectosigmoid colon) or completely peritonealized. To determine the radial margin status, pathologists differentiated between the nonperitonealized and peritonealized sides prior to fixation by inking the cut mesenteric edge as well as the nonperitonealized surface. The pathologist and pathology technician confirmed this, marked the specimen, and proceeded to fix it for further analysis.

Pathologic assessment of resected samples also included a more detailed assessment of tumor characteristics, including tumor grade, presence of lymphovascular and perineural invasion, absence of lymphocytic response, tumor border configuration, and mutation and microsatellite instability profiles. Pathologic analysis was performed according to current recommendations of the College of American Pathologists.

Follow-up was performed in a standardized manner following the guidelines and recommendations of the American Society of Clinical Oncology as part of the Massachusetts General Hospital multidisciplinary gastrointestinal cancer center and involved a team of surgeons, diagnostic radiologists, gastroenterologists, endoscopists, medical and radiation oncologists, oncology nurses, nurse practitioners, and, when relevant, nutritionists, psychiatrists, and palliative care professionals. Local recurrence was defined as the identification of recurrent disease at the site of the original disease during follow-up. Distant recurrence was defined as any disease identified outside the primary site during follow-up beyond 30 days of the original admission. Accordingly, metastatic disease confirmed within 30 days of the index admission was considered to be baseline metastasis.

### Statistical Analysis

Our primary research methods consisted mainly of comparing several dichotomous pathologic and clinical variables as well as survival and recurrence outcomes between patients with RMP and radial margin negativity. Frequency in dichoto-
mouseventswasexpressedinpercentageratesalongwiththerelativeriskand95%CIconstatisticalsignificanceofthedif-
ferences was assessed using a χ2 test. Continuous outcomes
were displayed using median values and the interquartile
range, using a Mann-Whitney
U
 test to assess for statistical
significance. Timed events, such as death or recurrence,
were compared using the Cox proportional hazards model,
which allows comparing univariable hazard ratios and the
95% CI of events with the multivariable hazard ratio after
adjusting for covariables. In addition to AJCC staging, poten-
tial covariables included neoadjuvant chemoradiation, age,
Charlson comorbidity score, obesity, smoking, or a history of
inflammatory bowel disease. Backward elimination was
used in the regression analysis, removing covariables if they
did not have a significant effect (P ≤ .05) in the correspond-
ing model. All analysis was performed using the SPSS statis-
tical software, version 22.0 (IBM Corp).

Results

Baseline Characteristics

Of the 984 patients included, 52 (5.3%) had an involved ra-
dial margin compared with a 0.7% proximal and 0.2% distal
margin involvement rate. Demographic characteristics, in-
cluding age, sex, and race/ethnicity, were not different de-
pending on radial margin status. Rates of smoking, alcohol
abuse, comorbidity burden, previous colorectal malignancy,
or rates of neoadjuvant chemotherapy did not show statisti-
cally significant differences. Obesity was much less preva-

ent in patients with RMP. Patients with RMP were obese
(BMI > 30) in 11.8% of cases vs 29.6% in patients with radial
margin negativity (P = .006). This discrepancy may relate to
advanced disease-associated weight loss. The possibility of
advanced and/or aggressive disease is also supported by pa-
tients with radial margin negativity having markedly higher
preexisting polyposis detection rates (13.4% vs 3.8%; P = .05)
and screening diagnoses (26.8% vs 3.8%; P < .001), both con-
sidered indicators of early detection.8,9 All baseline charac-
teristics are shown in Table 1.

Surgical Pathology

Table 2 shows rates of RMP for every tumor, node, and metas-
tasis stage as well as every seventh-edition AJCC stage (ie, I,
IIA, IIB, IIC, IIIA, IIIB, IIIC, and IV). The lowest stages with
radial margin involvement were T3, NO, MO, and AJCC stage
IIA. Patients with RMP with a T3 tumor had tumor involve-
ment in a nonperitonealized surface where the tumor could
grow directly into the subserosa without further extension
through the peritoneum or adjacent structures, which would
make it a T4 tumor. The percentage of patients with RMP
invariably increased with each major staging increment
(P < .001). In postoperative surgical pathology, patients with
RMP fared considerably worse in every aspect (Table 3),
including much higher rates of T4 disease (61.5% vs 21.5%;
P < .001), lymph node positivity (86.5% vs 38.8%; P < .001),
and, most substantially, metastatic disease identified in surgi-
cal pathology (relative risk, 5.20; 34.6% vs 6.7%; P < .001).
Radial margin involvement was also associated with aggres-
sive tumor properties, significantly higher rates of high-grade
disease (45.1% vs 18.2%; P < .001), small-vessel invasion
(75.0% vs 35.9%; P < .001), large-vessel invasion (69.2% vs

Table 2. Rates of Radial Margin Positivity Stratified by Pathological Stage

<table>
<thead>
<tr>
<th>Pathological Stage</th>
<th>Patients, No. (n = 984)</th>
<th>Patients With Radial Margin Positivity, No. (%)</th>
<th>P Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>162</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td>128</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>462</td>
<td>20 (4.3)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>232</td>
<td>32 (13.8)</td>
<td></td>
</tr>
<tr>
<td>N stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>581</td>
<td>7 (1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1</td>
<td>246</td>
<td>13 (5.3)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>157</td>
<td>32 (20.4)</td>
<td></td>
</tr>
<tr>
<td>M stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>904</td>
<td>34 (3.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1</td>
<td>80</td>
<td>18 (22.5)</td>
<td></td>
</tr>
<tr>
<td>AJCC stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>255</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>237</td>
<td>2 (0.8)</td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>52</td>
<td>3 (5.8)</td>
<td></td>
</tr>
<tr>
<td>IIC</td>
<td>19</td>
<td>2 (3.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IIIA</td>
<td>29</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>184</td>
<td>7 (3.7)</td>
<td></td>
</tr>
<tr>
<td>IIIC</td>
<td>96</td>
<td>20 (17.2)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>62</td>
<td>18 (22.5)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AJCC, American Joint Committee on Cancer; M, metastasis; N, node; T, tumor.
a Calculated using a χ2 test.
Table 3. Pathological Characteristics for Patients With Radial Margin Negativity and Radial Margin Positivity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients, No./Total No. (%)</th>
<th>With Radial Margin Negativity (n = 932)</th>
<th>With Radial Margin Positivity (n = 52)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>T stage 4</td>
<td>200 (21.5)</td>
<td>32 (61.5)</td>
<td></td>
<td>2.86 (2.23-3.67)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>N stage ≥1</td>
<td>362 (38.8)</td>
<td>45 (86.5)</td>
<td></td>
<td>2.23 (1.95-2.55)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>M stage 1</td>
<td>62 (6.7)</td>
<td>18 (34.6)</td>
<td></td>
<td>5.20 (3.34-8.11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>High-grade tumor</td>
<td>159/876 (18.2)</td>
<td>23/51 (45.1)</td>
<td></td>
<td>2.48 (1.78-3.47)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Table 4. Differences in Surgical Characteristics Among Patients With Radial Margin Negativity and Radial Margin Positivity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients, No./Total No. (%)</th>
<th>With Radial Margin Negativity (n = 932)</th>
<th>With Radial Margin Positivity (n = 52)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic surgery, %</td>
<td>246 (26.3)</td>
<td>8 (15.4)</td>
<td></td>
<td>0.58 (0.31-1.12)</td>
<td>.08</td>
</tr>
<tr>
<td>Conversion, %</td>
<td>23/174 (13.7)</td>
<td>3/6 (50.0)</td>
<td></td>
<td>3.78 (1.56-9.18)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivisceral resection, %</td>
<td>119 (12.8)</td>
<td>21 (40.4)</td>
<td></td>
<td>3.16 (2.18-4.58)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Surgical Outcomes

Patients with an involved radial margin who had laparoscopic index surgery had a 50% (3 in 6) chance of conversion vs 13.7% (23 in 174) in patients with negative margins (P = .01). Patients with RMP were also more often in need of multivisceral resection (40.4% vs 12.8%; P < .001); most frequently under suspicion of locally progressive disease, leading to resections of an adjacent small bowel or a gynecological resection; and were often paired with abdominal or pelvic sidewall resections or segmentectomies or histological biopsies of the liver. Patients with RMP were also more likely to have had right-sided colectomies (67.3% vs 51.9%; P = .01). The duration of the procedures was not significantly different (P = .52). However, the median duration of admission was 1 day longer in patients with RMP (6 vs 5 days; P = .006). Table 4 shows details on surgical outcomes.

Disease-Free Survival and Survival Outcomes

Patient outcomes during follow-up shown in Table 5 and Table 6 emphasize the differences in baseline staging and disease characteristics. Cumulative metastasis rates were 80.8% in patients with RMP compared with 24.4% (P < .001) in patients with radial margin negativity. Rates of local recurrence (1.9% vs 1.5%; P = .81) and distant recurrence (11.5% vs 11.4%; P = .97) were not statistically significantly different. However, recurrence rates were likely skewed owing to the considerable difference in baseline metastasis rates (Table 3) and the median follow-up duration, which was 15.5 months in patients with RMP vs 45 months in all patients (P < .001). This difference in follow-up duration was likely owing to differences in survival. In living patients, respective median follow-up durations were comparable at 49 months vs 51 months (P = .76). When focusing exclusively on patients without metastatic disease at baseline, the higher local recurrence rate in patients with RMP became noteworthy but was not statistically significant (6.3% vs 1.3%; P = .18) while distant recurrence rates became significantly higher (37.5% vs 13.1%;
Patients with RMP had a much higher overall death rate (86.4% vs 32.4%; \( P < .001 \)) as well as rates directly and uniquely attributable to colon cancer (65.4% vs 15.9%; \( P < .001 \)). The significant detrimental differences in these long-term outcomes in RMP also withstood multivariable analysis, as shown in the Cox proportional hazards model for survival adjusted for AJCC stage, age, comorbidity, smoking, and neoadjuvant chemotherapy (hazard ratio, 3.39; 95% CI, 2.41-4.77; \( P < .001 \)). Corresponding details of the multivariable analysis are shown in Table 4. To illustrate the stage-adjusted gap in survival and disease-free survival between patients with RMP and patients with radial margin negativity, survival curves based on the Cox proportional hazards survival models adjusted for baseline staging and other covariables mentioned previously are depicted in Figure 2.

### Discussion

The purpose of this study was to evaluate the effect of RMP in a cohort of 984 patients with surgically resected invasive colon cancer, focusing specifically on the association of RMP with...
Our principal finding was that RMP had a marked association with poor pathological characteristics, including more invasive tumors and a much more advanced baseline staging. This subsequently showed strong associations with hematogenous patterns of metastasis during follow-up, with significantly higher rates of liver and peritoneal metastasis, which may have been the major causes of increased mortality in this group. The analysis also showed that after adjusting for baseline AJCC stage and other significant predictors in the multivariable analysis, relative hazards of death remained more than 3 times as high in patients with RMP.

To our knowledge, this is the first study to demonstrate the effect of RMP in malignancies of the colon separately rather than including rectal cancers. Although it is a relatively low-occurrence finding, the effect of RMP on outcomes strongly magnifies its clinical effect and the relevance of our findings.

### Table 6. Multivariable Analysis of Survival and Disease-Free Survival During Follow-up

<table>
<thead>
<tr>
<th>Cox Regression Outcome</th>
<th>Univariable HR (95% CI)*</th>
<th>P Value</th>
<th>Covariables: Multivariable HR (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival duration**</td>
<td>5.58 (4.04-7.72)</td>
<td>&lt;.001</td>
<td>AJCC, age, Charlson, smoking, NeoChemo</td>
<td>3.39 (2.41-4.77)</td>
</tr>
<tr>
<td>Disease-free survival*</td>
<td>5.16 (3.68-7.23)</td>
<td>&lt;.001</td>
<td>AJCC, smoking, NeoChemo</td>
<td>2.03 (1.43-2.89)</td>
</tr>
</tbody>
</table>

* Comparing patients with radial margin positivity with patients with radial margin negativity.

* Included covariables were AJCC (P < .001), NeoChemo (P < .001), and smoking (P = .007). Excluded covariables from the model were adjuvant chemotherapy (P = .83), age (P = .23), Charlson (P = .44), sex (P = .66), and neoadjuvant radiation (P = .41).

** Included covariables were AJCC (P < .001), NeoChemo (P < .001), and smoking (P = .007). Excluded covariables from the model were adjuvant chemotherapy (P = .14).

### Figure 2. Stage-Adjusted Survival and Disease-Free Cox Proportional Hazards Curves

**A.** Multivariable Cox proportional hazards model for survival

- Overall survival, covariable-adjusted: Hazard ratio, 3.39; 95% CI, 2.41-4.77; P < .001
- Patients with an involved radial margin show significantly worse survival compared to those with an uninvolved margin.

**B.** Multivariable Cox proportional hazards model for disease-free survival

- Disease-free survival, covariable-adjusted: Hazard ratio, 2.03; 95% CI, 1.43-2.89; P < .001
- Patients with an involved radial margin show significantly worse disease-free survival compared to those with an uninvolved margin.
In rectal cancer, the phenomenon is much more studied and validated mostly because of the much higher prevalence of RMP in rectal cancer, as high as 22% in population-based studies and 28% in a single-center study prior to complete mesorectal excision and neoadjuvant treatment. With just more than 5% of patients with colon cancer with RMP, a cohort of nearly 1000 patients was necessary to have enough statistical power to demonstrate the colon cancer–specific effect of RMP.

This study had limitations. For specific subgroups of interest, we were unable to establish sufficient statistical power. In the key subgroup of patients with RMP without metastatic presentation, differences that appeared clinically significant based on percentages or point estimates did not reach statistical significance. The most noteworthy example was local recurrence, where incidence was 4 times higher in patients with RMP but not statistically significant. Considering that local recurrence is historically the main reason why circumferential margins are important in rectal resections, this lack of significance is historically the main reason why circumferential margins are important in rectal resections, and this lack of significance may be surprising. However, in the case of colonic tumors, the relatively lower overall rate of local recurrence combined with the lower incidence of RMP likely made the incidence numbers less than the statistical power threshold, potentially leading to a type II error. The number of patients with RMP was also too small to determine whether partially peritonealized segments of the colon had a relatively higher RMP rate compared with segments where the mesenteric margin was the only radial margin. Future research could explore this and evaluate whether radial margin involvement of these segments may explain why some T3N0 tumors yielded similar or even worse outcomes compared with patients with stage IIIA cancer.

This study was also inherently challenged by its retrospective nature, which despite all efforts to gather data as accurately and completely as possible, meant a few cases had to be excluded owing to the lack of data on margin status. However, the high procedure volumes of more than 100 yearly colon cancer surgeries, specimen reviews done by a small group of dedicated pathologists, and application of national guidelines and internal protocols for the processing and interpretation of specimens all mitigated interrater variability and made pathological analysis as reliable as realistically achievable.

Despite having largely comparable demographics, patients with RMP presented with much lower rates of screening and detected polyposis, reiterating the importance of screening to detect disease early and prevent degeneration to aggressive forms, especially because patients with RMP had more complex surgeries, longer admissions, and higher perioperative mortality. In terms of staging, patients with metastatic disease often had RMP and vice versa. However, one-third of patients with RMP did not have metastatic disease at baseline but had subsequently dramatically higher odds of developing metastatic disease in follow-up, along with the previously discussed noteworthy albeit not statistically significant quadruple rate of local recurrence. Patients with RMP without macroscopic metastatic disease at presentation may benefit from adjuvant chemotherapy to prevent local as well as distant recurrence, especially considering this same group also has a 4-fold increased incidence of long-term systemic metastasis. The addition of adjuvant radiotherapy could also be proposed in patients with RMP; however, because of the anatomical difficulties of this treatment approach and the high rates of systemic disease recurrence, adjuvant radiotherapy may not be prudent.

Another learning point that may be adopted from experience in rectal surgery would be the use of preoperative imaging to detect radial margin involvement. The use of magnetic resonance imaging in pelvic structures surrounding the rectum allows for a very accurate detection of circumferential involvement. As the quality of computed tomography continues to improve, it may be feasible in the future to make reliable assessments on radial margin status in the colon or, more generally, to systematically discuss and assess surrounding structures and organs in multidisciplinary tumor boards to guide surgeons toward a less improvised and more standardized multivisceral resection where needed and reduce conversion rates by preemptively abandoning laparoscopic approaches in these complex multivisceral surgeries. Future research could also explore the use of neoadjuvant chemotherapy if RMP is detected preoperatively.

Conclusions
Radial margin positivity is an unequivocally poor prognostic factor in colon cancer and is a strong predictor of recurrence and mortality. Although a relatively infrequent occurrence, it has important consequences for patient outcomes. Radial margin positivity must be a standard element of any preoperative assessment as well as the postoperative pathological assessment. Indications of radial margin involvement in preoperative imaging should weigh heavily in the planned operative approach as well as any decision regarding adjuvant therapy and may justify the development of specific standardized treatment approaches.
manuscript; and decision to submit the manuscript for publication.

Previous Presentation: This paper was presented at the 95th Annual Meeting of the New England Surgical Society; September 12, 2014; Stowe, Vermont.

Disclaimer: The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, or the National Institutes of Health.

REFERENCES


Invited Commentary

The Role of the Radial Margin: Further Call for Standardization of Colon Cancer Care

Jonathan Efron, MD

Amri and colleagues have provided a retrospective review on the effect of margin positivity on survival among patients with colon cancer. They have found that, although rare, radial margin positivity is associated with a higher recurrence rate, an increased risk of death, and a shorter survival. At first, the concept seems foreign. Generally, it is rare that a colon cancer should have a positive radial margin (unlike rectal cancer, in which the resection margins are limited by bony structures) because most structures adjacent to the colon are resectable. However, in this study, a radial positive margin was shown to be an independent predictor of survival.

In some ways, the data are not new. Gunderson et al examined the Surveillance, Epidemiology, and End Results database in 2010 and found that patients with T2N2a tumors have a prognosis that is similar to that of patients with T4aN0 tumors. T4a tumors are those that perforate the visceral peritoneum. The institutional study by Amri and colleagues provides a justification for the population review of Gunderson et al. Both studies stress the importance of a meticulous pathological evaluation of surgical technique.

Given the finding, it is therefore essential that all colon cancers are evaluated, just like rectal cancers, by the pathologist in a standard format, generating standard reports. We have known for some time that the evaluation of all resected lymph nodes is essential to adequately staging colon cancers and predicting patient outcomes. The same diligence that is currently advocated for rectal cancer is now required for the workup and evaluation of colon cancer.

It is the biology, genetic makeup, and epigenetic interaction of the tumors that ultimately predict survival. As our knowledge of the genetics of colorectal cancer continues to evolve at breakneck speed and as the cost of performing the analysis continues to decrease, one can only hope that the abovementioned tumor biology, and not classic TNM staging, will be used to predict survival.