Guideline for Optimization of Colorectal Cancer Surgery and Pathology

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for the Expert Panel on Colon and Rectal Cancer Surgery and Pathology

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Background and Objectives: There is evidence of gaps in care for colorectal cancer surgery related to obtaining negative resection margins and lymph node assessment. Recommendations on the surgical and pathological management of curable colon and rectal cancer were developed.

Methods: A systematic review on colorectal resection margins and lymph nodes was conducted. This evidence, combined with evidence from existing guidelines and expert consensus, was used to develop recommendations. The draft guideline was reviewed by an expert panel and was externally reviewed by practitioners in Ontario, Canada.

Results: The search of the recent literature identified 107 articles pertinent to resection margins and lymph node assessment. The majority of the evidence was of poor quality. Of the 63 practitioners who reviewed the guideline, 97% agreed with the draft recommendations and 92% thought that the report should be approved as a practice guideline.

Conclusions: Achieving optimized performance concerning margin status and lymph node assessment requires the coordinated efforts of surgeons and pathologists, as well as other medical professionals. Focus should be on ensuring that colorectal cancers are resected with negative (R0) margins and that an adequate number of lymph nodes are assessed to allow for accurate decision making relating to prognosis and adjuvant therapy. J. Surg. Oncol. 2010;101:5–12. © 2009 Wiley-Liss, Inc.

KEY WORDS: resection margins; lymphadenectomy; practice guideline

BACKGROUND

Colorectal cancer is a highly incident cancer, resulting in the second highest rate of cancer mortality for both males and females combined in Canada [1]. Surgical resection remains the cornerstone of curative management of colorectal cancer and this is performed by a wide range of surgeons. Pathological assessment is inextricably linked to surgical management and communicates the tumor extent (T-stage) and the absence or presence and number of lymph node metastases (N-stage). In addition, pathological assessment defines the quality of surgical management, including critical information on the completeness of resection (R-stage) [2]. This information, together with preoperative, intraoperative, and postoperative assessment for metastases (M-stage) is essential for accurate staging, treatment planning, and prediction of prognosis. Surgical and pathological management and assessment are complemented by radiologic assessment and medical and radiation oncology evaluation and/or management. A host of professionals working in close communication, with co-ordinated collaboration, are required to achieve optimal results [3,4].

There is evidence of shortcomings in aspects of colorectal cancer care relating to resection margins and lymph node assessment. Evidence suggests that some resections are suboptimal, resulting in lower survival rates. In a subset of cases, this gap results from errors in judgment preoperatively and intraoperative decision making [5]. Similarly, lymph node assessment of colorectal cancers often falls short of optimal levels despite the existence of evidence that higher lymph node counts are associated with improved staging [6] and survival [7–9]. Furthermore, pathology reporting may fail to comment on status of margins.

Cancer Care Ontario (CCO), which is the principal advisor to the Government of Ontario on cancer prevention, screening, and treatment, has made quality improvement a top priority. In an effort to improve gaps

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Received 31 March 2009; Accepted 17 July 2009
DOI 10.1002/jso.21395
Published online in Wiley InterScience (www.interscience.wiley.com).

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in quality of care, the CCO Surgical Oncology Program developed a guideline entitled “Optimization of Surgical and Pathological Quality Performance in Radical Surgery for Colon and Rectal Cancer,” in collaboration with CCO’s Program in Evidence-Based Care (PEBC) [10]. The recommendations, developed using a standardized approach, are based on evidence identified in existing guidelines, a review of the recent evidence, and expert consensus. It is anticipated that the guideline will form the basis of quality improvement efforts in Ontario pertaining to the management of patients undergoing radical surgery for curable colorectal cancer. This article outlines the process of guideline development and its major conclusions.

METHODS

This guideline was developed to provide advice on the management of a narrowly defined but common patient population. The recommenda-
dations apply to all patients with curable colon and rectal cancer in whom surgical management with curative excision is undertaken. This may include selected patients with M1 disease. In this guideline, curative surgery refers to resection of the luminal aspect of the intestine as well as the adjoining lymph node bearing tissues (mesorectum and mesocolon).

This is relevant to the majority of colorectal cancers. The guideline does not apply to patients with primary cancers that are managed by polypectomy or full thickness transanal excision, patients treated for recurrent tumors, or patients undergoing surgery with palliative intent.

In creating the guideline, the specific issues to be addressed by the authors included:

1. The recommended technique and extent of surgical resection for curable colorectal cancer, including extent of bowel resection, extent of lymph node resection, and surgical documentation requirements.
2. The recommended approach to pathological processing and reporting the resected specimen, including specimen marking in the operating room, as well as processing and reporting requirements in the pathology laboratory.

The methodology used to develop the guideline is well established and has been repeatedly used by CCO and the PEBC [11]. Key features of the process include a systematic literature review, rigorous examination of the evidence, engagement of a wide range of stakeholders, and external review by practitioners for whom the guideline is relevant. Evidence was selected and reviewed by PEBC methodologists and data abstraction was verified through a data auditing procedure. Authors disclosed information on potential conflicts of interest. The PEBC is editorially independent of CCO and the Ontario Ministry of Health and Long-term Care.

Adaptation of Existing Guidelines

Adaptation methodology allows for the incorporation of previous evidence-based guidelines as a basis for the development of a more contemporary guideline. For the development of this guideline, a systematic scoping review was conducted to identify contemporary guidelines of interest. The “Guidelines 2000 for colon and rectal cancer surgery” sponsored by the National Cancer Institute (NCI) and developed by Nelson et al. [12] was identified and chosen as a basis on which to build the evidence for this guideline. The NCI Guidelines 2000 were assessed for quality independently by three reviewers, using the AGREE instrument [13].

Study Selection Criteria

Studies were considered eligible for inclusion if they reported comparative outcome data for resection margin status or length, TME versus conventional surgery, inadvertent perforation versus no perforation, high versus low ligation, number of lymph nodes analyzed, or presence of occult tumor cells in lymph nodes. For studies reporting data for patients who received en bloc multivisceral resection, non-comparative data were also considered for inclusion. Case reports, narrative reviews, articles published in a language other than English, and studies of patients undergoing surgical resection for recurrent colorectal tumors were excluded. To be considered for inclusion, studies had to report at least one of the following outcomes of interest: local recurrence, disease-free survival, or overall survival.

Development of Recommendations

The foundation for the surgical recommendations is the NCI Guidelines 2000 document [12] and the systematic review of the evidence published between 1999 and 2007. Recommendations for the pathology issues are based on a systematic review of the published literature up to 2007, as well as a review of four key articles in the field [14–17]. Where evidence was not available or was not sufficient to reach definitive conclusions, recommendations are based on the consensus of the Expert Panel on Colon and Rectal Cancer Surgery and Pathology (Expert Panel).

Internal Review

Prior to submission of the draft report for external review, the draft report was reviewed by the Expert Panel, comprised of eight surgeons, three pathologists, one administrator, and methodologists. In addition, the report was reviewed by the PEBC Report Approval Panel, which consists of two members, including an oncologist with expertise in clinical and methodology issues.

External Review

Following approval of the draft systematic review and practice guideline by the Expert Panel and the PEBC Report Approval Panel, the document was distributed through a mailed survey to health care providers in Ontario, Canada for review and feedback. A sample of 168 practitioners (92 surgeons, 48 pathologists, 12 radiation oncologists, and 16 medical oncologists) received the survey, which consisted of items evaluating the methods, results, and interpretation of the evidence used to inform the draft recommendations, questions about whether the draft recommendations should be approved as a practice guideline, and questions related to guideline implementation; written comments were invited. The survey was mailed on December 10, 2007 and follow-up reminders were sent to non-responders at 4 and 6 weeks. The Expert Panel reviewed the results of the survey.

Journal of Surgical Oncology
RESULTS

Literature Search Results

The literature search of the recent evidence (subsequent to the NCI Guidelines 2000 [12]) identified 107 articles regarding issues pertinent to resection margins and lymph node assessment. Additional details regarding the literature search results, including evidence summary tables, can be found in the full text of the guideline report at www.cancercare.on.ca [10].

Quality of the Evidence

The NCI Guidelines 2000 [12] were assessed for quality independently by three reviewers, using the AGREE instrument [13]. While the guideline scored well for the Scope and Purpose and Clarity and Presentation domains, it scored lower for the Stakeholder Involvement, Applicability, and Editorial Independence domains. These lower scores were due in part to the fact that patients’ views and preferences were not sought, the guideline was not piloted among target users, potential costs, and barriers to implementation were not discussed, and editorial independence from the funding body and conflicts of interest were not explicitly stated. Problems in the domain of Rigour of Development included the lack of details regarding strategies used to search for the evidence, unclear criteria for including or excluding evidence, no description of external review of the guideline by experts not involved in developing the guideline, and no procedure reported for updating the guideline. Despite these issues, the authors did not feel that these shortcomings should preclude the use of this guideline as a basis for the current update of the evidence. In general, the quality of the available evidence was poor. No RCTs have been performed to specifically address the extent of tumor resection, resection margins, extent of lymphadenectomy, or lymph node evaluation techniques. The evidence on which recommendations are based is limited to retrospective reviews of charts or databases, subgroup analyses of RCTs, and non-randomized prospective studies. In evaluating the evidence, it is important to take the inherent limitations of these study designs into consideration. The available studies were often small and underpowered to detect statistically significant differences in relevant outcomes between patient subgroups. As these studies were not controlled, confounding factors such as adjuvant therapy and patient baseline characteristics could often not be taken into account. Statistical methods used to determine the effect of surgical and pathological variables on outcome varied between studies and are therefore difficult to compare. In addition, details regarding pathological techniques for the assessment of resection margins and evaluation of lymph nodes were frequently not reported.

Guideline Recommendations, Evidence Summary, and Consensus

Guideline recommendations are framed around issues in surgery and pathology and considered for each of colon and rectum as these two sites differ sufficiently with respect to anatomy, tumor biology and therapeutic standards. Below, the recommendations and key aspects of the evidentiary base are summarized. The full text of the guideline report can be found at www.cancercare.on.ca [10].

Tumor extent and margin guidelines

Surgery. Presence of tumor 1 mm or less from a radial margin (surgically cut margin) should be considered a positive resection margin. Surgeons must preoperatively consider the expected R status at the end of an operation. Clinical (e.g., evidence of tumor tethering or fixation on physical examination) and radiological (e.g., cross-sectional imaging with magnetic resonance imaging [MRI] or computed tomography [CT]) assessment is necessary to identify lesions that may have a threatened or involved radial margin. Patients with such a presentation should be considered for neoadjuvant therapy and/or multimodal resection. Close consultation between the surgeon and the pathologist is required in the postoperative assessment of margins.

Colon resection margins. Negative margins are the goal of colon resection. Studies reporting outcomes as a function of length of colon resected are limited, therefore recommendations on proximal and distal colon resection margins are based on expert consensus. An adequate minimum length for proximal and distal colon resection margin is 5 cm, although they are generally much greater. The primary determinant of the extent of colon resection is the need for adequate removal of associated lymph nodes which ostensibly follow the arterial supply to the removed segment [12].

Radial, non-peritonealized negative resection margins of >1 mm of the colon should be obtained and must be histologically free of disease (R0) to achieve a curative resection. When the tumor has involved a free serosal surface but is not adherent to adjacent structures, the margin is not considered positive.

Ideally, locally advanced adherent tumors should be diagnosed preoperatively through appropriate application of cross-sectional imaging, especially CT scanning, and should be assumed to be malignant in curative–intent operations. En bloc resection of adherent organs or parts of organs should be done where possible to obtain a R0 excision. If a surgeon finds a locally advanced, adherent tumor in an otherwise curable patient and is not prepared to perform a multivisceral resection, then consideration should be given to either aborting the operation or creating a proximal stoma and then referring the patient for multidisciplinary opinion regarding possible neoadjuvant therapy and more radical surgery.

The specimen must be labeled by the surgeon and areas of possible radial margin involvement, particularly segments not typically associated with a radial margin (e.g., transverse colon), should be marked for correct identification by the pathologist.

Rectal resection margins. Negative margins are the goal of rectal resection. The primary determinant of the extent of resection of the proximal rectum is the technical considerations for obtaining adequate lymphadenectomy and reconstruction. The available data for distal margin length are conflicting; however, the majority of studies demonstrate improved outcome with greater margin lengths [12,18–24]. For tumors of the proximal and mid rectum resected for curative intent, the distal margin length should be a minimum of 5 cm from the distal edge of the primary tumor to remove positive lymph nodes that are distal to the palpable leading edge of the tumor. The mesorectum and bowel must be transected transversely to avoid coning towards the distal resection margin and possible loss of lymph node tissue distal to the primary tumor. For tumors at or below the end of the mesorectum, ideally a distal margin length of 2 cm in the fresh specimen should be obtained, not including the circular stapler donut. In expert hands, a negative margin of less than 2 cm can be oncologically adequate to facilitate very low colorectal re-anastomosis. A negative distal margin must not be compromised in an effort to avoid a permanent colostomy. Abdominoperineal resection (APR) is indicated for patients in whom the rectal tumor invades or very closely encroaches upon the external anal sphincter.

A circumferential resection margin (CRM) is present in the mid-lower rectum, while the upper rectum has a peritonealized anterior surface and a non-peritonealized posterior radial margin similar to the ascending and descending colon. Thus, tumor extending to the peritonealized surface does not constitute a positive CRM. All rectal cancers should undergo preoperative workup to assess the extent to which the CRM is threatened. This includes pelvic CT or MRI and, for lesions within reach of the examining finger, a digital rectal exam. The CRM is positive if the tumor is located 1 mm or less from the cut edge of the specimen. The recommendation for a minimum CRM length of
1 mm is supported by the majority of the studies reviewed, with the exception of one study which recommended a minimum length of 2 mm [25]. The evidence consistently demonstrated improved outcome in patients with a negative CRM compared with those with an involved margin [25–28].

For lesions that are clinical stage II (i.e., T3 or T4) or III (i.e., likely positive lymph nodes on cross-sectional imaging), neoadjuvant therapy is recommended unless there are contraindications. Such preoperative determinations demand a high-quality MRI and, ideally for T status, a trans-rectal ultrasound [29]. Adherent rectal cancers should be diagnosed preoperatively and en bloc resection may be required to obtain an R0 resection in such cases.

**Total mesorectal excision (TME).** For rectal cancer, the technique of TME using sharp dissection under direct visualization in the plane between the parietal fascia of the pelvis and the visceral fascia of the mesorectum should be performed. Careful dissection in this plane offers protection to the pelvic autonomic nerves, which traverse under the parietal fascia, and offers the best chance for local tumor control. The goal of surgery should be wide anatomic resection to obtain radial clearance of the primary tumor and lymphatic, vascular, and perineural tumor deposits in the mesorectum, preserving the integrity of the mesorectal fascia propria. Eight studies were identified in the literature that compared TME versus conventional resection [19,30–36]. All eight studies demonstrated lower local recurrence rates for patients who underwent TME; however, not all were able to demonstrate a statistically significant difference between groups and none of the comparisons were randomized. There is evidence that tumors rarely extend in the bowel wall distal to their palpable edge, but deposits in lymph nodes 2–4 cm distal to the palpable edge of a tumor have been observed in a very small percentage of cases. While tumors of the high rectum do not require TME, the same operative technique with sharp dissection should be performed. In all cases at least 5 cm of mesorectum distal to the leading edge of the tumor should be removed if possible. Coning-in, or breaching the visceral fascia proximal or just distal to the tumor, should be avoided in both partial and TME to ensure the removal of all mesorectal nodes that are distal to the leading edge of the tumor.

**En bloc multivisceral resection.** Locally advanced, adherent colorectal tumors should be dissected en bloc with histologically negative margins for the resection to be considered adequate. If a tumor is transected at the site of local adherence, resection is not complete. If a surgeon finds a locally advanced, adherent tumor in an otherwise curable patient and is not prepared to perform a multivisceral resection, then consideration should be given to either aborting the operation or creating a proximal stoma and then referring the patient for multidisciplinary opinion regarding possible neoadjuvant therapy and more radical surgery. The evidence comparing en bloc multivisceral resection with standard resection is limited; however, the evidence in general suggests that multivisceral resection of adherent structures can result in satisfactory survival outcomes when negative margins are achieved [12,37].

**Inadvertent tumor perforation.** Every effort should be made to avoid inadvertent perforation of the colon or rectum during dissection. There is evidence to suggest that inadvertent perforation at the site of the tumor results in increased risk of local recurrence and decreased survival [12,38,39]. Inadvertent perforation should be documented in the operative report and the pathology requisition form.

**Pathology.**

**Colon resection margins.** The surgeon should communicate with the pathologist regarding the orientation of the specimen. Proximal and distal margins should be sampled for histological examination. The distance of the tumor to the proximal and distal margins should be reported in the fresh state, if possible. Measurement in the fixed state must take into account the fact that shrinkage will have occurred; pinning the fresh specimen to a board, under tension,

**Rectal resection margins.** Proximal and distal margins should be sampled for histological examination. Pathologists should pay close attention to mesorectal soft tissue, in addition to the mucosa, when assessing the distal margin.

Rectal cancer specimens should be assessed grossly by the pathologist using the method developed by Quirke [40]. The mesorectal tissue that constitutes the CRM, including all non-peritonealized bare areas anteriorly and posteriorly, should be inked.

The specimen should be fixed with the tumor segment unopened 5 cm above and below the proximal and distal edges of the tumor, respectively, and a gauze wick placed into the unopened segment to facilitate fixation. Following at least 48 hr of fixation, the segment with the tumor should be sliced into transverse sections. The relationship of the tumor to the CRM must be carefully assessed [41].

The CRM distance must be reported. The CRM is positive if the tumor is located 1 mm or less from the margin; this includes tumor cells within a lymph node, vein, or nerve, as well as direct tumor extension.

Note that tumors of the upper rectum have a peritonealized anterior surface and a non-peritonealized posterior (non-circumferential) radial margin similar to the ascending and descending colon.

**Serosal penetration.** Involvement of the serosa by tumor (pT4) is not equivalent to involvement of the radial margin by tumor (although there are circumstances in which an advanced tumor has penetrated the serosa and is adherent to adjacent soft tissue). Documentation of serosal involvement by tumor requires careful gross and microscopic examination and may require extensive sampling and/or serial sectioning of sampled tissue blocks. Gross clues to the presence of serosal penetration include: retraction/puckering, prominent blood vessels, granularity, exudate, and loss of the normal shiny serosal surface. Serosal penetration is defined as occurring when any of the following criteria are met:

1. Free tumor cells are present on the serosal surface with underlying ulceration.
2. Tumor is present at the serosal surface with an associated inflammatory reaction, mesothelial hyperplasia, and/or erosion or ulceration.

If tumor cells are not present at the serosal surface, but are close (within 1 mm), the tumor should be staged as T3 but a comment made that possible peritoneal involvement may be present. Serosal penetration is an independent prognostic variable and has a strong negative impact on prognosis [42,43]. The frequency of distant metastasis is greater in cases with perforation of the visceral peritoneum compared to cases with direct invasion of adjacent organs or structures without perforation of the visceral peritoneum, and the median survival time following surgical resection for cure is shorter for the former versus latter presentation (with or without distant metastasis).

**Lymph node assessment guidelines.**

**Surgery.**

**Extent of lymphadenectomy.** The goal of colon resection is the removal of the segment of the bowel with the tumor and all the mesentery containing the blood supply and the lymphatics at the level of the primary feeding arterial vessel (e.g., ileocolic, middle colic, left
When the primary tumor is equidistant from two feeding vessels, both vessels should be excised close to their origin. More radical lymphadenectomy is not supported by available evidence [12,44,45]. In curative operations, lymph node resection must be en bloc with the main vessel supplying the involved segment of colon. Lymph nodes at the origin of feeding vessels (apical nodes) should be included when feasible and tagged for pathologic evaluation. Appropriate proximal lymphatic resection and TME of the rectum provides adequate lymphadenectomy for rectal cancer. There is a lack of evidence about the benefit of ligating the IMA at its origin at the aorta, although nodes should be removed as high as technically possible to allow for complete removal of clinically involved nodes. Suspicious periaortic nodes should be biopsied for staging. The surgeon should report the named vessel and lymph node basin resected en bloc. Clinically suspicious nodes should be reported, and any lymph nodes outside the resected basin that are suspicious and biopsied should be reported.

**Number of lymph nodes assessed.** In general, and particularly for clinical T3/4 neoplasms, a minimum of 12 lymph nodes should be examined for colon and rectal cancer resection specimens, although an effort should be made to include all lymph nodes. There is ample evidence that survival increases with higher numbers of lymph nodes assessed [7,12]. The underlying mechanism is thought to be improved staging accuracy and subsequent improved use of adjuvant chemotherapy, though there is some controversy in this area [46]. Importantly, the 12-lymph node target may not be achievable in patients with T1 or T2 tumors and/or some patients who received neoadjuvant therapy. In summary, expert consensus supports a recommendation that a minimum of 12 lymph nodes be examined. This is consistent with recommendations in the NCI Guidelines 2000 [12].

### Pathology

**Technique of lymph node examination.** Pericolic fat should be carefully examined using inspection and palpation. For colonic tumors, examination should occur after pericolic fat has been stripped off the colon and after any appropriate sections have been taken to evaluate the radial margin. In the case of rectal tumors, the cross-sectional slices are examined for lymph nodes, taking care not to double count lymph nodes that might be present in more than one cross-sectional slice. All lymph nodes present must be examined histologically. Nodal examination must not stop once 12 nodes have been identified. It is particularly important to find small lymph nodes close to the underlying bowel wall. If less than 12 lymph nodes are found, consideration should be given to placing the fat into a lymph node highlighting solution. All grossly negative or equivocal lymph nodes must be submitted in their entirety. However, if a node is grossly positive, partial submission is acceptable.

**Lymph node assessment.** The pathology report should indicate the number of positive lymph nodes as well as the total number of nodes assessed. The number of lymph nodes involved by micrometastases (tumor deposits >0.2 mm but <2.0 mm) and isolated tumor cells (ITCs) (single cells or clusters 0.2 mm or less) should be reported separately from typical (macro) metastases. Micrometastases without typical (macro) metastases detected by routine histology are reported as pN1, whereas immunohistochemical detection is reported as pN0. The presence of ITCs does not affect the pN classification. Note that special measures to detect micrometastases or ITCs (e.g., multiple tissue levels of paraffin blocks, immunohistochemistry, polymerase chain reaction) are not recommended for the routine examination of regional lymph nodes [17].

### TABLE I. External Reviewers’ Responses to Selected Survey Questions

<table>
<thead>
<tr>
<th>Survey item</th>
<th>Rated “strongly agree” or “agree”</th>
<th>Rated “neither agree nor disagree”</th>
<th>Rated “disagree” or “disagree strongly”</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is a need for a guideline on this topic</td>
<td>61 (97)</td>
<td>2 (3)</td>
<td></td>
</tr>
<tr>
<td>The literature search is relevant and complete (i.e., no key trials were missed nor any included that should not have been)</td>
<td>52 (85)</td>
<td>9 (15)</td>
<td></td>
</tr>
<tr>
<td>I agree with the methodology used to summarize the evidence</td>
<td>57 (92)</td>
<td>5 (8)</td>
<td></td>
</tr>
<tr>
<td>The results of the trials described in the draft report are interpreted according to my understanding of the data</td>
<td>60 (98)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>The draft recommendations in the report are clear</td>
<td>61 (98)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>I agree with the draft recommendations as stated</td>
<td>60 (97)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>This draft report should be approved as a practice guideline</td>
<td>55 (92)</td>
<td>4 (7)</td>
<td></td>
</tr>
<tr>
<td>To apply the draft recommendations would require an increase in pathology technical staff</td>
<td>25 (41)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>To apply the draft recommendations would require training/mentoring of surgeons</td>
<td>45 (75)</td>
<td>11 (18)</td>
<td></td>
</tr>
<tr>
<td>Which do you foresee as the biggest obstacles to implementing these recommendations in your hospital setting?</td>
<td>23 (39)</td>
<td>21 (36)</td>
<td></td>
</tr>
<tr>
<td>Not enough pathologists</td>
<td>29 (49)</td>
<td>22 (37)</td>
<td></td>
</tr>
<tr>
<td>Not enough pathologist assistants</td>
<td>6 (10)</td>
<td>22 (38)</td>
<td></td>
</tr>
<tr>
<td>Not enough surgeons</td>
<td>6 (10)</td>
<td>22 (38)</td>
<td></td>
</tr>
<tr>
<td>Lack of training (technical skills)</td>
<td>15 (26)</td>
<td>21 (37)</td>
<td></td>
</tr>
<tr>
<td>Too many other competing priorities</td>
<td>17 (29)</td>
<td>16 (28)</td>
<td></td>
</tr>
<tr>
<td>Poor collaboration between surgeons and pathologists</td>
<td>16 (27)</td>
<td>16 (27)</td>
<td></td>
</tr>
<tr>
<td>I see myself playing an active role in contributing towards the implementation of this guideline</td>
<td>37 (73)</td>
<td>11 (22)</td>
<td></td>
</tr>
<tr>
<td>If the draft report were to become a practice guideline, how likely would you be to make use of it in your own practice?</td>
<td>55 (92)</td>
<td>3 (5)</td>
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</tbody>
</table>

*Journal of Surgical Oncology*
### Tumor extent and margin recommendations

#### Surgery

- ** Colon resection margins
  - Presence of tumor 1 mm or less from a margin should be considered a positive resection margin
  - Negative margins are the goal of colon resection
  - An adequate minimum length for proximal and distal colon resection margins is 5 cm, although they are generally much greater
  - Radial, non-peritonealized negative resection margins of the colon should be obtained and must be histologically free of disease to achieve a curative resection
  - The specimen must be labeled by the surgeon and areas of possible radial margin involvement should be marked for correct identification by the pathologist

- ** Rectal resection margins
  - Negative margins are the goal of rectal resection
  - For tumors of the proximal and mid rectum, the distal margin length should be a minimum of 5 cm. For tumors at or below the end of the mesorectum, ideally a distal margin length of 2 cm in the fresh specimen should be obtained; however, in expert hands, a negative margin of less than 2 cm can be adequate to facilitate very low colorectal re-anastomosis. A negative distal margin must not be compromised in an effort to avoid a permanent colostomy. Abdominoperineal resection (APR) is indicated for patients in whom the rectal tumor invades or very closely encroaches upon the external anal sphincter
  - A circumferential radial margin (CRM) should be considered positive if the tumor is located 1 mm or less from the cut edge of the specimen

- ** Total mesorectal excision (TME)
  - For rectal cancer, the technique of TME using sharp dissection under direct visualization in the plane between the parietal fascia of the pelvis and visceral fascia of the mesorectum should be performed

- ** En bloc multivisceral resection
  - Locally advanced, adherent colorectal tumors should be dissected en bloc with histologically negative margins for resection to be considered adequate. If a tumor is transected at the site of local adherence, resection is not complete

- ** Inadvertent tumor perforation
  - Every effort should be made to avoid inadvertent perforation of the colon or rectum during dissection. Inadvertent perforation should be documented in the operative report and the pathology requisition

#### Pathology

- ** Colon resection margins
  - Proximal and distal colon margins should be sampled for histological examination
  - The distance from the tumor to the proximal and distal margins should be reported in the fresh state, if possible
  - If the tumor is close to a margin, the distance between the tumor and the margin of concern should be reported as measured microscopically on the glass slide
  - The radial margins of the resected specimen should be inked and sectioned. The radial margin distance must be reported and should be reported as positive if tumor is located 1 mm or less from the inked non-peritonealized surface of the specimen

- ** Rectal resection margins
  - Proximal and distal rectal margins should be sampled for histological examination
  - All rectal cancer specimens should be assessed grossly by the pathologist using the method developed by Quirke. The mesorectal tissue that constitutes the CRM should be inked. The specimen should be fixed with the tumor segment unopened 5 cm above and below the proximal and distal edges of the tumor and a gauze wick placed into the unopened segment to facilitate fixation. Following at least 48 hr of fixation, the segment with the tumor should be sliced into transverse sections
  - The relationship of the tumor to the CRM must be carefully assessed and the CRM distance must be reported. The CRM is positive if the tumor is located 1 mm or less from the margin; this includes tumor cells within a lymph node, vein, or nerve, as well as direct tumor extension
  - Involvement of the serosa by tumor (pT4) is not equivalent to involvement of the radial margin by tumor. Documentation of serosal involvement by tumor requires careful gross and microscopic examination and may require extensive sampling and/or serial sectioning of sampled tissue blocks

- ** Serosal penetration
  - Involvement of the serosa by tumor (pT4) is not equivalent to involvement of the radial margin by tumor. Documentation of serosal involvement by tumor requires careful gross and microscopic examination and may require extensive sampling and/or serial sectioning of sampled tissue blocks

### Lymph node assessment recommendations

#### Surgery

- ** Extent of lymphadenectomy
  - The goal of colon resection is the removal of the segment of the bowel with the tumor and all the mesentery containing the blood supply and the lymphatics at the level of the primary feeding arterial vessel. More radical lymphadenectomy is not supported by available evidence
  - Appropriate proximal lymphatic resection and TME of the rectum provides adequate lymphadenectomy for rectal cancer
  - Clinically suspicious nodes should be reported, and any lymph nodes outside the resected basin that are suspicious and biopsied should be reported

- ** Number of lymph nodes
  - In general, and particularly for T3/4 tumors, a minimum of 12 lymph nodes should be examined for colon and rectal cancer resection specimens, although an effort should be made to identify all lymph nodes

#### Pathology

- ** Technique of lymph node examination
  - All lymph nodes present must be examined histologically; nodal examination must not stop once 12 nodes have been identified. If less than 12 lymph nodes are found, consideration should be given to placing the fat into a lymph node highlighting solution
  - All grossly negative or equivocal lymph nodes must be submitted in their entirety; however, if a node is grossly positive, partial submission is acceptable

- ** Lymph node assessment
  - The pathology report should indicate the number of positive lymph nodes as well as the total number of nodes assessed
  - The number of lymph nodes involved by micrometastases and isolated tumor cells (ITCs) should be reported separately from macrometastases. Special measures to detect micrometastases or ITCs (e.g., multiple tissue levels of paraffin blocks, immunohistochemistry, polymerase chain reaction) are not recommended for the routine examination of regional lymph nodes
A tumor nodule in the pericolonic/perirectal fat without histologic evidence of residual lymph node tissue is classified as a lymph node replaced by tumor if the nodule has the form and smooth contour of a lymph node. If the nodule has an irregular contour, the nodule should be classified as a discontinuous extramural extension, pT3 (based on the AJCC/UICC TNM 6th edition) [3].

**Internal Review**

The PEBC Report Approval Panel reviewed the guideline and provided feedback on the draft. Several key issues were raised by the Panel. One reviewer commented that the structure of the recommendations section should be reworked to separate key recommendations for which there is supporting evidence from technical and process recommendations, which are in general based on Expert Panel consensus. One reviewer requested that the AGREE instrument [13] be used to assess the quality of the guidelines on which the document is based. Another reviewer suggested that the authors clarify that the outcomes of interest driving recommendations are local recurrence and survival. The reviewer also suggested that the authors consider providing statements about the adverse effects associated with different surgical approaches. Feedback from the Report Approval Panel was incorporated into the draft guideline prior to external review by Ontario practitioners [10].

**External Review**

From among the 168 surveys sent, 80 responses were received (48% response rate). Of the practitioners who responded, 63 indicated that the report was relevant to their clinical practice and completed the survey. Responses were generally positive and reflected the view that the guideline was practical and the conclusions reached were sound. Table I presents the response of practitioners to some key survey questions. Written comments were received from 33% of practitioners who responded to the survey. The comments were reviewed by the Expert Panel and applied to the final wording of the guideline. Additional details on the comments received and the modifications made to the recommendations in response to those comments can be found in the full guideline report [10].

Several barriers to implementation of the guideline, in addition to those listed in Table I, were identified by external reviewers. These included availability of preoperative imaging, submission of fresh specimens at appropriate times, and communication between surgeons and pathologists regarding circumferential radial margins, serosal adhesions, and identification of proximal and distal margins.

**CONCLUSIONS**

The guideline process successfully resulted in the development of a guideline focusing on surgical and pathology issues relevant to the curative surgical management of colorectal cancer. The key recommendations are summarized in Table II. The strength of the guideline arises from the rigorous, often reproduced methodology from which it was created. The conclusions differed little if at all from Nelson et al. [12]. Importantly, the process identified a rich spectrum of new literature to help inform the conclusions.

Guidelines in and of themselves are relatively weak tools for knowledge translation [47]. Nonetheless, they may form an important basis for broader implementation strategies; this is the plan for this guideline. Gaps in colorectal cancer care exist and are postulated to arise from the rigorous, often reproduced methodology from which it is based. Another reviewer suggested that the authors consider providing statements about the adverse effects associated with different surgical approaches. Feedback from the Report Approval Panel was incorporated into the draft guideline prior to external review by Ontario practitioners [10].

**REFERENCES**


