

Evidence-Based Series 17-4 Version 2

A Quality Initiative of the Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)

Optimization of Surgical and Pathological Quality Performance in Radical Surgery for Colon and Rectal Cancer: Margins and Lymph Nodes

The Expert Panel on Colon and Rectal Cancer Surgery and Pathology

An assessment conducted in November 2024 deferred the review of Evidence-Based Series 17-4 Version 2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol).

EBS 17-4 is comprised of four sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/566

- Section 1: Guideline Recommendations (ENDORSED)
- Section 2: Evidence Summary
- Section 3: EBS Development Methods and External Review Process
- Section 4: Document Assessment and Review

November 29, 2016

For information about the PEBC and the most current version of all reports, please visit the CCO website at <u>http://www.cancercare.on.ca/</u> or contact the PEBC office at: Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: <u>ccopgi@mcmaster.ca</u> **Guideline Citation (Vancouver Style):** Smith AJ, Driman DK, Spithoff K, McLeod R, Hunter A, Rumble RB, et al. Optimization of surgical and pathological quality performance in radical surgery for colon and rectal cancer: margins and lymph nodes. Driman D, Kennedy E, Kellett S, Brown J, reviewers. Toronto (ON): Cancer Care Ontario; 2008 Apr. Program in Evidence-based Care Evidence-based Series No.: 17-4 Version 2.

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Guideline Report History

GUIDELINE	SYSTEMATIC REVIEW		PUBLICATIO	NOTES AND KEY
VERSION	Search Dates	Data	NS	CHANGES
Original Version April 2008	1999-2007	Full Report	Web publication	NA
Current Version November 2016	2007-2015	New data found in section 4: Document	Updated web	2008 recommendations
		Assessment and Review	publication	ENDORSED



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Evidence-Based Series #17-4 Version 2: Section 1

Optimization of Surgical and Pathological Quality Performance in Radical Surgery for Colon and Rectal Cancer: Margins and Lymph Nodes: Guideline Recommendations

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A Quality Initiative of Cancer Care Ontario (CCO)'s Program in Evidence-Based Care (PEBC) and CCO's Surgical Oncology Program (SOP). Developed by the Expert Panel on Colon and Rectal Cancer Surgery and Pathology

November 29, 2016

These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Assessment and Review for a summary of updated evidence published between 2007 and 2015, and for details on how this Clinical Practice Guideline was ENDORSED.

QUESTIONS

- 1. What is the recommended technique and extent of surgical resection for curable colorectal cancer (CRC), including extent of bowel resection, extent of lymph node resection, and reporting requirements?
- 2. What is the recommended approach to processing and reporting the resected specimen, including specimen marking in the operating room, as well as processing and reporting requirements in the pathology laboratory?

TARGET POPULATION

This document applies to all patients with curable colon¹ and rectal² cancer in whom surgical management with radical excision is undertaken. This may include selected patients

¹ For the purpose of this document, colon cancers are defined as those that lie within the large intestine from the cecum to the top of the rectum.

² Rectal cancers are defined as adenocarcinomas that lie between the termination of the sigmoid colon, usually at the level of the sacral promontory, and the dentate line. The mesorectum and its enveloping mesorectal fascia end at the pelvic floor or top of the puborectalis sling, while the most distal aspect of the rectum ends at the

with M1 disease. This document does not apply to patients with primary cancers that are managed by polypectomy or full thickness transanal excision, patients treated for recurrent tumours, or patients undergoing surgery with palliative intent.

RECOMMENDATIONS

The recommendations have been organized under two categories: Surgical Issues and Pathology Issues. The foundation for the surgical recommendations is the Guidelines 2000 document sponsored by the National Cancer Institute (NCI) and authored by Nelson et al (1). This report reviews the evidence on surgical issues up to 1999 and provides recommendations based on the reviewed evidence. Section 2 contains the systematic review of the evidence is lacking, the recommendations are based on the consensus of the panel. 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 papers in the field (2-5), also presented in Section 2. The outcomes of interest behind the recommendations are local recurrence, disease-free survival, and overall survival.

The following recommendations are offered by the Expert Panel on Colon and Rectal Cancer Surgery and Pathology, organized as follows:

- 1. Staging Definitions
- 2. Tumour Extent and Margin Guidelines
 - 2.1 Surgery
 - 2.1.1 Margins of Resection: Colon
 - 2.1.2 Margins of Resection: Rectum
 - 2.1.3 Total Mesorectal Excision
 - 2.1.4 En Bloc Multivisceral Resection
 - 2.1.5 Inadvertent Tumour Perforation
 - 2.2 Pathology
 - 2.2.1 Margins of Resection: Colon
 - 2.2.2 Margins of Resection: Rectum
- 3. Lymph Node Assessment Guidelines
 - 3.1 Surgery
 - 3.1.1 Extent of Lymphadenectomy
 - 3.1.2 Number of Lymph Nodes Assessed
 - 3.2 Pathology
 - 3.2.1 Technique of Lymph Node Examination
 - 3.2.2 Number of Lymph Nodes Assessed
- 1. Staging Definitions
 - The TNM classification of tumours described by the American Joint Committee on Cancer (AJCC) (6) is recommended for tumour-staging definitions.

2. Tumour Extent and Margin Guidelines

- Resections and Positive Resection Margin Definitions
 - AJCC categorizes resections as R0: no residual tumour; R1: microscopic residual tumour; R2: macroscopic residual tumour.

dentate line. The rectum is divided into three sections: lower rectum (0-5 cm from anal verge), mid rectum (5-10 cm from anal verge) and upper rectum (10-15 cm from anal verge). Rectal tumors are classified according to their location relative to the peritoneal reflection anteriorly, i.e., entirely above, astride or entirely below the peritoneal reflection.

- Presence of tumour 1 mm or less from a 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 tumour tethering or fixation on physical exam) 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 (See Related Guidelines).
- Close consultation between the surgeon and the pathologist is required in the assessment of margins.

2.1 Surgery

2.1.1 Margins of Resection: Colon

Key Recommendation

• Negative margins are the goal of colon resection.

Key Evidence

- The NCI Guidelines 2000 cited numerous studies demonstrating better outcome for patients with margins free of residual tumour.
- In the recent literature, one retrospective study demonstrated no significant association between proximal or distal margin lengths and local recurrence or disease-free survival.

Technical Recommendations

Technical recommendations are based on Expert Panel consensus and endorsement of the NCI Guidelines 2000 and, for recommendations for radial margins, evidence supporting en bloc resection with negative margins for adherent tumours.

Proximal and Distal Margins

• The primary determinant of the extent of bowel resection is the need for adequate removal of lymph nodes and arterial supply that is consistent with the creation of a well-vascularized anastomosis. An adequate minimum length for proximal and distal colon resection margin is 5 cm, although they are generally much greater.

Radial Margins

- Radial, non-peritonealized negative resection margins of the colon should be obtained and must be histologically free of disease (R0) to achieve a curative resection. This does not apply to surfaces of the colon where the tumour has penetrated through a free serosal surface but is not adherent to adjacent structures.
- Ideally, locally advanced adherent tumours 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 (See En Bloc Multivisceral Resection).
- The specimen must be labelled 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.

2.1.2 Margins of Resection: Rectum

Key Recommendation

• Negative margins are the goal of rectal resection.

Key Evidence

- The NCI Guidelines 2000 cited numerous studies demonstrating better outcome for patients with margins free of residual tumour.
- In the recent literature, retrospective and prospective studies reported decreased local recurrence rates and increased survival in patients with negative margins compared with positive margins.

Technical Recommendations for Proximal and Distal Margins

Technical recommendations are based on the Expert Panel consensus informed by the NCI Guidelines 2000 and evidence emerging in the recent literature update. No data were found to inform proximal rectal resection margin lengths. Distal margin length of 2 cm or greater and a minimally acceptable distal margin length of 1 cm were recommended by the NCI Guidelines 2000. The evidence update yielded 19 studies reporting clinical outcomes by distal margin length or distal tumour spread and provided conflicting findings for adequate distal margin length, ranging from 1 cm to 4 cm.

Proximal Margins

• The primary determinant of the extent of resection of proximal rectum is determined by technical considerations for obtaining adequate lymphadenectomy and reconstruction. The resection margin length should be a minimum 5 cm.

Distal Margins

- The main determinants of distal margin length are adequate clearance of intramural cancer spread and adequate removal of lymph nodes in pericolic fat.
- The distal margin length should be measured in the fresh, anatomically restored ex vivo condition immediately after removal.
- The distal aspect of the tumour should be marked or carefully measured at the time of initial assessment, recognizing that this may change following preoperative therapy.
- For tumours of the proximal and mid rectum, the distal margin length should be a minimum of 5 cm from the distal edge of the primary tumour in most patients to remove positive lymph nodes that are distal to the palpable leading edge of the tumour. The mesorectum and bowel edge must be transected transversely to avoid coning towards the distal resection margin and possible loss of lymph node tissue distal to the primary tumour.
- For tumours at or below the anterior peritoneal reflection, 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. Please see Section 2 for a full discussion of this issue.
- Intraoperative evaluation of the distal margin by a pathologist may be beneficial but shortcomings of this procedure (e.g., false negative results) must be recognized.

Qualifying Statements regarding the shaded text above - Added to Endorsement in November, 2016

The original 2008 recommendation on distal margin length was modified by the expert panel. The wording "end of the mesorectum" was replaced with "below the anterior peritoneal reflection" to more clearly specify the anatomical location being discussed (see Section 4, Table 9, Modification 1 and Impact on Recommendations)

The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

General

- Abdominoperineal resection (APR) is indicated for patients in whom the rectal tumour invades or very closely encroaches upon the external anal sphincter.
- The surgeon should scrupulously and systematically document details relevant to the proximal and distal margins on the operative report.
- It is common practice to submit the circular stapler donuts for histological examination; however, histology of the donuts should not be relied on to determine margin status.

Technical Recommendations for Circumferential Radial Margins

These recommendations are informed by numerous retrospective studies and case series cited in the NCI Guidelines 2000 and the updated literature search that demonstrated the importance of negative circumferential radial margins (CRM) to minimize local recurrence and increase disease-free survival and overall survival.

- A 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.
- 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.
- Patients with rectal cancer should undergo a high resolution MRI for proper assessment of T and N category and predicted CRM to pre-operatively stage patients (1). Patients with Stage II or Stage III rectal cancer should be offered pre-operative chemoradiotherapy (1, 2)
- Adherent rectal cancers should be diagnosed preoperatively and en bloc resection may be required to obtain an R0 resection in such cases (See En Bloc Multivisceral Resection).
- The technique of total mesorectal excision (TME) should be employed (See Total Mesorectal Excision).
- The CRM is positive if the tumour is located 1 mm or less from the cut edge of the specimen.
- The surgeon should scrupulously and systematically document details relevant to the CRM on the operative report.

<u>Qualifying Statements regarding the shaded text above - Added to Endorsement</u> <u>in November, 2016</u>

The original 2008 recommendation on high resolution MRI was modified by the expert panel. The recommendation was updated to align with recommendations in EBS 17-8 and a recent systematic review (see Section 4, Table 9, Modification 2 and Impact on Recommendations)

The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

2.1.3 Total Mesorectal Excision

Key Recommendations

• 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 run under the parietal fascia, and offers the best chance for local tumour control.

Key Evidence

• Five out of seven studies comparing TME to conventional resection reported decreased local recurrence rates in patients who underwent TME.

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000.

- The goal of surgery should be wide anatomic resection to obtain radial clearance of the primary tumour and lymphatic, vascular, and perineural tumour deposits in the mesorectum, preserving the integrity of the mesorectal fascia propria.
- There is evidence that tumours 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 tumour have been observed in a low percentage of cases.
- For tumours of the proximal and mid rectum, the distal margin length should be a minimum of 5 cm from the distal edge of the primary tumour in most patients to remove positive lymph nodes that are distal to the palpable leading edge of the tumour. The mesorectum and bowel edge must be transected transversely to avoid coning towards the distal resection margin and possible loss of lymph node tissue distal to the primary tumour.
- For tumours at or below the anterior peritoneal reflection, 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. Please see Section 2 for a full discussion of this issue.
- Coning-in, or breaching the visceral fascia proximal or just distal to the tumour, should be avoided in both partial and total mesorectal excision to ensure the removal of all mesorectal nodes that are up to 5 cm distal to the leading edge of the tumour.

<u>Qualifying Statements regading the shaded text above - Added to Endorsement</u> <u>in November, 2016</u>

The original 2008 recommendations on TME was modified by the expert panel. For clarification purposes, previous text was replaced by more detailed text appearing earlier in the document (see Section 4, Table 9, Modification 3 and Impact on Recommendations)

The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

2.1.4 En Bloc Multivisceral Resection

Key Recommendations

• Locally advanced, adherent colorectal tumours should be dissected en bloc with histologically negative margins for resection to be considered adequate. If a tumour is transected at the site of local adherence, resection is not complete.

Key Evidence

- Retrospective reviews and case series demonstrated acceptable outcome in patients who underwent en bloc multivisceral resection of adherent tumours when negative resection margins were achieved.
- One large study of registry data reported improved overall survival for colon and rectal cancer patients who had multivisceral resection of locally advanced adherent colorectal cancer compared to standard resection.

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000.

- Appropriate pre-operative imaging is recommended for proper surgical planning.
- An en bloc multivisceral resection is recommended for all locally advanced tumours involving adjacent structures.
- In the uncommon event that a tumour is unexpectedly found to be adherent to other structures intra-operatively and a multivisceral resection has not been planned, then resection of the primary tumour should be avoided and a proximal stoma should be created.
- The patient should be reviewed at multidisciplinary cancer conference for further surgical planning and opinion regarding possible neoadjuvant therapy.

Qualifying Statements regarding the shaded text above - Added to Endorsement in November, 2016

The original 2008 recommendations on En Bloc Multivisceral Resection were modified by the expert panel. The original recommendations were updated to reflect the recommendations outlined in EBS 17-8 "Optimization of Preoperative Assessment in Patients Diagnosed with Rectal Cancer" and to highlighted a key point that surgeons should NOT routinely be surprised by what is encountered during surgery (see Section 4, Table 9, Modification 4 and Impact on Recommendations). The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

2.1.5 Inadvertent Tumour Perforation

Key Recommendation

• Every effort should be made to avoid inadvertent perforation of the colon or rectum during dissection.

Key Evidence

 Several retrospective reviews and database audits demonstrated increased local recurrence and decreased survival in patients who had inadvertent perforation of the bowel.

Technical Recommendation

The technical recommendation is based on the Expert Panel consensus informed by the evidence demonstrating a worse outcome for patients with inadvertently perforated tumours.

• Inadvertent perforation should be documented in the operative report and the pathology requisition form.

2.2 Pathology

2.2.1 Margins of Resection: Colon

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in four key papers in the field (2-5), as well as pathology studies identified in the recent literature search.

Proximal and Distal 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 tumour 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, will produce less shrinkage. If the tumour is close to a margin, the distance between the tumour and the margin of concern should be reported as measured microscopically on the glass slide.

Radial Margins

- The surgeon must clearly indicate to the pathologist areas with close contact to other organs or the abdominal wall. The pathologist should be aware of the retroperitoneal margin that exists in certain locations (e.g., proximal ascending colon and descending colon).
- The radial margins of the resected specimen should be inked and sectioned.
- The radial margin distance must be reported. The radial margin should be reported as positive if tumour is located 1 mm or less from the inked nonperitonealized surface of the specimen.

2.2.2 Margins of Resection: Rectum

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in four key papers in the field (2-5), as well as pathology studies identified in the recent literature search.

Proximal and Distal 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.

Circumferential Radial Margins

- All rectal cancer specimens should be assessed grossly by the pathologist using the method developed by Quirke (7).
- 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 tumour segment unopened 5 cm above and below the proximal and distal edges of the tumour, respectively, and a gauze wick placed into the unopened segment to facilitate fixation. Following at least 48 hours of fixation, the segment with the tumour should be sliced into transverse sections. The relationship of the tumour to the CRM must be carefully assessed.
- The CRM distance must be reported. The CRM is positive if the tumour is located 1 mm or less from the margin; this includes tumour cells within a lymph node, vein, or nerve, as well as direct tumour extension.
- Note that tumours of the upper rectum have a peritonealized anterior surface and a non-peritonealized posterior radial margin similar to the ascending and descending colon.

Serosal Penetration

- Involvement of the serosa by tumour (pT4a) is not equivalent to involvement of the radial margin by tumour (although there are circumstances in which an advanced tumour has penetrated the serosa and is adherent to adjacent soft tissue).
- Documentation of serosal involvement by tumour requires careful gross and microscopic examination and may require extensive sampling and/or serial sectioning of sampled tissue blocks.
- Serosal penetration is defined as occurring when any of the following criteria are met:
 - Tumor present at the serosal surface
 - Free tumor cells on the serosal surface (visceral peritoneum) with underlying erosion/ulceration of mesothelial lining, mesothelial hyperplasia and/or inflammatory reaction
 - Perforation in which the tumor cells are continuous with the serosal surface through inflammation
- The significance of tumors that are <1 mm from the serosal surface and accompanied by serosal reaction is unclear, with some but not all studies indicating a higher risk of peritoneal recurrence. Multiple level sections and/or additional section of the tumor should be examined in these cases. If the serosal involvement is not present after additional evaluation, the tumor should be assigned to the pT3 category.

• Serosal penetration is an independent prognostic variable and has a strong negative impact on prognosis. 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 patients with pT4b tumours compared to those with pT4a tumours (with or without distant metastasis).

<u>Qualifying Statements regarding the shaded text above - Added to Endorsement</u> <u>in November, 2016</u>

The original 2008 recommendations on serosal penetration were modified by the expert panel. In the first bullet point pT4b was replaced by pT4a to reflect changes in the CAP (see Section 4, Table 9, Modification 5 and Impact on Recommendations). Bullet points 3 and 4 were also updated to align with the recent publication by CAP (based on the AJCC/UICC TNM 7th edition) (see Section 4, Table 9, Modification 6 and Impact on Recommendations).

The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

3. Lymph Node Assessment

3.1 Surgery

3.1.1 Extent of Lymphadenectomy

Technical Recommendations

Technical recommendations are based on Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000 and evidence suggesting no significant benefit for high arterial ligation over low ligation.

- The goal of colon resection is the removal of the segment of the bowel with the tumour 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 colic, inferior mesenteric artery, and all their branches). When the primary tumour is equidistant from two feeding vessels, both vessels should be excised close to their origin. More radical lymphadenectomy is not supported by available evidence.
- In curative operations, lymph node resection should 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 inferior mesenteric artery (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.

3.1.2 Number of Lymph Nodes Assessed

Technical Recommendations

Technical recommendations are based on Expert Panel consensus and an endorsement of the recommendation in the NCI Guidelines 2000 and are informed by evidence from a published systematic review and a review of the recent literature indicating an improved survival the greater the number of lymph nodes evaluated.

• In general, and particularly for T3/4 neoplasms, a minimum of 12 lymph nodes should be examined to adequately stage colon and rectal cancer, although an effort should be made to identify all lymph nodes. Importantly, the 12-lymph node target may not be achievable in patients with T1 or T2 tumours and/or some patients who receive neoadjuvant therapy.

3.2 Pathology

3.2.1 Technique of Lymph Node Examination

Technical Recommendations

Technical recommendations are based on Expert Panel consensus informed by four key papers in the field (2-5) and pathology studies identified in the recent literature search.

- Pericolic fat should be carefully examined using inspection and palpation. For colonic tumours, 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 tumours, the cross-sectioned 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.

3.2.2 Number of Lymph Nodes Assessed

Technical Recommendations

Technical recommendations are based on Expert Panel consensus informed by four key papers in the field (2-5) and pathology studies identified in the recent literature search.

- 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 (tumour deposits >0.2 mm but <2.0 mm) and isolated tumour cells (ITCs) (single cells or clusters 0.2 mm or less) should be reported separately from typical (macro) metastases. In cases where there are typical (macro) metastases, micrometastases or ITCs do not change the pN stage. 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 change the pN classification. Note that special measures to detect micrometastases or ITCs (e.g. multiple tissue levels of paraffin

blocks, immunohistochemistry [IHC], polymerase chain reaction [PCR]) are not recommended for the routine examination of regional lymph nodes.

 Discrete tumor deposits in pericolic or perirectal fat away from the leading edge of the tumor and showing no evidence of residual lymph node tissue, but within the lymphatic drainage of the primary carcinoma, are considered tumor deposits or satellite nodules and are not counted as lymph nodes replaced by tumor (based on the AJCC/UICC TNM 7th edition).

<u>Qualifying Statements regarding the shaded text above - Added to Endorsement</u> <u>in November, 2016</u>

The original 2008 recommendation on lymph node assessment was modified by the expert panel. The recommendation was updated to align with the recent publication by CAP (based on the AJCC/UICC TNM 7th edition) (see Section 4, Table 9, Modification 7 and Impact on Recommendations)

The original and the revisions to the recommendation are based on the expert opinion of the guideline panel. In the updated literature review (to February 2016) no new data were identified to inform the recommendation.

RELATED GUIDELINES

- Evidence-Based Series #17-8: Optimization of preoperative assessment in patients diagnosed with rectal cancer, January 2014.
- Practice Guideline Report #2-20-2: Laparoscopic Surgery for Cancer of the Colon, September 2005
- Practice Guideline Report #2-9: Follow-up of Patients with Curatively Resected Colorectal Cancer, January 2004
- Diagnostic Imaging Recommendations Report: Cross-sectional Imaging in Colorectal Cancer, April 2006
- Multidisciplinary Care Conference Standards, June 2006
- Evidence-Based Series: #2-29 Version 2: Adjuvant Systemic Chemotherapy for Stage II and III Colon Cancer Following Complete Resection, September 2015
- Evidence-Based Series #2-4 Version 2 Preoperative or Postoperative Therapy for the Management of Patients with Stage II or III Rectal Cancer, November 2013

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