Colorectal Cancer Association of Canada consensus meeting: raising the standards of care for early-stage rectal cancer

Colorectal Cancer Association of Canada

ABSTRACT

The purpose of the meeting reported here was to develop a set of national evidence-based standards for assessing and managing patients with potentially resectable rectal cancer. This report represents the consensus of the multidisciplinary group of Canadian rectal cancer experts attending that meeting.

KEY WORDS

Early-stage rectal cancer, consensus statement, raising the standard for rectal cancer, multidisciplinary guidelines for early rectal cancer

1. TERMS OF REFERENCE

1.1 Purpose

The purpose of the meeting reported here was to develop a set of national evidence-based standards for assessing and managing patients with potentially resectable rectal cancer. This report represents the consensus of the multidisciplinary group of Canadian rectal cancer experts attending that meeting.

1.2 Participants

A representative group of Canadian rectal cancer experts from the key disciplines (surgical, medical and radiation oncology, pathology, radiology) involved in managing resectable rectal cancer were invited (Table 1).

1.3 Target Audience

- Health care professionals involved in the care of patients with potentially curable rectal cancer
- Stakeholders (provincial cancer agencies, hospitals, and so on) responsible for program and funding decisions related to the management of potentially resectable cancer
- Patient advocacy and education groups such as the Colorectal Cancer Association of Canada

1.4 Basis of Recommendations

All recommendations are based on a structured presentation and discussion of the best available evidence.

2. PREAMBLE

2.1 Application of Recommendations

These standards provide the basis for a discussion with patients regarding management options. Treatment plans will depend on a more complete discussion of the risks and benefits of proposed therapies with individual patients.

Significant progress has been made in improving outcomes for patients with potentially resectable rectal cancer; however, further improvement is necessary. Offering patients the option of participating in clinical trials should be a priority.

Optimally, the approach for assessing and managing patients with rectal cancer should involve a collaborative, multidisciplinary team (including all relevant medical specialties and allied health professionals). For example, optimal rectal cancer management is predicated on open communication and quality assurance between the surgeon and the pathologist describing the extent of disease of the surgical specimen for optimal postsurgical treatment choices.

Radiologic assessment and imaging should be completed within 2–3 weeks to ensure that the appropriate information is available to make timely management decisions.

3. QUESTIONS AND CONSENSUS STATEMENTS

Question 1

For complete clinical staging of rectal cancer, what should the standard diagnostics and reporting be (preoperative assessment)?
Consensus Statement 1

All diagnostics should be completed within a timely period (42 days to treatment, including imaging within the first 2–3 weeks), starting from the date of biopsy. Services should include:

- Colonoscopy
- Imaging
  - Computed axial tomography of thorax, abdomen, and pelvis AND magnetic resonance imaging (MRI)
  - Slices of 3–4 mm should be routine
  - Mesorectal margin measurements or circumferential resection margin (CRM) with tumour distance should be reported
- Measurements for staging criteria should be provided (see the radiology protocol in Appendix A)
- When available, endorectal ultrasonography may be complementary to MRI in some T1/2 patients to better delineate T-stage

This statement utilizes Beets–Tan et al. 2001 1, Brown et al. 2003 2, Filippone et al. 2004 3, Nagtegaal et al. 2002 4, Iafrate et al. 2006 5, Kapiteijn et al. 2001 6, and Harisinghani et al. 2003 7.

Question 2

For complete clinical staging of rectal cancer, what should constitute standard pathology reporting?
Consensus Statement 2

For complete clinical staging of rectal cancer, synoptic reporting in accordance with the College of American Pathologists (CAP) protocol for the examination of specimens from patients with primary carcinomas of colon and rectum, based on the American Joint Committee on Cancer and International Union Against Cancer TNM, to include these points:

- Total mesorectal excision (TME) quality
  - Macroscopic assessment of mesorectum (complete, partially complete, or incomplete)
- CRM status
  - Positive if tumour is at 1 mm or less from the CRM or if a lymph node with metastasis is at 1 mm or less from the CRM
- If neoadjuvant therapy was received, pathologic tumour response grading should be recorded

For the complete protocol, see the CAP template (Appendix ii).

This statement utilizes Nagtegaal and van Krieken 2002 8, Quirke 1998 9, Heald and Ryall 1986 10, Dworak et al. 1997 11, Washington et al. 2008 13, Smith et al. 2008 14, Kapiteijn et al. 2001 15, Nagtegaal and Quirke 2008 16, Rödel et al. 2005 17, Glynne–Jones et al. 2006 18,19, Ruo et al. 2002 20, Nagtegaal et al. 2002 21, and Parfitt and Driman 2007 22.

Question 3

Which neoadjuvant radiation protocol or protocols should be standard when combined with chemotherapy?

Consensus Statement 3

Preoperative neoadjuvant radiotherapy is the standard of care for clinically staged II and III patients. Long-course radiation (minimum of 45 cGy over 5 weeks) with fluoropyrimidine chemotherapy or short-course radiation without chemotherapy can be considered. A multidisciplinary team approach (with or without a tumour board) is important to review individual cases and reach consensus on the appropriate course of treatment (short- vs. long-course radiation).

This statement utilizes Bujko et al. 2004 23, Marijnen et al. 2003 24, Swedish Rectal Cancer Trial 1997 25, Bosset et al. 2006 26, Gérard et al. 2006 27, and Sauer et al. 2004 28.

Question 4

Which neoadjuvant chemotherapy protocol or protocols should be standard when combined with long-course radiation?

Consensus Statement 4

The optimal fluoropyrimidine-based chemotherapy is based on extrapolation of data from randomized trials of combined-modality chemoradiation used in the postoperative setting. Use fluoropyrimidine-based chemotherapy with long-course radiation. Protracted fluoropyrimidine is preferable to bolus 5-fluorouracil because of improved tolerability and similar efficacy, as seen in the largest and most recent randomized trial (INT 0144) 29.

This statement utilizes Smalley et al. 2006 29, Wong et al. 2008 30, and O’Connell 1994 31.

Question 5

What should be the surgical standard of care for rectal cancer?

Consensus Statement 5

All stage II—III rectal cancers should be considered for neoadjuvant treatment. For all rectal cancers undergoing radical surgery, TME principles must be followed. Surgeons treating rectal cancer patients should be familiar with the TME surgery. Quality should be assured through independent evaluations by the surgeon and the pathologist. Synoptic operative reporting is encouraged.

Trans-anal excision represents an oncologic compromise for most rectal cancer patients. Consider it only in patients with comorbidities, realizing that it requires excellent preoperative assessment and high intraoperative expertise.

Because trans-anal endoscopic microsurgery is a new approach for local excision, patients being treated using this approach should preferably be enrolled in trials or prospective follow-up studies.

This statement utilizes MacFarlane et al. 1993 32, Cecil et al. 2004 33, Dahberg et al. 1998 34, Martling et al. 2000 35, Brown and Daniels 2005 36, Dubé et al. 1997 37, Karanjia et al. 1992 38, Ricciardi 2007 39, Murphy 2008 40, Ptok 2007 41, van den Brink 2004 42, Wibe 2002 43, Okabe 2004 44, and Nash 2009 45.

Question 6

What criteria should be standard for handling, evaluating, and reporting on the surgical specimen?

Consensus Statement 6

The surgeon should be aware of the standard macroscopic evaluation (grades 1, 2, 3) of the surgical specimen immediately after removal of the rectum. The pathologist receiving the specimen should also grade the macroscopic quality of the excision, independently of grading by the surgeon. Optimal management is predicated on productive, open
communication between the surgeon and the pathologist so that quality assurance and appropriate mechanisms for evaluation and improvement can be achieved (see also consensus statement 5). Collaboration is mandatory for optimal evaluation; that is, margin assessment, surgical difficulty encountered, neoadjuvant treatment given to the patient must be communicated. (For optimal assessment of the specimen, the pathologist has to be informed if neoadjuvant therapy was administered.)

This statement takes account of Nagtegaal and van Krieken 2002 8, Quirke 1998 9, Dworak 1997 11, Washington et al. 2008 13, Smith 2008 14, Kapiteijn 2001 15, Nagtegaal and Quirke 2008 16, Nagtegaal 2002 21, and Parfitt and Driman 2007 22.

**Question 7**

What is the standard adjuvant chemotherapy post neoadjuvant treatment and surgery?

**Consensus Statement 7**

All patients should be considered for 4–6 months of fluoropyrimidine-based therapy. Based on extrapolation of phase III trials for adjuvant treatment of colon cancer, adjuvant oxaliplatin-based therapy should be considered for patients at high risk for recurrence, including, but not limited to those who are

- ypN-positive.
- CRM-positive.

This statement utilizes Sauer et al. 2004 28, Wong et al. 2008 29, André et al. 2009 46, and Kuebler et al. 2007 47.

**4. ACKNOWLEDGMENTS**

The Colorectal Cancer Association of Canada (CCAC) thanks all contributors to this consensus guideline. Of particular note, the CCAC thanks Drs. S. Berry, C. Marginean, C. Richard, A. Smith, and T. Vuong, and Shaniah Leduc RN for their contributions to the writing of this paper.

**5. CONFLICTS OF INTEREST**

Participants disclosed potential conflicts of interest within the past 2 years:

- Scott Berry: Advisory boards for Sanofi–Aventis
- Celia Marginean: None
- Carole Richard: None
- Andrew Smith: None
- Te Vuong: Work as a consultant for Sanofi–Aventis

The Colorectal Cancer Association of Canada and the authors acknowledge the sponsors who provided unrestricted grants: Sanofi–Aventis, Bristol–Myers Squibb, and Amgen.

**6. REFERENCES**

1. Beets–Tan RG, Beets GL, Vliegen RF, et al. Accuracy of magnetic resonance imaging in prediction of tumour-free resection margin in rectal cancer surgery. *Lancet* 2001;357:497–504.
2. Brown G, Radcliffe AG, Newcombe RG, Dallimore NS, Bourne MW, Williams GT. Preoperative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. *Br J Surg* 2003;90:355–64.
3. Filippone A, Ambrosini R, Fuschi M, Marinelli T, Genovesi D, Bonomo L. Preoperative T and N staging of colorectal cancer: accuracy of contrast-enhanced multi-detector row CT colonography—initial experience. *Radiology* 2004;231:83–90.
4. Nagtegaal ID, Marijnen CA, Kranenbarg EK, van de Velde CJ, van Krieken JH on behalf of the Pathology Review Committee, Cooperative Clinical Investigators. Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma: not one millimeter but two millimeters is the limit. *Am J Surg Pathol* 2002;26:350–7.
5. Iafrate F, Laghi A, Paolontonio P, et al. Preoperative staging of rectal cancer with US imaging: correlation with surgical and histopathologic findings. *Radiographics* 2006;26:701–14.

6. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. on behalf of the Dutch Colorectal Cancer Group. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 2001;345:638–46.
7. Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med* 2003;348:2491–9. [Erratum in: *N Engl J Med* 2003;349:1010]
8. Nagtegaal ID, van Krieken JH. The role of pathologists in the quality control of diagnosis and treatment of rectal cancer—an overview. *Eur J Cancer* 2002;38:964–72.
9. Quirke P. The pathologist, the surgeon and colorectal cancer: get it right because it matters. *Prog Pathol* 1998;4:201–13.
10. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986;1:1479–82.

11. Dworak O, Keilholz L, Hoffmann A. Pathological features of rectal cancer after preoperative radiochemotherapy. *Int J Colorectal Dis* 1997;12:19–23.
12. Ryan R, Gibbons D, Hyland JM, et al. Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. *Histopathology* 2005;47:141–6.
13. Washington K, Berlin J, Branton P, et al. on behalf of the Members of the Cancer Committee, College of American Pathologists. Protocol for the Examination of Specimens from Patients with Primary Carcinomas of the Colon and Rectum. Northfield, IL: College of American Pathologists; 2008. [Available online at: www.cap.org/apps/docs/committees/cancer/cancer_protocols/2008/colonrectum08_pw.pdf; cited October 8, 2009]
14. Smith AJ, Driman DK, Spithoff K, et al. on behalf of the Expert Panel on Colon and Rectal Cancer. Optimization of Surgical and Pathological Quality Performance in Radical Surgery for Colon and Rectal Cancer: Margins and Lymph Nodes Guideline Recommendations. Sect. 1. Evidence-based series

COLORECTAL CANCER ASSOCIATION OF CANADA

CURREN ONCOLOGY—VOLUME 16, NUMBER 6

53
17-4. Hamilton, ON: Cancer Care Ontario; 2008. [Available online at: www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34416; cited October 8, 2009]

15. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. on behalf of the Dutch Colorectal Cancer Group. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med 2001;345:638–46.

16. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? J Clin Oncol 2008;26:303–12.

17. Rödel C, Martus P, Papadopoulos T, et al. Prognostic significance of tumor regression after preoperative chemoradiotherapy for rectal cancer. J Clin Oncol 2005;23:8688–96.

18. Glynn-Jones R, Mawdsley S, Pearce T, Buyse M. Alternative clinical end points in rectal cancer—are we getting closer? Ann Oncol 2006;17:1239–48.

19. Glynn-Jones R, Anyamene N. Just how useful an endpoint is complete pathological response after neoadjuvant chemoradiation in rectal cancer? Int J Radiat Oncol Biol Phys 2006;66:319–20.

20. Ruo L, Tickoo S, Klimstra DS, et al. Long-term prognostic significance of extent of rectal cancer response to preoperative radiation and chemotherapy. Ann Surg 2002;236:75–81.

21. Nagtegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH on behalf of the Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. J Clin Oncol 2002;20:1729–34.

22. Parfitt JR, Driman DK. The total mesorectal excision specimen for rectal cancer: a review of its pathological assessment. J Clin Pathol 2007;60:849–55.

23. Ricciardi R, Virnig BA, Madoff RD, Rothenberger DA, Baxter NN. The status of radical proctectomy and sphincter-sparing surgery in the United States. Dis Colon Rectum 2008;51:1435.

24. Murphy J, Boyle DJ, Bhan C, Williams NS. Why are so many patients with rectal cancer still treated with abdominoperineal resection in America? [Letter]. Dis Colon Rectum 2008;51:1435.

25. Improved survival with preoperative radiotherapy in resectable rectal cancer. Swedish Rectal Cancer Trial. N Engl J Med 1997;336:980–7. [Erratum in: N Engl J Med 1997;336:1539]

26. Bosset JF, Collette L, Calais G, et al. on behalf of the EORTC Radiotherapy Group Trial 22921. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med 2006;355:1114–23. [Erratum in: N Engl J Med 2007;357:728]

27. Gérard JP, Conroy T, Bonnetain F, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. J Clin Oncol 2006;24:4620–5.

28. Sauer R, Becker H, Hohenberger W, et al. on behalf of the German Rectal Cancer Study Group. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 2004;351:1731–40.

29. Smalley SR, Benedetti JK, Williamson SK, et al. Phase III trial of fluorouracil-based chemotherapy regimens plus radiotherapy in postoperative adjuvant rectal cancer. GI INT 0144. J Clin Oncol 2006;24:3542–7.

30. Wong R, Berry S, Spiroff K, et al. on behalf of the Gastrointestinal Cancer Disease Site Group. Preoperative or Postoperative Therapy for the Management of Patients with Stage II or III in Rectal Cancer: Guideline Recommendations. Sect. 1. Evidenced-based series 2-4. Hamilton, ON: Cancer Care Ontario; 2008. [Available online at: www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14008; cited October 8, 2009]

31. O’Connell MJ, Martenson JA, Wied AH, et al. Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery. N Engl J Med 1994;331:502–7.

32. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet 1993;341:457–60.

33. Cecil TD, Sexton R, Moran BJ, Heald RJ. Total mesorectal excision results in low local recurrence rates in lymph node-positive rectal cancer. Dis Colon Rectum 2004;47:1145–50.

34. Dahlberg M, Pahlman L, Bergström R, Glömelius B. Improved survival in patients with rectal cancer: a population-based register study. Br J Surg 1999;85:515–20.

35. Martling AL, Holm T, Rutqvist LE, Moran BJ, Heald RJ, Cedemar B. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm Colorectal Cancer Study Group, Basingstoke Bowel Cancer Research Project. Lancet 2000;356:93–6.

36. Brown G, Daniels IR. Preoperative staging of rectal cancer: the MERCURY research project. Recent Results Cancer Res 2005;165:58–74.

37. Dubé S, Heyen F, Jencek M. Adjuvant chemotherapy in colorectal carcinoma: results of a meta-analysis. Dis Colon Rectum 1997;40:35–41.

38. Karanjia ND, Schache DJ, Heald RJ. Function of the distal rectum after low anterior resection for carcinoma. Br J Surg 1992;79:114–16.

39. Ricciardi R, Virnig BA, Madoff RD, Rothenberger DA, Baxter NN. The status of radical proctectomy and sphincter-sparing surgery in the United States. Dis Colon Rectum 2007;50:1119–27.

40. Murphy J, Boyle DJ, Bhan C, Williams NS. Why are so many patients with rectal cancer still treated with abdominoperineal resection in America? [Letter]. Dis Colon Rectum 2008;51:1435.
45. Nash GM, Weiser MR, Guillem JG, et al. Long-term survival after transanal excision of T1 rectal cancer. Dis Colon Rectum 2009;52:577–82.

46. André T, Boni C, Navarro M, et al. Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial. J Clin Oncol 2009;27:3109–16.

47. Kuebler JP, Wieand HS, O’Connell MJ, et al. Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer: results from NSABP C-07. J Clin Oncol 2007;25:2198–204.

Correspondence to: Barry Stein, c/o Toula Chondrozoumakis, 1230–5 Place Ville Marie, Montreal, Quebec H3B 2G2. E-mail: toulac@colorectal-cancer.ca, bstein@ccac-accc.ca

APPENDIX A  MAGNETIC RESONANCE IMAGING PROTOCOL

Phased-array coil
Field strength: 1.5 T or more
High-resolution matrix T2 images
Small field of view (<25 cm)
Thin section (3–4 mm)
Axial, coronal, and sagittal planes
Oblique planes perpendicular to the tumour
Gadolinium-enhanced imaging

STANDARDIZED IMAGING REPORT

All Tumours
- Craniocaudal tumour extent
- Distance from anal verge
- T stage
- Circumferential (radial) margin–tumour distance
- Pelvic viscera and bones

Additions for Low-Rectal and Anorectal Tumours
- Distance from levator ani
- Distance from anorectal junction
- Involvement of sphincter complex
- Internal sphincter (partial or full)
- External sphincter and beyond

APPENDIX B  COLLEGE OF AMERICAN PATHOLOGISTS PATHOLOGY REPORTING TEMPLATE

Note: This consensus guideline is based on College of American Pathologists (CAP) guideline version 6 from early 2009. An updated CAP guideline (version 7) is expected to be available at the end of 2009 and should be consulted for additional pathology reporting recommendations.

- Procedure type
  - Rectal/rectosigmoid colon (low anterior resection)
  - Abdominoperineal resection
  - Trans-anal disk excision (local excision)
  - Other

- Tumour size
- Macroscopic tumour perforation
- Macroscopic assessment of mesorectum (Note 1)
  - Complete
  - Partially complete
  - Incomplete
  - Cannot be assessed
- Histologic type
  - Adenocarcinoma
  - Mucinous adenocarcinoma
  - Signet-ring cell carcinoma
  - Small cell carcinoma
  - Squamous cell carcinoma
  - Adenosquamous carcinoma
  - Medullary carcinoma
  - Undifferentiated carcinoma
  - Other (specify)
- Histologic grade
  - Cannot be assessed
  - Low grade (well differentiated to moderately differentiated)
  - High grade (poorly differentiated to undifferentiated)
- Tumour depth of invasion (pT)
  - pTX: Cannot be assessed
  - pT0: No evidence of primary tumour
  - pTis: Carcinoma in situ, intraepithelial (no invasion)
  - pTis: Carcinoma in situ, invasion of lamina propia
  - pT1: Tumour invades submucosa
  - pT2: Tumour invades muscularis propria
  - pT3: Tumour invades through the muscularis propria into the subserosa or the nonperitonealized perirectal soft tissues
  - pT4a: Tumor penetrates the visceral peritoneum
  - pT4b: Tumor directly invades adjacent structures
- Lymph node status (pN)
  - pN0: No metastases in ____ lymph nodes
  - pN1: ____ (1–3) nodes involved of ____ (total number)
  - pN2: ____ (≥4) nodes involved of ____ (total number)
- Proximal margin
  - Cannot be assessed
  - Uninvolved by invasive carcinoma
  - Involved by invasive carcinoma
- Distal margin
  - Cannot be assessed
● Uninvolved by invasive carcinoma
● Involved by invasive carcinoma
● Circumferential (radial) margin (Note 2)
  ● Cannot be assessed
  ● Uninvolved
  ● Involved by invasive carcinoma or a positive lymph node [tumour or positive lymph node present 0–1 mm from margin (or both); specify distance to margin (millimetres or centimetres)]
● Lateral margin (for noncircumferential trans-anal disk excision)
  ● Cannot be assessed
  ● Uninvolved by invasive carcinoma [specify distance of invasive carcinoma from closest lateral margin (millimetres or centimetres)]
  ● Involved by invasive carcinoma
● Neoadjuvant therapy received
  ● Yes
  ● No
  ● Information not available
● Tumour response to neoadjuvant treatment (Note 3)
  ● Present (% of fibrosis)
  ● No response identified
● Vascular (large vessel) invasion
  ● Not identified
  ● Present
  ● Indeterminate
● Lymphatic (small vessel) invasion
  ● Not identified
  ● Present
  ● Indeterminate
● Discontinuous extramural extension (irregular tumour nodules in pericolorectal adipose tissue without histologic evidence of residual lymph node)
  ● Not identified
  ● Present
  ● Cannot be determined

NOTES

1. Mesorectal Envelope

The nonperitonealized surface of the fresh specimen is examined circumferentially, and the completeness of the mesorectum is scored as complete, partially complete, or incomplete.\(^8\) The entire specimen is scored according to the worst area.

● Complete: Intact bulky mesorectum with a smooth surface. Only minor irregularities of the mesorectal surface. No surface defects greater than 5 mm in depth. No coning towards the distal margin of the specimen. After transverse sectioning, the circumferential margin appears smooth.

● Nearly complete: Moderate bulk to the mesorectum. Irregularity of the mesorectal surface with defects greater than 5 mm, but none extending to the muscularis propria. No areas of visibility of the muscularis propria except at the insertion site of the levator ani muscles.

● Incomplete: Little bulk to the mesorectum. Defects in the mesorectum down to the muscularis propria. After transverse sectioning, the circumferential margin appears very irregular.

2. Circumferential (Radial) Margin

In addition to addressing the proximal and distal margins, the circumferential (radial) margin (CRM) must be assessed for any segment either unencased or incompletely encased by peritoneum. The CRM represents the adventitial soft tissue margin closest to the deepest penetration of tumour and is created surgically by blunt or sharp dissection of the retroperitoneal or subperitoneal aspect respectively. The serosal surface (visceral peritoneum) does not constitute a surgical margin.

The distance between the tumour and the CRM should be reported. The CRM is considered negative if the tumour is more than 1 mm from the inked nonperitonealized surface, but should be recorded as positive if tumour is located 1 mm or less from the nonperitonealized surface. This description includes both tumour within a lymph node and direct tumour extension; however, if CRM positivity is based solely on intranodal tumour, this fact should be stated (CAP protocol).

3. Pathologic Tumour Response to Neoadjuvant Therapy (ypN)

The tumour response to neoadjuvant chemoradiation therapy should be recorded at least as present, recording the percentage of fibrosis in respect to residual tumour (or no response identified).

The entire scarred area of the rectum has to be blocked and scrutinized meticulously for any foci of residual tumour cells. Acellular mucin pools post neoadjuvant therapy are considered to represent a pathologic complete response. Tumour regression should be assessed only in the primary tumour; lymph node metastases should not be included in the assessment.

Several grading systems for tumour response are available.\(^11\)\(^,\)\(^12\) A 3-point system showed good interobserver reproducibility and may be clinically important, but it is not yet validated or regularly used in patient management and is not required for accreditation purposes for the Commission on Cancer.