Guideline Resource Unit
guru@ahs.ca

Rectal Cancer

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Cancer Care Alberta

Clinical Practice Guideline GI-005 – Version 5
www.ahs.ca/guru

Background

According to statistics provided by the Canadian Cancer Society in 2019, one in fourteen Canadian males and one in fifteen Canadian females will be diagnosed with colorectal cancer in their lifetime[1].

A patient may be predisposed to develop colorectal cancer by a hereditary condition (e.g.: hereditary non-polyposis colon cancer, familial adenomatous polyposis) or a personal history of either inflammatory bowel disease (e.g.: Crohn's disease, ulcerative colitis) or adenomatous polyps. Over 60 percent of colorectal cancers arise without a clearly identifiable predisposing factor, however.

After a diagnosis of colorectal cancer, prognosis depends upon the stage at diagnosis; that is, prognosis is better with less penetration of the tumor into the bowel wall, fewer involved regional lymph nodes, and no evidence of metastatic disease.

Because the prognosis is better when colorectal cancer is identified at an earlier stage, because of the relatively high incidence of colorectal cancer, and because of the simplicity and accuracy of screening tests, screening for colorectal cancer represent an important component of routine care for all adults aged fifty years or older. This is especially important in patients with first-degree relatives with colorectal cancer.

This guideline was developed to outline the management recommendations for patients with rectal cancer (adenocarcinoma) amenable to resection with curative intent.

Guideline Questions

1. What are the recommendations for the diagnostic workup and staging of adult patients with rectal cancer amenable to resection with curative intent?
2. What are the treatment recommendations for adult patients with rectal cancer amenable to resection with curative intent?
3. What is the optimal timing of surgery post radiation for rectal cancer?
4. What is the evidence for restaging after long course chemoradiation for rectal cancer?

Search Strategy

This guideline was developed to promote evidence-based practice in Alberta. It was compiled from the results of randomized controlled trials and systematic reviews, derived from an English language and relevant term search of PubMed and MEDLINE from 1990 forward. It takes into consideration related information presented at local, national, and international meetings as well as the Alberta Provincial Gastrointestinal Tumour Team's interpretation of the data.

Target Population

The recommendations outlined in this guideline apply to adults (18+ years) with early stage rectal cancer. Different principles may apply to pediatric patients.

Recommendations and Discussion

Diagnostic Work-up

- In addition to a digital rectal examination (DRE) and a baseline CT chest, abdomen and pelvis, magnetic resonance imaging (MRI) is strongly recommended[2] to provide additional information about the extent of the disease (e.g. depth of penetration, lymph node involvement, fixation to adjacent structures).
- Transrectal endoscopic ultrasound can provide complementary information to MRI, especially when there is uncertainty between T2 versus T3N0 tumours or if a lymph node assessment is required. It can also be used for patients with contraindications to MRI.
- For patients with locally advanced disease who undergo neoadjuvant therapy, restaging CT (chest, abdomen, pelvis) and/or MRI may be required to facilitate clinical decision making.

Stage Information

- Clinical staging should be performed according to the AJCC TNM – 8th Edition[3] (Appendix A).

Goals of Therapy

The goals of therapy are to render the patient free of disease, to delay or prevent recurrence, and to preserve anal sphincter, urinary, and sexual function.

Recommendations

- A multidisciplinary team is required to define and provide the optimal care for a patient with rectal cancer. It should be composed of gastroenterologists, general surgeons, hepatobiliary surgeons, and both radiation and medical oncologists.
- All patients with rectal cancer should consider treatment on a clinical trial, if available.

Table 2. Recommendations for Treatment of Patients with Rectal Cancer Amenable to Resection.

Stage	Recommendations
Stage 0	• Perform local or transanal excision[4]. • No adjuvant systemic therapy is indicated.

Stage	Recommendations
Stage I	• If sufficient rectum (i.e. middle third of rectum and distal clear bowel margin ≥ 1 cm) distal to the cancer permits a colorectal or coloanal anastomosis, perform a radical *en bloc* excision of the rectum by low anterior resection. Otherwise, perform an abdominoperineal resection (APR) (i.e. upper third of rectum and distal clear bowel margin of ≥5 cm). • To precisely dissect the rectum and para-rectal lymph nodes within the mesorectal envelope and to obtain an optimal circumferential radial margin (CRM), surgery should *only* be performed by a surgeon experienced with the total mesorectal excision technique (TME)[5,6]. • In a carefully selected patient with low-risk T_1 disease who accepts an increased risk of tumor recurrence, a prolonged period of post-operative surveillance, and a decreased success after salvage surgery, consider transanal excision[6-8]. A T_1 rectal cancer is considered "low-risk" if (1) it is T_{1sm1} or T_{1sm2} (invasion into the superficial or middle third of the submucosa). • No adjuvant systemic therapy is indicated.

Stage II / III	**Neoadjuvant therapy is the preferred approach**: Long and short-course RT are equally recommended in this setting due to similar efficacy and patient reported QoL.
	• **Long course chemoradiation:** Patients with rectal cancer not immediately amenable to surgical resection as well as patients with clinical stage II and III disease[9,10] may be offered long-course pre-operative radiotherapy (50 Gy in 25fx or 50.4 Gy in 28fx with the option of 9 Gy boost) with either protracted venous infusion 5-Fluorouracil (225 mg/m^2 per day by ambulatory infusion pump during the entire period of radiation therapy[11]) or Capecitabine (825 mg/m^2 po BID)[12]. If sufficient rectum distal to the cancer permits a colorectal or coloanal anastomosis, perform a radical *en bloc* excision of the rectum by low anterior resection. Otherwise, perform an APR. Either surgery should be performed six to eleven weeks after having completed long course radiation[13]. Long-course RT may be more appropriate for low rectal cancers compared to short-course RT. Pre-operative chemoradiotherapy is associated with a lower rate of grade 3/4 acute toxicities, long-term toxicities, and local recurrence, but no difference in five-year overall survival when compared to post-operative chemoradiotherapy[9].
	• **Short course radiation**: Patients with rectal cancer amenable to surgical resection can be offered short-course pre-operative radiotherapy (25 Gy in five fractions)[13-15]. If sufficient rectum distal to the cancer permits a colorectal or coloanal anastomosis, perform a radical *en bloc* excision of the rectum by low anterior resection. Otherwise, perform an abdominoperineal resection. Either surgery should be performed within one week or delayed until 4-8 weeks after the end of radiotherapy.
	• **Total neoadjuvant therapy** (TNT) refers to the use of chemotherapy and radiation prior to surgery. In a systematic review and meta-analysis of seven studies, TNT was associated with a higher rate of pathological complete response and improved disease-free survival compared to neoadjuvant chemoradiation and adjuvant chemotherapy.[21] The optimal use of this strategy is not clear and multidisciplinary discussion is recommended.
	  • Radiation may be short course or long course chemoradiation
	  • For patients receiving neoadjuvant chemotherapy as a component of a total neoadjuvant strategy, either FOLFOX or CAPOX is utilized (4 months if long course chemoradiation is given, 6 months if short course RT is given).
	  • Tumor characteristics suggested for considering total neoadjuvant therapy include at least one of the following[22]:

Stage	Recommendations
	○ cT4 ○ cN2 disease (4 or more nodes positive) ○ Distance between tumor and mesorectal fascia on MRI <=1 mm ○ Lateral lymph node >= 1 cm (internal iliac, external iliac, obturator or common iliac) ○ Extramural vascular invasion • To precisely dissect the rectum and para-rectal lymph nodes within the mesorectal envelope and to obtain an optimal circumferential radial margin, surgery should *only* be performed by a surgeon experienced with the total mesorectal excision technique[16,17]. • **Adjuvant therapy after neoadjuvant** treatment: adjuvant chemotherapy options are extrapolated from colon cancer, see the Clinical Practice Guideline for Early-Stage Colon Cancer. ○ After short course RT: A total of six months of chemotherapy is recommended ○ After long course chemoradiation: four months of chemotherapy is recommended ○ No further chemotherapy is recommended for patients who received Total Neoadjuvant Therapy **Adjuvant therapy for patients who have upfront surgery** • If a patient with rectal cancer undergoes a low anterior resection or an abdominoperineal resection without pre-operative radiotherapy, offer two months of adjuvant chemotherapy (as for colon cancer), then radiotherapy (4,500 to 5,400 cGy in twenty-five to thirty fractions) with either concurrent protracted venous infusion 5-Fluorouracil (225 mg/m^2 per day by ambulatory infusion pump)[9] or Capecitabine (825 mg/m^2 po BID)[12] and then two additional months of adjuvant chemotherapy (as for colon cancer)[18-20]. • As long as resection of a metachronous polyp, second colorectal cancer, or metastasis to liver or lung is appropriate, surveillance is recommended (see Clinical Practice Guideline for Colorectal Cancer Surveillance).
Locally Recurrent Cancer	• Care should be directed by the Multidisciplinary Gastrointestinal Tumor Team. • If the recurrence is not amenable to surgical resection, see Clinical Practice Guideline for Metastatic Colorectal Cancer.
Stage IV	• Consider palliative radiotherapy for local symptoms. • See Clinical Practice Guideline for Metastatic Colorectal Cancer.

Pathologic Assessment

Please refer to the Pathway for detailed information about pathologic assessment.

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Appendix A: 8th Edition Colon and Rectum Cancer Staging[3]

Stage	Depth of Tumour Penetration		Regional Lymph Node Involvement		Metastases	
Stage 0	T_{is}	Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage I	T_1	Invades submucosa (through muscularis mucosa but not into muscularis propria)	N_0	No regional lymph node involvement	M_0	No distant metastasis
	T_2	Invades muscularis propria	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_A	T_3	Invades through muscularis propria into pericolorectal tissues	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_B	T_{4a}	Invades* through visceral peritoneum (including gross perforation of bowel through tumour and continuous invasion of tumour through areas of inflammation to surface of visceral peritoneum)	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_C	T_{4b}	Directly invades* or adhere[§] to adjacent organs or structures	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage III_A	T_{1-2}	As described above	N_1	1-3 regional lymph nodes positive (tumour in lymph nodes measuring ≥0.2 mm), or any number of tumour deposits are present and all identifiable lymph nodes are negative	M_0	No distant metastasis
			N_{1c}	No regional lymph nodes positive, but tumor deposits in subserosa, mesentery, nonperitonealized pericolic, or perirectal/mesorectal tissues		
	T_1	Invades submucosa	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
Stage III_B	T_{3-4a}	As described above	N_1	1-3 regional lymph nodes positive (tumour in lymph nodes measuring ≥0.2 mm), or any number of tumour deposits are present and all identifiable lymph nodes are negative	M_0	No distant metastasis
			N_{1c}	No regional lymph nodes positive, but tumor deposits in subserosa, mesentery, nonperitonealized pericolic, or perirectal/mesorectal tissues		
	T_{2-3}	As described above	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
	T_{1-2}	As described above	N_{2b}	≥7 regional lymph nodes positive	M_0	No distant metastasis
Stage III_C	T_{4a}	Penetrates to surface of visceral peritoneum	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
	T_{3-4a}	As described above	N_{2b}	≥7 regional lymph nodes positive	M_0	No distant

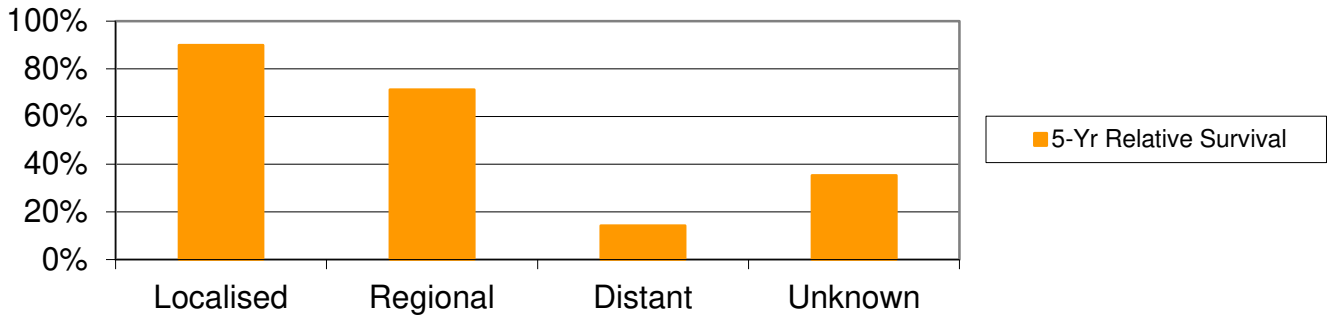
Stage	Depth of Tumour Penetration		Regional Lymph Node Involvement		Metastases	
						metastasis
	T_{4b}	Directly invades or is adherent to other organs or structures	N_{1-2}	As described above	M_0	No distant metastasis
Stage IV_A	T_{any}	As described above	N_{any}	As described above	M_{1A}	Metastasis to 1 site or organ without peritoneal metastasis
Stage IV_B	T_{any}	As described above	N_{any}	As described above	M_{1B}	Metastasis to ≥ 2 sites or organs without peritoneal metastasis
Stage IV_c	T_{any}	As described above	N_{any}	As described above	M_{1c}	Metastasis to peritoneal surface identified alone or with other site or organ metastases

*Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumour on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).

§Tumour that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.

Appendix B:

Figure 1. Observed survival rates with adenocarcinoma of rectum by SEER summary stage. Data from SEER 18 2009-2015, All Races, Both Sexes.



Development and Revision History

This guideline was reviewed and endorsed by the Alberta Gastrointestinal Tumour Team. Members include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Tumour Teams, external participants identified by the Working Group Lead, and a knowledge management specialist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in 2009.

Maintenance

A formal review of the guideline will be conducted in 2022. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AJJ, American Joint Committee; APR, Abdominoperineal resection; CAP, College of American Pathologists; CEA, Carcinoembryonic antigen; CRM, Circumferential resection margin; CT, Computed tomography; DRE, Digital rectal examination; FDG-PET, Fluorodeoxyglucose positron emission tomography; ME, Mesorectal excision; MRI, Magnetic resonance imaging; TME, Total mesorectal excision; TS, Tumour specific.

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Gastrointestinal Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

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