PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

GASTROINTESTINAL

RECTAL CANCER
These guidelines are evidence-based and thus subject to change. Some recommendations are currently funded in this jurisdiction, while others are in negotiation.
1. Introduction

It is estimated that 145,600 patients will be diagnosed with colorectal cancer in the United States in the year 2019, which represents 8.3% of all new cancer cases. In 2017 and according to the Canadian cancer society, an estimated 26,800 Canadians were diagnosed with colorectal cancer (13% of all new cancer cases in 2017). Moreover, 9,400 Canadians died from colorectal cancer. This represents 12% of all cancer deaths in 2017. The incidence of colorectal cancers is higher in developed countries than in developing countries.

2. Screening and early detection

The polyposis and colorectal cancer syndromes include familial adenomatous polyposis (FAP), Gardner syndrome, Turcot syndrome, flat adenoma syndrome, Hereditary nonpolyposis colorectal cancer or Lynch syndrome, Peutz-Jeghers syndrome and all increase the risk of colorectal cancer.

Inflammatory bowel disease, particularly ulcerative colitis is associated with an increased risk for colon cancer, estimated to be 5% to 10% by 20 years after diagnosis and is also associated with a high incidence of synchronous cancers affecting 10% to 20% of cases. Crohn’s disease may also have a role in increasing colorectal cancer, particularly in the ileocolic region.

The screening tests for colorectal cancer include digital rectal examination, FOBT, sigmoidoscopy, colonoscopy, barium enema and CT colonography.

Although sigmoidoscopy in conjunction with annual FOBT is an effective means of reducing mortality related to colon cancer, some cancers will be missed therefore colonoscopy is recommended every 5 to 10 years for a patient with average risk, starting at age 50 (Levin et al., 2008).

Screening should be more regular for patients at high risk such as those with inherited syndromes, inflammatory bowel disease, and previous adenomatous polyps or colorectal cancer.

Individuals with HNPCC should have screening by total colonoscopy every 1 to 3 years beginning between ages 20 and 25 because of the lack of a visible premalignant lesion in this population and the higher risk for right-sided colon cancers. Individuals with FAP should start screening colonoscopies as early as age 10.

3. Diagnosis

Diagnosis is based on a digital rectal examination including rigid sigmoidoscopy with biopsy for histopathological examination. Complete history and physical examination,
complete blood count, liver and renal function tests, carcinoembryonic antigen, CT scan of the chest and CT or MRI or ultrasound of liver and abdomen should be performed.

Endoscopic ultrasound (T1-T2) or rectal MRIs for all tumours is recommended in order to select patients for preoperative treatment and extent of surgery. Complete colonoscopy pre- or postoperatively is required.

4. Pathology

Histopathological examination should include surgical specimen with proximal, distal and circumferential margins and regional lymph nodes (at least 12 nodes are recommended to be examined). Tumours with distal extension to ≤ 15cm (as measured by rigid sigmoidoscopy) from the anal margin are classified as rectal, more proximal tumours as colonic.

Adenocarcinomas comprise the vast majority (98%) of colon and rectal cancers. Other rare rectal cancers include carcinoid (0.4%), lymphoma (1.3%), and sarcoma (0.3%). Squamous cell carcinomas may develop in the transition area from the rectum to the anal verge and are considered anal carcinomas. Very rare cases of squamous cell carcinoma of the rectum have been reported. The American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) TNM staging system (Rectal cancer) is available online at www.nccn.org

5. Management

5.1 Neoadjuvant therapy

The main indication for neoadjuvant therapy is locally advanced stage II and III rectal cancer as defined by transrectal ultrasound, CT or MRI and is recommended rather than initial resection.

Neoadjuvant therapy is also an appropriate option in patients who have distal mobile rectal cancers not amenable to local excision. Preoperative therapy might allow some patients to undergo sphincter-preserving low anterior resection rather than an abdominoperineal resection.

Neoadjuvant therapy is also recommended if the preoperative staging evaluation suggests the presence of tumour invading or in close proximity (within 2-5 mm) of the mesorectum on MRI even if the rectal cancer is T1/2, especially in the lower third, when an APR is required.

Continuous infusion 5-fluorouracil (225 mg/m²/24hours) may be administered during the course of 5 weeks of radiotherapy (50 Gy in 25 fractions) or oral capecitabine (825 mg/m² twice daily, five days per week) appears to be equivalent (Bosset et al., 2006, Hofheinz et al., 2012). The short course high dose preoperative radiotherapy (25 Gy in 5 fractions over 1 week) as reported in a Swedish study may be considered in mid rectal
cancers without threatened margins (Swedish rectal cancer trial, 1997). No significant difference in clinical outcome was achieved with the intensified capecitabine/oxaliplatin combination with radiotherapy in the neoadjuvant setting (Gérard et al., 2012). Surgical resection remains the standard approach after neoadjuvant chemoradiotherapy for patients who are medically operable, even if they appear to have a complete clinical response to induction therapy. Exceptions may be considered in low risk patients who have a complete response following preoperative therapy. This would require multidisciplinary assessment for patients interested in non-operative management.

5.2 Adjuvant therapy

Neoadjuvant rather than postoperative adjuvant chemoradiotherapy is a preferable approach for patients with transmural or node-positive tumours, particularly if they are low-lying within the rectum.

Following resection, due to the downsizing effect of neoadjuvant chemoradiotherapy, pathologic nodal staging is unreliable, therefore a six month course of postoperative 5-fluorouracil based chemotherapy regimen is recommended.

Options include weekly 5-FU/leucovorin (the Roswell Park regimen) (Haller et al., 2005), the de Gramont regimen of short-term infusional 5-FU and leucovorin (André et al., 2007) or FOLFOX as used in the MOSAIC trial (André et al., 2009).

Although FOLFOX is a reasonable option, clinicians should be aware that there is no evidence that FOLFOX is better than non-oxaliplatin-containing chemotherapy in the adjuvant setting of rectal cancer.

Chemotherapy dosing for obese patients should be based on actual and not ideal body weight, with subsequent dose modifications based upon toxicity.

For combined modality adjuvant therapy, the concurrent use of a fluoropyrimidine as a radiation sensitizer during postoperative radiotherapy is recommended rather than radiotherapy alone (Douglass et al., 1986, Krook et al., 1991).

Patients who are staged initially as having early disease, and thus are not considered for neoadjuvant therapy, but in whom the final pathology reveals more advanced stage II or III disease, may then be considered for post operative adjuvant therapy with 2 months FOLFOX, followed by 45 Gy in 25 fractions of pelvic radiotherapy with concurrent 5-fluorouracil or capecitabine, followed by a further 2 months of FOLFOX chemotherapy.

5.3 Recurrent or metastatic disease

Some cases of locoregional recurrence may be amenable to surgical resection. In selected cases, treatment may include surgery of resectable lung or liver metastases.
Surgical or stenting procedures should be considered if appropriate or radiotherapy as palliative procedures.

First-line palliative chemotherapy should be considered and consists of 5-FU/leucovorin in combination with oxaliplatin or irinotecan, with or without an antibody as utilized in the treatment of metastatic colon cancer. Cetuximab or panitumumab is indicated only in K-ras wild-type tumours. Bevacizumab can be used irrespective of K-ras mutation status.

Second and third line treatment should be considered in good performance status patients and agents not used in first or second line settings may be given.

For patients who have hepatic metastases at initial presentation, the optimal timing of primary and liver resection is uncertain. Pelvic radiotherapy may still be considered to optimize local control in the pelvis. Multidisciplinary discussion is advised.

5.4 Oncology Nursing

Refer to general oncology nursing practices

6. Supportive Care

6.1 Patient Education

Refer to general patient education practices

6.2 Psychosocial Care

Refer to general psychosocial oncology care guidelines

6.3 Symptom Management

Refer to general symptom management care guidelines

6.4 Clinical Nutrition

Refer to general clinical nutrition care guidelines

6.5 Palliative Care

Refer to general oncology palliative care guidelines

7. Follow-up care

In general, the value of regular clinical, laboratory and radiological examinations are not known. In patients treated with curative intent, at least postoperative imaging of the liver and lungs should be done 1 and 3 years after surgery.
A minimal recommendation would be history and rectosigmoidoscopy (if possible) every 6 months for 2 years. A completion colonoscopy if not done at the time of diagnostic work-up should be performed within the first year with history and colonoscopy and resection of colonic polyps every 5 years.

Following adjuvant treatment, in Princess Margaret Cancer Centre, a history and physical exam and CEA are recommended every 3 months for the first 2 years, every 4 months for year 3, every 6 months for year 4 and 5 and yearly from Year 6 to 10 (which can be done by primary physician). CT abdomen/thorax and pelvis are recommended every 6 months for year 1 and 2, and yearly in years 3, 4 and 5. A colonoscopy is recommended in year 3 and 8 and every 5 years thereafter.

For patients who are receiving palliative chemotherapy in the metastatic setting, it is recommended that the patient be re-evaluated with CEA and a CT scan of the involved regions every 2-3 months. History, physical examination and evaluation of general condition including side effects of chemotherapy need to be elucidated during systemic treatment as per physician choice (usually every 2-4 weeks depending on regimen being administered).
8. References


