GUIDELINES FOR THE MANAGEMENT OF COLON AND RECTAL CANCERS

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Introduction

Excluding cancer of the skin, colon and rectal cancers are the most common malignancies in western countries after lung and breast cancer in females, and lung and prostate cancer in males. In Lebanon, statistics are lacking, but from the data at the American University of Beirut Medical Center, the incidence is apparently increasing.

The following guidelines are up to date suggestions for the management of Colorectal Cancer. Needless to say that there should be a multidisciplinary approach with the involvement of the gastroenterologist, the surgeon, the oncologist and the radiotherapist. The outcome of treatment, in terms of cure, prolonging survival and improving quality of life is taken into consideration at each step in the management decision. Cost effectiveness and resources restrains will occasionally come into the picture to change some of the recommendations.

Rectal Cancer

1- Factors Influencing Therapy:

a- Level of the lesion: The distance from the lower edge of the tumor to the anal verge measured by rigid scope. It is probably the most important single variable but also should be put in context with other variables like fixity and pelvic anatomy.

b- Margins of resection: 5cm is an adequate proximal margin. The distal margin is important in deciding about a sphincter saving operation. 2 cm distal margin is safe but autopsy studies revealed that it is very rare for infiltration in the wall to spread beyond 0.8cm distally, when mesorectal tissue margin is considered a 5 cm margin is recommended to produce acceptable recurrence rate.

c- Size: Not significant
d- Macroscopic appearance: Not significant although infiltrative is worse than exophytic.

e- Circumferential involvement: Not significant

f- Fixity: As noted by any of the following: the examining finger, rigid scope, CT, transrectal U/S or MRI which show infiltration of the adjacent tissue especially posteriorly & laterally. Fixity implies poor prognosis or the likelihood of residual tumor left following resection. Preoperative radiation and chemotherapy are preferred. A-P resection doesn't yield better results in such tumors when compared to radiation and chemotherapy followed by low anterior resection and anastomosis. Mesorectal resection without chemorad gives similar results if fascia propria is not penetrated.

g- Histologic Appearance: Poor differentiation, perineural and perivascular invasion and greater than 20% microacinar picture are associated with poor prognosis. However, lymphocytic infiltration at the border of the tumor carries a better prognosis.

h- DNA content: Aneuploidy probably carries worse prognosis.

i- Depth of infiltration as measured by transrectal U/S or magnetic resonance imaging with endorectal coil is as significant as fixity.

2- Work up of patient with rectal cancer (1st Encounter):

a. Pathology review ± flow cytometry.
b. CBC (including platelets), PT, PTT, electrolyte, BUN, Cr, FBS, CEA, γGT, Alk phosphatase, and urinalysis.
c. Chest X-ray (PA and lateral).
d. CT of abdomen and pelvis with IV contrast and oral contrast that reaches the rectum. If liver is (+)ve for disease and if resection is entertained then liver-CT portography should be done.
e. Transrectal U/S esp. in distal 2/3 tumors.
f. Colonoscopy ± laser recanalization or stent insertion in obstructed lesions, if clinically needed

g. EKG +/- more extensive work up if clinically indicated.
h. Enterostomal therapist consultation pre-op.
3- **Staging**

To talk or to compare tumors and their management they should be of similar clinical pathologic staging. The TNM (T for Tumor N for Nodes M for Metastasis). Classification is agreed upon by UICC (International Union Against Cancer) and AJC (American Joint Committee) as the most representative.

**Current UICC/AJC Colorectal Staging System**

**Primary tumor (T)**
- TX Primary tumor cannot be assessed
- TO No evidence of primary tumor
- Tis Carcinoma-in-situ
- T1 Tumor Invades Submucosa
- T2 Tumor Invades Muscularis Propria
- T3 Tumor Invades through muscularis propria into the subserosa or into nonperitoneolized pericolic or perirectal tissues
- T4 Tumor perforates the visceral peritoneum or cavity, invades other organs or structures

**Regional lymph nodes (N)**
- NX Regional lymph nodes cannot be assessed
- NO No regional lymph node metastasis
- N1 Metastasis in 1 to 3 pericolic or perirectal lymph nodes
- N2 Metastasis in 4 or more pericolic or perirectal lymph nodes
- N3 Metastasis in any lymph node along the course of a named vascular trunk

**Distant metastasis (M)**
- MX Presence of distant metastasis cannot be assessed
- MO No distant metastasis
- MI Distant metastasis

**Stage grouping**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tis</th>
<th>NO</th>
<th>MO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>Stage II</td>
<td>T3</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>Stage III</td>
<td>Any T</td>
<td>N1</td>
<td>MO</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N2,3</td>
<td>MO</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M 1</td>
</tr>
</tbody>
</table>
## 4- Treatment According to Presentation and Stage:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Stage</th>
<th>Choices of Primary Rx</th>
<th>Adjuvant Rx</th>
</tr>
</thead>
</table>
|              | I(T1-2NoMo) | - Low anterior resection (LAR) with colo-anal pouch (CAP) anastomosis  
- Transmesorectal resection (TME) + CAP or A-P resection.  
- A-P resection if a distal margin cannot be attained, or in the presence of suboptimal anatomical conditions.  
- Transanal local excision, in the medically unfit, or patient preference.  
- Endocavitary radiation in medically unfit with well differentiated tumor. | chemorad only in T2, with poor prognosis i.e. perineural, perivascular and poorly differentiated |
|              | II (T3N0M0)  
(T4N0M0)  
(T1-3N1,3M0) | - LAR/TME + CAP or A-P resection or the next choice  
- Preop Chemorad followed by LAR + CAP or A-P resection | chemorad  
chemo |
|              | III (T1,3N1-3M0)  
(T4N1-3M0) | - Preop chemorad followed A-P resection or LAR/TME | chemo |
|              | I(T1-2N0M0)  
(T4N0M0)  
(T1-3N1,3M0) | - LAR/TME ± CAP  
- Rarely A-P resection depending on anatomical restrictions | chemorad in T2 with poor prognosis |
|              | II (T3N0M0)  
(T4N0M0)  
(T1-3N1,3M0) | - TME ± CAP or A-P in rare cases  
- LAR ±CAP  
- Rarely A-P resection  
- Pre-op chemorad followed by LAR/TME ± CAP or rarely A-P resection  
- Pre-op chemorad followed by LAR/TME ± CAP or rarely A-P resection | chemorad  
chemorad  
chemorad  
chemo |
|              | III (T1,3N1-3M0) | - LAR/TME ± CAP  
- chemorad followed by LAR/TME ± CAP | chemorad  
chemo |
|              | Obstru-cting Ca | - If partial obstruction chemorad followed by Rx according to stage.  
- Stent or laser recanalization followed by Rx according to stage.  
- Resection, anastomosis and proximal covering stoma  
- Resection, intraop colon prep & anastomosis.  
- Resection, proximal colostomy and Hartmans | chemo |
<p>|              | Perforated Ca | - Resect, peritoneal irrigation-if no gross abdominal seeding, | chemo/ |</p>
<table>
<thead>
<tr>
<th>Presentation</th>
<th>Stage</th>
<th>Choice of Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic disease to liver only</td>
<td>IV</td>
<td>If the liver metastasis is diagnosed preop and in the absence of other sites of metastasis (diagnosed by CEA, oncocint or PET scan or intra-op exploration) and the intraop U/S revealed a solitary lesion which is easily resectable then the rectal tumor and liver mets can be resected simultaneously, otherwise the rectal tumor is resected and documentation of liver mets is done by biopsy. The patient is given chemorad and in 3 months the liver mets is or are resected if feasible. If liver mets. is noted intraoperatively and exploration or intraop U/S revealed no other mets and it is easily resectable then resect rectal and liver lesions simultaneously followed by chemo &amp; radiation, otherwise you follow the above.</td>
</tr>
<tr>
<td>Metastatic Disease to lung only</td>
<td>IV</td>
<td>If the Lung lesions are resectable and there are no other sites of mets (ruled out by CEA* or PET scan) they should be excised 3 months after rectal resection and chemorad.</td>
</tr>
</tbody>
</table>
| Metastatic Disease to liver and lung | IV | - If either tumor is unresectable, give chemorad like in generalized mets and operate only if primary tumor bleeds or obstructs.  
- If tumors are resectable, resect primary tumor ± liver mets if simple. Otherwise, give chemo and reassess for possible resection of liver and lung. |
| Metastasis to intra abdominal sites | IV | - Prove mets by biopsy. If diffuse carcinomatosis, treat as generalized mets. If the lesions are resectable without the need for major surgery, then resect primary tumor and metastatic sites followed by chemorad. |
5- MONITORING AND SURVEILLANCE

1- Physical examination, digital rectal exam and sigmoidoscopy every 3 months for 2 years, and then every 6 months for 3 more years.

2- CEA should be done 2 weeks post-op if it was elevated pre-op and then every 2-3 months for 3 years, then every six months for 2 more years. If CEA is not elevated, pre-op CA 19-9 could be done and used to follow up the patient.

3- Chest x-ray every year for 5 years. If the patient had liver mets or other resected mets the chest x-ray should be done every 6 months. If lung mets are excised, the surveillance should be every 6 months.

4- CT of abdomen and pelvis with intravenous and oral contrast (reaching the rectum) every 3-6 months for the 1st year then every 6-12 months for 2 years, then yearly (most mets occur during the 1st 3 years)

5- Colonoscopy every year for 2 consecutive years then every 3-5 years.
POSITIVE MONITORING EXAMINATION

- Combined local & distal Metastasis
  - If both are resectable & after PET or CEA* & in very special cases resect all.
  - Unresectable or Multiple lesion are present
    - Progression on Chemotherapy
    - Supportive or Clinical Trial
  - Resectable isolated organ-confined Metastasis Liver, Lung or Liver & Lung
    - Resect & Chemotherapy
    - Had Radiation before
      - +/- Chemo
      - Non-Resectable
      - Resect if Resectable

- Distal Metastasis
  - (+)ve
    - Colonoscopy
      - (-)ve
        - Chest X-Ray +/- CT
          - CT of Abdomen & Pelvis
            - (-)ve
              - PET +/- or CEA*
                - or CT of chest Abdomen & pelvis every 3 mths until Dx

- Local recurrence
  - CEA
    - (+)ve
      - Colonoscopy
      - Chest X-Ray +/- CT
        - CT of Abdomen & Pelvis
          - (-)ve
            - PET +/- or CEA*
              - or CT of chest Abdomen & pelvis every 3 mths until Dx

* CEA: Carcinoembryonic antigen
Rectal Cancer- Chemotherapy Considerations

- The aims of incorporating chemotherapy into rectal cancer surgical adjuvant treatment are to:

  1- Improve local tumor control by enhancing the effect of irradiation.
  2- Decrease distant metastasis
  3- Improve survival

- There is strong evidence that 5-Fu based adjuvant chemotherapy can improve outcome when used as a component of a multidisciplinary approach to the curative treatment of stage II and III rectal cancer based in the controlled trials. (N Engl j Med 312:312:1465-1472, 1985) (JAMA 264:1444-1450,1990).

- Local control appears to be optimal when irradiation is given in conjunction with chemotherapy.

- In stage II and III (stages B & C) Rectal carcinoma the following is recommended.
  1- Bolus 5-Fu 425 mg/m² D₁ → D₅ with and without Leucovorin 20 mg/m² daily D₁ → D₅ for 2 cycles followed by concomitant pelvic irradiation and bolus 5-Fu with or without leucovorin for 3 days at the start of radiation and 3 days at the end of radiation followed by 5-Fu with or without Leucovorin 5 days/months for additional 2 cycles.
  2- Bolus 5-Fu (with or without LV) → 2 cycles followed by concomitent pelvic irradiation and continuous infusion 5-Fu 300m/d/day followed by bolus 5-Fu (with or without LV) for additional 2 cycles.

- The optimal sequence of surgery, irradiation and chemotherapy is not known. And is the subject of ongoing clinical trials.

- The decision of whether to use pre-operative therapy or preoperative combined modality therapy is based on the results of endorectal ultrasound.

  1- If it reveals T₂ disease the patient may have pathologic T₂N₀M₀ disease and the sole reason for preoperative therapy is sphincter preservation therefore preoperative radiation alone is recommended.
  2-If positive mesorectal and/or pelvic lymphnodes are identified at the time of surgery, then 6 months of adjuvant post-operative 5-Fu based chemotherapy is recommended.
3- For patient with transrectal ultrasound stage T3 disease, pre-operative combined modality therapy followed by surgery and post-operative 5-Fu based chemotherapy is recommended.
COLON CANCER GUIDELINES

1- Factors Influencing Therapy:

All factors that influence rectal cancer apply to colon cancer but the level of the lesion is less important because of the length of the colon and easiness of resection of any site. Only one area of the colon should be noted and that is the splenic flexure because of its duel blood supply from middle colic and from inferior mesenteric vessels and therefore similar lymphatic channels and thus may be necessitating a wider resection.

2- Work-Up Similar to Rectal Cancer Excluding Transrectal u/s

3- Staging Similar to Rectal Cancer

Treatment According To Presentation and Stage

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Stage</th>
<th>Choice of Rx</th>
<th>Adjuvant Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyp</td>
<td>-Tumor reaching muscularis Mucosa (Mm)</td>
<td>Polypectomy suffice</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>-Tumor across Mm at the base of the polyp</td>
<td>Resection, and in very special cases only polypectomy</td>
<td>None or according to stage.</td>
</tr>
<tr>
<td>Nonobstructed Nonmetastatic Tumor</td>
<td>-All colon except splenic flexure</td>
<td>Any Stage</td>
<td>Segmental resection or hemicolectomy</td>
</tr>
<tr>
<td></td>
<td>- Splenic Flexure</td>
<td>Any Stage</td>
<td>Subtotal colectomy or extended transverse colectomy</td>
</tr>
</tbody>
</table>

Chemo for ≥ stage III or stage II with poor prognosis.
<table>
<thead>
<tr>
<th>Presentation</th>
<th>Choice of Rx</th>
<th>Adjuvant Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructed non metastatic</td>
<td></td>
<td>Chemo for≥ stage III or stage II with poor prognosis.</td>
</tr>
<tr>
<td>- Right colon any stage</td>
<td>- Same like non-obstructed</td>
<td></td>
</tr>
<tr>
<td>- Rest of the colon any stage</td>
<td>- Subtotal colectomy with primary anastomosis.</td>
<td>Chemo for&gt; stage III or stage II with poor prognosis.</td>
</tr>
<tr>
<td></td>
<td>- Resect with Hartman's pouch and proximal temporary or permanent colostomy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Like in non-obstructing but with a covering temporary stoma.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Resection, intraoperative colon and rectum preparation and anastomosis.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Recanalization with laser or stenting followed by bowel preparation then Rx like non obstructing</td>
<td></td>
</tr>
<tr>
<td>- Perforated Colon Ca (Stage IV)</td>
<td>- Resection with proximal colostomy and Hartman pouch</td>
<td>chemo for all</td>
</tr>
<tr>
<td></td>
<td>- In optimal conditions in well kept patients, with no gross leakage, treat like obstructing tumor.</td>
<td></td>
</tr>
<tr>
<td>- Locally invasive (T₄NₓM₀)</td>
<td>Treat like non-obstructed with resection of all non-vital contiguous structures (even a whipple if necessary), Use metal Clips to delineate area of resection.</td>
<td>Post-op chemorad</td>
</tr>
<tr>
<td>Generalized Metastasis</td>
<td>- Segmental resection if there is impending obstruction and proof of metastasis.</td>
<td>chemo</td>
</tr>
<tr>
<td></td>
<td>- Rx complications, stent the obstruction</td>
<td>chemo</td>
</tr>
</tbody>
</table>
Preop Unidentified liver mets

Proper colonic resection, intraop liver ultrasound, if tumorectomies is/are simple and tolerable then resect. Otherwise give chemotherapy for 3 months, do CT portography and CEA* or PET scan, if liver mets is resectable and is the only metastasis (excluding resectable lung lesion) then proceed with major liver resection. Otherwise consider, cryotherapy or Intraarterial chemotherapy (systemic ± DAC), for the liver lesions.

Preop Identified Liver metastasis

If considered resectable do CT portography and preferably CEA* or PET scan, if the liver lesions are resectable and it is the only mets (excluding resectable lung lesions) and if intraop operative U/S is (-)ve then resect the colonic lesion and simultaneously resect the liver mets if simple resection is applicable and follow by chemotherapy, otherwise if liver mets needs major resection then give chemotherapy for 3 months, repeat above tests and if (-)ve, and the lesions are stable proceed to major liver resection. When there are other sites of mets or liver lesions that are nonresectable, resect colon and resect mets other than liver if few, or resect one to prove mets. And give chemotherapy ± cryo to liver or IAC.

Lung Metastasis

If lung mets is or are identified and are resectable, CT of lung should be done, if still resectable, the CT portography of abdomen should be done if there is no abd. mets confirmed preferably by CEA* or PET scan. Then proceed to colon resection followed by chemotherapy for 3 months and repeat above tests if still stable resect lung lesions. If liver mets is identified and are resectable, then resect also followed by chemotherapy.

Ovarian Mets

When macroscopic tumor is noted intraop there is no argument that oophorectomy should be done, also prophylactic bilateral oophorectomy should be done in all post menopausal pts with
colorectal cancer. In premenopausal it should be discussed with the pt since there is a conflict in the literature.
4- **Monitoring and Surveillance:**

1- Physical examination every 2-3 months for 3 years then every 6 months.
2- CEA 2 weeks post-operatively if CEA was elevated pre-op, Then CBC & CEA every 2-3 months for 3 years then every 6 months. (many studies recommended shorter interval of doing CEA). If CEA is not elevated preop, then CA 19-9 should be done and if elevated can be used for follow up.
3- CT of abd and pelvis with intravenous and oral contrast every 6 months for 3 years then every year for 3 years.
4- Chest X-ray every year for 5 years.
5- Colonoscopy, soon post-op if not done preop otherwise every 12 months for 3 years if (-)ve every 3 years.

5- **Recurrent WorkUp**

**Repeated elevation in CEA**

A colonoscopy and CT scan should be done, if there is local recurrence by colonoscopy and CT if CT is (-)ve do CT of chest, if (-)ve preferably do PET or CEA* before resection , if resectable, resect, and then give chemo. If colonoscopy is (+)ve and CT is (+)ve for mets that is non-resectable, treat like generalized mets. If mets is resectable as proven by PET or CEA* and following CT of chest which is negative then proceed according to the primary lesion guidelines.

If colonoscopy showed no local recurrence and CT (+)ve do PET or CEA* and or CT of chest if results suggests resectability proceed and if not treat as generalized mets. If CT is (-)ve do PET or CEA* and chest CT, if all are (-)ve then repeat CEA in 3 months if still elevated repeat the above or observe. If PET or CEA* or chest CT revealed resectable solitary lesion then resect, otherwise Rx as generalized mets.

**Positive Abdominal CT**

If CT revealed nonresectable liver or abdominal lesions then document and Rx as generalized metastasis. If CT suggests resectable liver lesions do colonoscopy if (+)ive Rx as generalized mets, and in very special cases resect both. If colonoscopy is (-)ve and CT of chest or and PET or CEA* are (-)ve resect the metastasis after doing a CT portogram, all followed by chemo.
↓ HCT or occult stools (+)ve

Do an upper GI endoscopy if negative proceed to a colonoscopy, if colonoscopy is (+)ve see (+)ve colonoscopy. If colonoscopy is (-)ve, do a small bowel series if negative, repeat colonoscopy in 3 months.
**Colonoscopy (+)ve**

Remove polyps if any is (+)ve for carcinoma Rx like primary lesion. If recurrence is noted, then a CT of abd and pelvis should be done, in special cases if (+) in liver and if both are resectable resect both, otherwise Rx as generalized mets. if CT is (-)ve and CEA* or PET are negative resect the recurrence. If CEA* or PET are (+)ve then Rx as generalized metastasis. In rare cases esp. young and the CT is (+)ve and CEA* or PET are (+)ve and on exploration all lesions can be resected, then resect all.

**Chest X-ray (+)ve**

CT of chest, abdomen and pelvis should be done, if it reveals either nonresectable chest lesion or intraabdominal lesions in the liver or the rest of the abdomen that are irresectable then Rx as generalized mets. If chest CT is resectable and CT of abdomen and pelvis revealed no mets or resectable liver mets preferably confirmed by PET or CEA* then resect both otherwise Rx as generalized mets.