Grand Rounds
Rectal Cancer Treatment

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March 3, 2008
Rectal Cancer

- Cancers arising in the distal 15 cm of the large bowel share many of the genetic, biologic, and morphologic characteristics of colon cancers.

- However, the unique anatomy of the rectum, with its retroperitoneal location in the narrow pelvis and proximity to the urogenital organs, autonomic nerves, and anal sphincters, makes surgical access relatively difficult.
Blood Supply

- Inferior mesenteric artery
- Marginal arteries
- Median sacral artery
- Superior rectal artery
- Right common iliac artery
- Right external iliac artery
- Right internal iliac artery
- Right superior gluteal artery
- Right inferior epigastric artery
- Right obturator artery
- Right superior gluteal artery
- Accessory middle rectal artery
- Right internal pudendal artery
- Right middle rectal artery
- Right inferior rectal artery
Lymphatic Drainage
## TNM Staging Classification of Colorectal Cancer

<table>
<thead>
<tr>
<th>TX</th>
<th>Primary tumor cannot be assessed</th>
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</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: intraepithelial or invasion of lamina propria</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades muscularis propria</td>
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<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into the subserosa or into nonperitonealized pericolic or perirectal tissues</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor directly invades other organs or structures, and/or perforates visceral peritoneum</td>
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</tbody>
</table>

### Regional lymph nodes (N)

<table>
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<tbody>
<tr>
<td>N0</td>
<td>No regional lymph-node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1 to 3 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
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</table>

### Distant metastasis (M)

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<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
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</table>
Local excision

• Excellent operation for a small cancer in the distal rectum that has not penetrated into the muscularis.
• Transanal approach, and usually involves excision of the full thickness of the rectal wall underlying the tumor.
• Local excisions do not allow complete removal of lymph nodes in the mesorectum, and therefore operative staging is limited.
• The operation is indicated for mobile tumors that are less than 4 cm in diameter, that involve less than 40% of the rectal wall circumference, and that are located within 6 cm of the anal verge.
• These tumors should be stage T1 (limited to the submucosa) or T2 (limited to the muscularis propria), well or moderately differentiated histologically, and with no vascular or lymphatic invasion.
Locally advanced rectal cancer
Stage II-III

• Since the early 90’s

• Radical surgery
• Fluoropyrimidine-based chemoradiotherapy (CHRT)
• Gold standards of treatment for locally advanced rectal cancer.
Gastrointestinal Tumor Study Group and the North Central Cancer Treatment Group

- Studies in 1990 concluded

- Combination of postoperative chemo-therapy with radiotherapy improved local tumor control and survival in stage II and III rectal cancer relative to surgery alone.

Milestones

• Improvement of the surgical technique, total mesorectal excision (TME).
• TME became the choice surgical procedure, with a relevant increase in local control.
• Actually, at some point it was thought that TME could make radiotherapy (RT) unnecessary.

Sagittal view of the pelvis demonstrating the plane of dissection for rectal resection
Milestones

• A randomized study soon followed showing the maintained benefit of RT and TME surgery, at least in terms of local control

• Outcomes that are improving with even longer follow-up.

Second landmark

- Move the CHRT segment before the surgery.
- Initially, preoperative radiotherapy was found to improve overall survival as compared with surgery alone.
- In the last decade, the dominant tendency in the therapeutic development of rectal cancer, both in Europe and North America, has been the use of preoperative radiotherapy with conventional protracted fractionation (45-50 Gy in daily fractions of 1.8-2 Gy during 5-6 wk) with concurrent chemotherapy followed by TME surgery at 4-8 wk.


Preoperative CHRT

Extensive experience with preoperative CHRT showed feasibility and promising results in terms of:

- down staging of tumor
- Use of sphincter preservation surgery
- Local disease control
- Overall survival parameters

Also interesting in the analysis was an improved toxicity profile.

- The most frequently used chemotherapy agent in this clinical context is 5-fluorouracil

- A phase III trial concluded comparing pre- vs post-operative CHRT
- Demonstrated better tolerance of the chemotx
- Ability to perform sphincter-saving surgical procedures and local control therapy with preoperative CHRT

Down-staging

- Preoperative radiotherapy alone (no chemotherapy) and delayed surgery reported down staging rates of 18%.
- However, the prolonged administration of CH-RT achieves down staging figures of around 65%.


Down-staging

- Additionally, induction of tumor down staging improves the probability of a complete resection and sphincter-preserving surgery.
- Complete pathologic response rates range from 8% to 27% using i.v. 5-FU with preoperative irradiation.


Low Anterior Resection
ABDOMINOPERINEAL RESECTION OF RECTUM
Toxicity

- In studies of postoperative 5-FU-based CHRT, severe acute toxicity ranges from 24%-40%.
- However, in Phase II studies of preoperative CH-RT
- Acute toxicity occurs in 15%-28% of patients.


Tumor control and survival for Stage II-III

- Published series vary in follow-up
- Preoperative CHRT in rectal cancer ranges at 5-year:
  - Local recurrence from 2% to 15%
  - Disease-free survival from 70% to 86%
  - Overall survival from 60% to 85%.


In summary

- Incorporation of TME surgical procedure and 5-FU-based preoperative CHRT have been translated to an improvement in local control.
- With the additional advantage of more tolerable treatments in terms of acute toxicity and saving-sphincter surgical procedures.
MANAGEMENT OF RECTAL CANCER
(Resectable metastatic disease not considered in this algorithm)

SUSPECTED RECTAL CANCER
Biopsy +

Non-obstructed

Consider metastatic work-up

(-) Transrectal ultrasound

Stage I
Preoperative neoadjuvant therapy***
Resection for curative intent#
Scheduled follow-up**

Stage II, III

(+) Palliative resection and/or observation and/or combined chemoradiation for local control#

Periodic assessment of response

Obstructed

Consider metastatic work-up*

(-) Emergency decompression: colonic stent as bridge to surgery or temporary stoma

Transrectal ultrasound]

Stage I
Preoperative neoadjuvant therapy***
Curative resection
Scheduled follow-up**

Stage II, III

(+) Palliation: palliative colonic stent, palliative resection, or diverting stoma

Systemic chemotherapy; consider radiation for local control

Periodic assessment of response