بسم الله الرحمن الرحيم
Digestive Disease Research Institute
Hazrate Rasoul Hospital
Tehran University of medical sciences

Shahram Agah
Associate professor of
gastroenterology
Rectal cancer present and future
Incidence in Iranian older age is currently very low compared to western population
In younger age: accelerated rate
Burden is increasing dramatically

Malekzadeh, MD, Ansari MD AIM 2009
Epidemiology (continue)

- Occurrence in family
- Younger probands
- Located in the right side
- In past 3 decades significant socioeconomic development
- Lifestyle changes (diet rich in fat & meat)
3rd most common cancer in males (ASR: 8.3/100000)

4th most common cancer in females (ASR: 6.5/100000)

Young CRC is considerably higher than western

Age < 40 : 1/5

Causes:

1. Different lifestyle
2. Inherited
Clinical manifestation

1. Abdominal pain: 21%
2. Change in bowel habit: 43%
3. Hematochezia or blood in stool: 60%
4. Weakness: 20%
5. Anemia without other gastrointestinal symptoms: 26% (occult GI bleeding)
6. Weight loss: 6%

Others: abdominal distention, nausea, vomiting
Metastasis 20% at first dx

- 1. hematogenous dissemination,
  2. contiguous and transperitoneal routes.

The most common metastatic sites:

- a. regional lymph nodes
- b. liver
- c. lungs (distal rectum: may first)
- d. Peritoneum
- e. bone
Alarming signs

- Weight loss very low sensitivity & specificity
- Dark red rectorrhagia & abdominal mass 95% specificity
- Involvement of sciatic & other nerves
- Others: abdominal distention, nausea, vomiting
Rare presentation

- Fistula to bladder or small bowel
- FUO or abdominal abscess
- Bacteremia with strep bovis
- Perforation
  - Obstruction and/or perforation, although uncommon, carry a poor prognosis
prognosis

- Distal rectum has the worst prognosis
Synchronous & metachronous lesions

- Synchronous 3% - 5%
- Has the same prognosis as metachronous: 1.5% - 3% during 5 years, 9% later in an alive person
A 72-year-old man who is in good general health came with cc of rectal bleeding on & off from 4 months ago

P/E: mild pallor, normal BP & PR

Digital Rectal Exam: mass at 6 cm from anal verge

Hb: 12.2, OB: +++
AST: 28, ALT: 34, ALK-P: 755

What you recommend for this patient?
case

1. rigid sigmoidoscope
2. flexible sigmoidoscope
3. total colonoscopy
4. double contrast barium enema + rectosigmoidoscopy
5. virtual colonography
6. capsule endoscopy
Diagnosis & staging
Diagnosis

1. digital rectal exam : relation and fixation to anal sphincter
2. rigid sigmoidoscope is better than flexible to determine the position
3. colonoscopy for synchronous lesions
4. double contrast barium enema + rectosigmoidoscopy
5. virtual colonography
6. capsule endoscopy
Digital rectal exam

- Anal canal length is about 4 cm

- It is located between anal verge & dentate (pectinate line)
- Anal verge is the margin of skin and mucosa

- Dentate line is the margin of squamous and columnar epithelium
- Ano-rectal ring (high pressure zone) is located 1-3 cm above dentate line
- Preserving sphincter tumor should be above this ring (more than 5-8 cm from anal verge)
Adenoma to Carcinoma Pathway

Normal Epithelium → Hyper-proliferation → Early Adenoma → Intermediate Adenoma → Late Adenoma → Cancer

APC loss → K-ras mutation → Chrom 18 loss → p53 loss
DD of colonic mass

- Malignant lesions
- Adenocarcinoma
- Lymphoma
- Carcinoid tumor
- Kaposi's sarcoma
- Prostate cancer
Benign lesions
Crohn's colitis
Diverticulitis
Endometriosis
Solitary rectal ulcer
Lipoma
Tuberculosis
Amebiasis
Cytomegalovirus
Fungal infection
Extrinsic lesion
Biopsy was performed and send for pathology

- Report:
- Well differentiated adenocarcinoma of rectum
What do you perform next?

1. refer the patient for immediate surgery
2. Abdominopelvic CT scan
3. Abdominopelvic MRI
4. trans rectal endosonography
Clinical staging

- Physical exam: (attention to: ascitis, LAP, hepatomegally)
- Abdominopelvic CT scan (more sensitive for rectal cancer than for colon cancer, no non-malignant LAP in this area)
- (liver metastasis does not necessarily alter the plan)
- Chest imaging
- LFT:
- ALK-P the most sensitive although may be normal
- CEA > 5-10 is an independent prognostic factor
Accuracy of methods for T staging

- TRUS: ranges from 80% - 95%
- CT: 65% to 75%
- MRI: 75% to 85%
- DRE: 62%
MRI scan for pre-operative staging
INVOLVEMENT OF MESORECTAL FASCIA
INVolVEMENT OF PUBORECTAL SPHINCTER
EXTRAMURAL VEIN INVASION
Bowel Cancer Staging

Outlook depends on spread

- Confined to bowel wall  Dukes’ A  85%
- Through the wall   Dukes’ B   65%
- Spread to glands  Dukes’ C   35%
- Spread to the liver  Dukes’ D   10%
T staging

- **TX**  Primary tumor cannot be assessed
- **T0**  No evidence of primary tumor
- **Tis**  Carcinoma in situ: intraepithelial or invasion of lamina propria*
- **T1**  Tumor invades submucosa
- **T2**  Tumor invades muscularis propria
- **T3**  Tumor invades through the propria into pericolorectal tissues
- **T4a** Tumor penetrates to the surface of the visceral peritoneum
- **T4b** Tumor directly invades or is adherent to other organs or structures Δ
N staging

- **NX** Regional lymph nodes cannot be assessed
- **No** No regional lymph node metastasis
- **N1** Metastasis in 1-3 regional lymph nodes
  - **N1a** Metastasis in one regional lymph node
  - **N1b** Metastasis in 2-3 regional lymph nodes
  - **N1c** Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
- **N2** Metastasis in four or more regional lymph nodes
  - **N2a** Metastasis in 4-6 regional lymph nodes
  - **N2b** Metastasis in seven or more regional lymph nodes
M staging

- M₀  No distant metastasis
- M₁  Distant metastasis
- M₁a Metastasis confined to one organ or site (e.g., liver, lung, ovary, non regional node)
- M₁b Metastases in more than one organ/site or the peritoneum
Tumor invades through the propria into pericolorectal tissues, 2 LN was detected at perirectal area

- Which stage should be considered in this patient?
- 1. T3N1a
- 2. T3N1b
- 3. T2N2
- 4. T2N1a
Which treatment do you recommend?

1. surgery
2. neoadjuvant chemo radiotherapy then surgery
3. surgery then adjuvant chemo radiotherapy
4. chemo radiotherapy alone
Treatment
Improved coordination of care
To consider each case from a variety of perspectives.
Patients are more likely to be offered a range of types of treatment at appropriate times
A supportive environment where professionals can share their concerns
Surgeons receive feedback from pathologists and other team members on the results of their work
Optimal setting for clinical research
A MULTIDISCIPLINARY TEAM APPROACH FOR RECTAL CANCER: CORE MEMBERS

- Experienced imaging specialist, particularly on MRI
- At least two well trained TME surgeons
- Pathologist able to report on specific requirements
- Radiation Oncologist with focused interest in rectal cancer
- Medical Oncologists
- Clinical Nurse specialist
- Other non core members
A MULTIDISCIPLINARY TEAM APPROACH FOR RECTAL CANCER

- Discussion of all new cases before surgery
- Discussion of MRI data
- Selection of patients for preoperative therapy
- Discussion of pathology report, stressing the assessment of the surgical plane and CRM
- Selection for postoperative therapy
- Detailed discussion of any relapse during follow up
- Yearly audits of all activities and results
THE IMPORTANCE OF MULTIDISCIPLINARY TEAM DISCUSSION:

Total no. Rectal cancer pts 298

Potentially curative 259 (87%)

Palliative cases 39 (13%)

Not discussed 62 (24%)

Surgery alone 62 (100%)

Histological CRM+ve 16/62 (26%)

Histological CRM-ve 46/62 (74%)

Histological CRM+ve 1/116 (1%)

Histological CRM-ve 113/116 (97%)

Discussed 197 (76%)

Surgery alone (Group 1) 116 (59%)

Preoperative therapy (Group 2 and 3) 81 (41%)

Refused surgery 2/116 (1%)
5 years survival after curative surgery

- Stage I: 80% to 90%
- Stage II: 50% to 60%
- Stage III: 30% to 40%
Type of surgery

- Low anterior resection
- Abdominopelvic resection
- Complicated cases: different surgery
Indication of neoadjuvant therapy

- Complete indications:
  - T₃/T₄ tumor even cT₃No

- Relative indications:
  1. presence of clinically node-positive rectal cancer in a patient with an MRI or TRUS-staged T₁/T₂ rectal cancer,
  2. distal rectal tumor for which an APR is thought to be necessary
  3. tumor which appears to invade the mesorectal fascia on preoperative imaging,
Effect of neoadjuvant

- Low controlled trials showed benefit for sphincter saving
- Decline risk of drug toxicity and postop complications
- Restaging after neoadjuvant is not sensitive and does not recommended
Guideline update

- MSI, KRAS, BRAF, testing
- FOLFOX cumulative dose/toxicity
- Transanal excision
Adjuvant therapy

- In stage II & III adjuvant is recommended
- RT does not decline the mortality but decline local recurrence
- RT + Chemo increase survival
Adjuvant in T3

- Presence of perineural invasion
- MSI instability
- 18q loss of heterozygosity

( 5FU/leukovorin/oxaliplatin )
Guideline continue

- Bevacizumab
- Cetuximab
- Panitumumab
- Irinotecan
- Only in stage IV
- In stage II & III Should not be used outside the setting of a clinical trial
High risk T3N0M0

- Grade 3-4
- Lymphatic, vascular invasion
- Bowel obstruction
- <12 lymph nodes examined
- Localized perforation
- Indeterminate or positive margins
Poor risk stage II

- T4
- Bowel perforation
- Lymphovascular invasion
- Poorly differentiate histology
- Perineural invasion
- Lymph node count < 12
- High tumoral thymidylate synthase
- 18q loss of heterozygosity
- Microsatellite – stable (MSI actually do worse when they receive adjuvant)
KRAS

- EGFR binding of cetuximab is inhibited with KRAS
BRAF mutation

- Unlikely to benefit from monoclonal antibody
Malignant polyp

- Polypectomy is enough unless:
  1. margin involvement
  2. poor differentiation
  3. lymphovascular invasion
Obstructing Colorectal Cancer

- Operate in day-time hours
  - Manpower
  - Resourse
- Exclude pseudo-obstruction
  - Gastrograffin enema
  - CT scan
- Avoid stoma if possible
  - Single stage operation
- Overall mortality <20%
Efficacy and Safety of Stents

Systematic Review *Khot et al BJS in press 2002*

29 series n=598

- Palliative 56.2%
- Bridge to surgery 43.8%

**Technical success** 92%

**Clinical success** 88%

- Palliation achieved 90%
- Bridge to surgery 85%
- One stage procedure 95%