Colorectal cancer guidelines from Yesterday till Today

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Introduction

- **The incidence of CRC**  **at a rate of approximately 2.9% per year or greater between 2005 till 2017.**
- **The incidence rates for colon and rectal cancers will**  **by 90.0% and 124.2%, respectively, for patients aged 20 to 34 years by 2030.**
- **Preoperative CEA is an independent predictor of OS in patients with stage I to III colon cancer.**
- **These guidelines are inclusive and not prescriptive. Their purpose is to provide information on which decisions can be made, rather than to dictate a specific form of treatment.**

I. AJCC/TNM staging system

- The eighth edition has expanded the definition of metastatic disease to include the M1c category for peritoneal implants,
- clarified the definition of tumor deposits, and
- highlighted the importance of lymphovascular invasion, microsatellite instability (MSI) status, and mutations in KRAS, NRAS, and BRAF in treatment considerations.

- **As with previous editions, a positive lymph node is defined as one containing a ≥0.2-mm deposit of cancer cells.**
- **Although debate continues regarding the prognostic value of "isolated tumor cells" or clumps of tumor cells measuring <0.2 mm in regional lymph nodes, these terms are not included in the AJCC/TNM staging system.**
- **At the present time the use of sentinel lymph nodes should be considered investigational.**

i. Tumor deposits (satellite nodules):N1c

- **Definition**
  - **Irregular discrete tumor deposits in pericolic or perirectal fat away from the leading edge of the tumor and showing no evidence of residual lymph node tissue.**
- **Associated with reduced disease-free and overall survival.**
- **Their number should be recorded in the surgical pathology report.**

ii. Radial (circumferential) margin evaluation for colon cancer

- **The circumferential resection margin corresponds to any aspect of the colon that is not covered by a serosal layer of mesothelial cells.**

- **The mesenteric resection margin is the only relevant circumferential margin in segments completely encased by the peritoneum.**

II. Pedunculated or sessile polyp (adenoma) with invasive cancer

- Pathology review ?.
- Full colonoscopy.
- Marking of cancerous polyp site.
- Single specimen, with clear margins.

Recent evidence supports a ≥1-mm margin, and most recently, a negative resection margin of any measure is adequate.

“Low risk” features:

- **Resection margins free of dysplasia or cancer,**
- **well or moderately differentiated cancer.**
- **without angiolymphatic invasion, and**
- **limited submucosal invasion with cancer cells ≤2 mm below the muscularis mucosa.**

III. PET-CT

PET/CT scan is not indicated in non metastatic colon cancer appropriate for resection.

Indications:

- **Suspected or proven metastatic synchronous/metachronous adenocarcinoma if potentially surgically curable M1 disease.**
- **CEA elevation with negative findings (radiological and colonoscopy).**

If done, PET/CT does not supplant a contrast-enhanced diagnostic CT scan.

IV. Stage II colon cancer adjuvant therapy

T3, N0, M0 (MSI-L or MSS and no high-risk features)

- **Observation or**
- **Consider capecitabine or 5-FU/leucovorin.**

T3, N0, M0 at high risk for systemic recurrence OR T4, N0, M0

- **Capecitabine or 5-FU/leucovorinn, or**
- **FOLFOX or CAPEOX or**
- **Observe.**

High-risk factors for recurrence:

- **Poorly differentiated histology (exclusive of those cancers that are MSI-H),**
- **lymphatic/vascular invasion,**
- **bowel obstruction,**
- **<12 lymph nodes examined,**
- **perineural invasion,**
- **localized perforation, or**
- **close, indeterminate margins.**

V. Locally advanced disease

- Clinical T4b consider neoadjuvant chemotherapy FOLFOX or CAPEOX
- Locally unresectable or medically inoperable …
  - Systemic Therapy or
  - Infusional 5-FU/RT (preferred) or
  - Capecitabine/RT (preferred) or
  - bolus 5-FU/leucovorin/RT
  - Re-evaluate for conversion to resectable disease.

VI. Resectable synchronous liver and/or lung metastases only

The treatment should be individualized and based on a comprehensive multidisciplinary approach.

i. **Synchronous or staged colectomy with liver or lung resection (preferred) and/or local therapy followed by adjuvant therapy or**
ii. **Neoadjuvant therapy (for 2–3 months) followed by synchronous or staged colectomy and resection of metastatic disease or**
iii. **Colectomy, followed by chemotherapy (for 2–3 months) followed by staged resection of metastatic disease.**

VII. Colon cancer with ovarian metastasis

- **The ovaries are the site for colorectal cancer metastasis (Krukenberg tumor) in 3% to 8% of patients.**
- **If 1 ovary is involved with metastatic disease, a bilateral oophorectomy should be performed with the expectation of prolonged survival in affected women who receive adjuvant chemotherapy.**

VIII. Synchronous abdominal/ peritoneal metastases

- **Consider colon resection only if imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms.**
- **Complete cytoreductive surgery and/or intraperitoneal chemotherapy can be considered in experienced centers for select patients with limited peritoneal metastases for whom R0 resection can be achieved**.

IX. Locoregional recurrence

- **The risk for locoregional recurrence as the first and only site of recurrence following curative resection of localized colon cancer is low, approximately 2% to 3%. Salvage surgical resection is possible in approximately 30% of patients.**
- **The treatment of patients with locoregionally recurrent colon cancer should be multidisciplinary.**
- **Potentially curative resection, including multivisceral resection, should be performed when indicated to improve overall survival.**

XI. EUS for rectal cancer staging

- **EUS cannot fully image high or bulky rectal tumors nor regions beyond the immediate area of the primary tumor (eg, tumor deposits, vascular invasion).**
- **Another disadvantage of EUS is a high degree of operator dependence.**
- **At this time, EUS should only be used to evaluate the pelvis if MRI is contraindicated (eg, due to a pacemaker).**

XII. Transanal local excision and TEM

Is only appropriate for

- **Selected T1,N0 early-stage cancers.**
- **Small (<3 cm).**
- **Well- to moderately differentiated tumors.**
- **Within 8 cm of the anal verge.**
- **limited to <30% of the rectal circumference,**
- **No evidence of nodal involvement.**
- **In addition, full thickness excision must be feasible.**

If pathologic examination reveals adverse features

- **Positive margins,**
- **lymphovascular invasion,**
- **poor differentiation, or**
- **invasion into the lower third of the submucosa (sm3 level)**

A more radical resection is recommended.

XIII. Total neoadjuvant therapy approach for rectal cancer

Possible benefits of using chemotherapy first include;

- **Early prevention or eradication of micrometastases,**
- **higher rates of pCR,**
- **minimizing the time patients need an ileostomy,**
- **facilitating resection, and**
- **improving the tolerance and completion rates of chemotherapy.**

XIIII. Short-course RT/conventional RT

- **Short-course RT gives effective local control and the same OS as more conventional RT schedules, and therefore is considered as an appropriate option for patients with T3,N0 or T1–3,N1–2 rectal cancer.**

- **Short-course RT is not recommended for T4 disease at this time.**

XV. Watch-and-Wait approach for clinical complete responders

- the NCCN panel believes that a nonoperative management approach may be considered in centers with experienced multidisciplinary teams after a careful discussion with the patient of their risk tolerance.

XVI. Genetic testing

KRAS, NRAS, and BRAF Mutation Testing

- **All patients with metastatic colorectal cancer should have tumor tissue genotyped for RAS (KRAS and NRAS) and BRAF mutations.**
- **Patients with any known KRAS mutation (exon 2, 3, 4) or NRAS mutation (exon 2, 3, 4) should not be treated with either cetuximab or panitumumab.**
- **BRAF V600E mutation makes response to panitumumab or cetuximab highly unlikely unless given with a BRAF inhibitor.**

Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing

- **Universal MMR* or MSI* testing is recommended in all patients with a personal history of colon or rectal cancer.**
- **The presence of a BRAF V600E mutation in the setting of MLH1 absence would preclude the diagnosis of Lynch syndrome.**
- **Stage II MSI-H patients may have a good prognosis and do not benefit from 5-FU adjuvant therapy.**


Thank
you