Radiation therapy for rectal cancer.

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Overview

Guideline Objective

To provide recommendations for the indications and appropriate technique and dose of neoadjuvant radiation therapy (RT) in the treatment of localized rectal cancer

Note: Outside the scope of this guideline are many other important questions that may be subjects of other guidelines, including indications, dose and technique for adjuvant therapy, RT in the setting of oligometastatic disease, locally recurrent disease, palliative RT, contact RT, proton RT, intraoperative RT, re-irradiation, and detailed discussions of surgical approaches and chemotherapy regimens. While outside the scope of this guideline, efforts to proactively address potential survivorship issues including fertility and sexual dysfunction should be made, especially given the increasing incidence of rectal cancer among young adults.

Patient Population

Adults ≥18 years with a diagnosis of operable primary rectal cancer

Recommendations

Recommendation Statements

Key Question (KQ) 1: What are the indications for neoadjuvant radiation therapy (RT) for operable rectal cancer?

1. For patients with rectal cancer, pelvic magnetic resonance imaging (MRI) with a rectal cancer protocol is recommended for preoperative clinical T and N staging. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

2. For patients with stage II-III rectal cancer, neoadjuvant RT is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

3. For patients with stage II rectal cancer at lower risk of locoregional recurrence, omission of neoadjuvant RT is conditionally recommended after discussion with a multidisciplinary team. (**Strength of recommendation: Conditional; Quality of evidence: Moderate**)

   Implementation Remark: Lower risk is defined as a cT3a/b N0 tumor that is >10 cm from the anal verge* and with MRI-determined circumferential resection margin (mrCRM) ≥2 mm and no MRI-determined extramural vascular invasion (mrEMVI).

4. For patients with cT1-2N0 rectal cancer who may need an abdominoperineal resection (APR), neoadjuvant chemoradiation is conditionally recommended to improve the chance of sphincter preservation. (**Strength of recommendation: Conditional; Quality of evidence: Expert Opinion**)

5. For patients with rectal cancer where radiation is indicated, RT should be performed preoperatively rather than postoperatively. (**Strength of recommendation: Strong; Quality of evidence: High**)

***** cT3a/b = 1 to 5 mm extramural tumor spread; tumor height should be surgeon defined.

KQ2: What are appropriate neoadjuvant regimens for operable rectal cancer when neoadjuvant therapy is indicated?

1. For patients with rectal cancer receiving neoadjuvant chemoradiation, conventional fractionation from 5000-5040 cGy in 25-28 fractions with concurrent chemotherapy is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

2. For patients with rectal cancer receiving neoadjuvant short-course RT, 2500 cGy in 5 fractions without concurrent chemotherapy is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

3. For patients with rectal cancer undergoing neoadjuvant chemoradiation, only concurrent 5-fluorouracil or capecitabine is recommended with RT for radiosensitization. (**Strength of recommendation: Strong; Quality of evidence: High**)

4. For patients with rectal cancer undergoing neoadjuvant therapy, chemotherapy alone (folinic acid, 5-fluorouracil, and oxaliplatin [FOLFOX] or capecitabine and oxaliplatin [CAPOX]) is conditionally recommended only in the context of a clinical trial or multi-institutional registry. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

5. For patients with rectal cancer undergoing neoadjuvant therapy *without* tumor factors that portend increased recurrence risk, (1) chemoradiation or (2) short-course RT are recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

   Implementation Remark: Risk factors for increased recurrence include cT3 tumors ≤5 cm from the anal verge or mrCRM <2 mm; cT4 tumor or cN2 disease, presence of mrEMVI.

6. For patients with rectal cancer undergoing neoadjuvant therapy without tumor factors that portend increased recurrence risk, addition of multiagent (FOLFOX or CAPOX) chemotherapy (1) before or after chemoradiation or (2) after short-course RT is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

   Implementation Remark: Risk factors for increased recurrence include cT3 tumors ≤5 cm from the anal verge or mrCRM <2 mm; cT4 or cN2 disease, presence of mrEMVI.

7. For patients with rectal cancer undergoing neoadjuvant therapy *with* tumor factors that portend increased recurrence risk, addition of multiagent (FOLFOX or CAPOX) chemotherapy (1) before or after chemoradiation or (2) after short-course RT is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Moderate**)

   Implementation Remark: Risk factors for increased recurrence include cT3 tumors ≤5 cm from the anal verge or mrCRM <2 mm; cT4 or cN2 disease, presence of mrEMVI.

8. For patients with rectal cancer receiving neoadjuvant chemotherapy as a component of a total neoadjuvant therapy strategy, 3-4 months of either FOLFOX or CAPOX (without additional agents, targeted therapy, or immunotherapy) is recommended. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

9. For patients with rectal cancer undergoing neoadjuvant chemoradiation with no further neoadjuvant chemotherapy planned, an interval of 6-11 weeks from the end of chemoradiation to surgery is recommended. (**Strength of recommendation: Strong; Quality of evidence: High [≥6 weeks], Moderate [6-11 weeks]**)

10. For patients with rectal cancer undergoing neoadjuvant short-course RT with no further neoadjuvant chemotherapy planned, an interval of either ≤3 days or 4-8 weeks from the end of RT to surgery is recommended. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

    Implementation Remark: An interval of 4-8 weeks is preferred for patients who may benefit from tumor downstaging before resection.

KQ3: What are the appropriate indications for consideration of a nonoperative management (NOM) or local excision (LE) approach after definitive/preoperative chemoradiation?

1. NOM is conditionally recommended after multidisciplinary discussion if a complete clinical response (cCR) is achieved after neoadjuvant treatment in patients with rectal cancer who:

    a. Would have a permanent colostomy or inadequate bowel continence after total mesorectal excision (TME); AND

    b. Decline TME; AND

    c. Agree to close follow-up by a multidisciplinary team.

    (**Strength of recommendation: Conditional; Quality of evidence: Moderate**)

2. Organ preservation through neoadjuvant chemoradiation followed by LE is conditionally recommended after multidisciplinary discussion for patients with cT2 N0 rectal cancer who:

    a. Would have a permanent colostomy or inadequate bowel continence after TME; AND

    b. Decline TME; AND

    c. Are found to have ≤ypT1 disease and R0 margins upon LE; AND

d. Agree to close follow-up by a multidisciplinary team.

(**Strength of recommendation: Conditional; Quality of evidence: Moderate**)

3. For patients with rectal cancer considering NOM or LE after RT, conventional fractionation from 5000-5400 cGy in 25-30 fractions with concurrent chemotherapy is recommended. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

4. For patients with rectal cancer considering NOM, concurrent chemoradiation with or without induction or consolidation chemotherapy is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Moderate**)

5. For patients with rectal cancer considering NOM, assessment for response is recommended with rectal protocol MRI, computed tomography (CT) abdomen/pelvis, and proctoscopy/sigmoidoscopy with digital rectal examination (DRE) 2-3 months after completion of treatment. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

6. For patients with rectal cancer undergoing NOM or LE, surveillance is recommended with:

    - Proctoscopy/sigmoidoscopy with DRE every 3 months for the first 2 years, then every 6-12 months thereafter;
    - Rectal protocol MRI every 3-6 months for the first 2 years, then every 6-12 months thereafter; and
    - Cross-sectional imaging of the chest, abdomen and pelvis every 6-12 months for the first 2 years, then every 12 months thereafter.

    (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

    Implementation Remark: Follow-up should continue for a minimum of 5 years.

KQ4: What are the appropriate treatment volumes, dose-constraints, and techniques for patients treated with RT?

1. For patients with cT3-4 and/or cN + rectal cancers, inclusion of the rectum, mesorectal nodes, presacral nodes, internal iliac nodes, and obturator nodes in the

clinical target volume (CTV) is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

2. For patients with rectal tumors invading an anterior organ or structure (e.g., prostate, seminal vesicles, cervix, vagina, and/or bladder), inclusion of the external iliac nodes in the CTV is conditionally recommended in addition to the rectum, mesorectal nodes, presacral nodes, internal iliac nodes, and obturator nodes. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

3. For patients with rectal cancer involving the anal canal, inclusion of inguinal and external iliac nodes in the CTV is conditionally recommended in addition to the rectum, mesorectal nodes, presacral nodes, internal iliac nodes, and obturator nodes. (**Strength of recommendation: Conditional; Quality of evidence: Expert opinion**)

4. For patients with rectal cancer treated with RT, an intensity modulated radiation therapy (IMRT)/volumetric modulated arc therapy (VMAT) technique is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

   Implementation Remark: IMRT/VMAT may be beneficial when the external iliac nodes and/or the inguinal nodes require treatment or when 3-dimensional (3-D) conformal techniques may confer a higher risk for toxicity.

5. For patients with rectal cancer receiving IMRT/VMAT, daily image guidance to verify localization is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Expert opinion**)

6. For patients with rectal cancer in whom the CTV does not include the inguinal nodes, simulation prone with a belly board is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

Evidence Rating Scheme

Overall Quality of Evidence Grade	Type/Quality of Study	Evidence Interpretation

High	• 2 or more well-conducted and highly-generalizable randomized controlled trials (RCTs) or meta-analyses of such trials.	The true effect is very likely to lie close to the estimate of the effect based on the body of evidence.
Moderate	• 1 well-conducted and highly-generalizable RCT or a meta-analysis of such trials **OR** • 2 or more RCTs with some weaknesses of procedure or generalizability **OR** • 2 or more strong observational studies with consistent findings.	The true effect is likely to be close to the estimate of the effect based on the body of evidence, but it is possible that it is substantially different.
Low	• 1 RCT with some weaknesses of procedure or generalizability **OR** • 1 or more RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes **OR** • 2 or more observational studies with inconsistent findings, small sample sizes, or other problems that potentially confound interpretation of data.	The true effect may be substantially different from the estimate of the effect. There is a risk that future research may significantly alter the estimate of the effect size or the interpretation of the results.

Expert Opinion*	• Consensus of the panel based on clinical judgment and experience, due to absence of evidence or limitations in evidence.	Strong consensus (≥90%) of the panel guides the recommendation despite insufficient evidence to discern the true magnitude and direction of the net effect. Further research may better inform the topic.

***** A lower quality of evidence, including expert opinion, does not imply that the recommendation is conditional. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials but there still may be consensus that the benefits of a treatment or diagnostic test clearly outweigh its risks and burden.

Recommendation Rating Scheme

Strength of Recommendation	Definition	Overall Quality of Evidence Grade	Recommendation Wording
Strong	• Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits. • All or almost all informed people would make the recommended choice.	Any (usually high, moderate, or expert opinion)	"Recommend/Should"
Conditional	• Benefits are finely balanced with risks and burden or appreciable uncertainty exists about the	Any (usually moderate, low, or expert opinion)	"Conditionally Recommend"

	magnitude of benefits and risks. • Most informed people would choose the recommended course of action, but a substantial number would not. • A shared decision-making approach regarding patient values and preferences is particularly important.		

Related Content

Supporting Documents

- Evidence Tables.
- Appendix 1: Peer Reviewers and Disclosures.
- Appendix 2: Abbreviations.
- Appendix 3: Literature Search Strategy.
- ASTRO Clinical Practice Guideline Methodology Guide; 2019 May.
- ASTRO Guideline Development Process Overview.

Implementation Tools

- Executive Summary; 2021 Jan-Feb.

- Slide Set; 2020.

Patient Education

No patient education materials available.

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TRUST Scorecard

Composition of Guideline Development Group (GDG)

Multidisciplinary GDG Members	**Yes**
Methodologist Involvement	**Yes**
Incorporation of Patient and Public Perspective	

Systematic Review of Evidence

Literature Search	
Study Selection	
Evidence Synthesis	

Foundations for Recommendations

Strength of Evidence Grade	
Description of Benefits and Harms of Recommendations	
Summary of Evidence Supporting Recommendations	
Strength of Recommendations Rating	
Clear Articulation of Recommendations	

Funding Source

Yes

Disclosure and Management of Financial Conflicts of Interests



External Review



Updating



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