Complete Summary

GUIDELINE TITLE

Resectable rectal cancer.

BIBLIOGRAPHIC SOURCE(S)

Suh WW, Johnstone PA, Blackstock AW, Herman J, Konski AA, Mohiuddin M, Poggi MM, Regine WF, Rich TA, Cosman BC, Saltz L, Expert Panel on Radiation Oncology-Rectal/Anal Cancer. Resectable rectal cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 7 p. [16 references]

GUIDELINE STATUS

This is the current release of the guideline.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
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IDENTIFYING INFORMATION AND AVAILABILITY
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SCOPE

DISEASE/CONDITION(S)

Resectable rectal cancer

GUIDELINE CATEGORY

Evaluation
Treatment

CLINICAL SPECIALTY

Gastroenterology
Oncology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of procedures for evaluation and treatment of respectable anal cancer

TARGET POPULATION

Patients with resectable rectal cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Blood tests: complete blood count (CBC), liver function tests, carcinoembryonic antigen (CEA)
2. X-ray
    - Chest
    - Colon (barium enema)
3. Computed tomography (CT)
    - Abdomen and pelvis
    - Chest
4. Endorectal magnetic resonance imaging (MRI)
5. Endorectal ultrasound (US)
6. Positron emission tomography (PET) scan
7. Invasive (INV) procedures
    - Colonoscopy
    - Bone marrow biopsy

Treatment

1. Radiation therapy
    - Dose
    - Technique
    - Endocavitary
    - Brachytherapy
2. Chemotherapy
    - Dose

3. Combination therapy: radiation therapy and chemotherapy
4. Simulation

MAJOR OUTCOMES CONSIDERED

- Survival: disease-free, overall
- Local control
- Anal sphincter-preservation rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Resectable Rectal Cancer

Variant 1: 60-year-old woman with rectal bleeding mass at 5 cm from verge, biopsy positive for adenocarcinoma. Staging workup.

Radiologic Procedure	Appropriateness Rating	Comments
CBC	9	
Liver function tests	9	
CEA	9	
CT, abdomen and pelvis	9	
CT or x-ray, chest	9	CT chest preferred
INV, colonoscopy	9	
Endorectal MRI	9	
Endorectal US	9	
INV, sigmoidoscopy	3	
X-ray, colon, barium enema	2	Only if colonoscopy cannot be performed
INV, bone marrow biopsy	1	
PET	1	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 70 year old woman staged with EUS, a T2NX rectal cancer at 3 cm from verge. Final pathology was T3N1 status post APR. KPS ≥70.

Treatment	Appropriateness Rating	Comments
Treatment Option		
RT + chemotherapy	9	
RT alone	2	

Treatment	Appropriateness Rating	Comments
Chemotherapy alone	2	
If RT + Chemo: RT Dose to Primary		
45 Gy/1.8 Gy	6	
50.4 Gy/1.8 Gy	9	
54 Gy/1.8 Gy	8	If small bowel is completely excluded after 50.4 Gy.
59.4 Gy/1.8 Gy	3	If small bowel is completely excluded after 50.4 Gy.
Simulation		
Patient prone	9	Unless physically unable
Small bowel contrast at simulation	9	
Patient immobilized	9	
Use belly board	9	
Perineal scar marker	9	
Bladder full at simulation	7	
If RT + Chemo: RT Volume		
L5/S1 pelvis to include perineal scar	9	
L5/S1 pelvis to bottom of ischial tuberosity	1	
RT Technique		
3 or 4 field with photons	9	Depending on clinical situation.
AP/PA	1	
3 field with electron boost to perineum	3	

Treatment	Appropriateness Rating	Comments
4 field with electron boost to perineum	3	
IMRT	1	Investigational use only.
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 70-year-old woman staged with EUS, aT2NX rectal cancer at 9 cm from verge, Final pathology was T3N1 status post LAR. KPS ≥70.

Treatment	Appropriateness Rating	Comments
Treatment Option		
RT + chemotherapy	9	
RT alone	2	
Chemotherapy alone	2	
If RT + Chemo: RT Dose to Primary		
45 Gy/1.8 Gy	6	
50.4 Gy/1.8 Gy	9	
54 Gy/1.8 Gy	8	If small bowel is completely excluded after 50.4 Gy.
59.4 Gy/1.8 Gy	3	If small bowel is completely excluded after 50.4 Gy.
Simulation		
Patient prone	9	Unless physically unable
Small bowel contrast at simulation	9	
Patient immobilized	9	
Use belly board	9	

Treatment	Appropriateness Rating	Comments
Bladder full at simulation	7	
If RT + Chemo: RT Volume		
L5/S1 pelvis to include anal marker	9	
L5/S1 pelvis to bottom of ischial tuberosity	1	
RT Technique		
3 or 4 field with photons	9	Depending on clinical situation.
AP/PA	1	
3 field with electron boost to perineum	3	
4 field with electron boost to perineum	3	
IMRT	1	Investigational use only.
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 60-year-old woman with circumferential lesion at 8 cm from verge. EUS stage T3N1. KPS ≥70.

Treatment	Appropriateness Rating	Comments
RT		
Preoperative RT + chemo	9	
Postoperative RT + chemo	3	
Preoperative RT alone	1	

Treatment	Appropriateness Rating	Comments
Postoperative RT	1	
Endocavitary RT	1	
Brachytherapy	1	
If Preoperative RT: RT Dose		
45 Gy/1.8 Gy	7	
50.4 Gy/1.8 Gy	9	
54 Gy/1.8 Gy	7	If small bowel is completely excluded after 50.4 Gy.
59.4 Gy/1.8 Gy	2	If small bowel is completely excluded after 50.4 Gy. For fixed lesions only.
5 Gy X 5	1	
Surgery		
LAR	9	
APR	1	Only if LAR not technically possible.
If Postoperative RT: RT Dose		
45 Gy/1.8 Gy	6	
50.4 Gy/1.8 Gy	9	
54 Gy/1.8 Gy	8	If small bowel is completely excluded after 50.4 Gy.
59.4 Gy/1.8 Gy	3	If small bowel is completely excluded after 50.4 Gy. For fixed lesions only.
5 Gy X 5	1	
Simulation		
Patient prone	9	Unless physically unable
Small bowel contrast at simulation	9	
Patient immobilized	9	
Use belly board	9	
Bladder full at simulation	7	

Treatment	Appropriateness Rating	Comments
RT Technique		
3 or 4 field with photons	9	Depending on clinical situation.
AP/PA	1	
3 field with electron boost to perineum	3	
4 field with electron boost to perineum	3	
IMRT	1	Investigational use only.
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 45-year-old woman with EUS staged T3N0, 4 cm lesion at 3 cm from verge. KPS ≥70.

Treatment	Appropriateness Rating	Comments
Treatment Options		
Preoperative RT + chemo followed by surgery	9	ELAR if possible.
Preoperative RT followed by surgery	1	
ELAR followed by adjuvant treatment if T3 and/or LN+	1	
APR followed by adjuvant treatment if T3 and/or LN+	1	
If Preoperative RT: RT Dose		
45 Gy/1.8 Gy	7	
50.4 Gy/1.8 Gy	9	

Treatment	Appropriateness Rating	Comments
54 Gy/1.8 Gy	7	If small bowel is completely excluded after 50.4 Gy.
59.4 Gy/1.8 Gy	2	If small bowel is completely excluded after 50.4 Gy. For fixed lesions only.
5 Gy X 5	1	
Simulation		
Patient prone	9	Unless physically unable
Small bowel contrast at simulation	9	
Patient immobilized	9	
Use belly board	9	
Perineal scar marker	9	
Bladder full at simulation	7	
If Preoperative RT: RT Volume		
Pelvis to L5/S1 + boost	9	
Local field only	1	
Pelvis to L2/L3 + boost	1	
Pelvis to L5/S1 + inguinal LN + boost	1	If extensive involvement of anal cancer.
RT Technique		
3 or 4 field with photons	9	Depending on clinical situation.
AP/PA	1	
3 field with electron boost to perineum	3	
4 field with electron boost to perineum	3	
IMRT	1	Investigational use only.

Treatment	Appropriateness Rating	Comments
If Preoperative RT + Chemo: time between RT & surgery		
2 weeks	1	
4 weeks	1	
6 weeks	9	
8 weeks	7	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

In what arguably may be the most pivotal recent trial in the area of resectable rectal cancer management, a randomized trial from Germany has established a regimen of preoperative chemoradiotherapy and surgery followed by additional cycles of chemotherapy alone as the standard of care for clinical stages T3 or T4, or for node-positive rectal cancer. Other clinical studies from the United States, Europe, and Asia have also influenced the treatment strategies of operable rectal cancer, as various approaches using preoperative or postoperative radiotherapy, with or without chemotherapy, have been examined. A summary of the major randomized clinical trials spanning the past several decades is provided below.

Postoperative Radiotherapy with or without Chemotherapy

Several classic trials have examined the use of postoperative irradiation alone or in combination with chemotherapy; in three of these (GITSG, NCCTG, Norway), radiotherapy delivered with concurrent chemotherapy improved both local control and survival.

The method of administration of chemotherapy appears to be important in obtaining optimal results. Infusional 5-FU was found to be superior to bolus 5-FU and is considered to be a standard adjuvant therapy; more recent studies have investigated alternate means of optimizing chemotherapy. The timing of early versus late radiotherapy with respect to chemotherapy may also be important according to the preliminary results of a recent randomized study and warrants further investigation.

Preoperative Radiotherapy with or without Chemotherapy

Exploring the role of preoperative radiotherapy alone (25 Gy in 5 fractions), a Swedish trial showed improvements in both local control and survival. However, given its long-term treatment toxicity and the inability to combine the

hypofractionated radiotherapy regimen with systemic chemotherapy, this approach is rarely used. More importantly, three recent trials from Europe have examined the role of incorporating concurrent chemotherapy with preoperative irradiation using standard radiotherapy fractionation, in keeping with the postoperative combined chemoradiotherapy model. Two studies (European Organisation for Research and Treatment of Cancer [EORTC] 22921, Fondation Française de Cancérologie Digestive [FFCD] 9203) demonstrated a significant improvement in local control, in the absence of a survival or sphincter-preservation benefit, with the addition of chemotherapy. The third trial from Poland reported no differences with respect to local control, survival, or late toxicity between the two arms. As expected, acute toxicity was increased with the addition of chemotherapy, as had been noted in the French trial (FFCD 9203).

Preoperative versus Postoperative Chemoradiotherapy

The important question of comparing preoperative versus postoperative chemoradiotherapy, as noted above, was addressed by a randomized trial from Germany. The preoperative regimen was associated with significantly improved local control and increased sphincter-preservation rates with no differences in disease-free or overall survival. It also resulted in decreased rates of acute and chronic treatment toxicity, when compared to the postoperative approach. Another randomized trial (National Surgical Adjuvant Breast and Bowel Project [NSABP] R03) exploring the same question in the United States was terminated early due to poor accrual. However, it did show a trend towards improved survival; clinical response to the preoperative therapy was associated with significantly improved disease-free and overall survival. The current standard of care in the United States is, therefore, to provide preoperative chemoradiotherapy, using standard radiotherapy fractionation and concurrent fluorouracil for clinical stages T3 or T4, or for node-positive rectal cancer.

Need for Future Trial

Despite the published data from randomized trials that support the shift to preoperative chemoradiotherapy, a subset of patients will require surgical resection upfront for a variety of clinical reasons. A pooled analysis of five randomized clinical trials in the United States suggests clinical reasons. A pooled analysis of five randomized clinical trials in the United States suggests that not all patients with resected tumors may require a trimodality (surgery, chemotherapy, radiotherapy) treatment approach. Patients with favorable or "intermediate-risk" (T3N0 or T1-2N1) tumors were found to have benefited equally from either postoperative chemoradiotherapy or chemotherapy alone. A future clinical study is warranted to validate the appropriateness of such a risk-adapted treatment-minimization strategy.

Abbreviations

- AP/PA, anteroposterior/posteroanterior
- APR, abdominoperineal resection
- CBC, complete blood count
- CEA, carcinoembryonic antigen
- CT, computed tomography
- EUS, endoscopic ultrasound

- IMRT, intensity modulated radio therapy
- INV, invasive
- KPS, Karnofsky performance scale
- LAR, low anterior resection
- MRI, magnetic resonance imaging
- PET, positron emission tomography
- RT, radiotherapy
- US, ultrasound

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for respectable rectal cancer

POTENTIAL HARMS

Radiotherapy or chemotherapy toxicity

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the

appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Suh WW, Johnstone PA, Blackstock AW, Herman J, Konski AA, Mohiuddin M, Poggi MM, Regine WF, Rich TA, Cosman BC, Saltz L, Expert Panel on Radiation Oncology-Rectal/Anal Cancer. Resectable rectal cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 7 p. [16 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel Radiation Oncology-Rectal/Anal Cancer

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: W. Warren Suh, MD; Peter A. Johnstone, MD; A. William Blackstock, MD; Joseph Herman, MD, MSc; Andre A. Konski, MD; Mohammed Mohiuddin, MD; Matthew M. Poggi, MD; William F. Regine, MD; Tyvin A. Rich, MD; Bard C. Cosman, MD; Leonard Saltz, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Relative radiation level information. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in

Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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