Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

ACR Appropriateness Criteria® pretreatment staging of colorectal cancer.

Bibliographic Source(s)

Fowler KJ, Kaur H, Cash BD, Feig BW, Gage KL, Garcia EM, Hara AK, Herman JM, Kim DH, Lambert DL, Levy AD, Peterson CM, Scheirey CD, Small W Jr, Smith MP, Lalani T, Carucci LR, Expert Panel on Gastrointestinal Imaging. ACR Appropriateness CriteriaÂ® pretreatment staging of colorectal cancer. Reston (VA): American College of Radiology (ACR); 2016. 13 p. [105 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dewhurst C, Rosen MP, Blake MA, Baker ME, Cash BD, Fidler JL, Greene FL, Hindman NM, Jones B, Katz DS, Lalani T, Miller FH, Small WC, Sudakoff GS, Tulchinsky M, Yaghmai V, Yee J, Expert Panel on Gastrointestinal Imaging. ACR Appropriateness Criteria® pretreatment staging of colorectal cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 7 p. [62 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Pretreatment Staging of Colorectal Cancer

Variant 1: Rectal cancer. Locoregional staging.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with IV contrast	9		O
MRI pelvis without IV contrast	8	Noncontrast MRI is sufficient for T staging, though with and without is routinely used as well.	O
US pelvis transrectal	8	For suspected early T-stage disease instead of MRI.	O
CT abdomen and pelvis with IV contrast	5	May be appropriate if MRI cannot be performed and tumor is locally advanced.	☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis without IV contrast	3	May be appropriate if MRI cannot be performed and tumor is locally advanced.	☢☢☢☢
CT abdomen and pelvis without and with IV contrast	3	May be appropriate if MRI cannot be performed and tumor is locally advanced.	☢☢☢☢
CT colonography	3	Low dose CTC without IV contrast	☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

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

Variant 2: Rectal cancer. Staging for distant metastases.

Radiologic Procedure	Rating	Comments	RRL*
CT chest abdomen pelvis with IV contrast	9		☢☢☢☢
MRI abdomen and pelvis without and with IV contrast	8	MRI or CT can be used. Usually performed along with a chest CT.	O
FDG-PET/CT whole body	6		☢☢☢☢
MRI abdomen and pelvis without IV contrast	5	Rarely used, but may be appropriate in situations when other exams cannot be performed due to contraindications. Usually performed along with chest CT.	O
CT chest abdomen pelvis without IV contrast	4	Only useful in a few very specific situations.	☢☢☢☢
CT chest abdomen pelvis without and with IV contrast	3	Limited added value of non-contrast series at the expense of increased dose.	☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

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

Summary of Literature Review

Introduction/Background

Colorectal cancers are the third most common tumors in the United States and the most common gastrointestinal cancer. The American Cancer Society estimates that over 93,090 new cases of colorectal cancer will be diagnosed in 2015. Most of these patients will undergo surgery for palliation or possible cure. Barring contraindications from associated medical conditions, virtually all patients with colorectal cancer will undergo some form of surgical therapy for attempted cure or palliation. Current treatment strategies are divided into those aimed at local/primary tumor management and those aimed at management of distant metastatic disease. Resection, if possible, of liver metastatic disease and in select oligometastatic sites provides the best overall survival. Although the evaluation and management of distant metastases is generally the same between colon and rectal cancer, the locoregional staging is quite different.

Colon Cancer

The local treatment of colon cancer relies primarily on what section of the colon is involved (right versus left hemicolectomy), with removal of the associated mesentery and regional nodes. The treatment strategy for colon cancer is governed by the location of the mass (generally radical hemicolectomy), with selective adjuvant chemotherapy dictated by lymph node positivity and extramural lymphovascular invasion on pathologic specimen. Locoregional staging (T and N stage) with imaging is not well supported in the literature. Most studies show that imaging is best utilized to identify advanced T stage and distant metastases with locoregional nodal staging being relatively less accurate and of marginal clinical utility.

Additionally, the role of preoperative imaging to predict T-stage and N-stage is of questionable value, given that neoadjuvant therapy has not been shown to significantly improve survival over surgery alone and the standard surgical approach is radical resection. Preoperative imaging of colon cancer appears to be of most benefit in identifying distant metastases, regardless of its ability to predict T-stage and N-stage. Given the limited role of locoregional staging, the imaging variant discussion for colon cancer will be limited to evaluation of distant metastases only.

Rectal Cancer

Surgical options for rectal carcinoma are more varied than for colon cancer and depend on the relationship of tumor to the sphincter and circumferential resection margins and peritoneal reflection. Several studies have evaluated the efficacy of transanal excision as an alternative to radical resection, with results suggesting this may be appropriate in carefully selected T1-stage patients. Close observation and accurate preoperative staging is essential to avoid high recurrence rates in these patients, likely related to involvement of local mesorectal nodes not detected by preoperative imaging. Furthermore, neoadjuvant chemotherapy and radiation added to primary resection in patients with radiologically determined high-risk rectal cancer has been shown to decrease local recurrence and improve survival. Thus, preoperative imaging for local staging of rectal cancer is important for determining the need for neoadjuvant therapy and surgical strategy.

Overview of Imaging Modalities

The diagnosis of colorectal cancer is often based upon clinical presentation of blood in stools, obstruction, anemia, or detection at colonoscopy surveillance. Computed tomography (CT), magnetic resonance imaging (MRI), and transrectal ultrasound (TRUS) have all been evaluated in initial staging of colorectal carcinoma. There are some studies supporting the use of CT colonography in local staging of colon cancer as well. Furthermore, an important role of imaging in staging patients with colorectal cancer is the detection of distant metastases, which can be accomplished with CT, positron emission tomography (PET)/CT, and MRI. All 3 of these modalities benefit from the use of intravenous (IV) contrast, with new MRI contrast agents allowing hepatobiliary phase imaging to improve accuracy. In rectal tumors, due to the need for high-resolution anatomic detail in determining local tumor extension, the local staging of tumor is often considered separately from the evaluation of distant metastatic disease, resulting in the need for a combination of modalities to fully stage the patient (i.e., MRI pelvis for local staging and CT chest, abdomen and pelvis for metastases). The optimal combination of imaging studies should take into consideration accuracy and cost-effectiveness.

Ideally CT is performed with IV contrast and can be performed as a single post-contrast portal venous phase of the chest, abdomen, and pelvis. Alternatively, a multi-phase protocol of the liver (generally consisting of arterial, portal venous, and delayed phases) can be paired with post-contrast imaging of the chest and pelvis. Acquiring multiple phases of the liver may improve diagnostic characterization of focal liver lesions. In addition to the phases of contrast, thin slices (ranging from 3 to 5 mm) and optimized technique (in relation to contrast bolus and imaging parameters) are essential for adequate staging accuracy with CT.

Liver MRI is ideally performed with and without IV contrast, with multiphase dynamic post-contrast imaging as the standard acquisition. There are 2 main types of MRI IV contrast for liver imaging, traditional extracellular agents (producing similar contrast kinetics to CT contrast) and hepatobiliary agents. Hepatobiliary agents allow for both dynamic contrast images (arterial, portal venous) and hepatobiliary phase images. The hepatobiliary phase images are acquired at a delayed timepoint that corresponds to greatest liver parenchymal enhancement due to uptake of the contrast agent by hepatocytes and where there is excretion of the administered contrast agent into the bile ducts. During the hepatobiliary phase, liver lesions are dark against a bright liver and may be more conspicuous than on traditional dynamic phases. MRI with diffusion-weighted imaging also produces greater diagnostic accuracy, especially when combined with hepatobiliary phase imaging. Although the use of IV contrast agents is ideal for staging, in patients who cannot receive an IV contrast agent due to severe allergy or renal failure, MRI without an IV contrast agent may be an option that provides better anatomic detail than CT without contrast.

A brief mention of IV contrast agents and renal function is essential to guide choices in the staging setting. Iodinated contrast agents used for CT are potentially nephrotoxic and should be avoided in patients with compromised renal function. Gadolinium-based IV contrast agents used in MRI are not nephrotoxic and may be a better option for patients with mild renal insufficiency. However, gadolinium agents carry a black box warning against use in severe renal dysfunction due to the risk of nephrogenic systemic fibrosis. More detailed discussion of contrast agents can be found in the ACR *Manual on Contrast Media* (see the "Availability of Companion Documents" field).

Variant 1: Rectal Cancer. Locoregional Staging

In this clinical scenario, a patient has a known diagnosis of rectal carcinoma and presents for staging of the primary tumor and locoregional nodes. Initial staging of rectal cancer should provide information regarding transmural extension (T-stage), locoregional nodal involvement, and involvement of adjacent organs or important anatomic structures (such as the sphincter complex and resection margin). These factors guide surgical planning and determine the need for neoadjuvant treatment. Surgical excision with satisfactory margins is necessary to provide a significant disease-free interval.

Transrectal Ultrasound

TRUS has been considered the gold standard for T-stage evaluation of rectal carcinoma with rich historical evidence to support its use. TRUS enables one to distinguish layers of the rectal wall and provides high accuracy in detecting and characterizing tumors within the superficial layers of the rectal wall. Reported accuracies range between 80% and 97% for T-stage determination. The T-stage accuracy for TRUS (84.6%) is far

superior to that of CT (70.5%). Evaluation of extent of tumor infiltration into the mesorectum (differentiating minimal from advanced T3 tumors and minimal T3 from T2 tumors) is of clinical interest in determining the need for neoadjuvant treatment but remains a challenge for TRUS. Although TRUS performs better than MRI for T1 tumors, similar for T2-3, it may be less accurate in characterizing locally advanced tumors (T4) with a tendency to understage. The use of TRUS in assigning patients to transanal endoscopic microsurgery (TEM) versus traditional surgery remains controversial. Despite some authors reporting good accuracy for some T stages, a retrospective evaluation of the use of TRUS in patients selected to undergo TEM for presumed early-stage disease showed disappointing results with inaccurate staging seen in 44.8% of the 165 patients who underwent TRUS preoperatively (32.7% were understaged and 12.1% were overstaged).

A significant limitation of TRUS is the limited field of view that compromises assessment of relationship of the tumor, mesorectal tumor implants, tumor invasion in extramural vessels and malignant nodes to the mesorectal fascia, in addition to limited assessment of high rectal tumors. MRI may better evaluate these findings as it offers a larger field of view.

Lymph Node Involvement

Detection of lymph node involvement with TRUS is limited to mesorectal nodes in the immediate vicinity of the tumor, which limits sensitivity. The sensitivity ranges from 45% to 74% and overall accuracy ranges from 62% to 83%. Although TRUS can frequently be used to detect regional lymph nodes, it has not been shown to be predictive of the histology of the visualized lymph nodes. Many lymph nodes measuring <5 mm in diameter have associated micrometastases, and some early-stage T1 and T2 tumors are likely to have lymph node micrometastases missed on TRUS. This may be responsible for the high rate of pelvic recurrence within this patient group. Lymph nodes along the superior rectal vessels and outside the mesorectal fascia along the internal iliac and obturator nodal stations also cannot be assessed with TRUS. This can also be clinically important; 1 series showed that 27% of the rectal cancer study cohort (Dukes class C; T2–4 tumors) demonstrated positive lateral lymph node involvement, with a small percentage with lateral lymph node involvement only (4%). TRUS similarly is limited in evaluating lateral lymph nodes.

Magnetic Resonance Imaging

Like TRUS, MRI can depict the separate layers of the rectal wall with high-resolution, especially when performed at 3 T and with an endorectal coil. Although the use of endorectal coils may provide improved diagnostic accuracy for T-stage as compared to phased-array coils alone, high-resolution imaging using phased-array MRI coils, as is used in multicenter trials (MERCURY), has performed well when done at either 1.5 or 3 T. Additionally, when going from 1.5 T to 3 T there may be only small incremental improvements in diagnostic accuracy. In a meta-analysis of 21 studies, phased-array coil MRI demonstrated a specificity of 94% (95% confidence interval [CI], 88–97) for determining circumferential resection margin involvement and a specificity of 75% (95% CI, 68–80) for determining T-stage. However, MRI technique and image quality play a critical role in the attainment of these objectives, accuracy is dependent on obtaining high-resolution images (0.5–0.6 cm in-plane voxel size) that are perpendicular to the plane of the tumor.

Agreement between high-resolution MRI and TRUS in determining early (<T3 stage) versus advanced tumors (≥T3 stage) was found to be high (kappa value = 0.93) in a study of 86 consecutive patients where detailed subclassification and distance of tumor extension beyond the wall were compared. In one study there was similar agreement between high-resolution MRI and endorectal ultrasound (EUS). In another study comparing MRI and TRUS for measurement of the closest radial tumor-mesorectal margin, there was substantial agreement; however, the correlation between observers and modalities was modest, suggesting significant influence of reader performance on the diagnostic accuracy/reproducibility of TRUS. This may be especially true for accuracy in lymph node detection with TRUS.

When used as a preoperative tool in advanced tumors, MRI has shown high diagnostic accuracy for both initial staging to determine surgical plan and determining resectability following neoadjuvant treatment. Studies have shown MRI sensitivities ranging from 94% to 100% and specificities from 85% to 88% in assessment of the circumferential resection margin. Hence, MRI is valuable in predicting complete resection with negative margins. In a multicenter cohort trial evaluating the use of high-resolution MRI with a phased-array coil in determining resectability, a total of 228 patients underwent curative-intent treatment based on the MRI characterization of tumor extent with 95.6% of patients achieving margin-negative results. High-risk MRI features (extramural vascular invasion, mesorectal tumor depth >5 mm, T4 stage, involved circumferential resection margin) may correlate with higher risk for distant metastases. In addition to initial staging prognostic features, MRI response to neoadjuvant treatment has been shown to be an indicator of long-term outcomes, including recurrence and survival.

Lymph Node Involvement

The differentiation of benign from metastatic locoregional nodes remains challenging. MRI is sensitive for detecting enlarged lymph nodes, but remains nonspecific for differentiating benign from malignant nodes with accuracies ranging from 59% to 83%. However, studies have shown high negative predictive value in the setting of node-negative determination by MRI, with negative predictive value ranging from 78% to 87%. Accuracy of lymph node staging may be improved with the use of specific lymph node agents taken up by the reticuloendothelial system; however, these agents are not currently available for clinical use in the United States.

Computed Tomography

CT was the first "locoregional staging" modality evaluated. Early enthusiastic reports of accuracy ranged between 85% and 90%, and it was reported to be an excellent preoperative staging method, with the ability to depict both the primary tumor and metastases. Larger, more carefully controlled studies, however, have shown that the overall accuracy of contrast-enhanced CT is in the 50% to 70% range, varying directly with the stage of the lesion. A limitation of CT is its inability to resolve the layers of the bowel wall; consequently, high T3 and T4 lesions are more accurately assessed than T2 or T3 lesions. A recent study using thin-section multidetector CT (MDCT) demonstrated a higher accuracy of 86% in T-staging. The accuracy of staging with CT may be improved with multiplanar reformats, allowing for true axial images through the rectum. Overstaging, predominantly due to desmoplastic peritumoral inflammation remains a challenge on CT, as with the other modalities (TRUS and MRI).

Lymph Node Involvement

Like all modalities that rely primarily on size as determinant of involvement (i.e., TRUS and MRI), CT remains relatively nonspecific for N-stage determination. There is little agreement on the critical cut-off diameter to determine if lymph nodes are involved in the disease process. One study suggests 4.5 mm; however, nodal size is not seen as a predictor of nodal status at surgery. Since detection of nodes involved with tumor remains a difficult problem, if a colonic resection is planned, local node groups should be encompassed in a properly performed cancer operation. Accuracies for CT detection of lymph node stage range from 56% to 84%.

Although EUS and MRI are the favored imaging modalities for locoregional staging, CT may be considered an option in instances where patients cannot undergo MRI and a thin-section optimized technique can be performed. Locoregional staging is not routinely performed for colon cancer; however, CT is still recommended in the initial evaluation of all patients scheduled for colorectal carcinoma surgery because of its ability to obtain a rapid global evaluation and demonstrate potential complications of the tumor (e.g., perforation, obstruction) that may not be clinically apparent.

CT Colonography

Virtual colonoscopy (or CT colonography [CTC]) has proven to be a valid tool in identifying both primary and synchronous colonic lesions. CTC is beneficial after incomplete colonoscopy to evaluate the remainder of the colon and is currently being advocated for use as a screening test. More than 95% of patients prefer CTC to routine colonoscopy, and its use may increase patient willingness to receive regular screening for colorectal cancer. CTC has a staging accuracy of 81%, lower than conventional CT due to the reduced radiation dose used and lack of IV contrast. It has a sensitivity of 93% and a specificity of 97% for detecting polyps >1 cm. Sensitivity and specificity fall to 86% and 86%, respectively, for polyps measuring <1 cm. There are no trials comparing CTC with other imaging modalities. It is likely not an optimal study for assessing local staging of distal rectal tumors due to the greater degree of noise related to reduced radiation and lack of IV contrast making soft tissue contrast less optimal.

Variant 2: Colorectal Cancer. Staging for Distant Metastases

Despite differences in locoregional staging between colon and rectal cancer, the evaluation of distant metastases is the same. The most common sites of metastatic involvement in colorectal cancer are the liver and lungs. Approximately 14.5% of patients present with synchronous liver involvement, and the 5-year cumulative metachronous liver metastasis rate is 14.5% (3.7% for stage I, 13.3% for stage II, and 30.4% for stage III [$P<0.001$]). The current paradigm of treatment is to remove all liver metastases if feasible because the survival for patients with liver metastases is <1% at 5 years. Hence, accurate depiction of the size, distribution, and number of liver metastases is the primary goal of staging. The most commonly used modalities for staging include CT, MRI, and PET/CT.

It is difficult to determine the best imaging modality for patients with colorectal liver metastases because very few studies have adequately compared the accuracy of MRI to high-quality CT. The available evidence supports that both MRI and CT detect liver lesions with high accuracy. The subsequent sections address CT, MRI, and PET/CT for staging patients.

Computed Tomography

Among a group of 100 patients who underwent contrast-enhanced CT, CT arterioportography (CTAP), and MRI without and with contrast, the sensitivity and specificity for liver metastases were 73% and 96.5% for CT, 87.1% and 89.3% for CTAP, and 81.9% and 93.2% for MRI. In addition, abdominal/pelvic CT with IV contrast has a high negative predictive value of 90%. The false-positive rate of CT in a prospective study was 3.9% (10 of 257 findings; 95% CI, 1.9% to 7.1%), with intraoperative ultrasound and histopathology serving as the reference standard. Although CT may have diminished sensitivity compared to MRI in detection of liver lesions, an important determinant of its accuracy is CT technique. The use of MDCT, multiphase imaging, appropriate IV contrast bolus and timing, and optimal imaging parameters significantly narrows the differential between CT and MRI. In studies evaluating IV contrast-enhanced optimized CT technique, detection rates for liver metastases range from 85% to 91%. CT may show more limited sensitivity in detecting metastases in the setting of fatty liver and following neoadjuvant therapy as compared with MRI. Particularly in this setting of serial imaging, MDCT has proven an effective tool in assessment of the extent of liver

disease in addition to providing a comprehensive assessment of extrahepatic disease. Recent studies have also noted CT morphologic criteria of responses in liver metastasis that have proven to be excellent predictors of overall survival and disease-free survival.

Detection of possible lung metastases is also an important part of the initial imaging evaluation of patients with colorectal carcinoma. Among patients with potentially resectable liver metastases and a negative initial chest PET, additional imaging with a chest CT revealed pulmonary metastases in only 5% of patients. In another study, approximately one-fourth of the indeterminate lesions on preoperative CT ultimately developed into metastases and 1 in 10 into other lung malignancies. However, in a single institution retrospective study including 200 consecutive patients, the findings at preoperative chest CT altered initial surgical management in only 1 patient. Despite the very low specificity and frequency of indeterminate findings on chest CT, most investigators still advocate its use at baseline and in patients with more advanced-stage rectal carcinomas (T3/T4).

Magnetic Resonance Imaging

Most studies show comparable or improved sensitivity for detection of colorectal liver metastases with IV conventional extracellular gadolinium agent-enhanced MRI compared to CT. As mentioned in the previous section, MRI is more accurate than CT in detecting liver metastases in the setting of fatty liver and following neoadjuvant therapy. Many recent studies focus on the value of hepatobiliary contrast agent-enhanced MRI and diffusion-weighted imaging. In a retrospective study of 242 patients undergoing surgical resection for colorectal liver metastases (n=92 with pre-chemotherapy and pre-surgical MRI with a hepatobiliary IV contrast agent and n=150 without both pre-chemotherapy and pre-surgical hepatobiliary IV contrast agent-enhanced MRI), patients who underwent hepatobiliary MRI both pre-chemotherapy and presurgically had significantly lower rates of intra-hepatic recurrence (48% versus 65%, P=0.04), and fewer repeat hepatectomies (13% versus 25%, P=0.03). On the basis of the results of this study, the authors suggested that a hepatobiliary IV contrast agent-enhanced MRI may improve outcomes in the era of highly active neoadjuvant chemotherapy and disappearing lesions. Because of limited sensitivity of MRI for lung nodules, a chest CT with or without contrast can be performed in addition to MRI for complete staging.

Nuclear Medicine

Although there is some evidence to support the use of PET/CT in the local staging of patients with rectal carcinoma, the more common clinical application of PET/CT is in identifying nodal and distant metastases. PET/CT is useful for determining overall stage and identifying patients with metastatic disease (sensitivity of 89% and specificity of 64%); however, the accuracy on a lesion-by-lesion basis is relatively low compared to contrast-enhanced CT and MRI for liver metastases (55% versus 89% in a study comparing PET/CT to MDCT). PET/CT may help to exclude other sites of disease beyond the liver or, in complex cases, to improve staging accuracy where it has been shown to result in a change in management in up to 8% to 11% of patients. Caution should be exercised, however, as the findings of PET/CT may be nonspecific, and could result in negative impact on patient care in up to 9% of patients. Additionally, PET/CT has further reduced sensitivity for lesions in the setting of neoadjuvant therapy and should be used in conjunction with contrast CT or MRI for presurgical planning of liver metastases. PET/CT may add value in the positive predictive value of avid lymph nodes as it has a higher specificity than other modalities. The sensitivity of detecting nodal metastases is only 43% with a specificity of 80%, and again size is not a helpful characteristic.

There is also a potential role for PET/CT in restaging colorectal cancer after chemoradiation therapy by measuring the pretreatment and post-treatment standard uptake volume (SUV) and assessing response by decreasing SUV. Limitations of PET include decreased sensitivity in detecting small colonic lesions ≤10 mm in diameter and decreased fluorine-18-2-fluoro-2-deoxy-D-glucose uptake by mucinous tumors.

Summary of Recommendations

- *Locoregional Staging of Rectal Cancer*: TRUS and high-resolution MRI are accurate modalities for evaluating local extent of tumor. TRUS may perform better for early stage tumors (T1-T2) and MRI for more advanced (T3 and above). High-resolution MRI with phased-array coil has high specificity for determining involvement of the circumferential resection margin (94%), which is an essential factor in presurgical planning. MRI holds advantages over TRUS in lateral pelvic lymph node and superior perirectal lymph node detection.
    - *Special circumstances*: In patients with advanced stage rectal carcinoma who cannot undergo MRI and for whom TRUS would be inadequate for evaluating nodes, CT may be appropriate to detect enlarged nodes or local organ invasion.
- *Evaluation of Distant Metastases*: Liver tumor involvement is best done with multi-phase contrast-enhanced MRI or contrast-enhanced CT (with both modalities, optimization of technique is essential for accuracy). The routine use of PET/CT is likely not indicated; however, it may provide guidance in cases of advanced, bilobar liver disease to exclude extrahepatic metastases prior to surgical intent to cure. The use of chest CT in preoperative planning is controversial, yet still widely performed along with abdomen pelvis CT or MRI.
    - *Special circumstances*: In patients with renal dysfunction who cannot undergo a contrast enhanced MRI or CT, either PET/CT or noncontrast MRI may be options to evaluate for metastatic liver disease. Noncontrast CT for liver staging is usually not indicated. However, there is little evidence to support an optimal/standardized-imaging algorithm in these patients. Discussion with a radiologist regarding local contrast administration policies and appropriate next steps is recommended.

Abbreviations

- CT, computed tomography
- CTC, CT colonography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- IV, intravenous
- MRI, magnetic resonance imaging
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Colorectal cancer

Guideline Category

Evaluation

Clinical Specialty

Colon and Rectal Surgery

Family Practice

Gastroenterology

Internal Medicine

Nuclear Medicine

Oncology

Radiology

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging modalities for pretreatment staging of colorectal cancer

Target Population

Patients with colorectal cancer

Interventions and Practices Considered

1. Magnetic resonance imaging (MRI)
    - Pelvis without and with intravenous (IV) contrast
    - Pelvis without IV contrast
    - Abdomen and pelvis without and with IV contrast
    - Abdomen and pelvis without IV contrast
2. Ultrasound (US), pelvis, transrectal
3. Computed tomography (CT)
    - Abdomen and pelvis with IV contrast
    - Abdomen and pelvis without IV contrast
    - Abdomen and pelvis without and with IV contrast
    - Chest, abdomen, and pelvis without IV contrast
    - Chest, abdomen, and pelvis without and with contrast
    - CT colonography (CTC)
4. 18-F-fluorodeoxyglucose–positron emission tomography (FDG-PET)/CT, whole body

Major Outcomes Considered

- Utility of imaging procedures in pretreatment staging of colorectal cancer
- Sensitivity, specificity, and accuracy of imaging procedures in pretreatment staging of colorectal cancer
- Detection rates for liver metastases
- Recurrence rates
- Overall survival

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 62 citations in the original bibliography, 27 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in September 2013 and updated in January 2014 as well as in October 2015 to identify additional evidence published since the *ACR Appropriateness Criteria® Pretreatment Staging Colorectal Cancer* topic was finalized. Using the search strategies described in the literature search companion (see the "Availability of Companion Documents"), 379 articles were found. Fifty articles were added to the bibliography. Three hundred twenty-nine articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

The author added 27 citations from bibliographies, Web sites, or books that were not found in the new literature search.

One citation is a supporting document that was added by staff.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 62 citations in the original bibliography, 27 were retained in the final document. The new literature search conducted in September 2013 and updated in January 2014 as well as in October 2015 identified 50 articles that were added to the bibliography. The author added 27 citations from bibliographies, Web sites, or books that were not found in the new literature search. One citation is a supporting document that was added by staff.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*

The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;

Or

The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness. When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the second

rating round, the recommendation is "May be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

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.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 105 references cited in the *ACR Appropriateness Criteria® Pretreatment Staging Colorectal Cancer* document, 89 are categorized as diagnostic references including 4 well designed studies, 34 good quality studies, and 29 quality studies that may have design limitations. Additionally, 10 references are categorized as therapeutic references including 2 well designed studies and 5 good quality studies. There are 25 references that may not be useful as primary evidence. There are 6 references that are meta-analysis studies.

While there are references that report on studies with design limitations, 45 well designed or good quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Preoperative imaging of colon cancer appears to be of most benefit in identifying distant metastases, regardless of its ability to predict T-stage and N-stage.
- Preoperative imaging for local staging of rectal cancer is important for determining the need for neoadjuvant therapy and surgical strategy.

Potential Harms

The findings of positron-emission mammography/computed tomography (PET/CT) may be nonspecific, and could result in negative impact on patient care in up to 9% of patients. See the “Nuclear Medicine” section under Variant 2.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Contraindications

Contraindications

Iodinated contrast agents used for computed tomography (CT) are potentially nephrotoxic and should be avoided in patients with compromised renal function. Gadolinium-based intravenous (IV) contrast agents used in magnetic resonance imaging (MRI) are not nephrotoxic and may be a better option for patients with mild renal insufficiency. However, gadolinium contrast agents carry a black box warning against use in severe renal dysfunction due to the risk of nephrogenic systemic fibrosis.

Qualifying Statements

Qualifying Statements

- The 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 examinations 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.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

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)

Fowler KJ, Kaur H, Cash BD, Feig BW, Gage KL, Garcia EM, Hara AK, Herman JM, Kim DH, Lambert DL, Levy AD, Peterson CM, Scheirey CD, Small W Jr, Smith MP, Lalani T, Carucci LR, Expert Panel on Gastrointestinal Imaging. ACR Appropriateness CriteriaÂ® pretreatment staging of colorectal cancer. Reston (VA): American College of Radiology (ACR); 2016. 13 p. [105 references]

Adaptation

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

Date Released

2016

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 on Gastrointestinal Imaging

Composition of Group That Authored the Guideline

Panel Members: Kathryn J. Fowler, MD (*Principal Author*); Harmeet Kaur, MD (*Co-Author*); Brooks D. Cash, MD; Barry W. Feig, MD; Kenneth L. Gage, MD; Evelyn M. Garcia, MD; Amy K. Hara, MD; Joseph M. Herman, MD, MSc; David H. Kim, MD; Drew L. Lambert, MD; Angela D. Levy, MD; Christine M. Peterson, MD; Christopher D. Scheirey, MD; William Small Jr, MD; Martin P. Smith, MD; Tasneem Lalani,

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dewhurst C, Rosen MP, Blake MA, Baker ME, Cash BD, Fidler JL, Greene FL, Hindman NM, Jones B, Katz DS, Lalani T, Miller FH, Small WC, Sudakoff GS, Tulchinsky M, Yaghmai V, Yee J, Expert Panel on Gastrointestinal Imaging. ACR Appropriateness Criteria® pretreatment staging of colorectal cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 7 p. [62 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2015 Sep. 3 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2016. 128 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2016 May. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® pretreatment staging of colorectal cancer. Evidence table. Reston (VA): American College of Radiology; 2016. 44 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® pretreatment staging of colorectal cancer. Literature search. Reston (VA): American College of Radiology; 2016. 3 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on March 19, 2001. The information was verified by the guideline developer on March 29, 2001. This summary was updated by ECRI Institute on June 23, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on February 22, 2012 and September 14, 2016.

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