Complete Summary

GUIDELINE TITLE

Staging and follow-up of ovarian cancer.

BIBLIOGRAPHIC SOURCE(S)

Javitt MC, Fleischer AC, Andreotti RF, Angtuaco TL, Horrow MM, Lee SI, Lev-Toaff AS, Scoutt LM, Zelop C, Expert Panel on Women's Imaging. Staging and follow-up of ovarian cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 5 p. [38 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Fishman EK, Mendelson E, Bohm-Velez M, Bree R, Finberg H, Hricak H, Laing F, Sartoris D, Thurmond A, Goldstein S, Walsh J. Staging and follow-up of ovarian cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 (Suppl):899-902.

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

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Ovarian cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Obstetrics and Gynecology
Oncology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of initial radiologic procedures for staging and follow-up of patients with ovarian cancer

TARGET POPULATION

Patients with ovarian cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. CA-125 antigen
2. Computed tomography (CT)
    - Abdomen and pelvis
    - Chest

3. Magnetic resonance imaging (MRI), abdomen and pelvis
4. Ultrasound (US), pelvis transvaginal
5. Fluorodeoxyglucose positron emission tomography (FDG-PET)
6. X-ray
    - Colon, barium enema
    - Intravenous urography

MAJOR OUTCOMES CONSIDERED

Utility of radiologic procedures in evaluation and staging of ovarian cancer

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: Staging and Follow-up of Ovarian Cancer

Variant 1: Pretreatment staging ovarian cancer.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis	9		High
CA–125	9		None
MRI abdomen and pelvis	5	Evidence shows equivalent staging accuracy compared to CT. Problem solving modality for patients who cannot have contrast enhanced CT. See comments regarding contrast in text under "Anticipated Expectations."	None
US pelvis transvaginal	5	Evidence shows equivalent staging accuracy compared to CT and MRI, but scan time and coverage may limit efficiency.	None
CT chest	4	For abnormal chest x-ray including pleural effusions, supraclavicular adenopathy	Med
X-ray colon barium enema	3		Med
X-ray intravenous urography	2		Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

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

Variant 2: Rule out recurrent ovarian cancer.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis	9		High
CA–125	9		None
CT chest abdomen	9	Indicated if abnormal chest x-ray,	High

Radiologic Procedure	Rating	Comments	RRL*
and pelvis		known extensive abdominal disease, or markedly elevated CA–125, or preoperatively for debulking to insure disease is limited to the abdomen.	
FDG-PET/CT abdomen and pelvis	7	If available, can substitute for CT.	High
MRI abdomen and pelvis	5	Problem solving modality. Appropriate for patients who cannot have contrast-enhanced CT. See comments regarding contrast in text under "Anticipated Expectations."	None
US pelvis transvaginal	4	May be used as problem solving tool for disease in the pelvis.	None
FDG-PET abdomen and pelvis	4	Limited due to difficulties in spatial localization, especially in the abdomen.	High
X-ray colon barium enema	3		Med
X-ray intravenous urography	2		Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

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

Summary of Literature Review

Ovarian cancer is the fifth most common cause of cancer death in women in the United States behind lung, breast, colorectal, and pancreatic cancers, accounting for more than 3% of all cancers in women and causing more deaths than any other gynecologic malignancy. Many common benign conditions of the ovaries have an acute presentation, while ovarian cancer is a silent killer, often presenting late with advanced stage III–IV disease after the disease has spread widely. The roles of diagnostic imaging have been ovarian mass characterization, determination of preoperative disease extent, and prediction of tumor resectability. Surgical staging is both diagnostic and therapeutic, and an experienced gynecologic surgeon is critical in optimum debulking of this tumor. However, up to 40% of patients may be understaged at laparotomy.

Transvaginal ultrasound (US) has a role in ovarian cancer screening and characterization of ovarian masses as benign or malignant. It can be used to determine the site of origin of a pelvic mass and to characterize the lesion. A combination of morphology and Doppler waveform analysis may provide the most accurate risk assessment for an adnexal lesion by US.

The proper choice of treatment for ovarian cancer depends on accurate staging. Computed tomography (CT) and magnetic resonance imaging (MRI) have been used to determine the resectability of tumors, the candidacy of patients for effective cytoreductive surgery, the need for preoperative chemotherapy if debulking is suboptimal, and the need for referral to a gynecologic oncologist. Limited disease means stage I or II. Regional disease means stage II, involving one or both ovaries with pelvic extension. Advanced disease means stages III and IV.

Cytoreductive surgery is the standard treatment for ovarian cancer. However, in patients with advanced disease, medical co-morbidities, or stage IV disease, using initial adjuvant chemotherapy and/or radiation therapy followed by cytoreduction results in optimal tailored patient management, decreased morbidity and mortality, and improved survival. Standard radiographic techniques such as chest radiograph, barium enema, and excretory urography have been replaced in many countries, including the United States, by cross sectional imaging, especially CT, for ovarian cancer staging. CT is the imaging modality of choice in the preoperative evaluation of ovarian cancer and has been validated as an accurate method to predict successful surgical cytoreduction. CT has been useful for detecting local tumor involvement of the pelvic ureter and uterine serosa, as well as metastases to the peritoneum, omentum, mesentery, liver, spleen, and lymph nodes. CT has a reported accuracy for ovarian cancer staging of up to 94%. Current high-resolution multidetector CT scanners can detect peritoneal implants as small as 5 mm (specificity 100%, accuracy 80% for all sites except diaphragm and pelvis) and improves the false negative rate (which is up to 50% for helical CT) when using multiplanar reconstruction for optimal depiction of disease. The most important limitation of CT in staging ovarian cancer is its inability to reliably detect bowel surface, mesenteric, or peritoneal tumor implants smaller than 5 mm, especially in the absence of ascites.

MRI is an excellent problem-solving technique by virtue of its ability to define common conditions such as fibroids, dermoid cysts, endometriomas, and other benign lesions. Two studies found no statistical difference between CT and MRI in defining disease extent. A multivariate analysis showed that the accuracy of MRI with gadolinium enhancement in diagnosing ovarian malignancy was 93%. Gadolinium enhancement improved diagnostic confidence and tissue characterization. However, the role of MRI has been limited because the use of intraluminal gastrointestinal contrast agents with MRI is not routine as it is with CT, MRI generally costs more than CT, and there are fewer experienced radiologists to interpret MRI. Thus, CT is currently the recommended modality to stage ovarian cancer. MRI is recommended for patients with a contraindication to the use of iodinated contrast agents (allergy, renal insufficiency), patients who are pregnant, and those for whom CT findings are inconclusive.

For predicting the nonresectability of ovarian cancer, cross sectional imaging (CT or MRI) plays a critically important role in finding significant lesions (greater than

2 cm) at the root of the mesentery, gastrosplenic ligament, omentum of the lesser sac, porta hepatic, intersegmental fissure of the liver, diaphragm, liver dome, lymphadenopathy at or above the celiac axis, presacral extraperitoneal disease, and pelvic sidewall invasion. Unresectable disease can be managed by needle or laparoscopic biopsy, chemotherapy, and possibly a later attempt at optimal debulking, resulting in improved survival by virtue of optimal response to chemotherapy.

The use of fluorodeoxyglucose positron emission tomography (FDG-PET) imaging in the primary diagnosis and tissue characterization of ovarian cancer is unsupported to date. Specificity has been reported as low as 54% and moderate sensitivity as high as 86%. Also, false negative results have been reported with borderline tumors, early carcinomas, and adenocarcinomas. False positive results have been reported with dermoid cysts, hydrosalpinges, and endometriosis.

However, FDG-PET, especially when combined with CT, is a valuable tool for diagnosing advanced disease and detecting recurrent tumor. The use of FDG-PET combined with serum tumor marker CA-125 has had a reported sensitivity as high as 98%, and PET alone has a sensitivity of 85%. Second look laparotomy is no longer routinely performed. The noninvasive diagnosis of recurrence obviates the need for unnecessary surgery.

Because optimal debulking after chemotherapy improves survival in patients with recurrence, this information is critical to patient management. MRI and CT are roughly equivalent for identifying lesions larger than 2 cm. CT is 58% sensitive and 100% specific in predicting unsuccessful debulking. The reported accuracy of MRI for detecting lesions larger than 2 cm is comparable to that of CT at 93% to 95%. CT remains the preferred imaging method for detecting recurrence for the same reasons as those that are discussed above for primary staging.

The preoperative evaluation of patients with suspected ovarian carcinoma usually includes a serum CA-125 determination. Only about 50% of all patients with ovarian cancer have a true positive result. Thus, this test alone is inadequate when used in isolation as a screening tool. However, with stage II or greater ovarian cancer, the true positive rate is as high as 80%. There is a very high correlation between CA-125 levels and the clinical course of the patient after surgery. False positive results have been reported with endometriosis, benign ovarian cysts, pregnancy, and pelvic inflammatory disease. Pancreatic cancer and cirrhosis have caused elevated CA-125 levels. CA-125 levels can also predict tumor recurrence among patients who are clinically tumor free.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF, a syndrome that can be fatal. Further studies are necessary

to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (e.g., >0.2 mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a "black box" warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Abbreviations

- CA, cancer antigen
- CT, computed tomography
- FDG-PET, fluorodeoxyglucose positron emission tomography
- Med, medium
- MRI, magnetic resonance imaging
- 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 staging and follow-up of patients with ovarian cancer

POTENTIAL HARMS

- The relative radiation level is high for computed tomography (CT) of the chest, abdomen and pelvis and fluorodeoxyglucose positron emission tomography (FDG-PET) of the abdomen and pelvis; FDG-PET/CT of the abdomen and pelvis medium for X-ray of the colon barium enema, CT of the abdomen and pelvis, CT of the chest, abdomen and pelvis,

fluorodeoxyglucose positron emission tomography (FDG-PET)/CT of the abdomen and pelvis; and low for X-ray intravenous urography.
- Fluorodeoxyglucose positron emission tomography (FDG-PET) can render false positive and false negative results.
- Cancer antigen (CA)-125 tests can render false positive results. When used as a screening tool, only about 50% of patients with ovarian cancer have a true positive result.
- Some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed nephrogenic systemic fibrosis, a syndrome that can be fatal. Until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

CONTRAINDICATIONS

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Iodinated contrast agents used for computed tomography (CT) is contraindicated in patients with allergy or renal insufficiency.

QUALIFYING STATEMENTS

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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)

Javitt MC, Fleischer AC, Andreotti RF, Angtuaco TL, Horrow MM, Lee SI, Lev-Toaff AS, Scoutt LM, Zelop C, Expert Panel on Women's Imaging. Staging and follow-up of ovarian cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 5 p. [38 references]

ADAPTATION

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

DATE RELEASED

1996 (revised 2007)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

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 Women's Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Marcia C. Javitt, MD; Arthur C. Fleischer, MD; Rochelle F. Andreotti, MD; Teresita L. Angtuaco, MD; Mindy M. Horrow, MD; Susanna I. Lee MD, PhD; Anna S. Lev-Toaff, MD; Leslie M. Scoutt, MD; Carolyn Zelop, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Fishman EK, Mendelson E, Bohm-Velez M, Bree R, Finberg H, Hricak H, Laing F, Sartoris D, Thurmond A, Goldstein S, Walsh J. Staging and follow-up of ovarian cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 (Suppl):899-902.

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

This NGC summary was completed by ECRI on April 3, 2006. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This NGC summary was updated by ECRI Institute on December 14, 2007.

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