

American College of Radiology ACR Appropriateness Criteria®

Clinical Condition: Staging and Follow-up of Ovarian Cancer

Variant 1: Pretreatment staging of ovarian cancer. (See narrative for comments regarding CA-125.)

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis with contrast	9		High
MRI abdomen and pelvis with contrast	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 with contrast	4	For abnormal chest x-ray including pleural effusions, supraclavicular adenopathy	Med
X-ray contrast enema	3		Med
X-ray intravenous urography	2		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 2: Rule out recurrent ovarian cancer. (See narrative for comments regarding CA-125.)

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis with contrast	9		High
CT chest abdomen and pelvis with contrast	9	Indicated if abnormal chest x-ray, known extensive abdominal disease, or markedly elevated CA-125, or preoperatively for debulking to insure disease is limited to the abdomen.	High
FDG-PET whole body with concurrent diagnostic CT abdomen and pelvis with contrast	9	If available, can substitute for CT.	High
MRI abdomen and pelvis with contrast	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 whole body without concurrent diagnostic CT	4	Limited due to difficulties in spatial localization, especially in the abdomen.	High
X-ray contrast enema	3		Med
X-ray intravenous urography	2		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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STAGING AND FOLLOW-UP OF OVARIAN CANCER

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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 [1]. 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 [2]. The roles of diagnostic imaging have been ovarian mass characterization, determination of preoperative disease extent, and prediction of tumor resectability [3-6]. 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 [7].

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 [8]. A combination of morphology and Doppler waveform analysis may provide the most accurate risk assessment for an adnexal lesion by US [4,9,10].

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 [11-16]. 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 [4,6,17].

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 [18-21]. 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 [19]. CT has a reported accuracy for ovarian cancer staging of up to 94% [7]. 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 [13]. 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 [11,14,22].

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 [6]. Two studies found no statistical difference between CT and MRI in defining disease extent [12,16]. A multivariate analysis showed that the accuracy of MRI with gadolinium enhancement in diagnosing ovarian malignancy was 93% [23]. Gadolinium enhancement improved diagnostic confidence and tissue characterization [23]. 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 [24,25].

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

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[7,19,26-28]. 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 [25].

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% [25,29-31]. 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 [25,30].

However, FDG-PET, especially when combined with CT, is a valuable tool for diagnosing advanced disease and detecting recurrent tumor [32]. The use of FDG-PET combined with serum tumor marker CA-125 has had a reported sensitivity as high as 98% [33], and PET alone has a sensitivity of 85% [33,34]. 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 [24]. MRI and CT are roughly equivalent for identifying lesions larger than 2 cm [7]. CT is 58% sensitive and 100% specific in predicting unsuccessful debulking [19]. The reported accuracy of MRI for detecting lesions larger than 2 cm is comparable to that of CT at 93%-95% [7]. 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 [4,31]. 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% [35]. 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 [33].

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 [36-38], 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 (eg, >0.2mM/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/1.73m²), 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) [37].

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. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

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References

1. American Cancer Society. Cancer facts and figures 2007. Atlanta, Ga. *American Cancer Society* 2007.
2. Johnson RJ, Blackledge G, Eddleston B, Crowther D. Abdominopelvic computed tomography in the management of ovarian carcinoma. *Radiology* 1983; 146(2):447-452.
3. Fukuda T, Ikeuchi M, Hashimoto H, et al. Computed tomography of ovarian masses. *J Comput Assist Tomogr* 1986; 10(6):990-996.
4. Jeong YY, Outwater EK, Kang HK. Imaging evaluation of ovarian masses. *Radiographics* 2000; 20(5):1445-1470.
5. Jung SE, Lee JM, Rha SE, Byun JY, Jung JI, Hahn ST. CT and MR imaging of ovarian tumors with emphasis on differential diagnosis. *Radiographics* 2002; 22(6):1305-1325.
6. Occhipinti KA, Frankel SD, Hricak H. The ovary. Computed tomography and magnetic resonance imaging. *Radiol Clin North Am* 1993; 31(5):1115-1132.
7. Forstner R, Hricak H, Occhipinti KA, Powell CB, Frankel SD, Stern JL. Ovarian cancer: staging with CT and MR imaging. *Radiology* 1995; 197(3):619-626.
8. Conway C, Zalud I, Dilema M, et al. Simple cyst in the postmenopausal patient: detection and management. *J Ultrasound Med* 1998; 17(6):369-372; quiz 373-364.
9. Bailey CL, Ueland FR, Land GL, et al. The malignant potential of small cystic ovarian tumors in women over 50 years of age. *Gynecol Oncol* 1998; 69(1):3-7.
10. Twickler DM, Forte TB, Santos-Ramos R, McIntire D, Harris P, Scott D. The Ovarian Tumor Index predicts risk for malignancy. *Cancer* 1999; 86(11):2280-2290.
11. Amendola MA, Walsh JW, Amendola BE, Tisnado J, Hall DJ, Goplerud DR. Computed tomography in the evaluation of carcinoma of the ovary. *J Comput Assist Tomogr* 1981; 5(2):179-186.
12. Buy JN, Ghossain MA, Sciort C, et al. Epithelial tumors of the ovary: CT findings and correlation with US. *Radiology* 1991; 178(3):811-818.
13. Buy JN, Moss AA, Ghossain MA, et al. Peritoneal implants from ovarian tumors: CT findings. *Radiology* 1988; 169(3):691-694.
14. Ghossain MA, Buy JN, Ligneres C, et al. Epithelial tumors of the ovary: comparison of MR and CT findings. *Radiology* 1991; 181(3):863-870.
15. Whitley N, Brenner D, Francis A, et al. Use of the computed tomographic whole body scanner to stage and follow patients with advanced ovarian carcinoma. *Invest Radiol* 1981; 16(6):479-486.
16. Semelka RC, Lawrence PH, Shoenuit JP, Heywood M, Kroeker MA, Lotocki R. Primary ovarian cancer: prospective comparison of contrast-enhanced CT and pre- and postcontrast, fat-suppressed MR imaging, with histologic correlation. *J Magn Reson Imaging* 1993; 3(1):99-106.
17. Walsh JW. Computed tomography of gynecologic neoplasms. *Radiol Clin North Am* 1992; 30(4):817-830.
18. Lund B, Jacobsen K, Rasch L, Jensen F, Olesen K, Feldt-Rasmussen K. Correlation of abdominal ultrasound and computed tomography scans with second- or third-look laparotomy in patients with ovarian carcinoma. *Gynecol Oncol* 1990; 37(2):279-283.
19. Meyer JI, Kennedy AW, Friedman R, Ayoub A, Zepp RC. Ovarian carcinoma: value of CT in predicting success of debulking surgery. *AJR* 1995; 165(4):875-878.
20. Nelson BE, Rosenfield AT, Schwartz PE. Preoperative abdominopelvic computed tomographic prediction of optimal cytoreduction in epithelial ovarian carcinoma. *J Clin Oncol* 1993; 11(1):166-172.
21. Pectasides D, Kayianni H, Facou A, et al. Correlation of abdominal computed tomography scanning and second-look operation findings in ovarian cancer patients. *Am J Clin Oncol* 1991; 14(6):457-462.
22. Pannu HK, Horton KM, Fishman EK. Thin section dual-phase multidetector-row computed tomography detection of peritoneal metastases in gynecologic cancers. *J Comput Assist Tomogr* 2003; 27(3):333-340.
23. Hricak H, Chen M, Coakley FV, et al. Complex adnexal masses: detection and characterization with MR imaging--multivariate analysis. *Radiology* 2000; 214(1):39-46.
24. Prayer L, Kainz C, Kramer J, et al. CT and MR accuracy in the detection of tumor recurrence in patients treated for ovarian cancer. *J Comput Assist Tomogr* 1993; 17(4):626-632.
25. Woodward PJ, Hosseinzadeh K, Saenger JS. From the archives of the AFIP: radiologic staging of ovarian carcinoma with pathologic correlation. *Radiographics* 2004; 24(1):225-246.
26. Megibow AJ, Bosniak MA, Ho AG, Beller U, Hulnick DH, Beckman EM. Accuracy of CT in detection of persistent or recurrent ovarian carcinoma: correlation with second-look laparotomy. *Radiology* 1988; 166(2):341-345.
27. Reuter KL, Griffin T, Hunter RE. Comparison of abdominopelvic computed tomography results and findings at second-look laparotomy in ovarian carcinoma patients. *Cancer* 1989; 63(6):1123-1128.
28. Silverman PM, Osborne M, Dunnick NR, Bandy LC. CT prior to second-look operation in ovarian cancer. *AJR* 1988; 150(4):829-832.
29. Cho SM, Ha HK, Byun JY, et al. Usefulness of FDG PET for assessment of early recurrent epithelial ovarian cancer. *AJR* 2002; 179(2):391-395.
30. Fenchel S, Grab D, Nuessle K, et al. Asymptomatic adnexal masses: correlation of FDG PET and histopathologic findings. *Radiology* 2002; 223(3):780-788.
31. Rieber A, Nussle K, Stohr I, et al. Preoperative diagnosis of ovarian tumors with MR imaging: comparison with transvaginal sonography, positron emission tomography, and histologic findings. *AJR* 2001; 177(1):123-129.
32. Nakamoto Y, Saga T, Ishimori T, et al. Clinical value of positron emission tomography with FDG for recurrent ovarian cancer. *AJR* 2001; 176(6):1449-1454.
33. Murakami M, Miyamoto T, Iida T, et al. Whole-body positron emission tomography and tumor marker CA125 for detection of recurrence in epithelial ovarian cancer. *Int J Gynecol Cancer* 2006; 16 Suppl 1:99-107.
34. Gadducci A, Cosio S, Zola P, Landoni F, Maggino T, Sartori E. Surveillance procedures for patients treated for epithelial ovarian cancer: a review of the literature. *Int J Gynecol Cancer* 2007; 17(1):21-31.
35. Jacobs I, Davies AP, Bridges J, et al. Prevalence screening for ovarian cancer in postmenopausal women by CA 125 measurement and ultrasonography. *BMJ* 1993; 306(6884):1030-1034.
36. Broome DR, Girguis MS, Baron PW, Cottrell AC, Kjellin I, Kirk GA. Gadodiamide-associated nephrogenic systemic fibrosis: why radiologists should be concerned. *AJR* 2007; 188(2):586-592.
37. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document for safe MR practices: 2007. *AJR* 2007; 188(6):1447-1474.
38. Sadowski EA, Bennett LK, Chan MR, et al. Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 2007; 243(1):148-157.

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