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Evaluation and Management of Adnexal Masses

Adnexal masses (ie, masses of the ovary, fallopian tube, or surrounding tissues) commonly are encountered by obstetrician–gynecologists and often present diagnostic and management dilemmas. Most adnexal masses are detected incidentally on physical examination or at the time of pelvic imaging. Less commonly, a mass may present with symptoms of acute or intermittent pain. Management decisions often are influenced by the age and family history of the patient. Although most adnexal masses are benign, the main goal of the diagnostic evaluation is to exclude malignancy. The purpose of this document is to provide guidelines for the evaluation and management of adnexal masses in adolescents, pregnant women, and nonpregnant women and to outline criteria for the identification of adnexal masses that are likely to be malignant and may warrant referral to or consultation with a gynecologic oncologist.

Background

Differential Diagnosis

A pelvic mass can have gynecologic or nongynecologic origins (Box 1). Consideration of the location of a pelvic mass in conjunction with patient age and reproductive status can help narrow the differential diagnosis. Adnexal masses of gynecologic origin may be benign or malignant ovarian lesions; tubal or paratubal processes such as hydrosalpinges or ectopic pregnancy; and uterine abnormalities such as leiomyomas or müllerian abnormalities. Nongynecologic causes of pelvic masses are less common and may be related to a variety of other organ systems, including gastrointestinal and urologic sources. Cases of metastatic cancer, especially those from the breast, colon, or stomach, may first present as adnexal masses.

Risk Factors for Malignancy

Age is the most important independent risk factor for ovarian cancer in the general population, with the incidence increasing sharply after the onset of menopause (1). According to data reported by the Surveillance, Epidemiology, and End Results program, from 2009 to 2013, the median age at ovarian cancer diagnosis was 63 years, and 69.4% of patients were 55 years or older (1). Most adnexal masses in postmenopausal women are benign neoplasms, such as cystadenomas, but the risk of malignancy is much greater than in premenopausal women (2).

The most important personal risk factor for ovarian cancer is a strong family history of breast or ovarian cancer (3). It is important to distinguish a family history of ovarian cancer from a familial ovarian cancer syndrome. For a 35-year-old woman with one affected family member, the lifetime probability of ovarian cancer increases from a general population risk of 1.6% to a risk of 5% (4). However, for a woman with a *BRCA1* mutation, the lifetime risk of ovarian cancer, fallopian tube cancer, or peritoneal cancer is approximately 41–46% by age 70 years (5–8). For a woman with a *BRCA2* mutation, the lifetime risk of ovarian cancer, fallopian tube cancer,

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Box 1. Differential Diagnosis of an Adnexal Mass ⇦

Gynecologic

- Benign
  - Functional cyst
  - Endometrioma
  - Tubo-ovarian abscess
  - Mature teratomas (dermoids)
  - Serous cystadenoma
  - Mucinous cystadenoma
  - Hydrosalpinx
  - Paratubal cysts
  - Leiomyomas
  - Müllerian anomalies
- Malignant
  - Epithelial carcinoma
  - Germ cell tumor
  - Metastatic cancer
  - Sex-cord or stromal tumor

Nongynecologic

- Benign
  - Diverticular abscess
  - Appendiceal abscess or mucocele
  - Nerve sheath tumors
  - Ureteral diverticulum
  - Pelvic kidney
  - Bladder diverticulum
- Malignant
  - Gastrointestinal cancers
  - Retroperitoneal sarcomas
  - Metastatic cancer

or peritoneal cancer is 10–27% by age 70 years (5–8). The risk of ovarian cancer through age 70 years for women with Lynch syndrome is estimated to be 5–10% (7–9). Additional factors that increase ovarian cancer risk include nulliparity, early menarche, late menopause, white race, primary infertility, and endometriosis (10–12).

General Evaluation

Individual patient characteristics, physical examination findings, imaging results, and serum marker levels help separate masses into the categories of probably benign, uncertain, and likely malignant, which can then guide appropriate management.

Medical and Family History

A personal medical history with a detailed gynecologic history and review of symptoms are critical components of patient evaluation. In addition, a family history and a review of other risk factors will help assess the likelihood of malignancy. See Committee Opinion No. 478, *Family History as a Risk Assessment Tool*, and the National Comprehensive Cancer Center's guidelines, *Genetic/Familial High-Risk Assessment: Breast and Ovarian*, for details on how to take a relevant and detailed family history (13, 14).

Patients with adnexal masses may present with symptoms that can refine the differential diagnosis. For example, a woman of reproductive age with acute onset abdominal or pelvic pain may have a hemorrhagic or bleeding ovarian cyst. The potential for pregnancy should be evaluated in all women of reproductive age because ectopic pregnancy is in the differential diagnosis of an adnexal mass in early pregnancy. Symptoms of unilateral, intermittent, and then acutely worsening pelvic pain may indicate an ovarian torsion. A more indolent, progressive pelvic pain associated with fevers, chills, vomiting, and vaginal discharge may indicate an infectious etiology such as a tubo-ovarian abscess. Women who report acute or chronic dysmenorrhea or pain with intercourse may have an endometrioma. Persistent bloating, generalized abdominal pain, and early satiety may be signs of malignancy (15). Abnormal uterine bleeding or postmenopausal bleeding may be caused by estrogen produced by sex cord-stromal tumors (16).

Physical Examination

The physical examination should start with evaluation of vital signs and general physical appearance. Whether the woman has a symptomatic adnexal mass or one that is incidentally discovered on imaging, a comprehensive physical examination should include palpation of cervical, supraclavicular, axillary and groin lymph nodes; pulmonary auscultation; abdominal palpation and auscultation; and pelvic examination (including visual inspection of the perineum, cervix, and vagina; and bimanual palpation, with rectovaginal examination as indicated). Although pelvic examination (even with the patient under general anesthesia) has shown limited ability to identify an adnexal mass, especially with patient body mass index greater than 30 (17), examination findings that are concerning for adnexal malignancy include a mass that is irregular, firm, fixed, nodular, bilateral, or associated with ascites.

Benign conditions that can produce these findings include endometriosis, chronic pelvic infections, hemorrhagic corpus luteum, tubo-ovarian abscess, and uterine leiomyomas (18).

Imaging

Transvaginal ultrasonography is the most commonly used imaging technique for the evaluation of adnexal masses. The ultrasound examination should assess the size and composition of the mass (cystic, solid, or mixed); laterality; and the presence or absence of septations, mural nodules, papillary excrescences, or free fluid in the pelvis. Spectral, color Doppler ultrasonography is useful to evaluate the vascular characteristics of pelvic lesions (19). Abdominal ultrasonography is a useful addition when pelvic structures are distorted by previous surgery, when masses extend beyond the pelvis, or if transvaginal ultrasonography cannot be performed.

Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are not recommended in the initial evaluation of adnexal masses. Based on limited data, MRI may have superior ability compared with transvaginal ultrasonography in correctly classifying malignant masses at the expense of a lower overall detection rate (20, 21). However, MRI often is helpful in differentiating the origin of pelvic masses that are not clearly of ovarian origin, especially leiomyomas (22, 23).

Currently, the best use of CT imaging is not to detect and characterize pelvic masses, but to evaluate the abdomen for metastasis when cancer is suspected based on ultrasound images, examination results, or serum markers. A CT scan can detect ascites, omental metastases, peritoneal implants, pelvic or periaortic lymph node enlargement, hepatic metastases, obstructive uropathy, and possibly an alternate primary cancer site, including pancreas or colon (24).

Laboratory Testing

Laboratory testing may clarify the suspected etiology of a pelvic mass. Pregnancy testing should be obtained in reproductive-aged women, if indicated. If an infectious etiology is suspected, a complete blood count and testing for gonorrhea and chlamydial infection should be performed. Other laboratory tests that may have value depending on the history and examination findings include urinalysis, fecal blood testing or other assessment of intestinal involvement, and serum marker testing.

Serum Marker Testing

Serum markers are used in conjunction with imaging to assess the likelihood of malignancy. The most extensively studied serum marker is cancer antigen 125 (CA 125), which is a protein associated with epithelial ovarian malignancies, but also frequently expressed at lower levels by nonmalignant tissue. Elevation of CA 125 levels may occur in endometriosis, pregnancy, pelvic inflammatory disease, and in nongynecologic cancer. In evaluating adnexal masses, CA 125 measurement is most useful in postmenopausal women and in identifying nonmucinous epithelial cancer (Table 1) (25). The CA 125 level is elevated in 80% of patients with epithelial ovarian cancer but in only 50% of patients with stage I disease (25). More recently, human epididymis protein 4 has been identified as a potentially useful biomarker in distinguishing benign from malignant masses (26, 27). If a less common ovarian histopathology is suspected based on risk factors, symptoms, or ultrasound findings, measurement of levels of ß-hCG, L-lactate dehydrogenase, alpha-fetoprotein, or inhibin may assist in the evaluation (Table 2).

Panels of biomarkers have been investigated to determine their ability to distinguish between benign and malignant adnexal masses when used in conjunction

Table 1. Serum Biomarker and Multimodal Test Results Considered Abnormal in Women With Adnexal Masses* ⇦

Test	Premenopausal	Postmenopausal
CA 125	—†	> 35 U/mL
MIA	≥ 5.0	≥ 4.4
ROMA	≥ 1.31	≥ 2.77
RMI	> 200	> 200

Abbreviations: CA, cancer antigen; MIA, multivariate index assay; ROMA, Risk of Ovarian Malignancy Algorithm; RMI, risk of malignancy index.

*Serum biomarker and multimodal testing may be helpful to identify a woman with an adnexal mass who would benefit from referral to or consultation with a gynecologic oncologist. Current evidence is insufficient to recommend any specific test.

†Specificity and positive predictive value of CA 125 levels are consistently higher in postmenopausal women compared with premenopausal women. Prior American College of Obstetricians and Gynecologists' guidance used a CA 125 threshold of greater than 200 U/mL for referral of a premenopausal woman with an adnexal mass to a gynecologic oncologist. This threshold was based on expert opinion; no evidence-based threshold is currently available; thus, gynecologic care providers should integrate the CA 125 level with other clinical factors in judging the need for consultation.

Data from Jacobs I, Bast RC Jr. The CA 125 tumour-associated antigen: a review of the literature. Hum Reprod 1989 Jan;4:1–12; Skates SJ, Mai P, Horick NK, Piedmonte M, Drescher CW, Isaacs C, et al. Large prospective study of ovarian cancer screening in high-risk women: CA 125 cut-point defined by menopausal status. Cancer Prev Res (Phila) 2011;4:1401–8; Bristow RE, Hodeib M, Smith A, Chan DW, Zhang Z, Fung ET, et al. Impact of a multivariate index assay on referral patterns for surgical management of an adnexal mass. Am J Obstet Gynecol 2013; 209:581.e1-8; Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol 1990;97:922–9; *and* Moore RG, McMeekin DS, Brown AK, DiSilvestro P, Miller MC, Allard WJ, et al. A novel multiple marker bioassay utilizing HE4 and CA 125 for the prediction of ovarian cancer in patients with a pelvic mass. Gynecol Oncol 2009;112:40–6.

with clinical and radiologic evaluation. The U.S. Food and Drug Administration has approved two different serum tumor marker panel tests to further assess the risk of ovarian cancer in adult women with pelvic masses: 1) the multivariate index assay, a qualitative serum tumor marker panel and 2) the Risk of Ovarian Malignancy Algorithm (28, 29). These panels are approved for use in women older than 18 years with an already identified adnexal mass that requires surgery. The multivariate index assay incorporates five serum biomarkers that are associated with ovarian cancer (CA 125 II, transferrin, transthyretin [prealbumin], apolipoprotein A-1, and β 2-microglobulin) into a malignancy risk score of 0–10 using a proprietary algorithm (30). The Risk of Ovarian Malignancy Algorithm includes CA 125, human epididymis protein 4, and menopausal status (31). Variable cut-off values specific to menopausal status have been established for the multivariate index assay and the Risk of Ovarian Malignancy Algorithm (Table 1).

Multimodal Tests

Diagnostic algorithms have been developed that incorporate serum markers, clinical information, and ultrasound findings. The United Kingdom's National Institute for Health and Clinical Excellence Guidelines for the recognition and initial management of ovarian cancer recommend the calculation of the risk of malignancy index version I as part of the evaluation (32). The risk of malignancy index is calculated using the product of the serum CA 125 level (U/mL), the ultrasound scan result (expressed as a score of 0, 1, or 3 depending on findings), and the menopausal status (1 if premenopausal and 3 if postmenopausal) (33). A systematic review found a risk of malignancy index score of 200 (Table 1) to have a pooled estimated sensitivity of 78% (95% confidence interval [CI], 71–85%) and a specificity of 87% (95% CI, 83–91%) (34).

Table 2. Serum Biomarkers in Ovarian Germ Cell Tumors ⇦

	β-hCG	AFP	LDH	CA 125
Dysgerminoma	+	-	+	-
Endodermal sinus tumo	-	+	-	-
Choriocarcinoma	+	-	-	-
Immature teratoma	-	+	+	+
Embryonal carcinoma	+	+	-	-

Abbreviations: AFP, alpha fetoprotein; CA, cancer antigen; LDH, lactate dehydrogenase.

Clinical Considerations and Recommendations

▶ ***What is the role of ultrasonography in the initial evaluation of a patient with a suspected or an incidentally identified adnexal mass?***

Transvaginal ultrasonography is the recommended imaging modality for a suspected or an incidentally identified pelvic mass. No alternative imaging modality has demonstrated sufficient superiority to transvaginal ultrasonography to justify its routine use.

High frequency, gray-scale transvaginal ultrasonography can produce high-resolution images of an adnexal mass that approximate its gross anatomic appearance. Although image quality is operator dependent, interobserver agreement among experienced ultrasonographers is high (35–37). The advantages of transvaginal ultrasonography, including its widespread availability, good patient tolerability, and cost-effectiveness, make it the most widely used imaging modality to evaluate adnexal masses (38, 39). The main limitation of transvaginal ultrasonography alone as a diagnostic tool to distinguish benign from malignant masses relates to its lack of specificity and low positive predictive value for cancer, especially in premenopausal women (38–40). Color Doppler ultrasonography permits measurement of blood flow in and around a mass and can increase the specificity of gray-scale two-dimensional ultrasonography (41, 42). However, the ranges of values of resistive index, pulsatility index, and maximum systolic velocity between benign and malignant masses overlap considerably (43). In an attempt to overcome the overlap, three-dimensional ultrasound examination of vascular architecture has been used and proved discriminatory in distinguishing benign masses from cancer in some reports (44, 45).

▶ ***What ultrasound findings suggest malignancy?***

Ultrasound findings that should raise the clinician's level of concern regarding malignancy include cyst size greater than 10 cm, papillary or solid components, irregularity, presence of ascites, and high color Doppler flow. There has been significant research on the use of ultrasound scoring systems alone or in combination with serum markers or historical information for predicting malignancy. Although promising, these systems have been validated only in research settings with specific ultrasound training and their suitability for routine clinical use has not been fully clarified.

The International Ovarian Tumor Analysis (IOTA) group has incorporated ultrasound features into its Logistic Regression model 2 and its Simple Rules, which were designed to help ultrasonographers predict the risk of malignancy of an adnexal mass before surgery (46, 47). The IOTA Logistic Regression model 2 includes six variables (patient age and five ultrasound findings suggestive of malignancy) that are entered into a formula that calculates the probability of malignancy (46). The IOTA Simple Rules include a total of 10 ultrasound findings characteristic of malignant adnexal masses and benign adnexal masses, with accompanying guidance on how to apply these rules (47).

Several other transvaginal ultrasound scoring systems have been developed that quantify cancer risk based on morphology (48). Whereas scoring criteria vary among the various models, most assign low risk scores to sonolucent cysts with smooth walls, thin or absent septations, and absence of solid components.

In general, the various morphologic ultrasound scoring systems are able to distinguish benign from malignant masses in most instances (48). However, a 2014 systematic review and meta-analysis that compared various malignancy prediction models (including ultrasound morphologic scoring systems, the IOTA Logistic Regression model 2, the IOTA Simple Rules, biomarker panels, and various versions of the risk of malignancy index multimodal test) found that the best performing models were the IOTA Logistic Regression model 2 with a risk cut-off of 10% and the IOTA Simple Rules model (49). The IOTA Logistic Regression model 2 and the IOTA Simple Rules model demonstrated high sensitivity (0.92 [95% CI, 0.88–0.95] for Logistic Regression model 2; 0.93 [95% CI, 0.89–0.95] for Simple Rules) and specificity (0.83 [95% CI, 0.77–0.88] for Logistic Regression model 2; 0.81 [95% CI, 0.76–0.85] for Simple Rules) based on pooled data (49).

▶ *What ultrasound findings suggest benign disease?*

Ultrasound characteristics of benign masses include simple appearance: thin, smooth walls; and the absence of solid components, septations, or internal blood flow on color Doppler ultrasound imaging. These simple cysts are highly likely to be benign in any age group (50–54). A definitive size cutoff to delineate the need for surgical intervention has not been established (52). Cysts of 10 cm or larger often are considered to be an indication for surgery (55); however, simple cysts (even those greater than 10 cm) often will spontaneously regress when examined with serial ultrasonography (56).

Simple cysts are almost always universally benign, regardless of menopausal status or cyst size, with malignancy rates in most series of 0–1% (41, 51–53, 57, 58). In the largest prospective study published to date, 2,763 postmenopausal women with unilocular cysts no larger than 10 cm were evaluated using serial transvaginal ultrasonography at 6-month intervals (53). Spontaneous resolution occurred in more than two thirds of patients, and no cases of cancer were detected after a mean follow-up of 6.3 years. A more recent series examined the risk of malignancy in 1,148 masses classified as unilocular cysts on ultrasonography (59). Of these cases, 11 (0.96% [95% CI, 0.48–1.71]) were malignant; however, in seven of the 11 malignancies, the ultrasound assessment (59) did not detect papillary projections or other solid components that subsequently were found macroscopically at surgery.

Small descriptive studies have reported ultrasound characteristics that may be specific for selected benign diagnoses. Typical findings reported for endometriomas include a round homogeneous-appearing cyst containing low-level echoes within the ovary (60). These characteristics allow differentiation from other types of ovarian cysts with sensitivity of 83% and a specificity of 89% and a positive and negative predictive value of 77% and 92%, respectively (61). Mature teratomas, which contain a hypoechoic attenuating component with multiple small homogeneous interfaces, were determined with 98% accuracy in a series of 155 suspected dermoid cysts (62). Overall, ultrasound assessment has shown a reported sensitivity of 58% and specificity of 99% in the diagnosis of mature cystic teratomas (63). Hydrosalpinges are another benign adnexal mass, which on transvaginal ultrasonography appear as tubular-shaped sonolucent cysts, with a sensitivity of 93% and specificity of 99% for differentiating them from other adnexal masses (64).

▶ *What is the role of serum marker testing in the initial evaluation of an adnexal mass?*

Serum marker testing is indicated to evaluate the likelihood of malignancy and need for surgery. Elevated CA 125 levels in combination with other findings can be useful to distinguish between benign and malignant adnexal masses and to identify patients who should be referred to or treated in consultation with a gynecologic oncologist. Specificity and positive predictive value of CA 125 levels are consistently higher in postmenopausal women compared with premenopausal women (65, 66). The combination of an elevated CA 125 level and a pelvic mass in a postmenopausal woman is highly suspicious for malignancy, and patients with these

findings should be referred to or treated in consultation with a gynecologic oncologist. Although CA 125 level measurement is less valuable in predicting cancer risk in premenopausal women than in postmenopausal women, extreme values increase suspicion for a malignant process. For example, although premenopausal women with adnexal masses and either normal or mildly elevated CA 125 levels usually have benign diagnoses, a markedly elevated CA 125 level raises greater concern for malignancy, even though women with benign conditions such as endometriomas can have CA 125 level elevations of 1,000 units/mL or greater (67). Prior guidance of the American College of Obstetricians and Gynecologists used a CA 125 threshold of greater than 200 U/mL for referral of premenopausal women to gynecologic oncologists. This threshold was based on expert opinion. No evidence-based threshold is currently available; thus, gynecologic care providers should integrate the CA 125 level with other clinical factors in judging the need for consultation.

The overall sensitivity of CA 125 testing in distinguishing benign from malignant adnexal masses reportedly ranges from 61% to 90%; specificity ranges from 71% to 93%, positive predictive value ranges from 35% to 91%, and negative predictive value ranges from 67% to 90% (65, 68–72). Wide variations in these figures reflect differences in cancer prevalence in the study population, the proportion of patients who are postmenopausal, and the threshold of CA 125 levels considered abnormal. Cancer antigen 125 testing has a low sensitivity for the detection of ovarian cancer because the CA 125 level is elevated in only one half of cases of early stage epithelial ovarian cancer and rarely in cases of germ cell, stromal, or mucinous cancer. Low specificity occurs because the CA 125 level is elevated in many nonmalignant clinical conditions, including uterine leiomyomas, endometriosis, pelvic inflammatory disease, ascites of any etiology, and even inflammatory conditions such as systemic lupus erythematosus and inflammatory bowel disease (73). Because most of these clinical conditions occur in premenopausal women and because most cases of epithelial ovarian cancer occur in postmenopausal women, the sensitivity and specificity of an elevated CA 125 for cancer diagnosis in the setting of a pelvic mass is highest after menopause.

Additional tumor marker testing may be useful if a less common ovarian histopathology is suspected (Table 2). Levels of β-hCG, L-lactate dehydrogenase, and alpha-fetoprotein may be elevated in the presence of certain malignant germ cell tumors. Granulosa cell tumors produce estrogen and inhibin and should be suspected in women with a solid pelvic mass and irregular or postmenopausal bleeding.

▶ *What is the role of serum biomarker panel testing in the evaluation of an adnexal mass?*

Serum biomarker panels may be used as an alternative to CA 125 level alone in determining the need for referral to or consultation with a gynecologic oncologist when an adnexal mass requires surgery. These biomarker panels are not recommended for use in the initial evaluation of an adnexal mass, but may be helpful in assessing which women would benefit from referral to a gynecologic oncologist. Trials that have evaluated the predictive value of these panels show potential for improved specificity, especially for evaluation of premenopausal women. However, comparative research has not yet defined the best testing approach.

The multivariate index assay has demonstrated higher sensitivity and negative predictive value for ovarian malignancy when compared with clinical impression and CA 125 alone (30, 74). In a study of 494 women enrolled by nongynecologic oncology providers, the multivariate index assay correctly predicted ovarian malignancy in 91.4% (95% CI, 77.6–97.0) of cases of early stage disease, compared with 65.7% (95% CI, 49.2–79.2) for CA 125 alone (30). The multivariate index assay was abnormal in 83.3% of malignancies in which the clinical impression was thought to be benign and was abnormal in 70.8% of cases of cancer in which the CA 125 was normal (30). In a larger cohort of 1,016 patients, the multivariate index assay combined with clinical assessment had greater sensitivity (95.3%; 95% CI, 88.6–98.2) compared with clinical assessment or CA 125 alone for early-stage ovarian malignancies (74). The addition of radiologic imaging to the multivariate index assay further increases sensitivity (98% for ultrasonography and 97% for CT scan) and the negative predictive value (99% for ultrasonography and 94% for CT scan). The false negative rate is less than 2% when the results of imaging and the multivariate index assay indicate low risk (75).

The Risk of Malignancy Algorithm includes human epididymis protein 4, which has been found to be more sensitive and specific than CA 125 for the evaluation of adnexal masses (76). In a cohort of 531 patients, the Risk of Ovarian Malignancy Algorithm successfully classified patients into high-risk and low-risk groups, with 93.8% of cases of epithelial ovarian cancer classified as high risk before surgical exploration (31). In postmenopausal women, the Risk of Ovarian Malignancy Algorithm had a specificity of 75% (95% CI, 66.9–81.4) and a sensitivity of 92.3% (95% CI, 85.9–96.4) in

distinguishing malignant pelvic masses (31). Conversely, in premenopausal women the Risk of Ovarian Malignancy Algorithm score exhibited a specificity of 74.8% (95% CI, 68.2–80.6) and a sensitivity of 76.5% (95% CI, 58.8–89.3) (31). In a prospective analysis that compared the efficacy of the multivariate index assay and the Risk of Ovarian Malignancy Algorithm in 146 patients with surgically confirmed malignancies, the multivariate index assay was found to be more sensitive (97% and 87%, respectively; *P*=.25). However, the Risk of Malignancy Ovarian Algorithm was more specific than the multivariate index assay (83% versus 55%, respectively; *P*<.0001) (77). The negative predictive values of both tests were similar (98.4% and 96.0%, respectively).

▶ *When is observation recommended for a patient with an adnexal mass?*

Observation is recommended when the morphology of the adnexal mass on ultrasonography suggests benign disease or when morphology is less certain but there is a compelling reason to avoid surgical intervention (57, 77, 78). Observation in the asymptomatic woman may be justified when the evaluation shows a normal CA 125 level in the absence of transvaginal ultrasound findings suspicious for cancer. With rare exception, simple cysts up to 10 cm in diameter on transvaginal ultrasonography performed by experienced ultrasonographers are likely benign and may be safely monitored using repeat imaging without surgical intervention, even in postmenopausal patients (53).

Additional benign diseases that may be managed expectantly include suspected endometriomas, mature teratomas, and hydrosalpinx. Repeat ultrasound imaging is recommended whenever the diagnosis is uncertain and when cancer remains within the differential diagnoses (2). The ideal interval and duration for ultrasound follow-up has yet to be defined. However, in one study, masses that were monitored and eventually diagnosed as malignancies all demonstrated growth by 7 months (78). Some experts recommend limiting observation of stable masses without solid components to 1 year, and stable masses with solid components to 2 years (79).

Surgical intervention is warranted for symptomatic masses or for suspected malignancy based on the results of radiologic imaging, serum marker testing, or both. However, some women for whom surgical intervention would normally be considered are at substantial risk of perioperative morbidity and mortality, such as women of very advanced age or with multiple comorbidities. In such instances, repeat imaging often is safer than immediate operative intervention, although the ideal interval for repeat imaging has not been determined.

▶ *What type of surgical intervention is appropriate for a presumed benign adnexal mass?*

Minimally invasive procedures are the preferred route of surgery for presumed benign adnexal masses. Regardless of the approach employed, fertility preservation should be a priority when managing masses in adolescents and premenopausal women who have not completed childbearing. Even in women who present with large ovarian cysts of 10 cm or greater, it is possible to save normal portions of the ovary and remove the cyst laparoscopically (80–82).

Given advancements in minimally invasive surgical techniques, laparoscopic management of presumed benign adnexal masses generally is appropriate and desirable. Several retrospective studies that addressed the laparoscopic management of adnexal masses have confirmed low complication rates (83–88). Three published, randomized trials that comprised 394 patients compared the findings and outcome of laparoscopy versus laparotomy in women with clinically benign pelvic masses (88–90). Conversion to laparotomy was performed only for endoscopic suspicion of cancer, with conversion rates ranging from 0% to 1.5%. Rates of intraoperative cyst rupture were equivalent between the two approaches. In each study, statistically significant decreases in operative time, perioperative morbidity, length of hospital stay, and postoperative pain after laparoscopy were demonstrated (88–90). When compared with women who underwent laparotomy, the most consistent, statistically significant findings in women whose masses were managed laparoscopically were shortened length of hospital stay, decreased pain, and decreased convalescence time (84–87, 91, 92). Robotic-assisted surgery and conventional laparoscopy offer a low-risk approach to benign ovarian masses, although conventional laparoscopy is preferred because of its shorter operative time (93). In cases in which the ovarian cyst is deemed too large for laparoscopic intervention, laparotomy may be performed as a vertical incision or as a low transverse incision.

▶ *Which patients may benefit from referral to a gynecologic oncologist?*

Consultation with or referral to a gynecologic oncologist is recommended for women with an adnexal mass who meet one or more of the following criteria:

- Postmenopausal with elevated CA 125 level, ultrasound findings suggestive of malignancy, ascites, a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis

- Premenopausal with very elevated CA 125 level, ultrasound findings suggestive of malignancy, ascites, a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis
- Premenopausal or postmenopausal with an elevated score on a formal risk assessment test such as the multivariate index assay, risk of malignancy index, or the Risk of Ovarian Malignancy Algorithm or one of the ultrasound-based scoring systems from the International Ovarian Tumor Analysis group

When a patient with a suspicious or persistent complex adnexal mass requires surgical evaluation, a physician trained to appropriately stage and debulk ovarian cancer should perform the operation (15). Surgical exploration should be performed in a hospital facility that has the necessary support and consultative services (eg, frozen section pathology) to optimize the patient's outcome (15). When a malignant ovarian tumor is discovered incidentally, a gynecologic oncologist should be consulted intraoperatively, if possible (15).

Women whose care is managed by physicians who have advanced training and expertise in the treatment of ovarian cancer, such as gynecologic oncologists, have improved overall survival rates compared with those treated without such collaboration. Improved survival rates reflect proper staging (thereby identifying some patients with unexpected occult metastasis who require adjuvant chemotherapy) and aggressive debulking of advanced disease, which is present in 75–80% of women with ovarian cancer (94–96).

▶ *What are the special considerations for the evaluation and management of adnexal masses in adolescents?*

The evaluation of adnexal masses in adolescents is similar to that in premenopausal women. Management of adnexal masses in adolescents should prioritize ovarian conservation to preserve fertility. Adnexal masses are common among adolescents, usually are benign, and often can be managed expectantly. The evaluation of adolescents with an adnexal mass should include menstrual history and a confidential inquiry regarding sexual activity. Transabdominal ultrasonography rather than transvaginal ultrasonography is recommended for young, virginal, or prepubertal adolescents (97). Alpha fetoprotein, β-hCG, and lactate dehydrogenase are indicated for evaluation of suspected germ cell tumors (98). Elevation of CA 125 levels can occur in adolescent and pediatric patients with ovarian malignancies but also has been observed in patients with noncommunicating uterine horns, ovarian fibromas, or torsed adnexa (99, 100).

Malignant and other adnexal masses that require surgery are uncommon in the adolescent population. Surgical indications include suspected malignancy, torsion, persistent mass, and acute abdominal pain. It is difficult to quantify the actual incidence of ovarian malignancy in adolescents; however, in the combined pediatric through adolescent age range, of those adnexal masses that require surgery in specialty care centers, 7–25% are malignant (101–103). Among those undergoing surgery, malignancy is more common in pediatric patients than adolescent patients (102). Germ cell tumors are the most common ovarian malignancies in children and adolescents (104, 105). The operative management of benign masses varies from a simple cystectomy to a unilateral salpingo-oophorectomy by laparoscopy or a staging laparotomy based on risk stratification (106). Ovarian preservation has been increasingly prioritized in the management of benign adnexal masses (107). Unilateral oophorectomy has not been shown to impair menstrual regularity or spontaneous pregnancy rates and, although possibly associated with lower follicular response to controlled ovarian stimulation, pregnancy and live birth rates are not decreased (108–110).

In cases in which malignancy is identified, the Children's Oncology Group recommends removal of the tumor without spilling its contents, sparing of the fallopian tube if not adherent, harvesting ascites for cytology, examination and palpation of the omentum with biopsy or removal of suspicious areas and examination and palpation of the iliac and aortocaval nodes with biopsy of abnormal areas (111). Several recent studies have confirmed the safety of conservative surgical approaches (112, 113). The presence of a gynecologic surgeon rather than a pediatric surgeon operating alone is associated with a higher rate of ovarian conservation (114, 107). The relative risk of incomplete surgical staging with malignant lesions was reduced when surgery was performed by a gynecologic oncologist (relative risk, 0.14; 95% CI, 0.02–0.89; P=.003) (107).

▶ *When is aspiration of an adnexal mass appropriate?*

Aspiration of an adnexal mass may be appropriate in cases of tubo-ovarian abscess (although antibiotic therapy is first-line treatment) and for the diagnosis of suspected advanced ovarian cancer for which neoadjuvant therapy is planned. Otherwise, aspiration of cyst fluid for diagnosis is contraindicated when there is a suspicion for cancer. Studies regarding diagnostic cytology have mixed results in the detection of malignancy, with sensitivity ranging from 50% to 74% (115, 116). Aspiration of a malignant mass can induce spillage and

seeding of cancer cells into the peritoneal cavity, which results in more-advanced-stage disease at diagnosis and potentially adversely affecting prognosis. There is strong evidence that spillage at the time of surgery decreases overall survival of patients with stage I gynecologic cancer compared with patients whose tumors were removed intact (117, 118). Even when a benign, simple cyst is aspirated, the procedure often is not definitively therapeutic. In one case series, the recurrence rate of cysts at 6 months was 44% for premenopausal women and 25% for postmenopausal women (119), whereas another series reported a 39% recurrence (120).

An exception to avoiding aspiration of a mass exists for those women who have clinical and radiographic evidence of advanced ovarian cancer and who are medically unfit to undergo surgery. In these patients, malignant cytology confirmed by aspiration will establish a cancer diagnosis, permitting initiation of neoadjuvant chemotherapy (121, 122).

Antibiotic therapy is the first-line treatment for tubo-ovarian abscess (123). The Centers for Disease Control and Prevention's *Sexually Transmitted Disease Treatment Guidelines* suggest hospitalization in cases of pelvic inflammatory disease complicated by tubo-ovarian abscess (124). The role of image-guided drainage versus surgical therapy depends on the clinical severity and patient's reproductive stage. Computed tomography and ultrasound-guided aspiration have been used successfully (125). Women of reproductive age may benefit from tubo-ovarian abscess drainage. In one study, women with abscesses of less than 10 cm were randomized to antibiotics alone or in combination with transvaginal aspiration. Women treated with drainage had shorter average hospital stay and were less likely to require surgical intervention (126). Surgical therapy is indicated for postmenopausal women with pelvic abscesses because they are at risk of underlying malignancy (127).

▶ *What is the recommended management for adnexal torsion?*

Adnexal torsion in women who want to remain fertile should be managed by reduction of the torsion with concomitant ovarian cystectomy, for identified ovarian pathology. In cases of a torsion, adnexal conservation should be prioritized because, in most cases, the residual ovary will regain perfusion and remain viable (128–130). Despite evidence of necrosis or ischemia at the time of surgical exploration, ovarian function is preserved in upwards of 90% of cases 3 months after intervention (131). Ovarian fixation remains controversial but may be considered in cases of recurrent torsion (132, 129).

▶ *What is the recommended management for mature teratomas and endometriomas?*

Surgical intervention for suspected endometriomas or mature ovarian teratomas is warranted if the masses are large, symptomatic, or growing in size on serial imaging or if malignancy is suspected. If these masses are managed expectantly, follow-up surveillance is warranted. In one series of 289 women who opted for expectant management of ultrasound-diagnosed mature teratomas, 26% eventually underwent surgical treatment. Women who failed expectant management were more likely to have larger or more rapidly enlarging cysts (133).

Surgical excision of endometriomas may adversely affect ovarian reserve (134). Although endometriomas of 5 cm or more have been associated with lower ovarian follicle density (135), several studies have found similar fertility outcomes among women with or without endometriomas who underwent assisted reproduction (136, 137). Thus, asymptomatic endometriomas do not require intervention for infertility (138). If surgery is required, as much ovarian tissue as possible should be conserved to preserve ovarian function.

▶ *How should adnexal masses be managed in pregnancy?*

Most adnexal masses in pregnancy appear to have a low risk of malignancy or acute complications and may be managed expectantly. Several investigators have examined the role of expectant management of adnexal masses through the duration of pregnancy. The authors report that 51–92% of adnexal masses will resolve during pregnancy (139–141), with predictors of persistence being mass size greater than 5 cm and "complex" morphology on transvaginal ultrasonography. The occurrence of acute complications is reportedly less than 2% (142).

The prevalence of adnexal masses in pregnant women is 0.05–3.2% of live births (139, 140, 142–144). The most commonly reported pathologic diagnoses are mature teratomas and paraovarian or corpus luteum cysts (144–146). Malignancy is diagnosed in only 1.2–6.8% of pregnant patients with persistent masses (140, 143, 147, 148).

Evaluation of the pregnant patient with an adnexal mass is similar to that of the premenopausal patient. Depending on gestational age, abdominal ultrasonography may be used in addition to transvaginal ultrasonography because the ovaries may be outside of the pelvis later in gestation. Magnetic resonance imaging is the modality of choice if additional imaging is needed because it has the ability to image deep soft tissue structures in a manner that is not operator dependent, and it

does not use ionizing radiation (149). Levels of CA 125 are elevated in pregnancy. They peak in the first trimester (range, 7–251 units/mL) and decrease consistently thereafter (150). Typically, low-level elevations in pregnancy are not associated with malignancy.

If intervention is warranted based on symptoms, laparoscopic approaches and laparotomy may be considered. Data support the relative safety and efficacy of laparoscopic management of persistent adnexal masses in the second trimester (151).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- Transvaginal ultrasonography is the recommended imaging modality for a suspected or an incidentally identified pelvic mass. No alternative imaging modality has demonstrated sufficient superiority to transvaginal ultrasonography to justify its routine use.
- Ultrasound findings that should raise the clinician's level of concern regarding malignancy include cyst size greater than 10 cm, papillary or solid components, irregularity, presence of ascites, and high color Doppler flow.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- The combination of an elevated CA 125 level and a pelvic mass in a postmenopausal woman is highly suspicious for malignancy, and patients with these findings should be referred to or treated in consultation with a gynecologic oncologist.
- Simple cysts up to 10 cm in diameter on transvaginal ultrasonography performed by experienced ultrasonographers are likely benign and may be safely monitored using repeat imaging without surgical intervention, even in postmenopausal patients.
- Minimally invasive procedures are the preferred route of surgery for presumed benign adnexal masses. Regardless of the approach employed, fertility preservation should be a priority when managing masses in adolescents and premenopausal women who have not completed childbearing.
- Consultation with or referral to a gynecologic oncologist is recommended for women with an adnexal mass who meet one or more of the following criteria:
  - Postmenopausal with elevated CA 125 level, ultrasound findings suggestive of malignancy, ascites, a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis
  - Premenopausal with very elevated CA 125 level, ultrasound findings suggestive of malignancy, ascites, a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis
  - Premenopausal or postmenopausal with an elevated score on a formal risk assessment test such as the multivariate index assay, risk of malignancy index, or the Risk of Ovarian Malignancy Algorithm or one of the ultrasound-based scoring systems from the International Ovarian Tumor Analysis group
- The evaluation of adnexal masses in adolescents is similar to that in premenopausal women. Management of adnexal masses in adolescents should prioritize ovarian conservation to preserve fertility.
- Aspiration of an adnexal mass may be appropriate in cases of tubo-ovarian abscess (although antibiotic therapy is first-line treatment) and for the diagnosis of suspected advanced ovarian cancer for which neoadjuvant therapy is planned. Otherwise, aspiration of cyst fluid for diagnosis is contraindicated when there is a suspicion for cancer.
- Adnexal torsion in women who want to remain fertile should be managed by reduction of the torsion with concomitant ovarian cystectomy for identified ovarian pathology.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Serum biomarker panels may be used as an alternative to CA 125 level alone in determining the need for referral to or consultation with a gynecologic oncologist when an adnexal mass requires surgery.
- Transabdominal ultrasonography rather than transvaginal ultrasonography is recommended for young, virginal, or prepubertal adolescents.
- Surgical intervention for suspected endometriomas or mature ovarian teratomas is warranted if the masses are large, symptomatic, or growing in size on serial imaging or if malignancy is suspected. If these masses are managed expectantly, follow-up surveillance is warranted.

▶ Most adnexal masses in pregnancy appear to have a low risk of malignancy or acute complications and may be managed expectantly.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and August 2016. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I	Evidence obtained from at least one properly designed randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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