REVIEW ARTICLE

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Lesions of the Ovary and Fallopian Tube

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LESIONS OF THE OVARY AND FALLOPIAN TUBE (COLLECTIVELY, THE ADNEXA) are found in up to 35% of premenopausal and 17% of postmenopausal patients.[1,2] They occur throughout the life cycle, with a spectrum of benign to malignant causes. Management of an adnexal mass has three goals: assessment of whether the lesion is due to an acute process that requires urgent surgical intervention; determination of the likelihood of a malignant process, with appropriate triage; and an approach to management that incorporates the patient's desires regarding fertility and endogenous hormonal preservation.

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ANATOMY AND PHYSIOLOGY

The ovaries are located in the ovarian fossae and have a whitish-gray appearance (Fig. 1). Ovarian size peaks at approximately 4 cm by 2.5 cm when women are in their 20s and decreases to the size of an almond by menopause.[3] Each ovary is nestled against a fallopian tube that is inserted proximally into the uterine cornua. Tubal blood supply and innervation are found in the mesosalpinx, which receives terminal blood vessels from both the uterine and gonadal arteries. Since the mesosalpinx and the gonadal vasculature support both the tube and the ovary, they are also considered to be adnexal structures.[1,2] Adnexal lesions are managed similarly, irrespective of the site of origin.

The ovary is a complex and dynamic organ, responsible for steroidogenesis and the genesis, support, and release of oocytes, which are essential to human reproduction. These physiologic activities are supported by three types of ovarian tissue: surface epithelium, sex cords and stroma, and primordial germ cells.[4,5] Each tissue type has the potential to develop a corresponding pathologic (benign or malignant) process. Epithelioid tumors arise from the surface epithelium and account for the majority of ovarian tumors, sex cord or stromal tumors originate in supporting epithelial cells and either secrete hormones or form masses of fibrous tissue, and germ-cell tumors emanate from the primitive germ cells and form a range of benign to malignant tumors, such as mature teratomas and yolk-sac tumors.

The fallopian tube comprises an outer muscularis layer and an inner mucosal layer, which in turn hosts ciliated columnar cells, secretory cells, and intercalated cells. The fimbriated end of the tube is in open communication with the peritoneum and is histologically similar to the epithelium of the ovary.[5] Historically, the fallopian tube was described as an inert organ accounting for 0.3 to 1.5 cases of malignant lesions per 100,000 women. However, the fimbriated end of the fallopian tube has been increasingly implicated as the progenitor of many serous adenocarcinomas previously thought to have arisen in the ovary.[6-12] As early as the 1980s, case reports described the paradoxical finding of "high grade serous ovarian cancers" in women with hereditary breast and ovarian cancer syndrome who had undergone removal of ovaries described as normal during histologic examination.[9,10] Histologic evaluation of prophylactically removed, presumably normal tubes and ovaries from women with *BRCA1* or *BRCA2* mutations showed that the fimbriated end of the fallopian tube harbored early serous carcinoma in 2 to 10% of

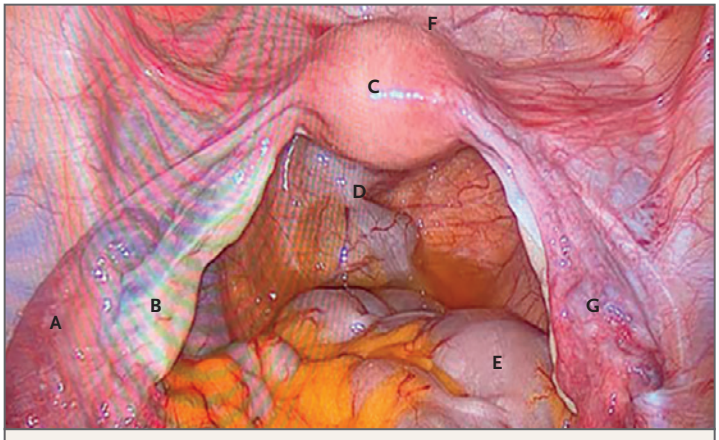

Figure 1. Normal Female Pelvis.
A laparoscopic image of the pelvis shows the fallopian tube (A), ovary (B), uterus (C), rectum (D), sigmoid colon (E), bladder (F), and mesosalpinx of the fallopian tube (G).

specimens. This lesion was frequently confined to the tube's endosalpinx endothelium, which supports a tubal origin.[11-13]

These serous tubal intraepithelial carcinomas, which account for 38 to 62% of all high-grade serous adenocarcinomas, may be missed on routine pathological examination.[14,15] Consequently, the National Comprehensive Cancer Network and the American College of Obstetricians and Gynecologists (ACOG) recommend complete resection of the fallopian tubes, as well as pathological examination according to the SEE-FIM (sectioning and extensively examining the fimbriated end) protocol,[16-18] in all patients undergoing risk-reducing surgery. This protocol allows for detailed, comprehensive examination of the fimbriated end of the fallopian tube, which is the portion of the tube that is susceptible to serous intraepithelial carcinoma lesions. This recommendation is followed by an estimated 91% of gynecologic oncologists but by only 41% of obstetrician-gynecologists.[19] Research on the physiology of the fallopian tube and its role in malignant processes is ongoing.

EVALUATION AND DIAGNOSIS

Although adnexal lesions have a wide differential diagnosis, they are always catalogued into one of three groups: benign, malignant, or borderline (Table 1). Tissue procurement is required for diagnosis, but biopsy of an adnexal lesion should almost always be avoided to prevent intraabdominal spillage and subsequent upstaging of a possible cancer.[18] Although a definitive diagnosis relies on histologic evaluation, the patient's age and clinical presentation are taken into account to rule out an acute process and assess the likelihood that the lesion is malignant. This evaluation usually consists of a history taking and physical examination, laboratory studies, and most important, imaging. Table 1 provides the differential diagnosis for an adnexal lesion, stratified by the appearance of the lesion on imaging.

ASCERTAINING THE NEED FOR URGENT SURGICAL INTERVENTION

A patient with an adnexal lesion may require emergency surgery on presentation (e.g., in the case of torsion, a ruptured ectopic pregnancy, or bowel obstruction due to a malignant lesion), may have chronic symptoms of pain or bloating (e.g., an endometrioma, large mucinous cystadenoma, or malignant process), or may be asymptomatic with incidental diagnosis of the adnexal lesion. The initial and most critical step in the evaluation is to ascertain the need for immediate surgical intervention. Patients with hemodynamic instability, peritonitis, or evidence of bowel or urinary obstruction should be evaluated in the emergency department for prompt surgical intervention. In addition, patients of reproductive age should immediately be tested for human chorionic gonadotropin to rule out an ectopic pregnancy, which can result in fatal hemoperitoneum. Once an acute process requiring urgent surgery has been ruled out, further evaluation should focus on assessing the risk of a malignant process and the likelihood of a benign process that would benefit from medical or surgical intervention by a specialist.

HISTORY AND PHYSICAL EXAMINATION

Evaluation of a suspected adnexal lesion should begin with the patient's age and family history. Older age is the greatest independent risk factor for ovarian or tubal cancer.[20,21] In addition, since approximately 20% of tubal or ovarian cancers are due to a heritable gene mutation, the family history is a critical component in the assessment of cancer risk for patients who present with an adnexal mass.[22-24]

Although a comprehensive physical examination includes pelvic examination, the pelvic examination has marked limitations. A prospective study of women undergoing examination while under anesthesia showed that the sensitivity of a pelvic examination for detecting an adnexal mass is low (range, 15 to 36%) and worsens markedly

with increasing body-mass index; it also showed that the experience of the clinician in performing the examination has no bearing on the sensitivity.[24] Multiple studies have also shown that the pelvic examination cannot reliably differentiate between a benign mass and a malignant mass.[25-29] Sensitivity is particularly poor in premenopausal patients (pooled sensitivity, 31% in premenopausal patients and 59% in postmenopausal patients).[25] However, the pelvic examination can inform surgical planning (e.g., by providing information about whether the mass feels fixed to the rectum or pelvic sidewall) and can provide valuable information about whether to use a laparoscopic or open approach.

IMAGING

Because of the limitations of the physical examination, pelvic ultrasonography is the most important imaging tool in the evaluation of the adnexa and should be the initial radiologic test.[22] However, pelvic ultrasonography also has limitations. There is evidence of interobserver variation, the examination can be difficult to perform and painful for patients, and pelvic ultrasonography cannot be used reliably to diagnose ovarian torsion.[1,30-32] Nevertheless, no other imaging approach has the performance characteristics, safety profile, and cost-effectiveness of transvaginal ultrasound in the workup of adnexal lesions.[26]

The morphologic features of the mass on ultrasonography are used to categorize the risk of a malignant process. Succinctly stated, the more complex a mass is, the higher the likelihood that it is malignant.[33] Though several ultrasonographic classification systems have been proposed, there is no universally accepted, standard classification system for adnexal lesions. Two promising tools are the International Ovarian Tumor Analysis (IOTA) simple rules, published in 2010, and the Ovarian-Adnexal Reporting and Data System (O-RADS), published in 2020 by the American College of Radiologists.[34-36] The IOTA simple rules categorize ultrasonographic features as benign (B features) or malignant (M features); each category has five features (Table 2). Tumors are considered likely to be benign if only B features are seen or malignant if only M features are seen. If these features are not observed or if they are not consistently B or M features, the mass is considered to be indeterminate. The simple rules have a sensitivity of 93% and a specificity of 81% for predicting a malignant process.[37] The IOTA trial was primarily performed in high-volume centers. These rules have not been validated in lower-volume centers with presumably less experienced clinicians.

Similarly, the American College of Radiologists O-RADS system offers a five-tiered classification for assessing the risk of cancer and offering the clinician follow-up recommendations (Table 3). Lesions in O-RADS category 2 are managed by observation or repeat imaging, patients with lesions in category 3 are referred to a specialist, and patients with lesions in categories 4 and 5 require the involvement of a gynecologic oncologist.[36] In a validation study analyzing 1054 adnexal masses, 300 of 304 malignant masses were categorized as O-RADS 4 or O-RADS 5, which led to 98.7% sensitivity (95% confidence interval [CI], 96.4 to 99.6) and 83.2% specificity (95% CI, 80.2 to 85.8) for the detection of cancer.[38] Though the O-RADS classification system is new, its initial performance data show that it is a highly reliable system for the categorization of adnexal masses.

Magnetic resonance imaging (MRI) can be a useful adjunct for masses described as indeterminate, but it is costly and should not be the first-line imaging study. MRI has a sensitivity of 81% and a specificity of 98% for categorizing as malignant a lesion thought to be of indeterminate risk on ultrasound.[39,40] Computed tomography (CT) is the test of choice for clinical staging of a known ovarian cancer and assessment for metastases or recurrence, but it has poor performance characteristics in the assessment of an adnexal mass.[39,40]

LABORATORY TESTING

All women of reproductive age should be screened for pregnancy if there is a concern about the possibility of an ectopic pregnancy, gestational trophoblastic neoplasia, or pregnancy concurrent with an adnexal mass. A complete blood count is helpful in guiding clinical management for women suspected of having a tubo-ovarian abscess or ovarian torsion. Clinicians may order other laboratory tests as appropriate. However, the most important laboratory studies for assessment of an adnexal mass are serum tumor marker tests.

Assessment of the serum level of the tumor marker CA-125 is the most extensively studied and most commonly used method of assessing lesions of the ovary. CA-125 is a large, transmembrane glycoprotein secreted by both coelomic (pleural and peritoneal) epithelium and müllerian epithe-

Table 1. Differential Diagnosis for Adnexal Lesions in Reproductive-Age and Postmenopausal Patients, According to Radiologic Appearance.*

Radiologic Appearance and Lesion Type	Benign, Malignant, or Borderline†	Age Group	Potential Laboratory Markers	Comments
Cystic lesions with or without thin septations			CA-125 level is generally normal but may be elevated if inflammation present	Purely cystic lesions are almost never cancerous
Follicular cyst	Benign	Reproductive age		
Serous cystadenoma	Benign	Any age		
Mucinous cystadenoma	Benign	Any age		
Hydrosalpinx	Benign	Any age		
Paraovarian cyst	Benign	Any age		
Paratubal cyst	Benign	Any age		
Peritoneal inclusion cyst	Benign	Any age		Associated with previous surgery or inflammation
Polycystic ovarian syndrome	Benign	Any age		
Solid lesions				
Leiomyoma	Benign	Any age		Can occur anywhere in gynecologic tract
Fibroma	Benign	Postmenopausal	CA-125	Ascites present in 10–15% of cases
Thecoma	Benign	Postmenopausal		Secretes estrogen; causes endometrial hyperplasia or carcinoma in up to 25% of cases
GCT	Malignant	Juvenile GCT: children and adolescents Adult GCT: postmenopausal	Inhibin A and B, CA-125	Secretes estrogen; causes endometrial hyperplasia or carcinoma in up to 50% of cases
Sertoli–Leydig cell tumor	Benign or malignant	Reproductive age or postmenopausal	Inhibin A and B, CA-125, alpha-fetoprotein, testosterone	May present with virilization or signs of estrogen excess
Sertoli-cell tumor	Benign or malignant	Reproductive age	Renin	May present with virilization, signs of estrogen excess, or both
Sex-cord tumor with annular tubules (sporadic or associated with Peutz–Jeghers syndrome)	Benign or malignant	Reproductive age		
Brenner tumor	Benign, borderline, or malignant	Postmenopausal		Rare; of epithelioid origin
Luteoma	Benign	During pregnancy		Can lead to virilization; spontaneous involution after delivery
Solid and cystic lesions				
Corpus luteum cyst	Benign	Reproductive age		
Ectopic pregnancy	Benign	Reproductive age	hCG	Must be evaluated; possible surgical emergency
Endometrioma	Benign	Reproductive age; occasionally seen in premenarchal and postmenopausal patients	CA-125 (level can be elevated, in the hundreds and rarely thousands of U/ml)	

Table 1. (Continued.)

Radiologic Appearance and Lesion Type	Benign, Malignant, or Borderline†	Age Group	Potential Laboratory Markers	Comments
Tubo-ovarian abscess	Benign	Reproductive age; rare cases in children and postmenopausal persons	Elevated white-cell count, sedimentation rate	Occurs as a result of seeding from another source (e.g., upper genital tract or colon)
Mature cystic teratoma	Benign	Reproductive age		Bilateral in 10% of patients, most common benign neoplasm in 20-to-30-yr-old patients
Monodermal, highly specialized teratoma	Benign or malignant	Reproductive age	5-HIAA (if carcinoid)	Most common are struma ovarii and carcinoid
Borderline tumors				
Mucinous borderline tumor	Borderline	Reproductive age or postmenopausal	CA-125, CEA	Generally unilateral; dissemination should prompt workup for cancer
Serous borderline tumor	Borderline	Reproductive age or postmenopausal	CA-125	Most common borderline tumor
Endometrioid borderline tumor	Borderline	Usually postmenopausal	CA-125	Generally unilateral, with good prognosis
Malignant germ-cell tumors				
Dysgerminoma	Malignant	Children, adolescents, or young adults; rare cases in older adults	Alkaline phosphatase, LDH, hCG	Most common germ-cell tumor
Yolk sac tumor	Malignant	Children, adolescents, or young adults	Alpha-fetoprotein, LDH	
Mixed germ-cell tumor	Malignant	Children, adolescents, or young adults	Alpha-fetoprotein, LDH	
Embryonal carcinoma	Malignant	Adolescents	Alpha-fetoprotein, LDH, hCG	
Choriocarcinoma or gestational trophoblastic neoplasia	Malignant	Adolescents or reproductive age	hCG (both free and glycosylated)	Nongestational choriocarcinoma extremely rare
Malignant epithelial and stromal lesions				CA-125 is a reliable marker in only 80% of stromal or epithelial cancers
Serous adenocarcinoma	Malignant	Reproductive age or postmenopausal	CA-125, HE4	Can be low grade or high grade
Endometrioid adenocarcinoma	Malignant	Reproductive age or postmenopausal	CA-125, HE4	Often associated with endometriosis and endometrial cancer
Mucinous adenocarcinoma	Malignant	Reproductive age or postmenopausal	CA-125, CEA, CA 19-9	Often arises with mucinous, borderline tumors†
Clear-cell adenocarcinoma	Malignant	Reproductive age or postmenopausal	CA-125, HE4	Associated with endometriosis
Carcinosarcoma	Malignant	Reproductive age or postmenopausal	CA-125	Majority of lesions are monoclonal (arise from the same cell, then metaplasia occurs)
Transitional-cell carcinoma	Malignant	Reproductive age or postmenopausal	CA-125	Believed to be a subtype of high-grade serous ovarian cancer

* CEA denotes carcinoembryonic antigen, hCG human chorionic gonadotropin, HE4 human epididymis protein 4, 5-HIAA 5-hydroxyindoleacetic acid, GCT granulosa-cell tumor, and LDH lactate dehydrogenase.
† Borderline classification indicates lesions that are also known as "low malignant potential" tumors.

Table 2. International Ovarian Tumor Analysis Simple Rules.

Benign features
Unilocular cyst (any size)
No solid components, or solid components <7 mm in diameter
Presence of acoustic shadowing
Smooth multilocular cyst <10 cm in diameter
No blood flow
Malignant features
Irregular solid tumor
Ascites
≥4 Papillary structures
Irregular solid multilocular tumor, with largest diameter >10 cm
Very strong color Doppler flow

lium, and levels are elevated in approximately 80% of women with epithelial ovarian or tubal cancers. Testing for CA-125 is approved by the Food and Drug Administration (FDA) for monitoring the response to treatment in women with ovarian cancer, but the testing is frequently used off label to help categorize adnexal masses and is particularly helpful in postmenopausal women. A meta-analysis showed that CA-125 testing has a sensitivity between 69% and 87% and a specificity between 81% and 93% for diagnosing cancer in postmenopausal women, and the performance of testing improves when it is combined with pelvic ultrasonography.[41] Because of its improved performance in postmenopausal women, the ACOG recommends that all postmenopausal women with a worrisome adnexal mass and a CA-125 level of 35 U per milliliter or higher be referred to a gynecologic oncologist.[22]

CA-125 testing has some important limitations. Up to 20% of women with metastatic ovarian or tubal cancers have a normal CA-125 level.[42] CA-125 testing is also unreliable in women with early-stage disease (sensitivity as low as 25% for stage I disease), in premenopausal women, and in those with epithelial subtypes of cancer other than high-grade serous adenocarcinoma (e.g., mucinous ovarian cancer).[42,43] The CA-125 level can also be elevated in many benign conditions, such as pregnancy, endometriosis, inflammatory bowel disease, renal failure, nonmalignant ascites, and any process that causes inflammation of the peritoneum or decreased clearance of CA-125. Thus, although an elevation in the CA-125 level is clinically relevant in the workup for an adnexal mass, CA-125 testing used alone is not diagnostic of epithelial ovarian cancer.

Because of these performance characteristics, the ACOG states that a "very elevated" CA-125 level should arouse concern for cancer in premenopausal women; unfortunately, there is no definition of "very elevated." In the 2011 ACOG practice bulletin on adnexal masses, the ACOG recommended that a premenopausal patient with an adnexal mass and a CA-125 level exceeding 200 U per milliliter should be referred to a gynecologic oncologist. However, this cutoff point was removed in the more recent practice bulletin, since it had been based on expert opinion alone. Currently, there is no established cutoff point for the CA-125 level in premenopausal women.

Human epididymis protein 4 (HE4) is another tumor marker that has been approved for determining the likelihood that an ovarian mass is cancerous. It has also been used to assess adnexal masses, with a sensitivity similar to that of CA-125 but superior specificity.[44] HE4 is included in the Risk of Malignancy Algorithm (ROMA), a nonproprietary online calculator that includes the serum levels of CA-125 and HE4 and age. It is also included in the serum Overa test, a commercial multivariate index assay based on serum levels of CA-125, transferrin, apolipoprotein A1, HE4, and follicle-stimulating hormone. These tests can help physicians decide whether a mass should be surgically removed by a gynecologist or a gynecologic oncologist. OVA1 is another multivariate index assay with FDA approval for the same indication. Though data suggest that multimodal tests are more sensitive than the clinical assessment of nongynecologic oncologists for the detection of cancer, the tests are costly and of uncertain clinical benefit.[44-46] An elegant economic modeling study performed by Havrilesky et al.[46] showed that multimodal laboratory assays are both more expensive and less effective than simply referring all women with indeterminate or suspicious lesions to a gynecologic oncologist for evaluation and treatment.

MANAGEMENT

LESIONS THAT APPEAR BENIGN ON IMAGING

Once it is clear that emergency surgery is not warranted, and once a malignant process has been ruled out, treatment is based on whether patients are symptomatic and on their individual preferences regarding surgery, fertility preservation, and endogenous hormone production (see text box).

Simple Cysts with or without Septations

The most innocuous lesion is a simple, unilocular cyst, which is commonly found in women of all ages.[44] These cysts are invariably benign. Large, prospective studies have shown that they resolve spontaneously 50 to 70% of the time; cysts that do not spontaneously resolve and are surgically removed are also benign.[45-47] The presence of thin septations does not increase the risk of cancer. The University of Kentucky Ovarian Cancer Screening program followed a total of 2870 women with septated cystic ovarian lesions over a 20-year period; none of these lesions were found to be an invasive cancer.[48] Symptomatic or very large cysts may require surgery, but otherwise, it is appropriate to manage simple cysts with ultrasound and observation.[25,49] Currently, there is no agreement on either the frequency or the duration of follow-up imaging. A large longitudinal study of adnexal lesions showed that tumors that would ultimately be diagnosed as malignant slowly increased in complexity each month.[44] In a study involving 1363 women who were over the age of 50 years and had small, complex lesions that were thought to be benign or indeterminate, all cancers and borderline tumors grew within 7 months of observation.[50] The ACOG suggests that clinicians consider 1 year of follow-up for stable cysts without solid components and up to 2 years of follow-up for stable, low-risk lesions with solid components.[22]

Complex Lesions

Hemorrhagic cysts, endometriomas, and mature teratomas are all benign, complex lesions with well-described ultrasonographic features (Table 1). Surgery should be considered for symptomatic patients. Minimally invasive (laparoscopic or robotic) approaches are associated with shorter recovery, fewer postoperative complications, lower cost, and greater patient satisfaction than laparotomy.[51] Conventional laparoscopy costs less and involves less operative time than robot-assisted surgery.[52]

For asymptomatic patients, observation is appropriate. Previously, the majority of patients with teratoma underwent surgery because of concern about an increased risk of ovarian torsion.[53] Today, however, most patients with asymptomatic teratomas are offered observation. In a 2017 study that followed 408 women with teratoma, torsion developed in only 1 woman (0.2%), and no other emergencies requiring surgery occurred.[54] Similarly, management of endometrioma has evolved in asymptomatic women who wish to preserve their fertility. A 2008 Cochrane review showed that women with documented subfertility and an endometrioma had increased spontaneous conception rates after removal of the endometrioma (odds ratio, 5.21; 95% CI, 2.04 to 13.29).[55] However, later studies showed that removal of an endometrioma was associated with a reduced ovarian reserve.[56-58] For women who wish to conceive, referral to an infertility specialist is appropriate.

Table 3. American College of Radiologists O-RADS System for Classification of Adnexal Lesions.*

Category	Description (Risk of Cancer)
O-RADS 1	Normal ovary (no risk of cancer)
O-RADS 2	Almost certainly benign lesion (<1% chance of cancer)
O-RADS 3	Low-risk lesion (1 to <10% chance of cancer)
O-RADS 4	Intermediate-risk lesion (10 to 50% chance of cancer)
O-RADS 5	High-risk lesion (>50% chance of cancer)

* O-RADS denotes Ovarian-Adnexal Reporting and Data System.

INDETERMINATE OR MALIGNANT LESIONS

Multiple studies have shown that for women with high-risk adnexal lesions, referral to a gynecologic oncologist, who has training in comprehensive surgical staging and tumor debulking, is associated with an increase in overall survival. Despite these findings, only approximately 40 to 50% of these patients are referred to a gynecologic oncologist.[59-65] The 2016 ACOG guidelines recommend consultation with a gynecologic oncologist for women with an adnexal mass who meet one of the following sets of criteria[22]: postmenopausal status with an elevated CA-125 level, ultrasound findings suggestive of cancer, ascites, or a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis; premenopausal status with a very elevated CA-125 level, ultrasound findings suggestive of cancer, ascites, or a nodular or fixed pelvic mass, or evidence of abdominal or distant metastasis; or premenopausal or postmenopausal status with an elevated score on a formal risk assessment test, such as the multivariate index assay, risk of malignancy index, or ROMA, or one of the ultrasound-based scoring systems from the IOTA group.

SPECIAL POPULATIONS

PEDIATRIC PATIENTS

Adnexal masses are rare in children and adolescents, with an incidence of roughly 3 cases per

Box 1. Key Points in the Management of an Adnexal Lesion.

- Appropriate management of an adnexal mass requires an assessment of whether the patient's presentation warrants emergency surgery, determination of the likelihood that the lesion is cancerous, and incorporation of the patient's desires concerning fertility and endogenous hormone preservation.
- Any germ layer of the ovary can create a benign, borderline, or malignant process.
- Most, but not all, ovarian cancers probably arise from serous tubal intraepithelial carcinoma lesions in the fimbriated end of the fallopian tube.
- A thorough family history is critical in assessing the likelihood that a mass is malignant.
- Ultrasound imaging is the most important study for assessing an adnexal lesion; MRI can be helpful but is usually not necessary. The more complex a mass, the greater the likelihood that it is malignant.
- The serum CA-125 level is elevated in roughly 80%, not 100%, of ovarian cancers. The level is also elevated in many benign, nononcologic conditions.
- Simple, unilocular lesions can be managed with observation.
- Complex lesions that are likely to be benign can be managed with observation or surgery, according to the clinical scenario and the patient's preference.
- All patients with high-risk adnexal lesions should be referred to a gynecologic oncologist for evaluation and treatment.

100,000 children per year.[66] Lesions found in pediatric populations are more likely to be malignant than those found in adults and are less likely to be diagnosed incidentally, with children generally presenting with pain, menstrual disorders, or precocious puberty.[67,68]

Most data on the workup and management of pediatric adnexal lesions come from studies in adults. Imaging and tumor markers remain the most important tools in ascertaining the risk of cancer.[69] Simple cystic structures are almost always benign, whereas the likelihood that a solid tumor larger than 9 cm in diameter is cancerous approaches 70%.[70] For asymptomatic lesions that are thought to be benign, observation is appropriate. For benign symptomatic lesions, surgical intervention is warranted, with the goal of removing the lesion but maximizing ovarian conservation when possible. Adnexal lesions are often associated with ovarian torsions, requiring operative management in children and adolescents. For patients with a cyst and a twisted ovary, the goal is ovarian preservation with detorsion and cystectomy.[71] Pediatric patients with a germ-cell cancer isolated to an ovary may undergo fertility-sparing treatment with unilateral salpingo-oophorectomy, pelvic washings, and sampling of any abnormal or enlarged structures and lymph nodes.[70]

PREGNANT PATIENTS

Most adnexal masses in pregnant patients are diagnosed incidentally on routine obstetrical ultrasonography, and ovarian or tubal cancer during pregnancy is rare. The most common mass diagnosed in pregnancy is a dermoid cyst.[72]

The diagnostic workup is more complex and less reliable in a pregnant patient than in a patient who is not pregnant. The CA-125 level is elevated during pregnancy, as are the levels of other tumor markers such as human chorionic gonadotropin and lactate dehydrogenase. Ultrasonography remains the mainstay of diagnosis, but ultrasonographic evaluation of the adnexa can become difficult with advancing gestation, since the ovaries are less proximal to a transvaginal probe. Women should not receive a substandard workup because they happen to be pregnant. For suspicious adnexal lesions in pregnant women, MRI is the study of choice because of its performance characteristics and because the fetus is not exposed to ionizing radiation. Gadolinium administration is avoided, since fetal safety with the use of gadolinium has not been established. Though abdominal and pelvic CT scans do expose the fetus and patient to ionizing radiation, the overall dose is low (<50 mGy). There is no evidence that doses below 50 mGy increase the risk of fetal anomalies.[73] Similarly, although iodinated contrast materials do cross the placenta and can cause transient depressive effects on the fetal thyroid gland, they do not appear to be teratogenic or carcinogenic.[74]

Management of adnexal lesions in pregnant patients is similar to that in nonpregnant patients. Lesions with ultrasonographic features that are consistent with benign disease can be managed expectantly. For patients with symptomatic masses or lesions that may be malignant, surgery is appropriate. Historically, laparoscopy was not considered in pregnant women, given concerns that elevated intraabdominal pressure might reduce placental perfusion, carbon dioxide absorption might result in fetal acidosis, or the fetus could be injured by trocar placement. However, studies in general surgery and gynecology have shown that laparoscopy results in lower rates of surgical-site infection, shorter hospitalization, and a lower risk of preterm labor than laparotomy. Longitudinal studies have shown no association between laparoscopy and an increase in fetal malformations or missed developmental milestones.[75] Although laparoscopy can be performed at any time during pregnancy, the second trimester is preferred, since the risk of spontaneous abortion has diminished by the second trimester and uterine size does not yet compromise surgical exposure of the pelvis.

CONCLUSIONS

Lesions of the adnexa are common and span a wide differential diagnosis, ranging from benign to malignant conditions. The goals of management require clinicians to quickly recognize a surgical emergency, to have a high suspicion for the presence of a malignant process, to consider the patient's preferences concerning fertility and endogenous hormone production, and to refer patients to an appropriate specialist as required. The mainstay of evaluation is imaging. Patients with adnexal masses would benefit from further research toward the standardization of imaging guidelines and recommendations, as well as from the consistent application of these guidelines in the management of masses that may be cancerous.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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