# Ovarian Masses from Anatomy to Its Complications: Review Article

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## ABSTRACT
Ovarian mass represents a common problem in clinical practice. Of all gynecologic carcinoma, ovarian carcinoma represents the greatest clinical challenge. The majority of ovarian masses are benign (80%) with cystic, solid, and mixed characteristics and a favorable diagnosis. The other 20% masses are malignant.

## INTRODUCTION

An adnexal mass (mass of the ovary, fallopian tube, or surrounding connective tissues) is a common gynecologic problem. It is estimated that there is a 5 to 10 percent lifetime risk for women undergoing surgery for a suspected ovarian neoplasm [1].

### Clinical approach:
A mass in the adnexa may be symptomatic or discovered incidentally on pelvic examination or imaging. There are many different types of adnexal masses. The type of mass is identified with pelvic imaging, use of biomarkers, and/or surgical exploration and pathologic evaluation. Most adnexal masses arise from the ovary or fallopian tube. However, other gynecologic structures may give rise to an adnexal mass, including the mesovarium or mesosalpinx (e.g., paratubal cysts). Uterine leiomyomas may protrude toward the adnexa and be palpated or visualized as an adnexal mass [2]. In addition, adnexal masses may arise from other proximal structures, including the urinary tract (e.g., bladder diverticulum), bowel (e.g., appendiceal abscess, diverticular abscess, bowel neoplasm), or pelvic connective tissue (e.g., peritoneal cyst) or nerves (nerve sheath tumor). Some adnexal masses require immediate attention; these include ectopic pregnancy, adnexal torsion, a ruptured ovarian cyst with hemorrhage, or a tubo-ovarian abscess. A serious concern when an adnexal mass is discovered is the possibility that it is malignant. A consensus paper from the Society of Radiologists in Ultrasound in 2010 indicated that transvaginal ultrasound, supplemented by transabdominal ultrasound, was the best technique for imaging and characterizing an adnexal cyst [3].

### Anatomy and Histology:
### a) Gross anatomy:
The uterine adnexa consist of the ovaries, fallopian tubes, and surround vascular, lymphatic, and connective tissues. The ovaries are suspended lateral and/or posterior to the uterus. The supporting structures of the ovaries include the utero-ovarian ligament that attaches the ovary to the uterus; the infundibulopelvic ligament (also referred to as the suspensory ligament of the ovary), through which the ovarian vessels travel, that attaches the ovary to the pelvic sidewall; and the broad ligament, which condenses to form the mesovarium. It is also attached to the broad ligament through the mesovarium. The ovary consists of an outer cortex, where the ova and follicles are located, and a medulla, where the blood vessels and connective tissue compose a fibromuscular tissue layer. The fallopian tubes arise from the uterine corpus posterior and superior to the round ligaments. The broad ligaments support the tubes with a condensation of connective tissue called the mesosalpinx [4].

### Histology:
The ovary includes several different tissue types. The most common neoplasms are epithelial. These derive from the stem cells that would typically give rise to fallopian tube epithelium (most high-grade serous carcinomas), or ovarian surface epithelium and inclusions (e.g., cystadenomas). Ovarian germ cell tumors are derived from primordial germ cells of the ovary. Ovarian sex cord-stromal tumors derive from stem cells that would normally give rise to supporting epithelial cells, including ovarian stroma (e.g., fibromas) and follicles (e.g., granulosa cell tumors, Sertoli-Leydig cell tumors).

The fallopian tubes consist of an outer muscularis layer of the tube with longitudinal smooth muscle fibers and an inner layer with circular fibers. The fallopian tube mucosa is composed of numerous delicate papillary folds (plica) consisting of three cell types: ciliated columnar cells; nonciliated, columnar secretory cells; and intercalated cells, which may simply represent inactive secretory cells [5].

### Gynecologic tract masses:
There are many different types of adnexal masses. The likely etiology of an adnexal mass differs by age and reproductive status. This is because some masses are stimulated by reproductive hormones [6].

### Premenopausal women:
There is a broad differential diagnosis of an adnexal mass in women of reproductive age. Adnexal masses stimulated by reproductive hormones are found

almost exclusively in this age group. These include physiologic cysts, endometriomas, and leiomyomas. Ovarian or tubal malignant neoplasms are uncommon in this age group, although the peak age for ovarian germ cell tumors is between ages 10 and 30 years. Adnexal masses in the reproductive age women that are associated with reproductive hormones include some that result from an aspect of the menstrual cycle, including: [7]

- Functional/physiologic cysts
- Corpus luteal cyst
- Theca lutein cyst
- Polycystic ovaries

Other types of masses are stimulated by reproductive hormones:

- Endometrioma
- Uterine leiomyoma

Premenopausal women may develop benign or malignant neoplastic adnexal masses. These occur most commonly in the ovary but may develop in the fallopian tube [8].

Common benign neoplasms include mature teratomas and cystadenomas. In general, ovarian or tubal cancers increase in incidence with increasing age and so are more common in postmenopausal women. However, ovarian germ cell tumors (e.g., teratomas) arise primarily in young women between 10 and 30 years of age; they represent 70 percent of ovarian neoplasms in this age group [9].

**Ovulatory**:

Some adnexal masses are associated with normal or abnormal ovulatory function [10].

**1) Functional or corpus luteal cysts:**

In the process of normal ovulation, a follicle develops to maturity and then ruptures to release an ovum; this is followed by formation and subsequent involution of the corpus luteum. Follicular cysts (also referred to as physiologic cysts) arise when rupture does not occur and the follicle continues to grow; corpus luteal cysts occur when the corpus luteum fails to involute and continues to enlarge after ovulation (the corpus luteum enlarges for the first six weeks of pregnancy and doubles its prepregnancy size. These cysts are therefore called physiologic or functional. Either type may become hemorrhagic. Follicular cysts appear smooth, thin-walled, and unilocular on ultrasound examination, while corpus luteum cysts can look complex and grossly are yellow. Simple cysts <3 cm in diameter are considered to be normal physiologic cysts. Physiologic cysts can become quite large but are usually less than 10 cm in size. Although simple cysts are most likely benign, there are no data to support which asymptomatic simple cysts are to be followed and which can be ignored [11].

Corpus luteal cysts in the normal menstrual cycle may have a variety of appearances on ultrasound. They can be simple or complex, containing internal debris

(hemorrhage) and thick walls. They can also be enlarged, up to 8 cm, but typically resolve spontaneously. An early intrauterine pregnancy is always associated with a corpus luteum cyst, which is typically <2.5 cm in diameter. However, the corpus luteum may occasionally become enlarged and painful due to hemorrhage. Functional and corpus luteal cysts are generally asymptomatic unless they rupture, they become hemorrhagic, or torsion occurs. Most spontaneously resolve within a few weeks, but some persist for several months [12].

**2) Theca lutein cysts**:

Theca lutein cysts (also called lutein cysts or hyperreactio luteinalis) are luteinized follicle cysts that form as a result of overstimulation from high human chorionic gonadotropin (hCG) levels or extreme sensitivity to hCG. Bilateral multiseptated cystic adnexal masses in a woman with gestational trophoblastic disease, multiple gestation, ovarian hyperstimulation, or a pregnancy complicated by fetal hydrops are likely to be theca lutein cysts rather than malignant neoplasm. This type of cyst can also occur in a normal pregnancy due to hypersensitivity to normal levels of hCG. Most theca lutein cysts are asymptomatic, but maternal virilization, hyperemesis gravidarum, preeclampsia, or thyroid dysfunction may occur. The cysts gradually resolve weeks to months after the source of hCG is eliminated [13].

**Polycystic ovaries:** Polycystic ovary syndrome (PCOS) results in enlarged ovaries with multiple small follicular cysts in some women. Although the ovaries are enlarged, patients with PCOS rarely present with an adnexal mass. The classic phenotype of PCOS is a woman who is obese, hirsute, and anovulatory [14].

**Pregnancy-related** [15, 16]:

Some types of adnexal mass are found only in pregnant women.

- **Corpus luteum of pregnancy**: An early intrauterine pregnancy is always associated with a corpus luteum cyst.
- **Luteoma**: Luteoma is a non-neoplastic ovarian mass associated with pregnancy; it is essentially a corpus luteum that is solid rather than cystic. A luteoma is sometimes mistaken for a neoplasm on clinical, gross, or microscopic examination. Luteomas involute spontaneously after delivery or are adequately treated by a conservative surgical approach. The diagnosis should be suspected in the presence of a solid adnexal mass and maternal hirsutism or virilization.
- **Decidualization of endometrioma:** Endometriomas may become decidualized during pregnancy. This can raise suspicion of a malignant mass due to the presence of a solid element with flow.

**3) Ectopic pregnancy**: An ectopic pregnancy may present as an adnexal mass noted on pelvic examination or ultrasound. Signs and symptoms

suggestive of ectopic pregnancy include a history of a missed menstrual period, abdominopelvic pain, and vaginal bleeding. An ectopic pregnancy is potentially life-threatening, and any woman with a possible ectopic pregnancy should be evaluated immediately.

## 4) Endometrioma:

An endometrioma is a benign cause of an adnexal mass arising from the ectopic growth of endometrial tissue. Patients with endometriosis often complain of pelvic pain, dysmenorrhea, and dyspareunia. An endometrioma, or "chocolate cyst," appears as a complex mass on ultrasound, typically containing homogeneous internal echoes. The ultrasound appearance of an endometrioma is often described as containing "ground glass" internal echoes. The chocolate-colored fluid, or old blood contained in the cyst, has a classic appearance.

### Leiomyoma:

A leiomyoma (fibroid) is a benign neoplasm of smooth muscle origin, which usually arises from the uterus but may also be found in the broad ligament. A fibroid arising from the posterior uterus and projecting into the posterior cul-de-sac (pouch of Douglas) or coming from the fundus as a pedunculated mass can be confused with an ovarian neoplasm. Cystic degeneration of a fibroid can result in the appearance of a complex mass on ultrasound. This, coupled with the fact that fibroids can cause an elevation in the serum CA 125 concentration, results in further concern that the mass may be a malignant ovarian neoplasm. Transvaginal imaging is key to differentiating between a leiomyoma in the adnexa from a solid ovarian tumor. First, the ovary must be found intact, normal, and completely separate from the leiomyoma. Also, Doppler flow can be used to see the vascular communication between the uterus and the pedunculated leiomyoma [2].

## Infectious or inflammatory:

### ■ Tubo-ovarian abscess:

A tubo-ovarian abscess (TOA) is an inflammatory mass involving the fallopian tube, ovary, and, occasionally, other adjacent pelvic organs (eg, bowel, bladder). This may manifest as a tubo-ovarian complex (an agglutination of those structures) or a collection of pus. These abscesses are found most commonly in reproductive age women and typically result from upper genital tract infection. TOA is usually a complication of pelvic inflammatory disease (PID). Findings of abdominopelvic pain, fever, purulent cervical discharge, and cervical motion tenderness in association with an adnexal mass suggest a diagnosis of TOA [17].

### ■ Hydrosalpinx:

Untreated or undertreated cases of PID result in scarring or "clubbing" of the tubal fimbriae. This leads to a collection of either tubal secretions or pus, resulting in a hydrosalpinx or pyosalpinx, respectively. After acute infection had resolved, a hydrosalpinx may remain. The tubal function is often compromised and this may contribute to infertility. A hydrosalpinx should be suspected when a dilated, tubular cystic structure is seen adjacent to the ovary. Hydrosalpinges often have incomplete septations. Three-dimensional ultrasound using sectional planes is useful to visually reconstruct the hydrosalpinx. Luminal contents vary from serous (hydrosalpinx) to blood (hematosalpinx) or pus (pyosalpinx) [18].

## Benign neoplasms:

Ovarian/tubal neoplasms may arise from stem cells, which typically give rise to the surface epithelium, fallopian tube epithelium, germs cells, or sex cord-stromal cells. The most common types of benign neoplasms in reproductive-age women are cystadenoma, Brenner tumor, and mature cystic teratoma (dermoid cyst). Mature cystic teratomas are a type of germ cell tumor; these ovarian neoplasms are found most commonly in women ages 10 to 30 years [19].

### ■ Serous or mucinous cystadenoma:

Serous and mucinous cystadenomas are among the most common benign ovarian neoplasms. They are thin-walled, uni- or multilocular, and range in size from 5 to <20 cm. Compared with serous cystadenomas, mucinous cystadenomas occur less frequently, are more likely to be multiloculated, are larger (they can attain an enormous size), and are less often bilateral (less than 5 versus 20 to 25 percent). A definitive diagnosis depends on pathologic evaluation to determine the cell type lining the cysts. Serous lining is similar to fallopian tube lining and mucinous lining cells collect mucin in their cytoplasm and resemble either endocervical or gastrointestinal epithelium. Many of these tumors are asymptomatic and found incidentally on pelvic examination or with ultrasound. As the masses grow they can cause pressure or pain, bloating, and urinary symptoms and can present with ovarian torsion [20].

## Mature cystic teratoma:

A mature cystic teratoma (dermoid cyst) is a benign germ cell tumor and is the most common ovarian neoplasm in the second and third decades of life. Mature teratomas can contain elements differentiated to all three germ cell layers: ectodermal (e.g., skin, hair follicles, sebaceous glands), mesodermal (e.g., muscle, urinary), and endodermal origin (e.g., lung, gastrointestinal). Transvaginal ultrasound usually reveals a complex mass, which can contain hyperechoic contents, hyperechoic lines or dots, fluid, and areas of acoustic shadowing. Mature teratomas may have a variety of appearances depending on their content. The tumors are bilateral in 10 to 15 percent of patients [21].

### ■ Endosalpingiosis:

Endosalpingiosis is the presence of non-neoplastic, ectopic, cystic glands outside the fallopian tube that are lined with fallopian tube-type ciliated epithelium.

Endosalpingiosis may occur in pelvic organs, including ovaries, fallopian tube serosa, uterine serosa, myometrium, or pelvic peritoneum. It may also occur in the bladder or in a retroperitoneal or axillary lymph node. Endosalpingiosis is not well-studied, and the clinical features remain uncertain. Similar Müllerian inclusions occur less frequently and may be lined by mucinous or endometrioid epithelium. Rarely, endosalpingiosis presents as large, tumor-like cystic masses involving the uterine serosa or bladder epithelium [22].

**Paraovarian/paratubal cysts and tubal and broad ligament neoplasms**:

Neoplasms arising from the fallopian tube or broad ligament are rare, although it is now believed that most high-grade serous carcinomas in the adnexa arise in the fallopian tubes. Since the tubes and broad ligaments are not usually visualized on ultrasound examination, the source of these tumors may be erroneously attributed to the ovary or uterus, which are more common sites for neoplasms. The most common findings in this area are simple cysts that originate from the remnants of paramesonephric (Müllerian) or mesonephric (Wolffian) ducts that are present during urogenital embryologic development. These are not neoplastic. The histology of these lesions may also be mesothelial. Paramesonephric cysts are most common, in particular the hydatid cyst of Morgagni. A hydatid cyst of Morgagni is attached to the tubal fimbriae and contains serous fluid surrounded by a translucent wall. These are non-neoplastic cysts lined by either mesothelium or fallopian tube-like epithelium. Rarely, a leiomyoma may arise in the fallopian tube or broad ligament. An adenomatoid "tumor" may arise in the fallopian tube. It is unclear whether a tumor is neoplastic. It is a benign mesothelial proliferation which grossly resembles a leiomyoma and histologically may be confused with a carcinoma [23].

**Malignant neoplasms:**

The incidence of ovarian malignant neoplasms in women of this age group with an adnexal mass ranges from 6 to 11 percent. Most primary ovarian neoplasms are partially cystic and derive from epithelial cells, although they can also arise from other cell types, such as germ cell, sex cord-stromal, and mixed cell types. Germ cell tumors are the second most common type of ovarian neoplasm in females younger than 30 years old, but they become rare after this age. The ovary can also be involved by metastatic malignant neoplasms forming in the gynecologic tract or nongynecologic primary sites ("Krukenberg tumor"), especially from endometrial carcinoma or gastrointestinal tract or breast cancer [24].

**5) Postmenopausal women**:

Most adnexal cysts in postmenopausal women are benign, but the incidence of ovarian cancer increases with advancing age; at least 30 percent of ovarian masses in women over age 50 are malignant neoplasms. Malignant adnexal masses include those of primary ovarian or tubal origin or metastatic lesions from other primary malignant neoplasms (e.g., endometrial, breast, or gastrointestinal tract). Nonmalignant etiologies of an adnexal mass in postmenopausal women include many of those also seen in patients of reproductive age, such as cystadenoma, paraovarian cyst, or hydrosalpinx. Leiomyomas or endometriomas are stimulated by estrogen, serum levels of which decrease significantly after menopause. Thus, these lesions typically decrease in size in postmenopausal women but may remain as smaller masses [25].

**Neoplastic**
■ **Epithelial neoplasms**:

Epithelial carcinoma is the most common histologic type of cancer of the ovary, fallopian tube, and peritoneum, accounting for 90 percent of all cancers at these sites. Ovarian carcinoma is traditionally referred to as a single entity, but it consists of a heterogeneous group of neoplasms with multiple histologic subtypes. Based upon histopathology, immunohistochemistry, and molecular genetic analysis, the five main subtypes of epithelial ovarian, fallopian tubal, and peritoneal carcinomas and their relative proportions are: [26].

- High-grade serous carcinoma (HGSC, 70 to 80 percent)
- Endometrioid carcinoma (10 percent)
- Clear cell carcinomas (10 percent)
- Mucinous carcinoma (3 percent)
- Low-grade serous carcinoma (LGSC, <5 percent)

The different subtypes also differ in risk factors and clinical behavior. It has been proposed that what had been diagnosed as ovarian or peritoneal serous carcinomas (HGSC and LGSC) may originate from fallopian tube precursors, serous tubal intraepithelial neoplasia/carcinoma in the case of HGSC, and endosalpingiosis/Müllerian rests in the case of LGSC. High-grade tubal intraepithelial neoplasia/carcinoma is typically seen either associated with an ovarian or tubal mass or as a pathology result after risk-reducing salpingo-oophorectomy in a patient with a breast cancer gene (BRCA) mutation. These are microscopic lesions and do not present as a mass [27].

**Germ cell tumors**:

Ovarian germ cell tumors are derived from primordial germ cells of the ovary. They may be benign or malignant. The most common germ cell tumor in postmenopausal women is malignant degeneration of a teratoma. These neoplasms comprise approximately 20 to 25 percent of ovarian neoplasms overall but account for only approximately 5 percent of all malignant ovarian neoplasms. Ovarian germ cell tumors arise primarily in young women between 10 and 30 years of age and represent 70 percent of ovarian neoplasms in this age group. Mature teratomas are sometimes seen in

postmenopausal women, but malignant germ cell tumors are exceedingly rare in the postmenopausal age group [28].

■ **Sex cord-stromal tumors**:

Ovarian sex cord-stromal tumors are a heterogeneous group of benign or malignant neoplasms that develop from the dividing cell population that would normally give rise to cells surrounding the oocytes (the non-germ cell and nonepithelial components of the gonads). These neoplasms are rare, comprising only 1.2 percent of all primary ovarian cancers (malignant neoplasms). The average age at diagnosis is approximately 50 years. The histologic types of sex cord-stromal tumors include granulosa-stromal cell (eg, granulosa cell tumor, fibroma, thecoma), Sertoli-stromal (e.g., Sertoli-Leydig cell tumor), and granulosa and Sertoli-Leydig elements (e.g., gynandroblastoma). Sex cord-stromal tumors are often comprised of cells that produce ovarian hormones, including estrogen and androgens. These may result in symptoms of estrogen excess or other effects, and measurement of these and other tumor markers may play a role in diagnosis. They rarely may be associated with Meigs syndrome. Meigs syndrome includes findings of an adnexal mass, ascites, and pleural effusions [29].

**Simple ovarian cysts**:

Simple (anechoic) ovarian cysts are common in postmenopausal women. Simple cysts often resolve spontaneously but require surveillance to detect malignancy. If a simple cyst develops complex features or is accompanied by an elevated tumor marker level, surgery is required to exclude ovarian cancer. Simple cysts that develop during menopause probably represent either persistent physiologic/functional cysts from the premenopausal period or nonovulatory ovarian activity. High levels of gonadotropins or androgens may cause small epithelial lined structures in the ovary to secrete fluid into their inner cavity and enlarge to become cysts. This is not uncommon, especially in the first few years after menopause [30].

**WHO Classification of Ovarian Cancer [26]:**
The WHO has classified ovarian cancer into the following types:
1) Epithelial tumors.
2) Mesenchymal tumors.
3) Mixed epithelial and mesenchymal tumors.
4) Sex-cord stromal tumors.
5) Germ cell tumors.
6) Monodermal teratoma and somatic type tumors arising in dermoid cyst.
7) Miscellaneous tumors.
8) Mesothelial tumors.
9) Soft tissue tumors.
10) Tumor-like lesions.
11) Lymphoid/myeloid tumors.
12) Secondary tumors.

**Adnexal mass complications:**

In addition to the presence of an adnexal mass, complications may occur that have characteristic symptoms, patterns, or findings on pelvic imaging.

1) **Hemorrhagic ovarian cyst**:

An ovarian cyst may become hemorrhagic, i.e., there may be bleeding within the cyst. Women with a hemorrhagic cyst may be asymptomatic or may present with mild to severe pelvic pain. If the patient is stable and bleeding is not ongoing, then the patient may be managed expectantly. Ultrasound features typically include a cystic mass with internal echoes, which vary depending on the evolution of a blood clot. There may be a fluid level if there has been fresh bleeding or a blood clot that appears as an avascular solid internal mass. Or there can be "cobweb" internal echoes as the blood clot resolves. Hemorrhagic cysts or hemorrhagic corpus luteum cysts usually occur with ovulatory dysfunction. Patients who are on anticoagulation are at increased risk [31].

2) **Ruptured ovarian cyst**:

An ovarian cyst may rupture. This is typically accompanied by the sudden onset of moderate to severe pelvic pain. Ruptured ovarian cysts may bleed. Most may be managed expectantly, but some surgical management is required in some cases [32].

3) **Adnexal torsion**:

Ovarian torsion refers to the complete or partial rotation of the ovary on its ligamentous supports, often resulting in ischemia. The fallopian tube often twists along with the ovary; when this occurs, it is referred to as adnexal torsion. The primary risk factor for ovarian torsion is an ovarian mass and is most common if the ovary is 5 cm or larger [33].

4) **Infected Ovarian Cyst.**

Cysts can develop in response to a pelvic infection (called an abscess). If an infected cyst ruptures, it can trigger sepsis, a life-threatening immune response to harmful bacteria. Women with infected cysts are treated with antibiotics and sometimes require hospitalization for surgical drainage of the cyst.

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