

Use of the ESCAPE Mnemonic May Help Differentiate Functional Ovarian Masses from Ovarian Neoplasms

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Adnexal masses are often identified incidentally on physical and pelvic examinations and during cross-sectional imaging studies, such as CT scan, being performed for other reasons.

Many of these masses are functional cysts—these can be managed conservatively without the need for surgical intervention. Although contemporary management of adnexal masses often involves imaging, understanding the pathophysiology of functional lesions and implementing the mnemonic

ESCAPE may provide additional information in the initial management of a patient with a palpable adnexal mass. This approach, in conjunction with sonographic imaging, may further minimize unnecessary surgery in patients with palpable adnexal masses. (J Reprod Med 2020;65:335–340)

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The ESCAPE mnemonic can be useful in the initial evaluation as well as an adjunct to imaging modalities such as pelvic ultrasound in patients with an adnexal mass.

With the advent of sophisticated imaging techniques, including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), it has become routine to perform one or perhaps several of these studies in patients found to have an adnexal mass on physical examination. In addition, adnexal masses are often discovered incidentally during imaging performed for other reasons.

Most adnexal masses detected either on physical examination or imaging are ovarian in origin. The clinician and patient are often faced with the decision of whether to proceed with surgical intervention of these incidental ovarian masses. This determination revolves around the nature of the lesion, i.e., neoplasm versus functional cyst. A functional ovarian mass is the sequelae of normal physiologic function during the reproductive years. Functional lesions typically resolve spontaneously with observation over a 6–8-week time period. Neoplastic lesions, whether benign or malignant, may ultimately require surgical intervention. There is no evidence that a 6–8-week time period delay affects prognosis in the setting of an ovarian malignancy. Therefore, it may be prudent to reevaluate

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an adnexal mass that is most consistent with a functional cyst rather than proceeding with surgical excision.

In 1977 Greiss first described use of the mnemonic ESCAPE for the management of ovarian lesions. The purpose of this approach was to identify lesions that did not warrant surgical intervention.¹ We assert that this mnemonic is still valid today and can be useful in the initial evaluation as an adjunct to pelvic ultrasound in the assessment of ovarian lesions. Additionally, thorough understanding of the pathophysiology of functional lesions of the ovary is crucial in minimizing surgical intervention in patients with an adnexal mass.

Pathophysiology of Functional Ovarian Cysts

The types of functional ovarian lesions are listed in Figure 1. Follicular and persistent corpus luteum cysts are the most common of these entities. Each of these functional lesions is associated with different pathophysiology, clinical presentation, and differential diagnosis.

The follicular cyst develops as an accumulation of serous-type fluid in a follicle that is destined to become atretic. This lesion is typically discovered incidentally in the asymptomatic patient as a mobile cystic structure palpated on pelvic examination. The patient, prior to examination, typically does not have any specific symptoms or menstrual abnormalities. Vigorous or repetitive examinations may actually lead to rupture of the cyst. Cyst rupture causes localized pain for a brief period of time, improving over the ensuing 30–60 minutes and completely resolving over the next 24 hours. The differential diagnosis includes a benign neoplastic process, such as a serous or mucinous cystadenoma.

A persistent corpus luteum cyst involves hemorrhage into a corpus luteum. Unlike the follicular cyst, the persistent corpus luteum cyst may be associated with pain related to either distention of the ovarian capsule or peritoneal irritation secondary to leakage. Continued hormonal production with these cysts leads to menstrual abnormal-

-
- Follicular cyst
 - Persistent corpus luteum cyst
 - Theca lutein cyst
 - Luteoma of pregnancy
-

Figure 1 The types of functional ovarian lesions.

ities, including irregular bleeding or delayed onset of menses. Pelvic examination typically reveals a tender mass of “doughy” consistency due to the hematoma in the cyst wall. The main differential diagnosis with the constellation of these findings (pelvic pain, menstrual abnormalities, and an adnexal mass) is an ectopic pregnancy. This diagnosis can be readily excluded with a negative pregnancy test.

Finally, a theca lutein cyst is the result of overstimulation of the ovary by human chorionic gonadotropin (hCG). The source of hCG can be endogenous, as seen either in gestational trophoblastic disease or exogenous administration associated with hyperstimulation related to ovulation induction. These lesions often require a longer period of observation for resolution. For example, in a study by Montz et al, when discovered in association with hydatidiform moles, approximately 25% of theca lutein cysts persisted beyond 8 weeks regardless of the course of the trophoblastic disease. In this series, theca lutein cysts persisted in 3 patients for 15–18 weeks after hCG regression.²

It is suggested that luteoma of pregnancy is a functional lesion with spontaneous regression postpartum. However, others have reported recurrences in subsequent pregnancies associated with maternal virilization.³ Since these lesions are rare and often not diagnosed until after surgical resection, this diagnosis should not be considered very often when evaluating a patient with an adnexal mass.

ESCAPE Mnemonic

In addition to understanding the pathophysiology of functional lesions of the ovary, the use of the mnemonic ESCAPE (Figure 2) may also facilitate developing an accurate differential diagnosis for a patient with an adnexal mass. Use of this mnemonic only requires a pertinent history and physical examination.

Enlargement
Size
Consistency
Age
Persistence
Endocrine

Figure 2 The ESCAPE mnemonic.

Enlargement

Typically, when a functional lesion is in the differential diagnosis, a follow-up examination is indicated in 6–8 weeks. A functional lesion should have either resolved completely or at least diminished in size on follow-up examination. By contrast, enlargement of an ovarian lesion over a 6–8-week time period suggests a neoplastic process.

Size

Functional lesions of the ovary are generally 4–8 cm in diameter, although these lesions may rarely reach 10 cm. Certainly, lesions over 8–10 cm are worrisome for an ovarian neoplasm.

Consistency

Functional lesions are either cystic or “doughy” in consistency on examination, indicative of a fluid or blood-filled structure. In contrast, a solid ovarian mass is usually neoplastic. Most solid ovarian masses are benign neoplasms such as an ovarian fibroma or cystadenofibroma. Malignant solid ovarian masses are usually due to metastatic disease from another primary cancer such as colon or breast cancer.

Age

Ovulatory activity is necessary for development of functional lesions of the ovary. Therefore, premenarchal or postmenopausal women should not have functional ovarian lesions. In fact, Barber described the postmenopausal palpable ovary syndrome based on the principle that the postmenopausal ovary undergoes atrophy and thus typically is not palpable on pelvic examination. Therefore, any palpable ovary in a postmenopausal patient should raise the suspicion of a neoplastic process, although the risk of a malignant lesion is only about 10%.^{4,5}

In a related clinical situation, any temporary suppression of ovulatory function should prevent the development of a functional lesion. This would include use of contraceptive hormones and GnRH analogs. However, the frequency of functional ovarian cysts developing in patients using low-dose oral contraceptives (≤ 35 μ g ethinyl estradiol) appears to be increased in comparison with those who have used higher-dose pills.⁶ The incidence of functional ovarian cysts is even higher in progestin-only pill users.⁷ Thus, managing these patients conservatively with a follow-up examination would be prudent prior to surgical intervention.

Persistence

Ovarian lesions that remain unchanged on repetitive examinations are not likely functional and thus should be considered neoplastic in nature. Certainly, a persistent or stable lesion would be more consistent with a benign ovarian neoplasm rather than a malignant process.

Endocrine

Ovarian lesions associated with excessive hormone production are neoplastic although generally benign or of low malignant potential. These lesions may produce excessive amounts of estrogens, such as a granulosa cell tumor or androgens characteristic of a Sertoli-Leydig cell tumor. For example, a patient who presents with rapid onset of virilization associated with an ovarian mass likely has a neoplastic process.

The algorithms in Figures 3–4 depict use of the ESCAPE mnemonic in the evaluation of a patient with an adnexal mass. The mnemonic is used to aid in the diagnosis of a neoplastic process, with the major concern revolving around identifying a malignant lesion. As seen in Figure 3, the initial history and physical examination may denote a neoplastic process (benign or malignant). If a neoplastic process is suspected, a follow-up examination in 6–8 weeks is necessary. If the adnexal mass has enlarged or has persisted at this point, the mass is most likely a neoplasm (Figure 4).

Using ESCAPE in Conjunction with Pelvic Sonogram

Most patients with an adnexal mass will undergo a pelvic sonogram during initial evaluation. The ESCAPE mnemonic can be used in conjunction with ultrasound to further differentiate a functional lesion from a neoplastic one. For example, ultrasound imaging of a persistent corpus luteum may have concerning features for a neoplastic process. Use of the ESCAPE mnemonic may provide useful information in the differential diagnosis. In addition, sonography may help differentiate a benign from a malignant neoplasm once a functional lesion is excluded. For example, a recent ultrasound study found that the risk of an ovarian malignancy was extremely low in postmenopausal women with unilocular ovarian cysts under 10 cm.⁸ At the other end of the age spectrum, Millar et al evaluated the incidence of ovarian cysts in prepubertal females as noted by ultrasound and found cysts >2 cm infrequently in young girls over 2 years of age. They recommended con-

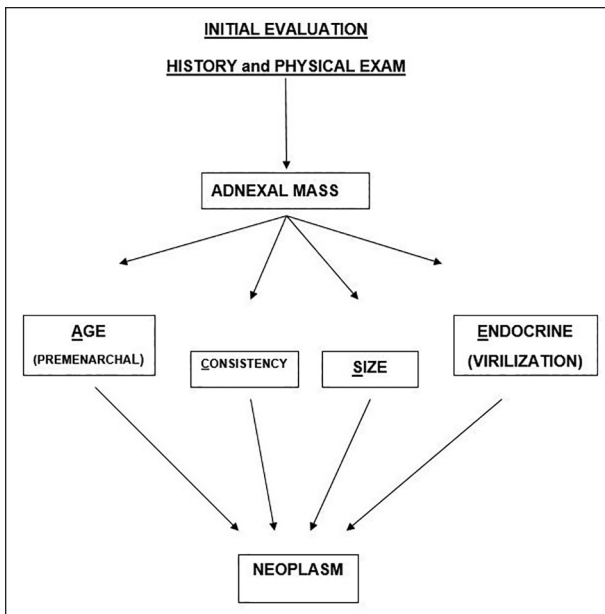


Figure 3 Incorporation of the ESCAPE mnemonic into the initial evaluation of a patient with an adnexal mass.

servative follow-up until regression for unilocular lesions <5 cm, noting no malignancies in their series.⁹

When a neoplastic process is favored after applying the ESCAPE mnemonic, a pelvic sonogram may further differentiate a benign from a malignant process. Ultimately, neoplasms with benign-appearing imaging features could be managed conservatively, thereby further minimizing additional surgical intervention in these patients.

For example, the International Ovarian Tumor Analysis (IOTA) group identified 4 reliable sonographic predictors of benign neoplasms and 2 reliable sonographic predictors of malignant neoplasms.¹⁰ However, approximately 20% of the time either both benign and malignant features are present or no features are present. In these inconclusive cases, more complex algorithms such as the IOTA LR2 model,¹⁰ ADNEX (Assessment of Differential Neoplasias in the Adnexa),¹¹ and RMI (Risk of Malignancy Index)¹² have been developed to discriminate benign versus malignant processes. These complex algorithms also incorporate clinical data such as patient age and CA-125. However, accuracy of these more complex algorithms has not reached a very reliable threshold for use in the clinical arena.

We suggest that patients with an adnexal mass suggestive of a neoplasm using the ESCAPE mnemonic with IOTA group malignant features be triaged to surgery. Reciprocally, surveillance should be considered in asymptomatic patients deemed to have an ovarian neoplasm with benign features using the ESCAPE and IOTA criteria. Serial ultrasonographic follow-up is indicated rather than surgical intervention in this clinical situation.^{13,14}

Case

A 38-year-old woman presented to the emergency room with left-sided flank pain consistent with nephrolithiasis. The patient had had a subtotal hysterectomy in 2007 for postpartum hemorrhage and an abdominal radical trachelectomy for cervical cancer in 2018. In the emergency room a CT scan of the abdomen and pelvis revealed a 1–2 mm punctate kidney stone along the inner margin of the left distal ureter. There was also an incidental finding of a 6.1 cm oval low attenuation cystic

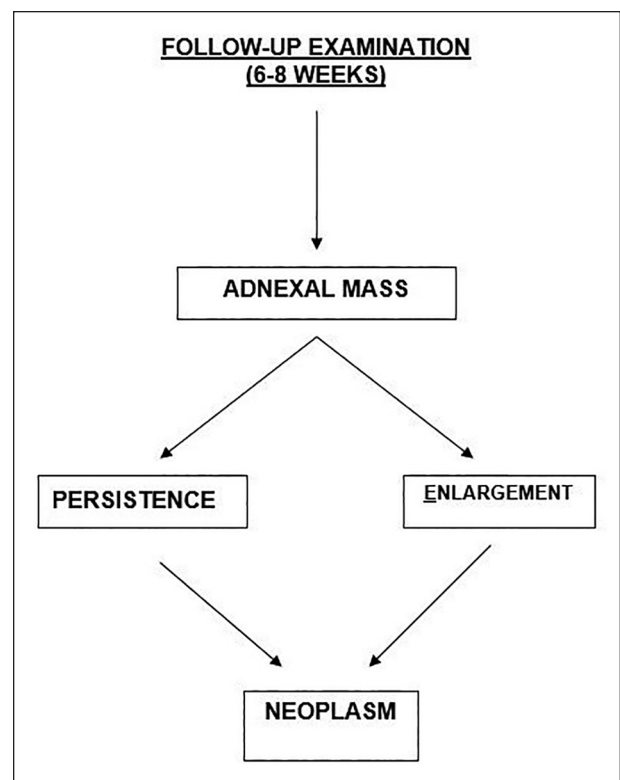


Figure 4 Incorporation of the ESCAPE mnemonic into follow-up management of a patient with an adnexal mass.

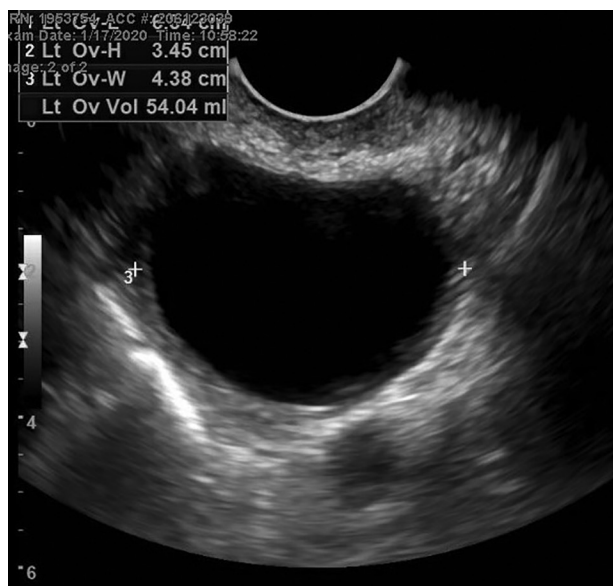


Figure 5 Pelvic sonogram reveals a 6.5 cm hypoechoic to anechoic cystic lesion in the left adnexa.

lesion in the left adnexa. A pelvic ultrasound was performed to further characterize the adnexal lesion (Figure 5). The patient's pain subsequently resolved. A follow-up pelvic sonogram 4 months later revealed a similar-appearing lesion. Subsequently, the patient underwent a laparoscopy converted to laparotomy with adhesiolysis and resection of the left adnexa. Final pathology revealed no evidence of malignancy.

In this case, application of the ESCAPE mnemonic would have led to reassurance in the following categories: enlargement, size, consistency, age and endocrine. The persistence of the cyst suggests a neoplastic process, likely a benign neoplasm since the size was stable. On ultrasound this cyst had IOTA group sonographic predictors of a benign mass (with no IOTA group sonographic predictors of a malignant process). If the ESCAPE and IOTA group criteria had been used in this case, this patient may have been spared an unnecessary operation.

Discussion

There are some exceptions to the ESCAPE mnemonic. As previously noted, theca lutein cysts may require somewhat longer than 6–8 weeks to resolve. Similarly, with pregnancy the corpus luteum is important in gestational support during

the first trimester, regressing by approximately 12 weeks' gestation. Surgical resection of a persistent corpus luteum cyst during this critical time would potentially jeopardize the pregnancy.

Hyperthecosis represents another exception to the ESCAPE mnemonic guidelines. This is a clinical variant of polycystic ovary syndrome characterized by more intense androgenization, which can be associated with a rapid onset of virilization and ovarian enlargement, though not a neoplastic condition.^{15,16} Finally, ovarian endometriomas are neither neoplastic nor functional—the ESCAPE mnemonic may not be very helpful with this diagnosis. Symptoms of pelvic endometriosis, including secondary dysmenorrhea, dyspareunia, and dyschezia, associated with an adnexal mass would suggest an endometrioma. Endometriomas also have a characteristic appearance on pelvic sonography.

Some adnexal masses will be difficult to classify after utilizing the ESCAPE mnemonic and IOTA group sonographic descriptors. In these cases, pelvic MRI with intravenous contrast should be considered. An IOTA study evaluating MRI performance in assessing these masses is currently ongoing.¹⁷ More complex algorithms (IOTA LR2, ADNEX, or RMI) should also be considered when triaging a patient with an indeterminate adnexal neoplasm after employing the ESCAPE mnemonic and IOTA sonographic descriptors. Further optimization of these models may lead to improvement in identification of women with benign ovarian neoplasms who can be spared unnecessary surgery.

In conclusion, knowledge of (1) pathophysiology of functional lesions of the ovary and (2) the ESCAPE mnemonic may be useful, efficient, and cost-effective tools in the evaluation and management of patients with an adnexal mass diagnosed on examination or incidentally on imaging. As Greiss stated, "appropriate observation of functional ovarian cysts will obviate diagnostic surgery 90% of the time, thus permitting an "escape" from the sequelae of unnecessary and often extirpative operations."¹ The ESCAPE mnemonic can be useful in the initial evaluation as well as an adjunct to imaging modalities such as pelvic ultrasound in patients with an adnexal mass.

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