THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Occam's Razor and the Adnexal Mass

John O Schorge, MD, FACS

William of Ockham (or Occam)

- b 1287 – d 1347
- English Franciscan friar & philosopher
- Major figure of medieval thought
- “Law of parsimony”

Occam's Razor: No more things should be presumed to exist than are absolutely necessary, i.e., the fewer assumptions an explanation of a phenomenon depends on, the better the explanation.

(William of Occam)

izquotes.com


Occam's Razor Example: You hear hoofbeats.
YOUR DICTIONARY
The answer that requires the fewest assumptions is generally the correct one.

Ockham chooses a razor

Ockham chooses a razor

OCCAM'S RAZOR

A Parsimonious Shave Every Time!

Educational objectives

1. Learn which adnexal masses can be safely observed and which require some form of intervention.
2. Better understand the appropriate workup: exam, labs, imaging depending on the patient's clinical circumstances.
3. Become familiar with the ACOG/SGO criteria for what constitutes sufficient risk to refer to GYN Oncology.
4. Review the many different options for preop testing such as OVA1, ROMA, RMI, other markers and their utility.

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31 y/o with LLQ pain x weeks. Pelvic exam with mild tenderness to palpation but no obvious mass. UPT negative.
What is next BEST step?

1. Expectant management
2. Transvaginal ultrasound
3. Pelvic MRI
4. Tuning fork to forehead
5. Diagnostic laparoscopy

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SYMPTOMS OF OVARIAN CYST

- Bloating, swelling or pressure in the lower abdomen
- Painful bowel movements
- Irregular periods
- Unusually heavy or light menstrual flow
- Pain that spreads from the pelvis to the lower back or thighs
- Feeling of heaviness even after eating very little
- Frequent need to pass a stool or urinate
- Feeling of pressure in the bladder or rectum
- Difficulty in emptying the bladder
- Nausea & vomiting
- Pain during sex
- Rare instances of hormonal fluctuations
- Painful tenderness in the breasts

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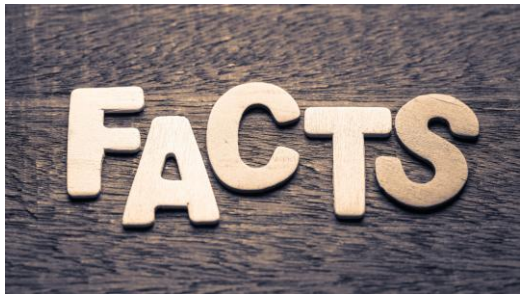
WHAT WE KNOW



- Ovarian cysts are ***incredibly*** common and are considered a normal part of having a menstrual cycle. Because they rarely cause symptoms, they often develop and disappear completely unnoticed

- Screening via TVS reveals that simple ovarian cysts are found in **nearly all premenopausal women** at some point during their childbearing years

- About **10% of women worldwide** have a noticeable ovarian cyst at any given time

- Cysts become less frequent after menopause, but they still appear in **up to 20% of postmenopausal individuals**.

- About **1 in 10 women** will require surgery to remove a cyst during their lifetime

31 y/o with LLQ pain. Pelvic exam with mild tenderness to palpation and adnexal fullness. UPT negative. TVS c/w a 4-cm ovarian cyst. Report recommends MRI. What is next BEST step?

1. Expectant management
2. Pelvic MRI
3. IR-guided biopsy
4. Need more info
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2

Types

COMPLEX

Risk of Malignancy in Unilocular Ovarian Cystic Tumors Less Than 10 Centimeters in Diameter

Susan C. Modesitt, MD, Edward J. Pavlik, PhD, Frederick R. Ueland, MD, Paul D. DePriest, MD, R. J. Kryscio, PhD, and J. R. van Nagell, Jr, MD

OBJECTIVE: To determine the natural history and to estimate the risk of malignancy of unilocular ovarian cystic tumors less than 10 cm in diameter followed conservatively by transvaginal ultrasound.

METHODS: From 1987 to 2002, 15,106 asymptomatic women at least 50 years old entered the University of Kentucky's Ovarian Cancer Screening Program and underwent initial transvaginal ultrasonography. If the screen revealed nothing abnormal, women were asked to repeat transvaginal ultrasonography yearly. If the screen revealed abnormalities, transvaginal ultrasonography was repeated in 4 to 6 weeks, along with Doppler flow ultrasonography and CA 125 testing.

RESULTS: Of the 15,106 women at least 50 years old, 2763 women (18%) were diagnosed with 3259 unilocular ovarian cysts. A total of 2261 (69.4%) of these cysts resolved spontaneously, 537 (16.5%) developed a septum, 189 (5.8%) developed a solid area, and 220 (6.8%) persisted as a unilocular lesion. During this time, 27 women received a diagnosis of ovarian cancer, and ten had been previously diagnosed with simple ovarian cysts. All ten of these women, however, developed another morphologic abnormality, experienced resolution of the cyst before developing cancer, or developed cancer in the contralateral ovary. No woman with an isolated unilocular cystic ovarian tumor has developed ovarian cancer in this population.

CONCLUSION: The risk of malignancy in unilocular ovarian cystic tumors less than 10 cm in diameter in women 50 years old or older is extremely low. The majority will resolve spontaneously and can be followed conservatively with serial transvaginal ultrasonography. (Obstet Gynecol 2003;102:594–9. © 2003 by The American College of Obstetricians and Gynecologists.)

Ovarian cancer is the second most common gynecologic malignancy in the United States and is the fifth leading cause of cancer death among US women.[1] Most women are diagnosed with advanced-stage cancer and undergo extensive surgical debulking, followed by combination chemotherapy. Initial complete response to therapy can be achieved in most women; however, relapse is the rule, and once ovarian cancer recurs, it is almost universally fatal. The dismal outcomes associated with the diagnosis of ovarian cancer in advanced stages has prompted the investigation of potential screening methods in an effort to detect the cancer at an earlier stage and to decrease mortality.

The use of transvaginal ultrasonography for ovarian cancer screening has been increasing in recent years. Sonography is also routinely performed in patients whose clinical examinations reveal ovarian enlargement. Transvaginal ultrasonography is a sensitive procedure that tests for ovarian abnormalities. It has limited interobserver variability but low positive predictive value.[2–4] As a result of the increasing use of sonography, the diagnosis of unilocular ovarian cysts in postmenopausal women has been increasing. Women with cystic ovarian tumors had been treated surgically until it was recognized that the malignant potential of a simple cyst was extremely low.[5,6] The purpose of this study was to determine this disease's natural history and to estimate the risk of malignancy of unilocular cystic ovarian tumors 10 cm or less in diameter in women at least 50 years old followed conservatively by transvaginal sonography.

MATERIALS AND METHODS

From 1987 to 2002, a total of 18,464 women were enrolled onto the University of Kentucky's Ovarian Cancer Screening Program, and 15,106 of these women were at least 50 years old. Eligibility criteria for the screening program included the following: all women at

From the Division of Gynecologic Oncology, Department of Obstetrics and Gyne-

Zero chance malignancy

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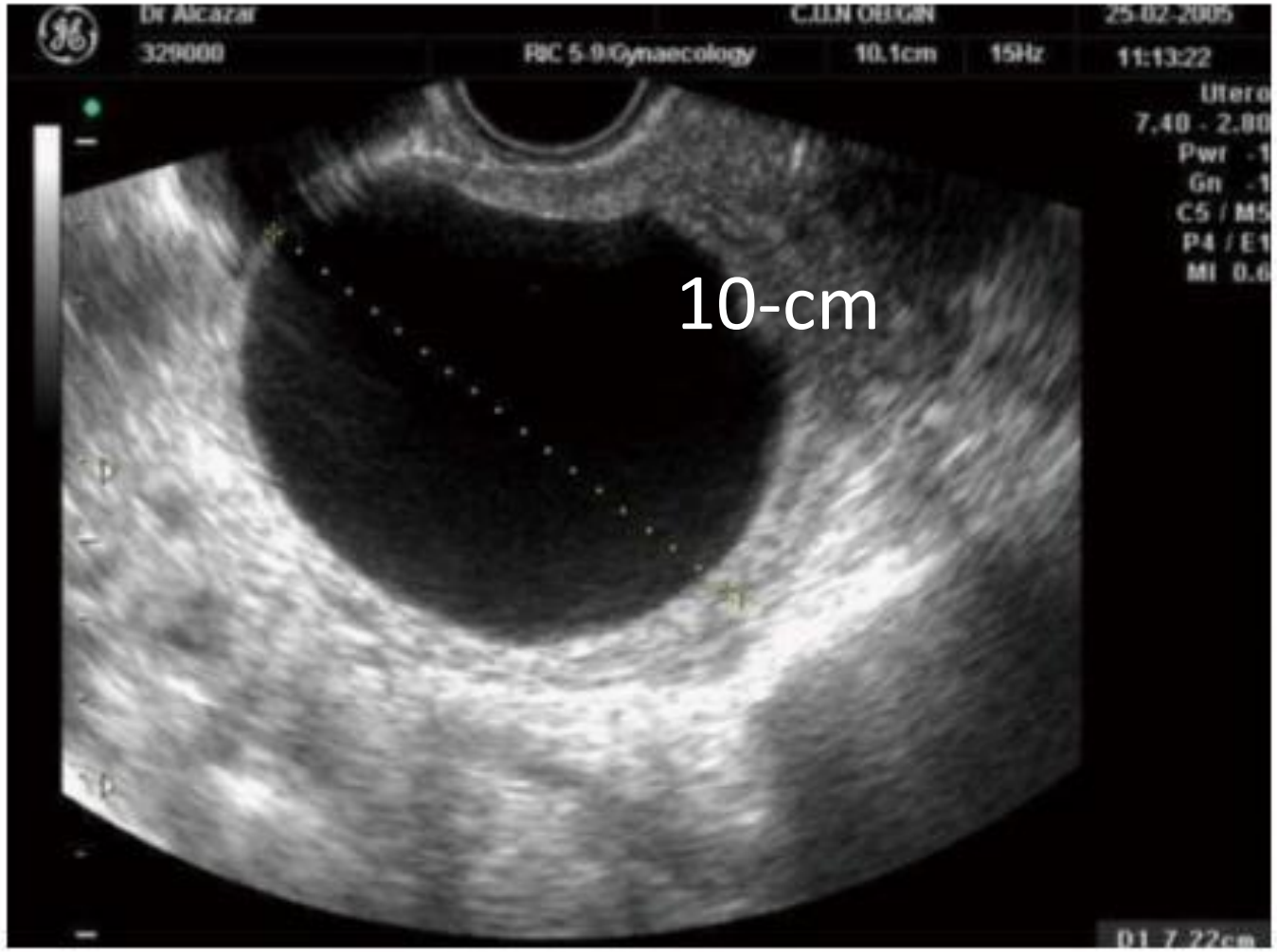

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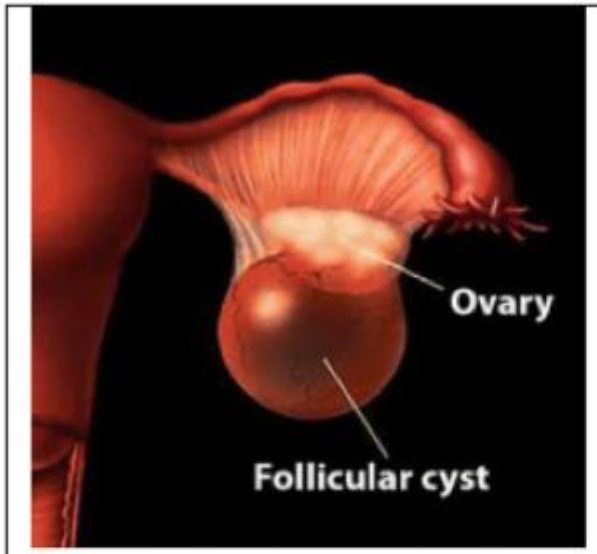
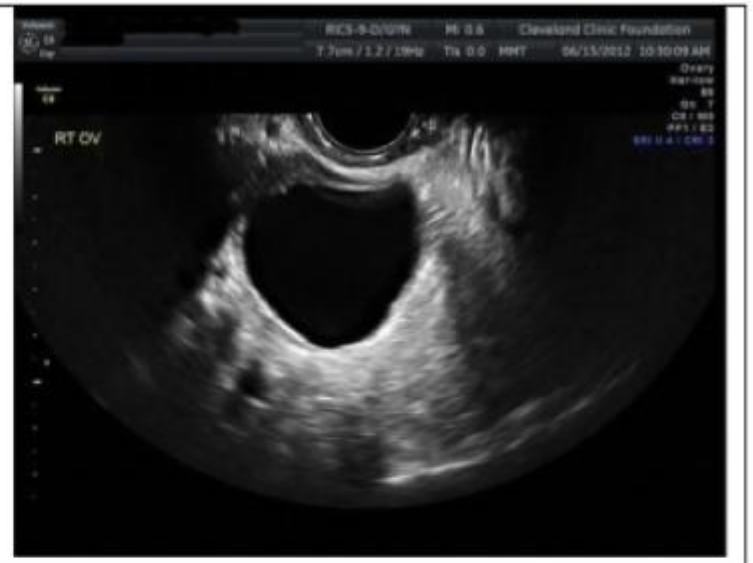
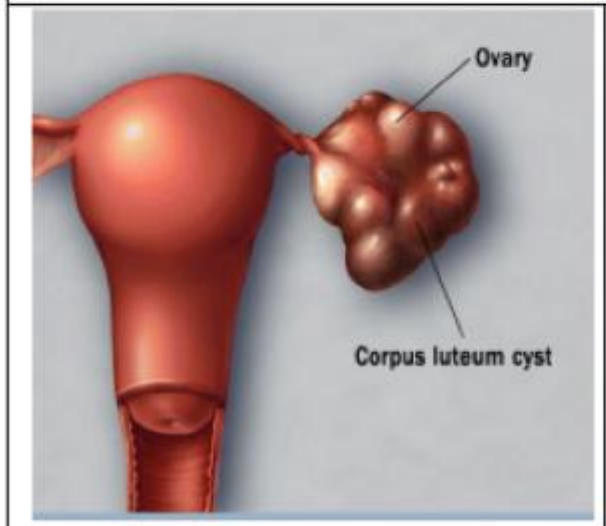
COMPLEX

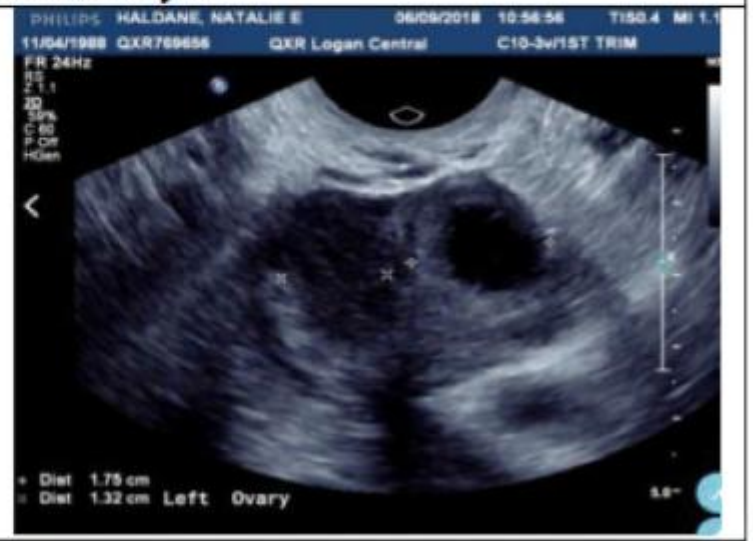
Physiologic cyst
normally 2-5 cm





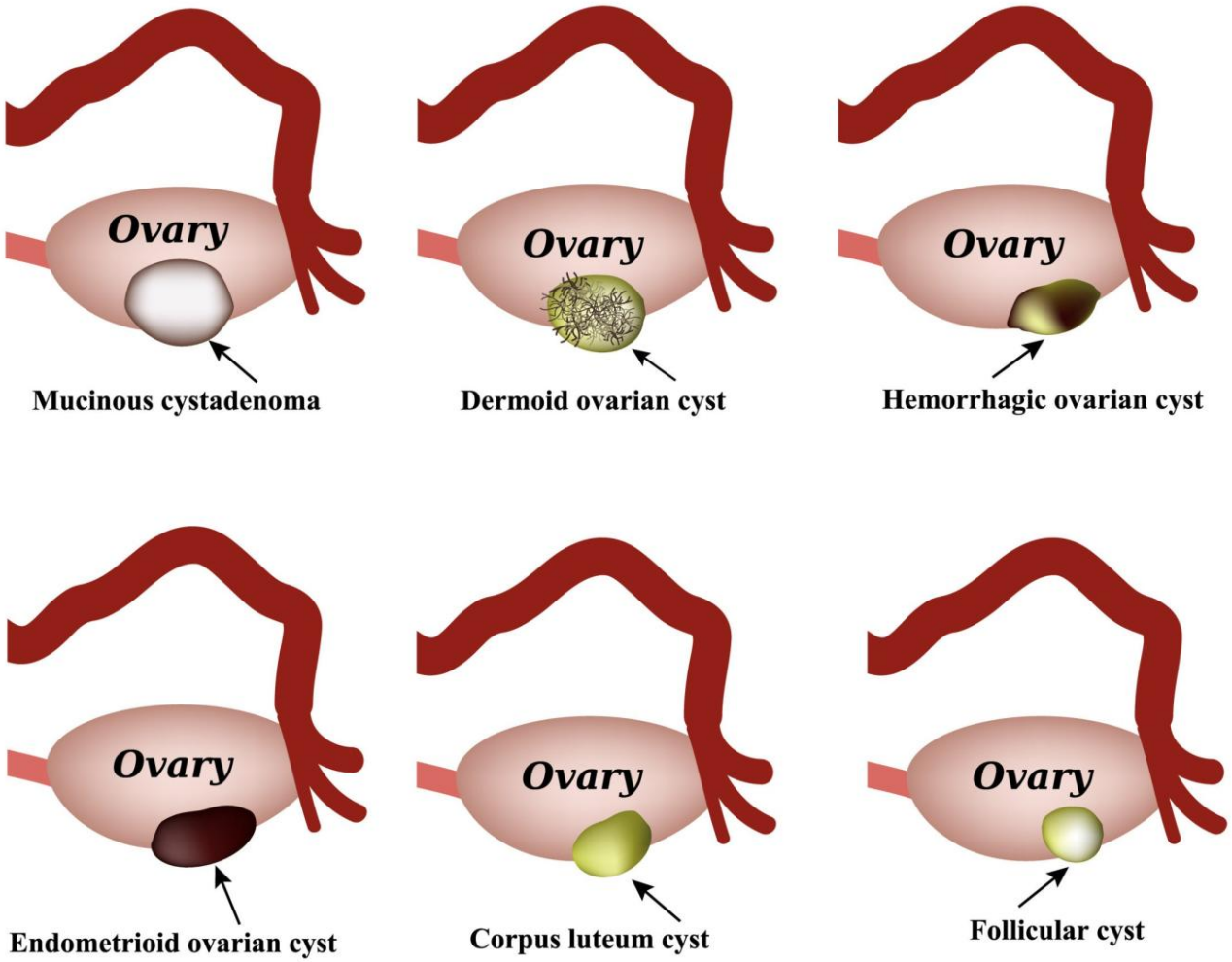
Follicle Cyst





Corpus Luteum Cyst

TYPES OF OVARIAN CYSTS



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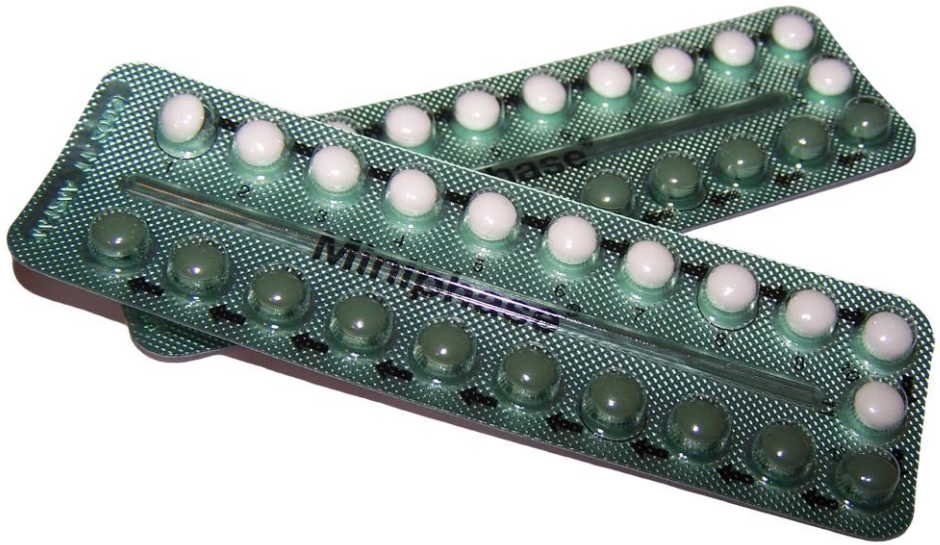
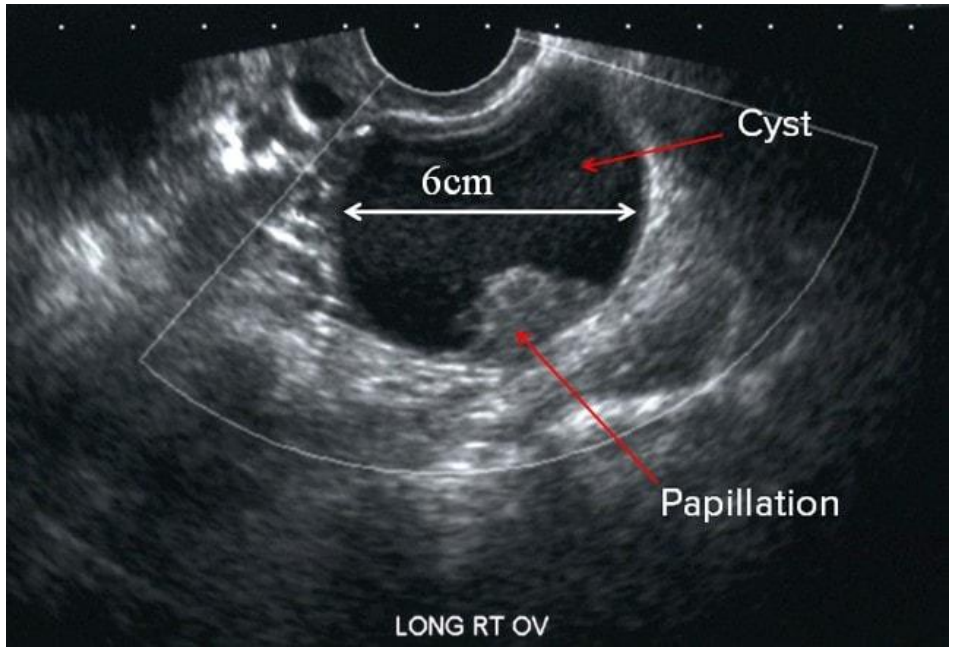


31 y/o with 4-cm complex ovarian cyst.

Repeat TVS 6 weeks later shows 5.5-cm enlargement with new excrescences & abnormal feeding vessel.



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WOMEN'S HEALTH CARE PHYSICIANS

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 174, NOVEMBER 2016 (Replaces Practice Bulletin Number 83, July 2007)

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

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

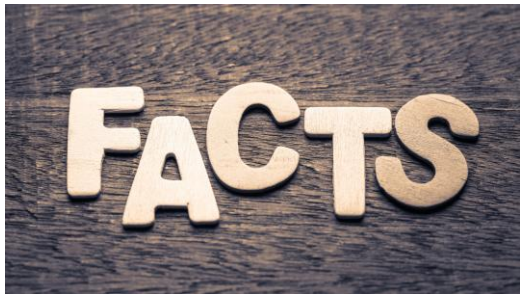
Box 1. Differential Diagnosis of an Adnexal Mass

Gynecologic

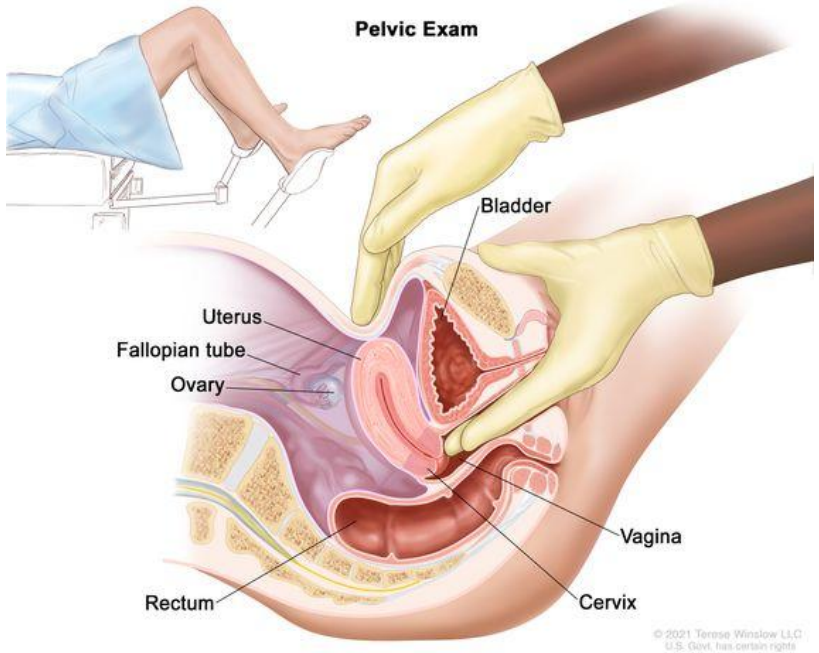
- Benign
  - Functional cyst
  - Endometrioma
  - Tubo-ovarian abscess
  - Mature teratomas (dermoids)
  - Serous cystadenoma
  - Mucinous cystadenoma
  - Hydrosalpinx
  - Paratubal cysts
  - Leiomyomas
  - Müllerian anomalies
- Malignant
  - Epithelial carcinoma
  - Germ cell tumor
  - Metastatic cancer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



- ***Age*** is the most important independent risk factor for ovarian cancer in the general population
- The most important personal risk factor for ovarian cancer is a strong ***family history*** of breast or ovarian cancer
- A personal medical history with a detailed gynecologic history and review of symptoms are **critical** components of patient evaluation
- The **potential for pregnancy** should be evaluated in all women of reproductive age because ectopic pregnancy is in the DDx of an adnexal mass in early pregnancy



- Start with VS and general physical appearance
- Pelvic exam (even EUA) has shown limited ability to identify an adnexal mass, especially with BMI > than 30
- Exam findings that are concerning include a mass that is irregular, firm, fixed, nodular, bilateral, or associated with ascites

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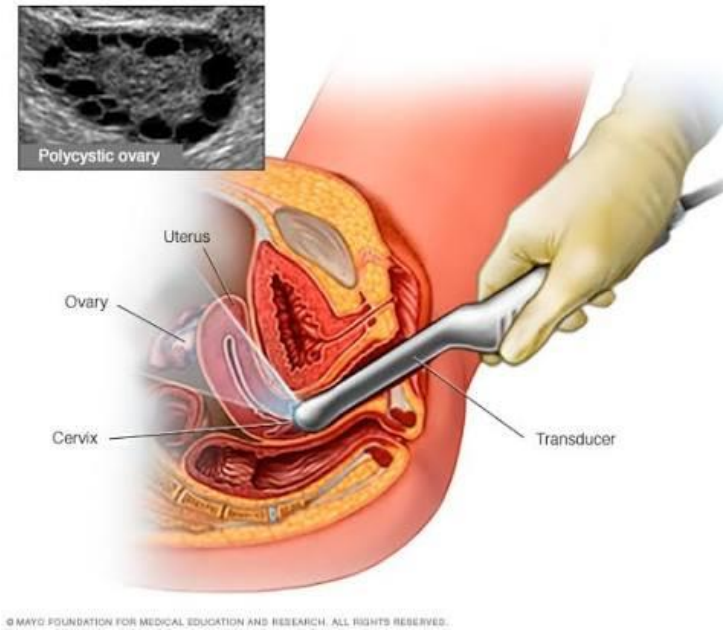
- CBC and testing for gonorrhea and chlamydial infection should be performed if an infectious etiology is suspected.
- Other labs will depend on the H&P findings: potentially U/A, fecal blood testing or other assessment of intestinal involvement, and serum marker testing
- CA125 is most commonly used in conjunction with imaging to assess the likelihood of malignancy

Imaging



- TVS 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
- MRI often is helpful in differentiating the ***origin*** of pelvic masses that are not clearly of ovarian origin, especially leiomyoma
- Best use of CT imaging is to evaluate the abdomen ***when cancer is suspected***

67 y/o with chronic RLQ discomfort. Pelvic exam with mild tenderness to palpation and fullness.

TVS c/w a 4-cm complex ovarian cyst. Report recommends MRI.
What is next BEST step?

1. Expectant management
2. Pelvic MRI
3. It depends
4. Repeat TVS in 6-8 weeks
5. Diagnostic laparoscopy

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CLINICAL OBSTETRICS AND GYNECOLOGY
Volume 58, Number 1, 53–65

Adnexal Mass in the Postmenopausal Patient

JOSE A. RAUH-HAIN, MD,* ALEXANDER MELAMED, MD,*† AMA BUSKWOFIE, MD,*† and JOHN O. SCHORGE, MD*

**Division of Gynecologic Oncology, Vincent Obstetrics and Gynecology, Massachusetts General Hospital; and † Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts*

Abstract: The adnexal mass in a postmenopausal patient poses an important diagnostic and management dilemma for primary care providers and gynecologists. Postmenopausal women are at a significantly increased risk of gynecologic malig-

Key words: adnexal mass, postmenopausal, ovarian cancer

Introduction

The adnexal mass in a postmenopausal

- Women with a complex ovarian tumor <5-cm in diameter and a normal serum CA-125 should undergo repeat TVS + CA-125, in 4 weeks.
- If the tumor is increasing in volume or complexity, or if the CA125 is rising, the tumor should be removed surgically.
- Any postmenopausal woman with a complex ovarian tumor and an elevated serum or rising CA-125 should undergo immediate surgery.

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KEEP
REFER

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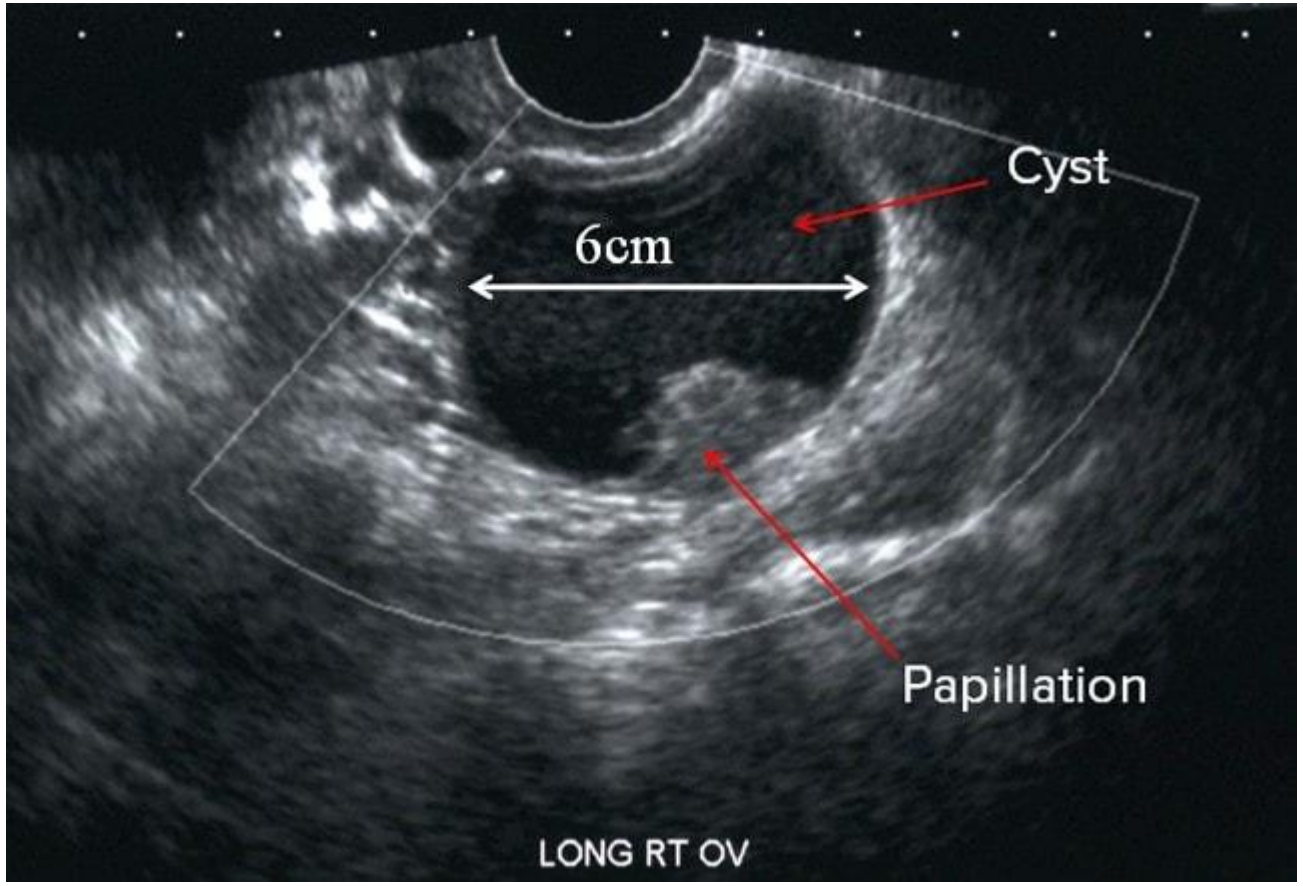

Concerning findings

- Solid component
- Excrescences
- Ascites
- Increased vascularity
- Size >10-cm
- Mural nodules
- Papillations

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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,

Committee on Practice Bulletins—Gynecology. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology in collaboration with Ramez Eskander, MD; Michael Berman, MD; and Lisa Keder, MD, MPH.

- ***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:

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

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- 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

Table 1. SGO and ACOG Referral Guidelines for a Newly Diagnosed Pelvic Mass

Age Group
Premenopausal (< 50 years old)
CA-125 > 200 U/mL
Ascites
Evidence of abdominal or distant metastasis (by exam or imaging study)
Family history of breast or ovarian cancer (in a first-degree relative)
Postmenopausal (> 50 years old)
CA-125 > 35 U/mL
Ascites
Nodular or fixed pelvic masses
Evidence of abdominal or distant metastasis
Family history of breast or ovarian cancer (in a first-degree relative)

Abbreviations: SGO, Society of Gynecologic Oncology; ACOG, American College of Obstetricians and Gynecologists.

67 y/o with chronic RLQ discomfort. Pelvic exam with mild tenderness to palpation and fullness.

TVS c/w a 4-cm complex ovarian cyst. ***CA125 = 38***
What is next BEST step?

1. Get more serum markers
2. Get that pelvic MRI
3. Refer to GYN Oncology
4. Obtain CT CAP due to risk malignancy
5. Take her for planned RSO

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The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 174, NOVEMBER 2016 *(Replaces Practice Bulletin Number 83, July 2007)*

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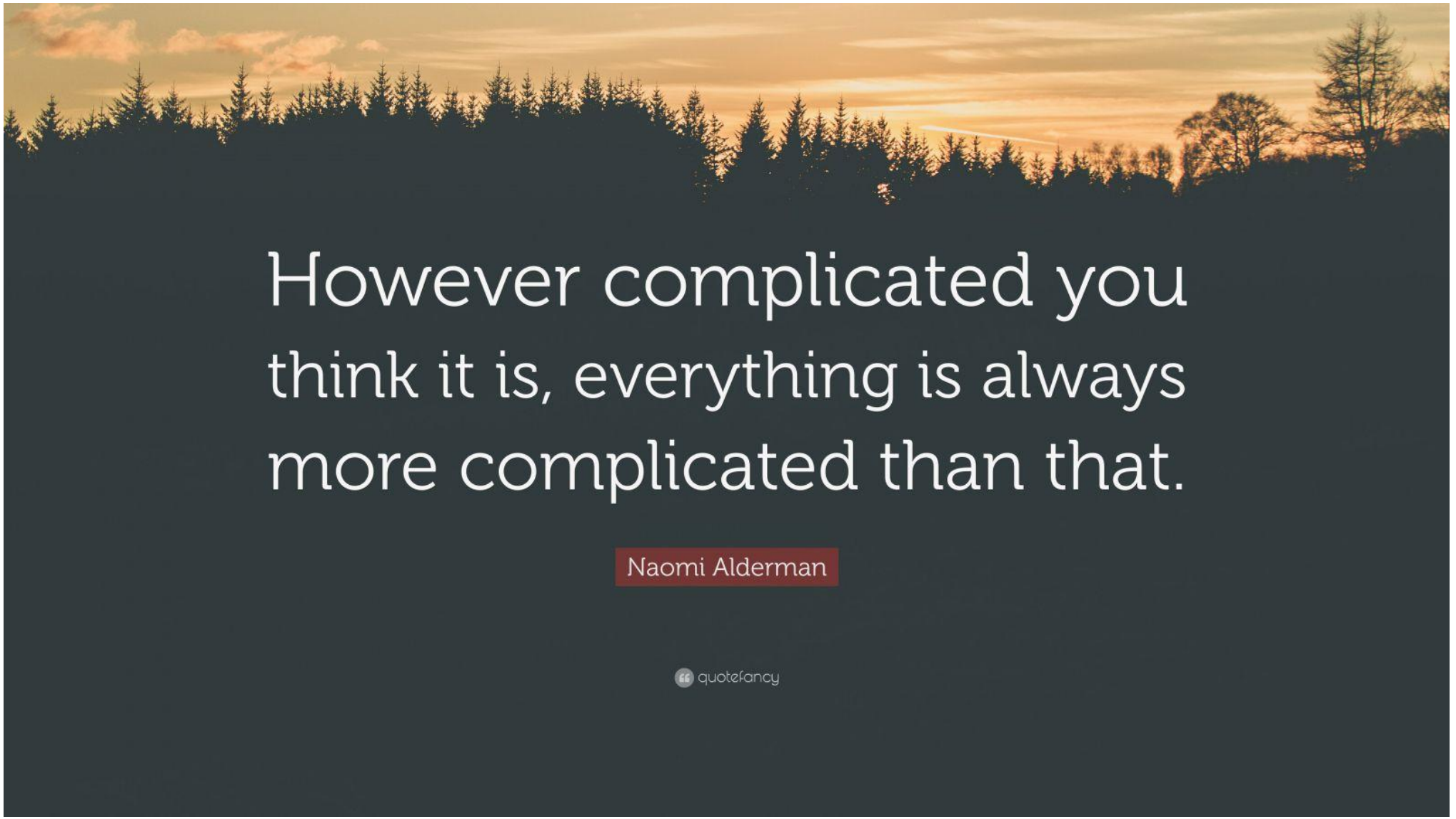
- ***Which patients may benefit from referral to a gynecologic oncologist?***

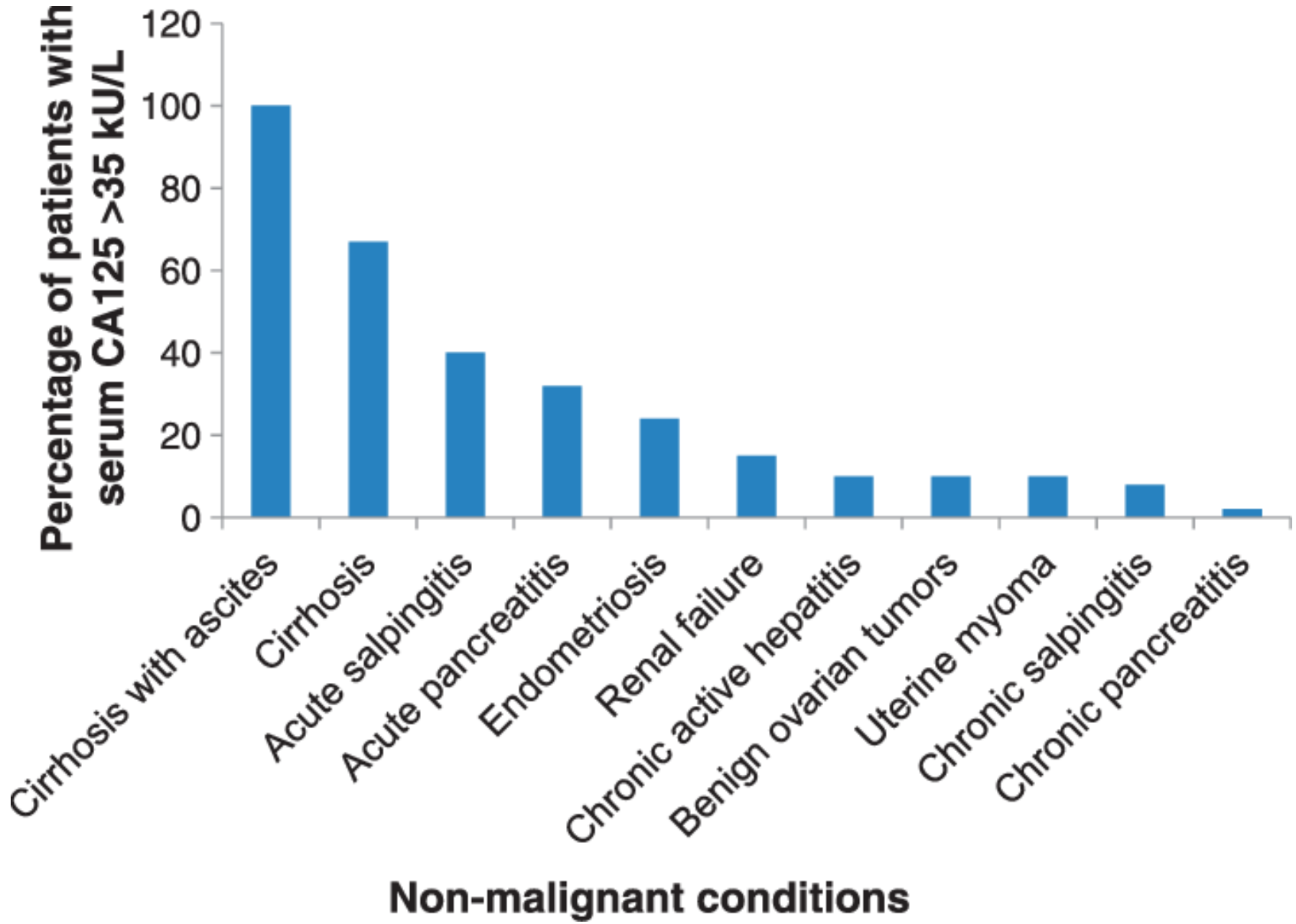
Consultation with or referral to a gynecologic oncologist is recommended for women with an adnexal mass who meet one or more of the following criteria:

- 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

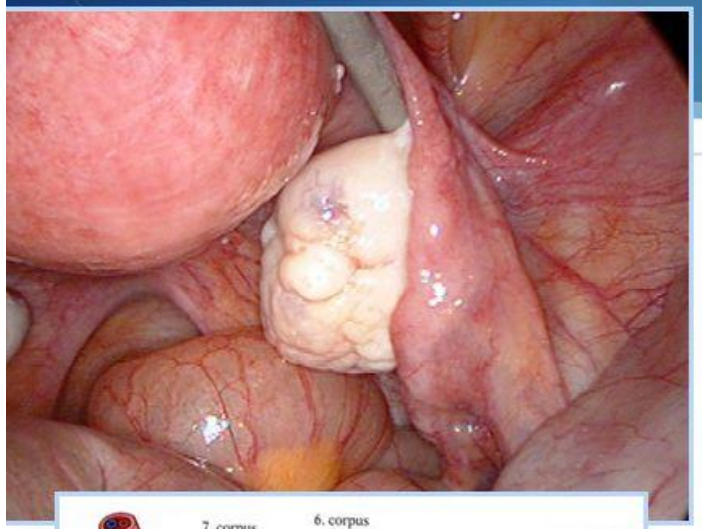
Educational objectives

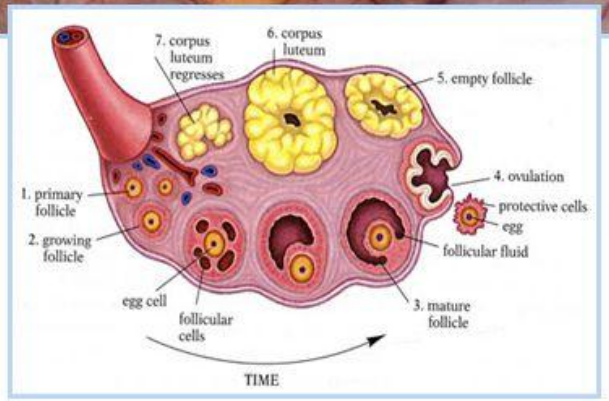
1. Learn which adnexal masses can be safely observed and which require some form of intervention.
2. Better understand the appropriate workup: exam, labs, imaging depending on the patient's clinical circumstances.
3. Become familiar with the ACOG/SGO criteria for what constitutes sufficient risk to refer to GYN Oncology.
4. Review the many different options for preop testing such as OVA1, ROMA, RMI, other markers and their utility.


However complicated you think it is, everything is always more complicated than that.
Naomi Alderman
quotefancy


Percentage of patients with serum CA125 >35 kU/L
120
100
80
60
40
20
0
Cirrhosis with ascites
Cirrhosis
Acute salpingitis
Acute pancreatitis
Endometriosis
Renal failure
Chronic active hepatitis
Benign ovarian tumors
Uterine myoma
Chronic salpingitis
Chronic pancreatitis
Non-malignant conditions

Types of Ovarian Cancer





1. Epithelial Ovarian Cancer (90%)
   - Serous/Papillary serous (80%)
   - Mucinous (10%)
   - Endometrioid (10%)
   - Clear Cell
   - Brenner Tumors
   - *Borderline Tumors*

CA125, HE4, ROMA, RMI
OVA1, CEA, CA19-9

2. Germ Cell Tumors
   - Dysgerminoma
   - Yolk Sac Tumors/Endodermal sinus tumor
   - Embryonal Carcinoma
   - Choriocarcinoma
   - Teratomas

LDH, AFP, hCG, CA125

3. Sex-cord Stromal Tumors
   - Granulosa Cell Tumors
   - Fibrosarcoma
   - Sertoli-Leydig Tumors

Inhibin A&B, testosterone

HE4 (Human Epididymal Protein 4)

- Initially discovered to be over-expressed in epididymal tissue and later in ovarian cancer tissue.
- Tumour expression is histologic dependent.
  - Most Serous and Endometrioid tutors
  - 50% of Clear Cell Tumours
  - 0 % of Mucinous tumours.

Snapshots of Clinical Evidence:HE4+CA125

Gynecol Oncol. 2009 January ; 112(1): 40–46. doi:10.1016/j.ygyno.2008.08.031.

A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass

Richard G. Moore[a], D. Scott McMeekin[b], Amy K. Brown[c], Paul DiSilvestro[a], M. Craig Miller[d], W. Jeffrey Allard[d], Walter Gajewski[e], Robert Kurman[f], Robert C. Bast Jr[g], and Steven J. Skates[h]

Moore et al. examined a panel of biomarkers and found the dual marker combination of HE4 and CA125 produced the highest sensitivity of the various tumor marker combinations and increased the sensitivity of CA125 alone(11). Maggino et al. examined the sensitivity and

Conclusion—An algorithm utilizing HE4 and CA125 successfully classified patients into high and low risk groups with 93.8% of EOC correctly classified as high risk. This model can be used to effectively triage patients to centers of excellence.

Moore et al; 2009

Thyrocare

Tests you can trust

ROMA (RISK OF OVARIAN MALIGNANCY)

4 TESTS

Only @

~~2838~~

₹2399

- ROMA - Premenopausal
- ROMA - Postmenopausal
- Human Epididymis Protein 4
- CA-125

BOOK NOW

8595219293

How does ROMA work?

Under the ROMA stratification, 3 patient variables are used:

1. HE4 levels
2. CA125 levels
3. Patient's menopausal status

Based on these variables, a numerical score is derived for each individual patient by using an established formula

The score determines the risk of malignancy in an individual patient, classified as either high or low.

How to Calculate ROMA™

For premenopausal woman:
Predictive Index (PI) = -12.0 + 2.38*LN[HE4] + 0.0626*LN[CA 125]

For postmenopausal woman:
Predictive Index (PI) = -8.09 + 1.04*LN[HE4] + 0.732*LN[CA 125]

ROMA = exp(PI) / [1/exp(PI)]

LN - Natural Log
exp – Exponential function

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exp – Exponential function

Interpretation (in the current set-up):

- **Pre-menopausal : 11.4 %**
  - < 11.4 % : Low risk of finding epithelial ovarian cancer
  - ≥ 11.4 % : High risk of finding epithelial ovarian cancer
- **Post-menopausal : 29.9 %**
  - < 29.9 % : Low risk of finding epithelial ovarian cancer
  - ≥ 29.9 % : High risk of finding epithelial ovarian cancer

Risk of Malignancy Index (RMI) for Ovarian Cancer

Predicts risk that an adnexal mass is malignant.

Pearls/Pitfalls

Ultrasound features

Multiloculated cysts	No	Yes
Solid areas	No	Yes
Bilateral lesions	No	Yes
Ascites	No	Yes
Intra-abdominal metastases	No	Yes

Other features

Ultrasound features

Multiloculated cysts	No	**Yes**
Solid areas	**No**	Yes
Bilateral lesions	**No**	Yes
Ascites	**No**	Yes
Intra-abdominal metastases	**No**	Yes

Other features

Menopausal status Postmenopausal status = >1 year of amenorrhea or age ≥50 years if patient is status post hysterectomy	Premenopausal or perimenopausal	**Postmenopausal**
Serum CA-125, U/mL	38 U/mL	

114 points

RMI

Low risk of malignancy

Copy Results | Next Steps »

- TVS is the 1st-line method for characterizing adnexal masses. If performed by an expert, subjective assessment of the images is the ***best*** method for distinguishing benign from malignant masses.

- For less experienced ultrasound examiners, there are other methods. RMI is a scoring system using clinical and TVS information that can be used to estimate the likelihood of an ovarian mass being malignant.

- In Europe, RMI is widely used to triage women with an adnexal mass for referral to an oncological center

Ova1 plus®

Planned for Surgical Management

- For adnexal masses that are planned for surgery
- Ova1® has a greater than 96% sensitivity with clinical assessment[2]
- Biomarkers (including CA-125), menopausal status, and ultrasound for a personalized risk score

Ova1Plus is a reflex process: Ova1® is performed3 first. If an intermediate risk is detected, Overa® is automatically performed.

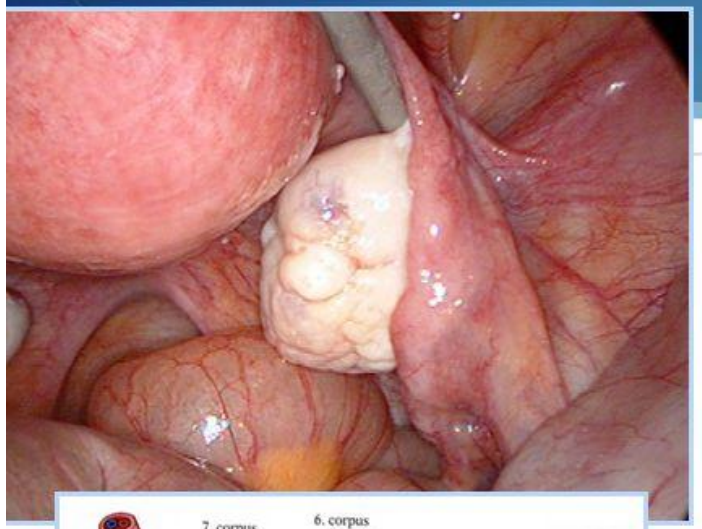
The OVA1 Test

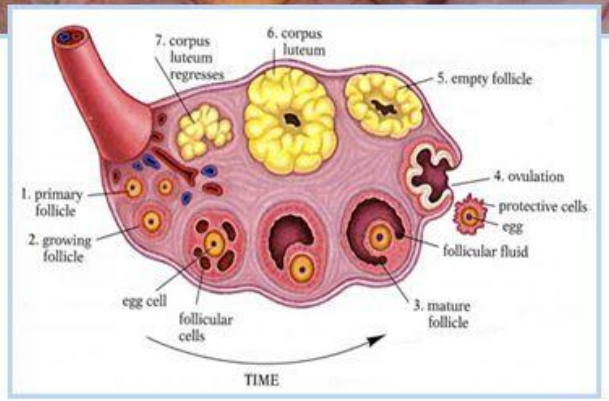
- Biomarker panel
  - CA125, transthyretin (prealbumin), apolipoprotein A1 beta 2 microglobulin, transferrin
- OvaCalc software algorithm
- OVA1 risk index, range 0-10

	Premenopausal	Postmenopausal
Low Risk	< 5.0	< 4.4
High Risk	≥ 5.0	≥ 4.4

TABLE 2	Comparison of OVA1 and Overa
OVA1	**Overa**
Apolipoprotein A-1	Apolipoprotein A-1
Transthyretin	Human epididymis protein 4 (HE4)
Beta-2-microglob-ulin	Follicle-stimulating hormone (FSH)
Transferrin	Transferrin
CA125	CA125

Types of Ovarian Cancer





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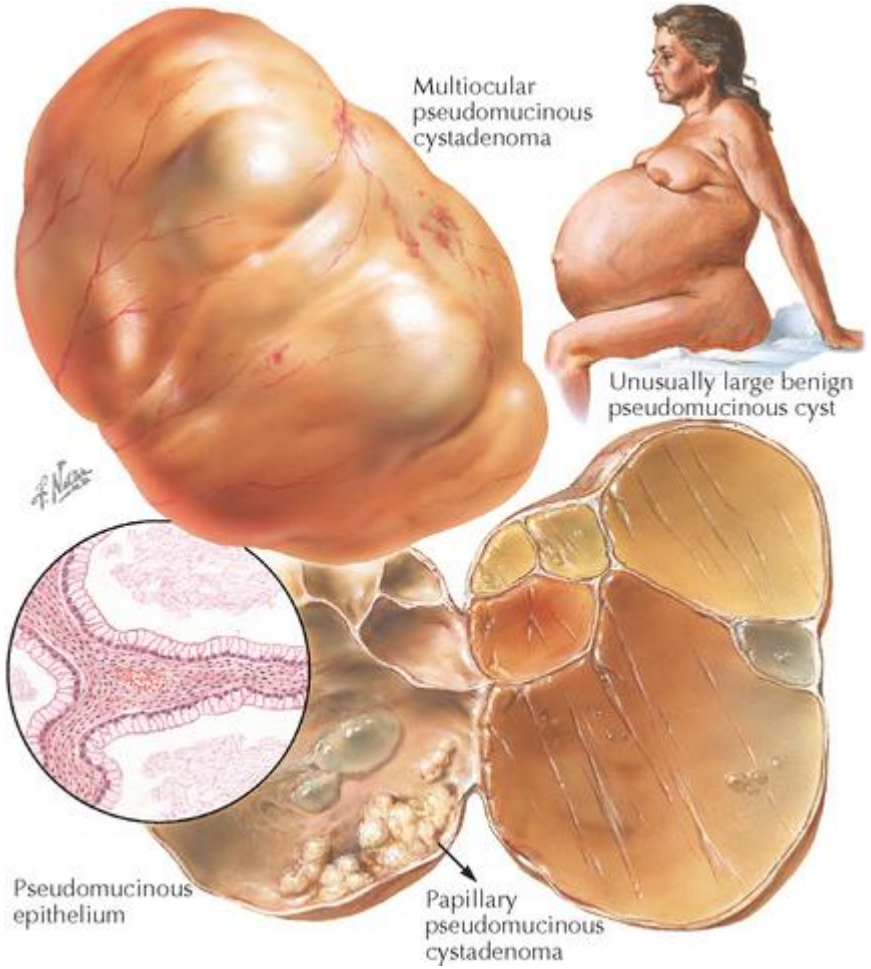

Mucinous tumors are big!!!

- Mass >10-cm
- CEA
- CA19-9

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GYNECOLOGY

External validation of ultrasound-based models for differentiating between benign and malignant adnexal masses: a nationwide prospective multicenter study (IOTA phase 6)

Francesca Moro, PhD; Marina Momi, MD; Ashleigh Ledger, MD; Lasai Barreñada, MD; Jolien Ceusters, PhD; Davide Sturla, MD; Elisa Mor, MD; Letizia Fornari, MD; Floriana Mascilini, MD; Francesca Ciccarone, MD; Federica Pozzati, MD; Wouter Froyman, PhD; Ben Van Calster, PhD; Tom Bourne, PhD; Dirk Timmerman, PhD; Anna Fagotti, PhD; Lil Valentin, PhD; Antonia Carla Testa, PhD; IOTA 6 Collaborators*

BACKGROUND: The diagnostic performance of the IOTA methods, the O-RADS lexicon, and the RMI has been validated in prospective and retrospective studies, but most validation studies tested the performance in the hands of experienced ultrasound examiners.

OBJECTIVE: To prospectively validate the performance of the Risk of Malignancy Index, the International Ovarian Tumor Analysis Simple Rules Risk Model, the International Ovarian Tumor Analysis Assessment of Different NEoplasias in the adneXa model, and the International Ovarian Tumor Analysis 2-step strategy across different types of ultrasound centers in Italy. A retrospective post hoc analysis estimates malignancy prevalence in Ovarian-Adnexal Reporting and Data System risk groups when using the 2-step strategy or the Ovarian-Adnexal Reporting and Data System lexicon.

STUDY DESIGN: ...including regional ref...

METHODS: Conse...

For Risk of Malignancy Index, the area under the receiver operating characteristic curve was 0.85 (95% confidence interval, 0.81 to 0.87), whereas for all International Ovarian Tumor Analysis models (Simple Rules Risk Model, Assessment of Different NEoplasias in the adneXa with and without CA125, and 2-step strategy with and without CA125), the area under the receiver operating characteristic curves ranged from 0.91 (95% confidence interval, 0.88–0.93) to 0.92 (95% confidence interval, 0.89–0.94). All International Ovarian Tumor Analysis models demonstrated a higher net benefit than Risk of Malignancy Index across risk thresholds (exchange rates) from 1% to 50%. All International Ovarian Tumor Analysis models slightly underestimated the risk of malignancy, but Simple Rules Risk Model showed the least degree of underestimation.

...responding 95% confidence ...and Data System risk cate- ...rategy and Ovarian-Adnexal

4 mathematical models:

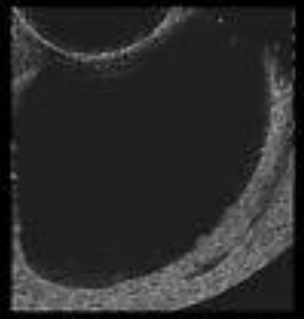
- LR Model 1
- LR Model 2
- SRRisk
- ADNEX

DECEMBER 2025 AJOG

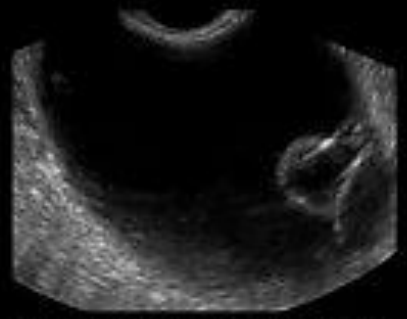
a

The IOTA simple rules

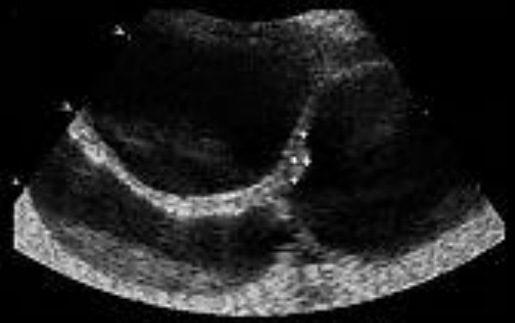
Benign ultrasound features



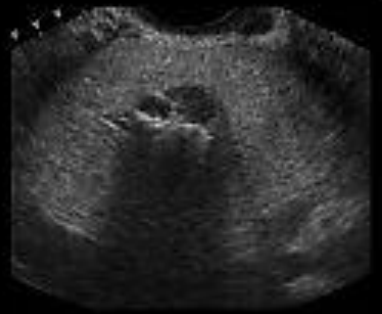
Unilocular cyst



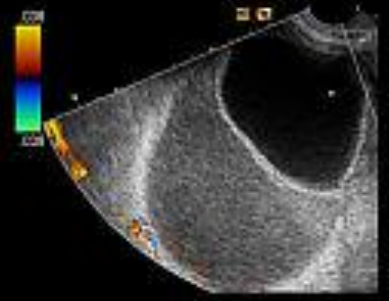
Smooth multilocular cyst <100 mm



Largest solid component <7 mm

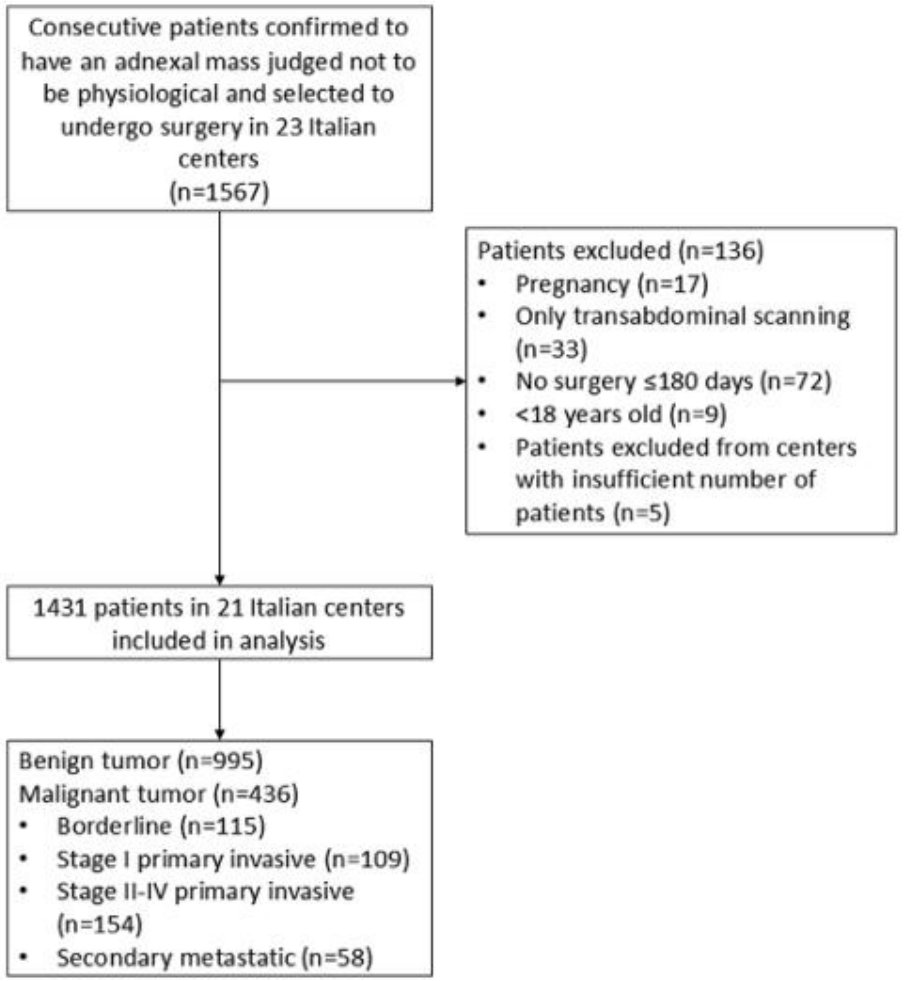


Shadows



No detectable flow (Color score = 1)

FIGURE 1
Flowchart of the patients included for the analysis



Assessment of Different NEoplasias in the adneXa (ADNEX) is the most extensively validated model.

ADNEX is a multinomial logistic regression model that incorporates 3 clinical and 6 ultrasound variables to calculate the probability of 5 types of tumor

CONCLUSION: RMI had lower ability than the IOTA models to distinguish between benign and malignant adnexal tumors in patients examined by either expert or nonexpert ultrasound operators in Italy

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RESEARCH ARTICLE

MEDICAL PHYSICS

Hybrid artificial intelligence echogenic components-based diagnosis of adnexal masses on ultrasound

Roni Yoeli-Bik[1] | **Heather M. Whitney**[2] | **Hui Li**[2] | **Agnes Bilecz**[1] | **Jacques S. Abramowicz**[1] | **Li Lan**[2] | **Ryan E. Longman**[1] | **Maryellen L. Giger**[2] | **Ernst Lengyel**[1]

[1]Department of Obstetrics and Gynecology, The University of Chicago, Chicago, Illinois, USA

[2]Department of Radiology, The University of Chicago, Chicago, Illinois, USA

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Email: hwhitney@uchicago.edu

Roni Yoeli-Bik, Heather M. Whitney are co-first authors.

Maryellen L. Giger, Ernst Lengyel are co-senior authors.

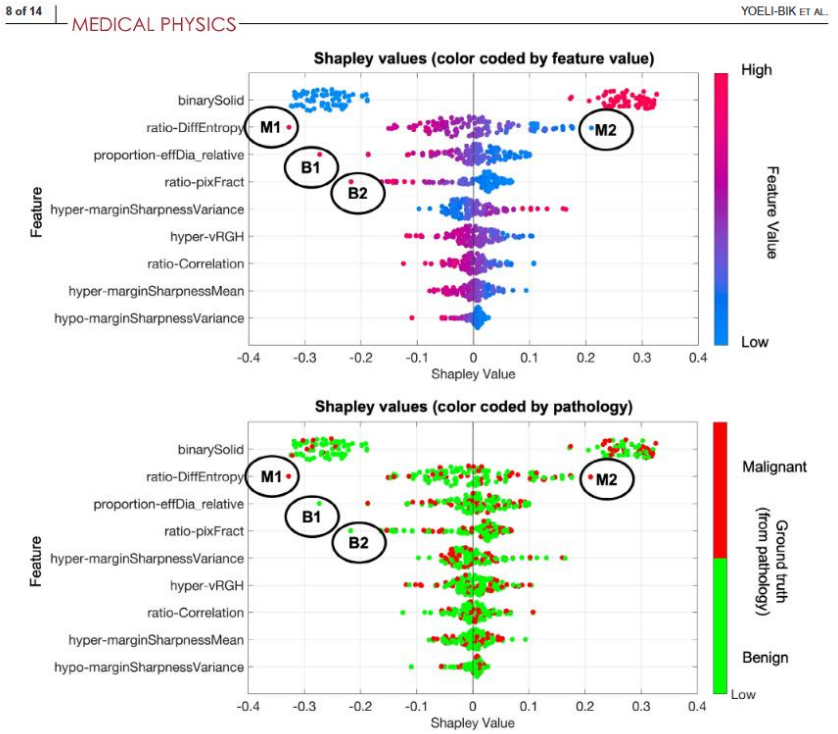
Abstract

Background: Adnexal masses are heterogeneous and have varied sonographic presentations, making them difficult to diagnose correctly.

Purpose: Our study aimed to develop an innovative hybrid artificial intelligence/computer-aided diagnosis (AI/CADx)-based pipeline to distinguish between benign and malignant adnexal masses on ultrasound imaging based upon automatic segmentation and echogenic-based classification.

Methods: The retrospective study was conducted on a consecutive dataset of patients with an adnexal mass. There was one image per mass. Mass borders were segmented from the background via a supervised U-net algorithm. Masses were spatially subdivided automatically into their hypo- and hyperechogenic components by a physics-driven unsupervised clustering algorithm. The dataset was separated by patient into a training/validation set (95 masses; 70%) and an independent held-out test set (41 masses; 30%). Eight component-based radiomic features plus a binary measure of the presence or absence of solid components were used to train a linear discriminant analysis classifier to distinguish between malignant and benign masses. Classification performance was evaluated using the area under the receiver operating characteristic curve (AUC), along with sensitivity, specificity, negative predictive value, positive predictive value, and accuracy at target 95% sensitivity.

Results: The cohort included 133 patients with 136 adnexal masses. In distinguishing between malignant and benign masses, the pipeline achieved an



Occam's Razor: No more things should be presumed to exist than are absolutely necessary, i.e., the fewer assumptions an explanation of a phenomenon depends on, the better the explanation.

(William of Occam)

izquotes.com

THE KISS PRINCIPLE

KEEP IT SIMPLE, STUPID

Table 1. SGO and ACOG Referral Guidelines for a Newly Diagnosed Pelvic Mass

Age Group
Premenopausal (< 50 years old)
CA-125 > 200 U/mL
Ascites
Evidence of abdominal or distant metastasis (by exam or imaging study)
Family history of breast or ovarian cancer (in a first-degree relative)
Postmenopausal (> 50 years old)
CA-125 > 35 U/mL
Ascites
Nodular or fixed pelvic masses
Evidence of abdominal or distant metastasis
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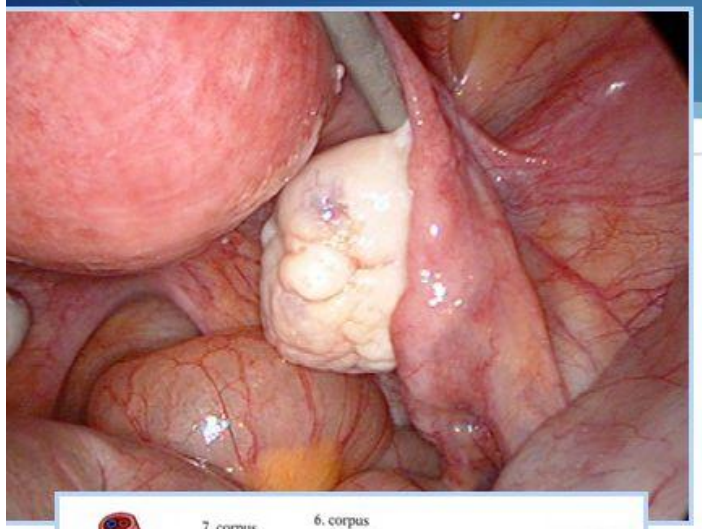
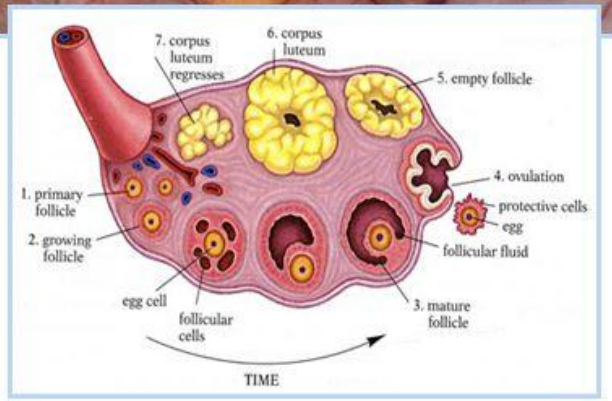
Abbreviations: SGO, Society of Gynecologic Oncology; ACOG, American College of Obstetricians and Gynecologists.

Types of Ovarian Cancer





1. Epithelial Ovarian Cancer (90%)
   - Serous/Papillary serous (80%)
   - Mucinous (10%)
   - Endometrioid (10%)
   - Clear Cell
   - Brenner Tumors
   - *Borderline Tumors*

2. Germ Cell Tumors
   - Dysgerminoma
   - Yolk Sac Tumors/Endodermal sinus tumor
   - Embryonal Carcinoma
   - Choriocarcinoma
   - Teratomas

3. Sex-cord Stromal Tumors
   - Granulosa Cell Tumors
   - Fibrosarcoma
   - Sertoli-Leydig Tumors

CA125, CEA, CA19-9
****<u>***BE VERY WARY***</u>**
<u>*OF HE4, ROMA, RMI, OVA1***</u>****

LDH, AFP, hCG, CA125
****<u>***TEENAGERS/EARLY 20S ONLY***</u>****

Inhibin A&B, testosterone
****<u>***NEVER GET THESE***</u>****

- Know the quality of your ultrasound unit
- Radiology will always recommend MRI
- Stay adherent to ACOG guidelines
- Know when to get markers & which ones
- ROMA, RMI, OVA1, ADNEX are no substitute for clinical judgment

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