EVALUATION & MANAGEMENT OF ADNEXAL MASSES

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10/23/19 Grand Rounds
Outline

1) Differential Diagnosis

2) Ovarian Neoplasms

3) Ultrasound Characteristics

4) Cases and Questions
Introduction

- 4% of women will be hospitalized due to ovarian cyst by age 65
- 6-7% of 20-40 year old women will have an incidental adnexal mass located on ultrasound
- 5-10% lifetime risk to undergo surgery for suspected ovarian neoplasm
- 200,000 women undergo surgery per year for pelvic mass, but only 21,000 confirm malignancy
- Surgical exploration of benign lesions is not without potential consequences, with reported complication rates ranging from 2-15%
- Diagnosis is often difficult as definitive diagnosis requires surgical evaluation
DIFFERENTIAL DIAGNOSIS

GYNECOLOGIC
- Benign
  - Functional or paratubal cyst
  - Fibroma
  - Endometrioma
  - Tuboovarian abscess
  - Ectopic pregnancy
  - Hydrosalpinx
  - Mature teratoma
  - Serous cystadenoma
  - Mucinous cystadenoma
- Malignant
  - Germ cell tumor
  - Sex-cord stromal tumor
  - Epithelial carcinoma

NONGYNECOLOGIC
- Benign
  - Peritoneal pseudocyst
  - Diverticular abscess
  - Appendiceal abscess
  - Mucocele
  - Nerve sheath tumors
  - Ureteral diverticulum
  - Pelvic kidney
  - Bladder diverticulum
- Malignant
  - GI cancers
  - Retroperitoneal sarcomas
  - Metastases
CASE #1

- Patient presents to the ED with unilateral right pelvic pain that was abrupt in onset. Accompanied nausea and vomiting are present.
- Vital Signs Stable except tachycardia
- Right lower quadrant tenderness

- Additional Information?
CASE #1

- Patient presents to the ED with unilateral right pelvic pain that was abrupt in onset. Accompanied nausea and vomiting are present.
- Vital Signs Stable except tachycardia
- Right lower quadrant tenderness

- Additional Information?
- Labs
  - hCG negative
  - WBC 12
  - Hgb 13.4
CASE #1

- Imaging
CASE #1

- Imaging

- Whirlpool sign
- Absent or reduced intra-ovarian venous flow
- Multiple small peripheral follicles
- Ovarian enlargement compared to contralateral ovary
CASE #1

- **Ultrasound**

- posterior enhancement, low level echogenity of part of the content, focal areas of high echogenicity, some of which also cause shadowing
OVARIAN TORSION

- Accounts for 3% of gynecologic emergencies
- Diagnosed between age 20-39 in 70% of cases
- Most likely located on right side
- Risk factors:
  - ovarian enlargement greater than 6cm
  - increased length of ovarian ligaments
  - Pregnancy
  - Fertility treatment

- Sensitivity of ultrasound for diagnosis of ovarian torsion ranges from 46-75%
- Treatment:
  - Surgical management and detorsion
  - May require oophorectomy if necrosis has developed
TERATOMA

- Most common type of germ cell tumor
- Mature teratomas
  - most common ovarian tumor in second and third decades
  - ectoderm, mesoderm, endoderm
  - Rokitansky Protuberence
  - Chemical peritonitis if rupture
  - Bilateral 10%
  - Malignant transformation in less than 1%
    - most common squamous cell component
- Monodermal teratomas
  - Struma Ovarii
    - 2.7% of ovarian teratomas
    - predominantly thyroid tissue
    - Carcinoid
- Immature teratomas
  - Less than 1% of ovarian teratomas
  - Most common in first two decades
  - Contain three germ cell layers
  - Immature tissue, most often with neural differentiation
OVARIAN MASS

- **Surface epithelium-stroma**
  - Serous
  - Mucinous
  - Endometrioid
  - Clear cell
  - Transitional cell

- **Sex cord-stroma**
  - Granulosa cell
  - Thecoma
  - Fibroma
  - Sertoli cell
  - Sertoli-Leydig
  - Steroid

- **Germ cells**
  - Dysgerminoma
  - Yolk sac
  - Embryonal carcinoma
  - Choriocarcinoma
  - Teratoma
GERM CELL TUMORS

- Derived from primordial germ cell of ovary
- Approximately 20-25% of ovarian neoplasms
- Approximately 5% of malignant ovarian neoplasms
- Primarily in **young women between 10-30 years of age**
  - represent 70% of neoplasms in this age group

- **Diagnosis**
  - Teratomas
  - Dysgerminomas
    - LDH
  - Yolk sac tumors
    - AFP
  - Mixed
DYSGERMINOMA

- 2% of all ovarian tumors
- 32% of all malignant germ cell tumors
- Primarily in adolescents and young adults, but can present at any age
- Fast growth
- “Fried egg” appearance on pathology

- AIS, Swyer syndrome and Mosaic Turner may develop
  - Prophylactic removal of streak gonads is recommended
YOLK SAC TUMOR

- 14-20% of germ cell tumors
- Average age of diagnosis: 23
- Schiller-Duval bodies
- AFP elevation
OVARIAN CHORIOCARCINOMA

- Very rare compared to gestational choriocarcinoma
- Estimated incidence of primary ovarian choriocarcinoma is 1 in 369,000,000
- Histologically identical to gestational choriocarcinoma
- Early hematogenous spread
- Relatively chemoresistant
- hCG
SEX CORD STROMAL TUMORS

- Arise from cells surrounding oocytes
- May produce hormones
- Incidence is 0.2 per 100,000
- Comprises 1.2% of ovarian malignancies, but majority are benign
- Average age at diagnosis: 50

Diagnosis

- Sertoli-Leydig Tumors
  - Testosterone/Estrogen
- Granulosa Cell Tumors
  - Inhibin
- Fibromas
- Fibrothecoma
SERTOLI - LEYDIG NEOPLASM

- Rare (0.5% of ovarian neoplasms)
- Most common in second and third decade of life
- Produce androgens
  - results in virilization
  - Follow testosterone for recurrence
  - If total testosterone >150ng/dL on clinical evaluation for virilization, ultrasound is indicated
GRANULOSA-THECA CELL TUMORS

- Two subtypes: Adult (95%) and juvenile
- **Call Exner bodies and Coffee Bean Nuclei**
- Estrogen excess
  - Theca cells produce androstenedione and granulosa cells convert this to estradiol
  - May present with menorrhagia, postmenopausal bleeding or precocious puberty
  - EMB will detect hyperplasia in 25-50% and carcinoma in 5-10%
- Most common type of sex cord stromal malignancy (2-5% of all malignancies)
- Tumor markers: **Inhibin A/B**, estradiol, AMH
FIBROMA

- Most common sex cord stromal neoplasm
- **Meig’s syndrome**
  - Ovarian fibroma and ascites or hydrothorax
  - **Ascites occurs in 10-15% of these neoplasms**
- May also contain theca cells termed fibrothecoma
  - If contains theca cells, may produce estrogen
EPITHELIAL CELL TUMORS

- Most common type of neoplasm
- Benign
  - Serous cystadenoma
  - Mucinous cyst adenoma are more likely to be larger and multiloculated
  - Thin walls
- Borderline
- Malignant

- Diagnosis
  - Serous
  - Mucinous
  - Endometrioid
  - Clear Cell
  - Brenner
BENIGN ADNEXAL MASSES

- Simple cysts up to 10cm may be safely monitored using repeat imaging without surgical intervention, even in postmenopausal patients.
- Endometriomas, mature teratomas and hydrosalpinx may also be managed expectantly.
- Repeat ultrasound is recommended when diagnosis is uncertain or cancer remains in differential.
  - Ideal interval and duration for follow up has yet to be defined.
  - IOTA: Phase 5 currently ongoing for future recommendations.
- If symptomatic, may consider laparoscopic cystectomy.
IOTA

- 2008 International Ovarian Tumor Analysis group described *Simple Rules*
  - 5 US features indicative of a benign tumor (B-features)
  - 5 US features indicative of a malignant tumor (M-features)

**TABLE 5**
Model coefficients for 11 predictors obtained on development data (n = 2445)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-1.10</td>
<td>0.26</td>
</tr>
<tr>
<td>B1 (unilocular cyst)</td>
<td>-3.10</td>
<td>0.34</td>
</tr>
<tr>
<td>B2 (solid components present, but &lt;7 mm)</td>
<td>-1.55</td>
<td>0.59</td>
</tr>
<tr>
<td>B3 (acoustic shadows)</td>
<td>-1.58</td>
<td>0.27</td>
</tr>
<tr>
<td>B4 (smooth multilocular tumor with largest diameter &lt;100 mm)</td>
<td>-3.59</td>
<td>0.60</td>
</tr>
<tr>
<td>B5 (no blood flow; color score 1)</td>
<td>-1.96</td>
<td>0.24</td>
</tr>
<tr>
<td>M1 (irregular solid tumor)</td>
<td>2.38</td>
<td>0.39</td>
</tr>
<tr>
<td>M2 (ascites)</td>
<td>2.87</td>
<td>0.29</td>
</tr>
<tr>
<td>M3 (at least 4 papillary structures)</td>
<td>1.72</td>
<td>0.28</td>
</tr>
<tr>
<td>M4 (irregular multilocular-solid tumor with largest diameter &gt;100 mm)</td>
<td>1.12</td>
<td>0.23</td>
</tr>
<tr>
<td>M5 (very strong flow; color score 4)</td>
<td>1.53</td>
<td>0.24</td>
</tr>
<tr>
<td>Oncology center</td>
<td>0.95</td>
<td>0.31</td>
</tr>
</tbody>
</table>

IOTA

- 2008 International Ovarian Tumor Analysis group described *Simple Rules*
  - 5 US features indicative of a benign tumor (B-features)
  
  - B1: Unilocular Cyst
  - B2: Solid components present but less than 7mm
  - B3: Acoustic Shadows
  - B4: Smooth multilocular tumor with largest diameter <100mm
  - B5: No color flow
IOTA

- 2008 International Ovarian Tumor Analysis group described *Simple Rules*
  - 5 US features indicative of a malignant tumor (M-features)

  - M1: Irregular Solid Tumor
  - M2: Ascites
  - M3: At least 4 papillary structures
  - M4: Irregular multilocular-solid tumor with largest diameter >100mm
  - M5: Very Strong Flow
BENIGN VS. MALIGNANT
BENIGN VS. MALIGNANT

- Almost Certainly Benign
- Hemorrhagic Cyst
- Fine Reticular Pattern composed of interdigitating fibrinous strands, which do not traverse the entirety of the cystic lesion
- Peripheral Vascularity, avascular internal contents
BENIGN VS. MALIGNANT
BENIGN VS. MALIGNANT

- Almost Certainly Benign
- Endometrioma
- Commonly multilocular with varying levels of echogenicity
- “Ground Glass”
BENIGN VS. MALIGNANT
BENIGN VS. MALIGNANT

- Almost Certainly Benign
- Dermoid
- Echogenic nodule with posterior acoustic shadowing
- Echogenic lines and dots representing hair in sebum
- “Tip of the iceberg”
- Fluid-fat levels
BENIGN VS. MALIGNANT
BENIGN VS. MALIGNANT

- Suspicious for Malignancy
- Solid vascular component
BENIGN VS. MALIGNANT
BENIGN VS. MALIGNANT

A: Cyst with several smooth thin septations on a background of low-level echoes. When persistent, these likely represent benign serous or mucinous cystadenoma.

B: A large (>10 cm) cystic lesion with multiple septations (>10) of varying thickness, with low-level echoes, is suspicious for malignancy.
MALIGNANCY

- Age is the most important risk factor for ovarian malignancy
- CA 125
  - Antigen derived from both coelomic and mullerian epithelia
  - Expressed by 80% of epithelial ovarian cancers. Unreliable for mucinous, clear cell, and mixed mullerian tumors.
  - Elevated in 90% of advanced-stage ovarian cancer but elevated in only 50% of clinically detectable stage I ovarian cancer
  - Benign elevations include endometriosis, adenomyosis, pelvic inflammatory disease, liver disease, pancreatitis, and diverticulitis
- Multimodal tests
  - RMI
  - ROMA
  - OVA1
RMI/ROMI

- RMI score = ultrasound score x menopausal score x CA125 level in U/mL

Table 2. The risk of malignancy index (RMI) scoring system

<table>
<thead>
<tr>
<th>Ultrasound features</th>
<th>RMI I score</th>
<th>RMI II score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multilocular cyst</td>
<td>0 = no abnormality</td>
<td>1 = no or one abnormality</td>
</tr>
<tr>
<td>Presence of solid areas</td>
<td>1 = one abnormality</td>
<td>4 = two or more abnormalities</td>
</tr>
<tr>
<td>Bilaterality of lesions</td>
<td>3 = two or more abnormalities</td>
<td></td>
</tr>
<tr>
<td>Presence of ascites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of intra-abdominal metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>CA125 level</td>
<td>U/mL</td>
<td>U/mL</td>
</tr>
</tbody>
</table>
ACOG GYN ONC REFERRAL GUIDELINES

Premenopausal

- Elevated CA 125 levels (> 200 U/mL)
- Ascites
- Evidence of abdominal or distant metastasis
- Family history of breast or ovarian cancer (in a first degree relative)

Postmenopausal

- Elevated CA 125 levels (> 35 U/mL)
- Ascites
- Nodular or fixed pelvic mass
- Evidence of abdominal or distant metastasis
- Family history of breast or ovarian cancer (in a first degree relative)
CASE #2

- Patient presents to emergency room with sudden onset of severe focal right lower quadrant pain following sexual intercourse
- Vital Signs
  - Temperature 99.3 F
  - Pulse 87
  - Respirations 16
  - Oxygen 98%
- Additional Information?
CASE #2

- Patient presents to emergency room with sudden onset of severe focal right lower quadrant pain following sexual intercourse
- Vital Signs
  - Temperature 99.3 F
  - Pulse 87
  - Respirations 16
  - Oxygen 98%
- Additional Information?
- Labs
  - Hcg negative
  - Hgb 12.4
  - UA negative
- Cullen’s sign negative
CASE #2

- Patient presents to emergency room with sudden onset of severe focal right lower quadrant pain following sexual intercourse

- Imaging

- 5cm ovarian cyst with a fine reticular pattern and small amount of free fluid
PHYSIOLOGIC CYSTS

• Normal Ovulation
  • Follicle develops to maturity and releases an ovum
  • Followed by formation of corpus luteum
  • Follicular cysts develop when follicle fails to release ovum and continues to grow
  • Corpus luteal cyst occurs when corpus luteum fails to involute
  • Either type may become hemorrhagic

• Management
  • Expectant management / observation
  • Emergent surgical evaluation if torsion occurs or hemoperitoneum with hemodynamic instability
  • May require inpatient observation if no hemodynamic instability, but large amount of pelvic fluid on ultrasound
PHYSIOLOGIC CYSTS

- **Ultrasound characteristics**
- **Follicular Cysts**
  - Simple Cyst
- **Corpus Luteal Cysts**
  - Thickened walls, circumferential color Doppler flow, and small central lucency containing echoes
- **Hemorrhagic Cyst**
  - Fine network of thin linear to curvilinear echoes, sometimes called a fishnet or reticular pattern
CASE #3

- Patient presents to clinic for follow up on chronic pelvic pain, dyspareunia and TVUS with 5cm left ovarian cyst
- Vital Signs Stable
- Bimanual exam with left adnexal mass
ENDOMETRIOMAS

- Characteristics
  - Ground Glass
  - Associated malignancies:
    - Endometrioid
    - Clear Cell
  
- Management
  - Surgical Removal
  - Observation
  - Hemorrhagic Cyst
CASE #4

- Patient present to emergency room with right lower quadrant pain and vaginal bleeding.
- Vital Signs Stable
- Abdominal Exam shows diffuse pelvic tenderness
- Pelvic Exam shows trace blood in vault with no active bleeding
- Additional Information?
CASE #4

- Patient present to emergency room with right lower quadrant pain and vaginal bleeding.
- Vital Signs Stable
- Abdominal Exam shows diffuse pelvic tenderness
- Pelvic Exam shows trace blood in vault with no active bleeding
- Additional Information?
- Labs
  - Hcg 2000
  - Hgb 11.1
  - UA negative
- Ultrasound
  - Adnexal mass with a concentric echogenic rim of tissue surrounding a hypoechoic center. 2.4cm ovarian cyst with thickened walls. No IUP. Trace free fluid.
- Type and Screen
ECTOPIC PREGNANCY

**Management**

- Repeat hcg in 48 hours with rupture precautions
- Emergent surgical evaluation if suspected rupture with hemodynamic instability
- May require inpatient observation if no hemodynamic instability, and unable to confirm ectopic and intense pain

**Ultrasound**

[Image: Ultrasound scan showing Ipsilateral corpus luteum and Tubal ectopic]
QUESTIONS

- An 18 year old woman present to the ED with acute left sided pelvic pain. She denies nausea and vomiting. Her exam shows left adnexal tenderness without cervical motion tenderness. Ultrasonography shows a hyperechoic ovarian cyst with a “lace-like” pattern and posterior acoustic enhancement. What is the most likely diagnosis?
  
  - A. Cystic Teratoma
  - B. Endometrioma
  - C. Functional Ovarian Cyst
  - D. Hemorrhagic Cyst
  - E. Tubo-ovarian abscess
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- A. Cystic Teratoma
- B. Endometrioma
- C. Functional Ovarian Cyst
- **D. Hemorrhagic Cyst**
- E. Tubo-ovarian abscess
QUESTIONS

• A 29 year old woman presents with chronic cycle pelvic pain. She reports that this pain has worsened over the last few cycles. She undergoes transvaginal ultrasound that shows an endometrioma. Which of the following ultrasonographic findings in MOST consistent with this diagnosis?

  • A. Anechoic cyst with a thin, well defined wall
  • B. Cystic mass with irregular walls: thick, irregular septations; and solid echogenic elements
  • C. Heterogeneous ovarian mass with an echogenic mural nodule
  • D. Homogeneous cyst with low level internal echoes
  • E. Hyperechoic “lace-like” cystic mass with posterior acoustic enhancement
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REFERENCES


• Hoffman, M., Hachberg, L et al. (2019). Differential diagnosis of the Adnexal Mass. UpToDate

• Patel, M. et al. (2019) Ultrasound Differentiation of Benign Versus Malignant Adnexal Masses. UpToDate


• TruLearn
QUESTIONS?
QUESTIONS

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- C. Heterogeneous ovarian mass with an echogenic mural nodule
- D. Homogeneous cyst with low level internal echoes
- E. Hyperechoic “lace-like” cystic mass with posterior acoustic enhancement
CA125 PREDICTIVE ABILITY

- Premenopausal women
  - Sensitivity 50-74%
  - Specificity 26-92%
  - PPV 5-64%
- Postmenopausal women
  - Sensitivity 69-87%
  - Specificity 81-100%
  - PPV 73-100%
- Serial assessments increase the sensitivity and preclinical ovarian cancer detection

OVA1

- Biomarkers
  - Upregulated
    - CA125
    - Beta-2-microglobulin
  - Downregulated
    - Transferrin
    - Transthyretin/Prealbumin
    - Apolipoprotein A1
- Algorithm to render a score from 0.0 to 10.0
  - High risk > 5.0 (premenopausal), > 4.4 (postmenopausal)
## OVA1 PREDICTIVE ABILITY

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>OVA1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Clinical assessment</th>
<th>OVA1 + clinical assessment</th>
<th>CA 125-II&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Modified ACOG&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>92.2</td>
<td>74.5</td>
<td>95.3</td>
<td>70.6</td>
<td>80.0</td>
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<tr>
<td>n/N</td>
<td>235/255</td>
<td>190/255</td>
<td>243/255</td>
<td>180/255</td>
<td>204/255</td>
</tr>
<tr>
<td>95% CI</td>
<td>88.2—94.9</td>
<td>68.8—79.5</td>
<td>92.0—97.3</td>
<td>64.7—75.8</td>
<td>74.7—84.4</td>
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<tr>
<td>Specificity</td>
<td>49.4</td>
<td>86.3</td>
<td>44.2</td>
<td>89.6</td>
<td>76.5</td>
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<tr>
<td>n/N</td>
<td>376/761</td>
<td>657/761</td>
<td>336/761</td>
<td>682/761</td>
<td>582/761</td>
</tr>
<tr>
<td>95% CI</td>
<td>45.9—53.0</td>
<td>83.7—88.6</td>
<td>40.7—47.7</td>
<td>87.2—91.6</td>
<td>73.3—79.4</td>
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<tr>
<td>Positive predictive value</td>
<td>37.9</td>
<td>64.6</td>
<td>36.4</td>
<td>69.5</td>
<td>53.3</td>
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<tr>
<td>n/N</td>
<td>235/620</td>
<td>190/294</td>
<td>243/668</td>
<td>180/259</td>
<td>204/383</td>
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<tr>
<td>95% CI</td>
<td>34.2—41.8</td>
<td>59.0—69.9</td>
<td>32.8—40.1</td>
<td>63.6—74.8</td>
<td>48.3—58.2</td>
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<td>Negative predictive value</td>
<td>94.9</td>
<td>91</td>
<td>96.6</td>
<td>90.1</td>
<td>91.9</td>
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<tr>
<td>n/N</td>
<td>376/396</td>
<td>657/722</td>
<td>336/348</td>
<td>682/757</td>
<td>582/633</td>
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<tr>
<td>95% CI</td>
<td>92.3—96.7</td>
<td>88.7—92.9</td>
<td>94.1—96.0</td>
<td>87.8—92.0</td>
<td>89.6—93.8</td>
</tr>
</tbody>
</table>

ACOG: American Congress of Obstetricians and Gynecologists; CI, confidence interval.

<sup>a</sup> Subjects stratified as high risk with OVA1 (Vermillion, Inc., Austin, TX) scores ≥5.0 (premenopausal) or ≥4.4 (postmenopausal).

<sup>b</sup> Subjects stratified as high risk with CA 125-II scores ≥200 U/mL (premenopausal) or ≥35 U/mL (postmenopausal).

<sup>c</sup> De KDing-modified ACOG criteria for consultation with gynecologic oncologist.

OVA1 + IMAGING

ROMA

- Algorithm that combines CA125 and HE4 in premenopausal and postmenopausal women
- Classifies tumors as high or low risk
  - Postmenopausal women
    - Sensitivity 92%
    - Specificity 75%
  - Premenopausal women
    - Sensitivity 76%
    - Specificity 75%
## ROMA PREDICTIVE ABILITY

### Distribution of patients into low risk and high risk groups: Benign vs. EOC and LMP Tumors.

<table>
<thead>
<tr>
<th>Menopausal Status</th>
<th>Disease</th>
<th>Low Risk</th>
<th>High Risk</th>
<th>Total (N)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N</td>
<td>%I</td>
<td>N</td>
<td>%I</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Benign</td>
<td>Cancer</td>
<td>17</td>
<td>6.1</td>
<td>134</td>
<td>60.1</td>
<td>88.7%</td>
<td>74.7%</td>
<td>60.1%</td>
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<tr>
<td></td>
<td>Total</td>
<td>280</td>
<td>100</td>
<td>223</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Benign</td>
<td>151</td>
<td>95.0</td>
<td>51</td>
<td>66.2</td>
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<td></td>
<td>Combined</td>
<td>17</td>
<td>6.1</td>
<td>134</td>
<td>60.1</td>
<td>88.7%</td>
<td>74.7%</td>
<td>60.1%</td>
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<tr>
<td></td>
<td>Total</td>
<td>202</td>
<td></td>
<td>151</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>Cancer</td>
<td>8</td>
<td>5.0</td>
<td>26</td>
<td>33.8</td>
<td>76.5%</td>
<td>74.8%</td>
<td>33.8%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>159</td>
<td>100</td>
<td>77</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Benign</td>
<td>112</td>
<td>92.6</td>
<td>38</td>
<td>26.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Combined</td>
<td>17</td>
<td>6.1</td>
<td>134</td>
<td>60.1</td>
<td>88.7%</td>
<td>74.7%</td>
<td>60.1%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>121</td>
<td>100</td>
<td>146</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Percentage of cases within low risk group and within high risk group.

MORPHOLOGY INDEX FROM THE UNIVERSITY OF KENTUCKY

- Based on 2 categories
  - Ovarian volume: Prolate Ellipsoid Formula (length x width x height x 0.523)
    - Tumor volume > 20mL in premenopausal females and >10mL in postmenopausal females is considered abnormal.
  - Morphological complexity
- A numerical score is assigned for each category of volume (0-5) and morphology (0-5) for a total score of 0 to 10
- Using morphology-index value of greater than or equal to 5 as indicative of malignancy
## MORPHOLOGY INDEX

<table>
<thead>
<tr>
<th>TUMOR VOLUME</th>
<th>TUMOR STRUCTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;10 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Smooth wall, sonolucent</td>
</tr>
<tr>
<td>1</td>
<td>10-50 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Smooth wall, diffuse echogenicity</td>
</tr>
<tr>
<td>2</td>
<td>&gt;50-100 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Wall thickening, &lt; 3mm fine septa</td>
</tr>
<tr>
<td>3</td>
<td>&gt;100-200 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Papillary projection ≥ 3mm</td>
</tr>
<tr>
<td>4</td>
<td>&gt;200-500 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Complex, predominantly solid</td>
</tr>
<tr>
<td>5</td>
<td>&gt;500 cm$^3$</td>
</tr>
<tr>
<td></td>
<td>Complex, solid and cystic areas with extratumoral fluid</td>
</tr>
</tbody>
</table>

### Lerner Criteria

**a simple 4-cm cyst**

<table>
<thead>
<tr>
<th>Risk of Ovarian CA</th>
<th>US Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>cystic, unilocular, size &lt; 5 cm</td>
</tr>
</tbody>
</table>
## Lerner Criteria

A multiloculated 3.5-cm cyst. Color doppler unremarkable.

<table>
<thead>
<tr>
<th>Risk of Ovarian CA</th>
<th>US Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate Risk</td>
<td>cystic, multilocular, complex, thin septations</td>
</tr>
</tbody>
</table>
Lerner Criteria

A complex $12 \times 10$-cm mass with multiple septations with solid elements that had marked vascular flow.

<table>
<thead>
<tr>
<th>Risk of Ovarian CA</th>
<th>US Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk</td>
<td>Solid, nodules, thick septations, size $&gt; 5$ cm</td>
</tr>
</tbody>
</table>
### Table 3. Test Performance in Predicting Ovarian Malignancy*

<table>
<thead>
<tr>
<th>Performance</th>
<th>CA 125† (67 Units/mL) (n=524)</th>
<th>CA 125‡ (200 Units/mL) (n=524)</th>
<th>Multivariate Index Assay (n=524)</th>
<th>Physician Assessment (n=516)</th>
<th>Physician Assessment Plus Multivariate Index Assay (n=516)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>77 (124/161)</td>
<td>69 (111/161)</td>
<td>93 (149/161)</td>
<td>75 (154/161)</td>
<td>96 (154/161)</td>
</tr>
<tr>
<td>95% CI</td>
<td>69.9–82.8</td>
<td>61.4–75.6</td>
<td>87.4–95.7</td>
<td>67.9–81.2</td>
<td>91.3–97.9</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>73 (266/363)</td>
<td>84 (304/363)</td>
<td>43 (156/363)</td>
<td>79 (281/355)</td>
<td>35 (123/355)</td>
</tr>
<tr>
<td>95% CI</td>
<td>77–87</td>
<td>79.6–87.2</td>
<td>38.0–48.1</td>
<td>74.6–83.1</td>
<td>29.9–39.7</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>56 (124/221)</td>
<td>65 (111/170)</td>
<td>42 (149/356)</td>
<td>62 (121/195)</td>
<td>40 (154/386)</td>
</tr>
<tr>
<td>95% CI</td>
<td>49.5–62.5</td>
<td>57.9–72.0</td>
<td>36.8–47.0</td>
<td>55.1–68.6</td>
<td>35.1–44.9</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>88 (266/303)</td>
<td>86 (304/354)</td>
<td>93 (156/168)</td>
<td>88 (281/321)</td>
<td>95 (123/130)</td>
</tr>
<tr>
<td>95% CI</td>
<td>83.6–91.0</td>
<td>81.9–89.1</td>
<td>87.9–95.9</td>
<td>83.5–90.7</td>
<td>89.3–97.4</td>
</tr>
</tbody>
</table>

Cl, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

* Malignancies include epithelial ovarian cancer, other primary ovarian malignancies, borderline ovarian tumors, metastatic malignancy to the ovary, and pelvic malignancies with no ovarian involvement.

† Premenopausal patients more than 67 units/mL; postmenopausal patients more than 35 units/mL.

‡ Premenopausal patients more than 200 units/mL; postmenopausal patients more than 35 units/mL.

### IOTA PREDICTIVE ABILITY

**TABLE 6**
Sensitivity, specificity, likelihood ratios, and predictive values for *Simple Rules* risk estimates (different cutoffs) on validation data (n = 2403)

<table>
<thead>
<tr>
<th>Cutoff for risk of malignancy</th>
<th>Size of high-risk group, n (%)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>LR+</th>
<th>LR−</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>1856 (77.2)</td>
<td>99.7 (97.8–99.9)</td>
<td>33.7 (25.5–43.0)</td>
<td>44.8 (35.4–54.7)</td>
<td>98.9 (97.3–99.5)</td>
<td>1.502</td>
<td>0.010</td>
</tr>
<tr>
<td>3%</td>
<td>1637 (68.1)</td>
<td>98.2 (96.9–98.9)</td>
<td>49.6 (41.0–58.2)</td>
<td>52.0 (43.6–60.2)</td>
<td>98.1 (96.4–99.1)</td>
<td>1.947</td>
<td>0.038</td>
</tr>
<tr>
<td>5%</td>
<td>1500 (62.4)</td>
<td>97.6 (96.0–98.6)</td>
<td>62.5 (52.2–71.1)</td>
<td>59.2 (50.9–67.1)</td>
<td>98.1 (96.2–99.1)</td>
<td>2.601</td>
<td>0.039</td>
</tr>
<tr>
<td>10%</td>
<td>1454 (60.5)</td>
<td>97.5 (95.8–98.5)</td>
<td>64.8 (53.4–74.7)</td>
<td>61.5 (53.9–68.6)</td>
<td>98.0 (96.2–99.0)</td>
<td>2.771</td>
<td>0.039</td>
</tr>
<tr>
<td>15%</td>
<td>1376 (57.3)</td>
<td>95.7 (93.2–97.3)</td>
<td>70.9 (61.7–78.6)</td>
<td>64.7 (56.0–72.5)</td>
<td>97.3 (94.8–98.7)</td>
<td>3.289</td>
<td>0.061</td>
</tr>
<tr>
<td>20%</td>
<td>1299 (54.1)</td>
<td>94.9 (92.2–96.7)</td>
<td>75.8 (69.0–81.5)</td>
<td>68.8 (59.4–76.8)</td>
<td>97.0 (94.0–98.5)</td>
<td>3.924</td>
<td>0.068</td>
</tr>
<tr>
<td>25%</td>
<td>1294 (53.8)</td>
<td>94.8 (92.3–96.5)</td>
<td>75.8 (69.1–81.5)</td>
<td>68.6 (59.2–76.8)</td>
<td>96.8 (93.9–98.3)</td>
<td>3.919</td>
<td>0.069</td>
</tr>
<tr>
<td>30%</td>
<td>1165 (48.5)</td>
<td>89.0 (78.2–94.8)</td>
<td>84.7 (75.2–91.0)</td>
<td>75.4 (68.3–81.3)</td>
<td>93.9 (90.8–96.0)</td>
<td>5.811</td>
<td>0.130</td>
</tr>
</tbody>
</table>

Sensitivities, specificities, PPV, and NPV computed using metaanalysis of center-specific results.

CI, confidence interval; LR+ , positive likelihood ratio; LR− , negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

The Ability to Achieve a High Negative Predictive Value

1. MIA (OVA-1) or ROMA: NPV of 96-98.4%

2. Parallel Combination of MIA (OVA-1) + Imaging Results Can Achieve High Sensitivity (98%) And High NPV (98%)

1. ACOG #174 / Nov. 2016, pg. 7
2. AJOG / July 2014, pg. 66
Consider Gyn Onc Consult / Consider Laparotomy for Mgmt:

1. PMP + CA 125 2X Nml + USG with suspicious Malignant features
2. PeriMenopausal + Markedly Elevated CA 125 + Worrisome USG
3. Pre or PMP Status with Increased Risk Noted on Formal Assessment:
   (OVA1 (MIA) / ROMA / RMI / IOTA)

ACOG #174 / Nov. 2016, pg 10
THANK YOU!
SUPPLEMENTAL MATERIAL
TUMOR MARKERS

• CA-125: nonspecific marker for ovarian cancer diagnosis, used primarily in monitoring response to treatment
  • Postmenopausal <35
  • Premenopausal <200

• CA 19-9: Carbohydrate antigen 19-9 is a monoclonal antibody initially discovered in the serum of patients with colon and pancreatic cancer
  • Normal: 0-37 U/mL

• CEA: Carcinoembryonic antigen, expressed by most epithelial neoplasms including metastases to the ovary from mammary or GI origin
  • Normal: ≤3 ng/mL

• AFP: normal fetal protein produced by the liver, yolk sac, and GI tract
  • Normal: <20 mg/mL

• hCG: produced by syncytiotrophoblasts
  • Normal: 20-30 mIU/mL

• PLAP: Placental Alkaline Phosphatase, normally produced by the placenta
  • Normal: <35 U/L (varies by lab)

• LDH: enzyme normally produced by hepatic cells
  • Normal: 140-280 U/L

• Inhibin: peptide hormone normally produced by ovarian granulosa cells to inhibit the secretion of FSH
  • Postmenopausal: <5 pg/mL
  • Premenopausal: 2-80 pg/mL