Gynecologic Ultrasound: Clarifying the Grey Areas

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Objectives

- Review ultrasound images of common and uncommon, typical and atypical gynecologic findings which have questionable clinical significance
- Be familiar with recent literature on appropriate management of these findings
- Provide more clinically useful gynecologic ultrasound examinations and interpretations

Disclosures

- No relevant financial relationships
- No discussion of products which are investigational or not labeled for the use under discussion

Common indications for gynecologic ultrasound

- Pelvic pain
- Adnexal mass
- Enlarged uterus
- IUD localization
- Family history of breast cancer or ovarian cancer
- Abdominal bloating, pain

Physiologic ovarian findings

- Immature follicles (2-4mm)
- Dominant follicle, days 8-10 (8-10mm)
- Dominant follicle, prior to ovulation (20-25mm)
- Corpus luteum...solid appearing after collapse of fluid, with rim of vascularity, “ring of fire” (15-20mm)
- Hemorrhagic corpus luteum...re-expansion of CL with blood (up to 4 cm)

http://www.seattlefertility.com/images/follicles.jpg
Adnexal mass characterization

- Wall thickness
  - Thin or Thick
- Loculations
  - Uni-locular or Multi-locular
- Papillations
  - Yes or No
- Septations
  - Yes or No
- Echogenicity
  - Sonolucent, Low level echos, highly echogenic, solid appearing
- Shadowing
  - Yes or No
- Complex – has cystic and/or solid components
  - Yes or No

Adnexal Mass

- Simple cyst
  - Unilocular
  - Walls thin, smooth, regular
  - No extramural projections
  - No solid areas
  - Avascular
  - No internal debris
  - Hypoechoic

- Complex
  - Partially solid, partially cystic...should indicate which is predominant
  - Cyst walls
  - Vascularity
  - Septations
  - Internal echoes...heterogeneous or homogeneous
Adnexal Mass

- Solid
  - Internal echoes are hyperchoic
  - Vascular?
  - Homogeneous vs. heterogeneous internal echoes

http://brighamrad.harvard.edu/Cases/bwh/images/59/R22A4.GIF

Ultrasound diagnosis of adnexal mass

- Sokalska et al, Ultrasound Obstet Gynecol, 2009 Oct
- 1066 women with one adnexal mass examined by ultrasound
- Examiners performed standard exam with suggestion of specific diagnosis compared to surgically removed tumors
  - Dermoid, hydrosalpinges, peritoneal pseudocysts, endometriomas were most commonly correctly identified
  - Functional cysts, paraovarian cysts, simple cysts, struma ovarii, adenofibromas were most likely misidentified.
  - Dermoid, hydrosalpinges, functional cysts, peritoneal pseudocysts, fibromas, simple cysts never misdiagnosed as malignancy
  - Inflammatory processes, adenofibromas, rare benign ovarian tumors misdiagnosed as cancer
  - Overall specificity 94-100%

Ultrasound is pretty good for NOT missing cancer.

Easily identified adnexal pathology

- Endometrioma
- Teratoma
- Simple cyst
- Physiologic: corpus luteum, functional cyst
- Abscess
- Solid fibroma

IOTA: Use of Instant Descriptors

- Defined six descriptors that should enable the examiner to make an instant diagnosis
  - Demonstrated excellent diagnostic accuracy, sensitivity of 98% and specificity of 97%
- If an instant diagnosis is not able to be made...
  - Perform a second stage test such as CA 125
  - Refer for expert opinion
- Basically pattern recognition
- Let’s try it!
Unilocular tumor with ground glass echogenicity in premenopausal woman

Endometrioma
Unilocular tumor with ground glass echogenicity in premenopausal woman


Unilocular tumor with mixed echogenicity and acoustic shadows in premenopausal woman

Benign cystic teratoma
Unilocular tumor with mixed echogenicity and acoustic shadows in premenopausal woman


Unilocular tumor with regular walls and largest diameter < 10 cm

Simple Cyst
Unilocular tumor with regular walls and largest diameter < 10 cm

https://iame.com/online/ovary/ovary.html
Remaining unilocular, regular walls

Hemorrhagic, complex, benign cyst

Remaining unilocular, regular walls


Tumor with ascites and at least moderate color Doppler blood flow in postmenopausal women

Ovarian Cancer

Tumor with ascites and at least moderate color Doppler blood flow in postmenopausal women


International Ovarian Tumor Analysis (IOTA)

- Standardized the approach to the ultrasound description of adnexal pathology
- Establishes simple rules for characterizing ovarian pathology (study found that almost half of ovarian masses have features that can easily characterized)
  - No risk estimates are produced
  - Tumors are classified as: benign, malignant, or unclassifiable/inconclusive

- Sayashneh, et al., Gynecol Oncol, Jul 2013
  - IOTA strategy shows good performance in ultrasonographers with different background training and experience

Simple Rules

- Five ultrasound features of malignancy
  - Five ultrasound features of a benign mass
  - A mass is classified as malignant if it has at least ONE M-feature and NO B-features
  - A mass is classified as benign if it has at least ONE B-feature and NO M-features
  - If both are present, results are inconclusive and a different diagnostic method should be used
Not so easy adnexal masses

- Benign cystadenoma (mucinous or serous)
- Hydrosalpinx
- Salpingitis
- Granulosa cell tumor
- Some ovarian cancers

Cyst in Postmenopausal Woman

- Postmenopausal ovarian cyst
  - Study examined the prevalence, incidence and natural history of simple ovarian cysts among women >50 years of age. Study examined a cohort of 15,734 women from the intervention arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.
  - Incidence: 14% of women had a simple cyst the first time ovaries were visualized
  - Prevalence: 54% retained cyst at one year
  - 32% had no cyst at one year
  - Conclusions:
    - Simple cyst did not increase risk of subsequent cancer
    - Simple cyst are common and appear stable or resolve over time

Postmenopausal ovarian cyst

- Bailey et al (Gynecol Oncol 1998)
  - 7705 asymptomatic postmenopausal women followed 1987-2002 with annual ultrasound
  - 256 (3.3%) with unilocular cyst
    - 100% < 10 cm; 90% < 5 cm in diameter
    - 125 (49%) resolved over 60 days
    - 131 (51%) persisted
    - 45 surgically removed - no ovarian carcinoma
  - 86 followed with ultrasound, > no ovarian carcinoma
  - 250 (3.2%) with complex cysts
    - 100% < 10 cm; 89% < 5 cm in diameter
    - 135 (55%) resolved over 60 days
    - 115 (45%) persisted
    - 114 surgically removed
    - 7 ovarian carcinomas
    - 1 peritoneal carcinoma
    - 1 metastatic breast to ovary

Bottom line: Unilocular cyst <10 cm associated with minimal risk of malignancy, but those with complex characteristics (wall abnormalities or solid areas) have significant risk

Postmenopausal ovarian cyst

- Modesitt et al (Obstet Gynecol 2003 Sep)
  - 15106 asymptomatic women >50 years old
  - Followed 1987-2002 with annual ultrasound
  - 2763 (18%) with unilocular cyst <10cm
    - 2261 (69.4%) resolved
    - 537 (16.3%) developed septum
    - 189 (5.8%) developed solid area
    - 220 (6.8%) persisted
    - 10 (0.1%) ultimately diagnosed with cancer, all developed an additional morphological abnormality (solid area, septum, persistence)

Risk of malignancy <1% if cyst is unilocular and <10cm.

Postmenopausal ovarian cyst

- McDonald & Modesitt (Clin Obstet Gynecol 2006 Sep)
  - In asymptomatic postmenopausal patients
    - Unilocular cyst and if CA-125 = followup scan 3-6 months
    - Complex mass < 5cm, normal CA-125 = repeat CA-125 and TVS in 4 weeks
    - Surgery for increasing complexity of morphology or rising CA-125 or for complex cyst and elevated CA-125 on baseline scan
Risk of Malignancy in Adnexal Mass

- Granberg S, et al., Gynecol Oncol. 1989
  - Macroscopic description of tumor correlated to histopathologic diagnosis (benign, borderline, malignant) in 1017 women. Of those that were classified as malignant,
    - 0.3% (4/1200) was described as unilocular
    - 2.0% (42/2030) unilocular solid tumor
    - 5.0% (20/395) multi-locular cysts
    - 36% (147/209) complex multi-loculated cysts
    - 39% (118/200), predominant solid cysts

Summary of Ovarian Cancer Risk Factors

- Age
- Size
- Doppler
- Morphologic characteristics on:
  - Inner wall structure/papillations
  - Septa and septa thickness
  - Wall thickness
  - Echogenicity
  - Multilocularity

Predicting risk of malignancy in adnexal masses

- McDonald, et al., Obstet Gynecol, April 2010
  - Premise - the combination of patient demographics, tumor morphology from ultrasonographic images and serum CA 125 is useful in estimating risk of malignancy
  - High risk women = complex or solid adnexal mass and serum CA 125 value more than 35 units/mL
  - PPV = 84.7%
  - NPV = 92.4%

Risk of malignancy in adnexal masses

- Ekerhovd et al., Am J Obstet Gynecol, 2001
  - Evaluated the risk of malignancy in surgically removed ovarian cysts that were described as unilocular by TVUS pre-operatively
    - 1.0% of all simple cysts were classified as borderline or malignant
    - 4.0% of all complex ovarian cyst were classified as borderline or malignant
  - In both groups, the frequency of finding borderline or malignant cysts increased with diameter
    - < 20 mm: 0.0%
    - 20–49 mm: 1.6%
    - 50–79 mm: 2.1%
    - > 79 mm: 6.9%

Family history of breast cancer or ovarian cancer

- National Ovarian Cancer Early Detection Program
  - 4326 women at high risk (family history, personal history, genetic mutation)
  - 12,709 scans
  - All ovarian, primary peritoneal, fallopian tube cancers detected were Stage III, no early stage disease

TVUS in Ovarian Cancer Screening

- van Nagell, Int J Womens Health, Dec 2013
  - Article reviewed major ovarian cancer screening trials
  - Ultrasound has been shown to lower stage of at detection, but no proven decrease in mortality/survival benefit

| Table 2 Ovarian cancer screening trials using transvaginal sonography |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Serum CA 125 (U/mL) | 101-199 | 200-299 | 300-499 | ≥500 | Serum CA 125 (U/mL) | 101-199 | 200-299 | 300-499 | ≥500 | Serum CA 125 (U/mL) | 101-199 | 200-299 | 300-499 | ≥500 |
| Sensitivity | 87% | 75% | 50% | 25% | Specificity | 87% | 75% | 50% | 25% | Accuracy | 87% | 75% | 50% | 25% |
| Positive Predictive Value | 87% | 75% | 50% | 25% | Negative Predictive Value | 87% | 75% | 50% | 25% | Positive Predictive Value | 87% | 75% | 50% | 25% |
| Negative Predictive Value | 87% | 75% | 50% | 25% | Positive Predictive Value | 87% | 75% | 50% | 25% | Negative Predictive Value | 87% | 75% | 50% | 25% |
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TVUS in Ovarian Cancer Screening - van Nagell, Int J Womens Health, Dec 2013

- Article reviewed major ovarian cancer screening trials
- Ultrasound has been shown to lower stage of at detection, but no proven decrease in mortality/survival benefit
Family history of breast cancer or ovarian cancer

- Sensitivity 85%
- Specificity 98.7%
- PPV 14.01%
- NPV 99.9%

Bottom line: ultrasound when performed annually associated with decrease in disease stage at diagnosis but not effective in detecting cancers in women with normal ovarian volume.

Patients with symptoms

- Olson et al., Obstet Gynecol 2001 Aug
  - 168 women with ovarian cancer compared to 251 healthy controls
  - Queried about 8 symptoms and use of 3 medications prior to diagnosis
  - Symptoms more common in cancer patients: unusual bloating, fullness or pressures (71% v. 6%), abdominal pain or back pain (52% v. 15%), lack of energy (43% v. 16%)

Patients with symptoms

- Goff et al., Obstet Gynecol 2002 Aug
  - 128 women preop for adnexal mass compared to 1709 women in primary care clinics
  - Most common in patients with malignant neoplasia
  - Back pain (45%)
  - Fatigue (14%)
  - Bloating (27%)
  - Constipation (22%)
  - Abdominal pain (12%)
  - Urinary symptoms (10%)

Patients with symptoms

- Goff et al., JAMA 2004 Jun
  - When compared to controls, odds ratios:
    - Increased abdominal size 7.4
    - Bloating 3.6
    - Urinary urgency 2.5
    - Pelvic pain 2.2
    - Also 20-30 times per month, higher severity, more recent onset
    - Triad of bloating, increased abdominal size, urinary symptoms (43% v. 8%)

Patients with symptoms

- Goff et al., Cancer 2007 Jan
  - 149 women with ovarian cancer
  - 255 women in a screening program
  - 233 referred for ultrasound
  - Important symptoms included pelvic/abdominal pain, urinary urgency/frequency, increased abdominal size/bloating, difficulty eating/feeling full when present for < 1 year and > 12 days per month

Symptoms

- Goff et al., Cancer 2007 Jan
  - Developed Symptom Index
    - Positive if patient had any of the 6 symptoms, > 12 times per month, < 1 year
    - Sensitivity
      - 56.7% for early stage
      - 79.5% for advanced
    - Specificity
      - 90% for women ≥60
      - 86.7% for women < 60
Putting it All Together

- Pavlik et al, Cancer 2009 August
- 450 women who had had surgery as a result of TVS screening program (Van Nagell), all are high risk
- 272 of those women who had a positive symptom index (Goff)

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TVUS in Ovarian Cancer Screening

- van Nagell, Int J Womens Health, Dec 2013
- Article also discussed future directions of research
  - Fundamental questions remaining: who should be screened, frequency of screening, and order of tests within a specific algorithm
  - TVUS can identify minimal changes in ovarian volume and morphology, but has not been reliable in differentiating benign from malignant
  - Possible solutions
    - Biweekly serial morphology for complex ovarian tumors
    - Contrast enhanced ultrasound using microbubble contrast-agent particles

Fundamental questions remaining:

- Who should be screened?
- Frequency of screening?
- Order of tests within a specific algorithm?

TVUS can identify minimal changes in ovarian volume and morphology, but has not been reliable in differentiating benign from malignant.

Possible solutions:

- Biweekly serial morphology for complex ovarian tumors
- Contrast enhanced ultrasound using microbubble contrast-agent particles

Postmenopausal endometrial fluid

- Takacs et al (J Ultrasound Med 2005 Nov)
- 343 postmenopausal women with endometrial fluid
- Retrospective chart review (endometrial evaluation, path, clinical characteristics, sonographic characteristics)
- Non-benign (endometrial hyperplasia, cervical cancer, endometrial cancer)
  - Thicker endometrium (9.9mm v. 5.9mm)…none with endometrial cancer had thickness <3mm (single layer thickness)
  - Non-echogenic fluid (4.8% of non-benign had echogenic fluid v. 45.8% of benign)

Bottom line: If with echogenic fluid AND endometrial lining <3mm, consider endocervical sampling only. Otherwise sample endometrium also.

Postmenopausal Endometrium

- Felix et al., Int J Cancer, Feb 2014
- Endometrial thickness was measured using transvaginal ultrasound in a cohort of 1272 women, aged 55 to 74, from the PLCO Cancer Screening Trial
  - Compared to baseline endometrial thickness of 1 – 3 mm
    - Those with endometrial thickness greater than or equal to 5.0 mm had increased risk of breast (HR = 2.0) and endometrial (HR = 5.0) cancers

Additional references:

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- Epstein and Valentin, Ultrasound Obstet Gynecol, Jul 2006
- 95 women with postmenopausal bleeding and endometrial thickness <4.5mm
- Heterogeneous echogenicity, irregularity of endometrial surface, focal lesion associated with abnormal endometrium
- Vascularity (branching and 2 or more vessels) showed trend but not statistically significant for abnormality of endometrium
- Endometrial fluid no difference
Postmenopausal endometrium

- Smith-Bindman et al. Ultrasound Obstet Gynecol 2004 Oct
- Using theoretical cohort and published numbers (sensitivity, specificity, incidence of cancer in various populations, etc.), calculated the following risks for cancer:
  - In women with postmenopausal bleeding, not on HRT
    - >5mm: 7.3%
    - ≤5mm: 0.07%
  - In asymptomatic postmenopausal women, not on HRT
    - >11mm: 6.7%
    - ≤11mm: 0.002%
- Risk increases with age of patient

Bottom line: In the asymptomatic postmenopausal patient, consideration should be given to endometrial sampling if the endometrium >11mm.