ADNEXAL MASSES: CONSENSUS STATEMENT & GUIDELINES

FIRST INTERNATIONAL CONSENSUS REPORT ON ADNEXAL MASSES: MANAGEMENT RECOMMENDATIONS

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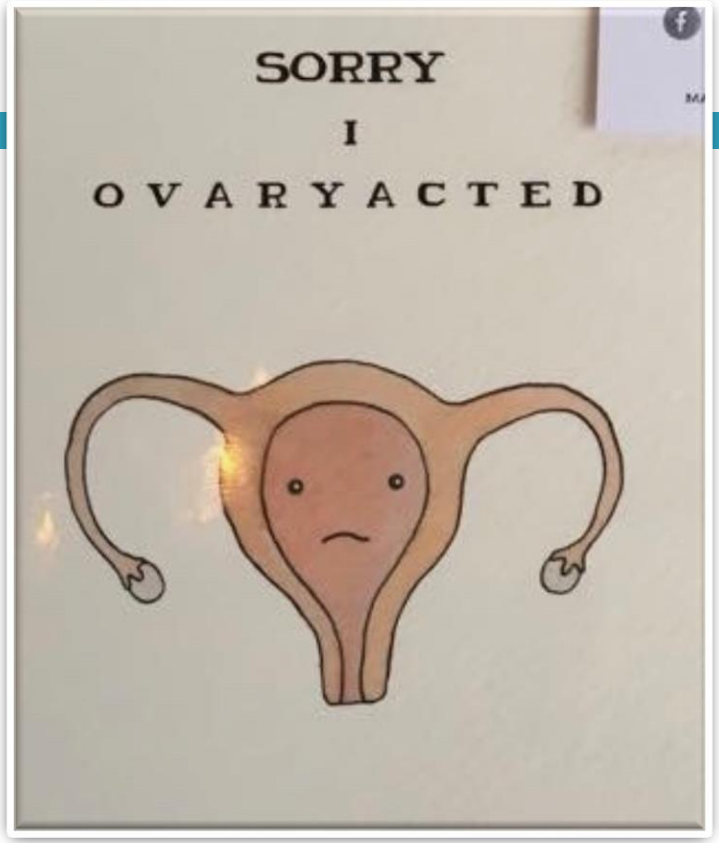
Disclosures

- No disclosures



Special Acknowledgement

- Dr. Stephen Goldstein
  - Co-Chair

- AIUM
  - Provided an unrestricted educational grant to permit face-face consensus meeting and administrative support

Talk is to share…..

First International Consensus Report on Adnexal Masses: Management Recommendations

- AIUM convened a multi-disciplinary / international consensus panel to address the diagnosis and management of asymptomatic women with pelvic masses November 2014
  - Co-Chairs: Drs. S Goldstein & P Glanc

	Academic Affiliation	Society Affiliation	Country	Specialty
S Goldstein , Co-Chair	Professor, NYU	**AIUM**	USA	Gynecology
P Glanc, MD, Co-Chair	Associate Professor, U of Toronto	**CAR** Canadian Association of Radiologists	Can	Radiology
B Benacerraf MD	Professor of Radiology Harvard Medical School	President, **AIUM**	USA	Radiology
T Bourne MD PhD	Adjunct Professor, Imperial College, London	**ISUOG**	UK	Gynecology
D Brown, MD	Professor Mayo Clinic	**SRU** Society of Radiologists in Ultrasound	USA	Radiology
B Coleman MD	Professor Emeritus Univ of Penn; Professor, CHOP	**ACR** American College of Radiology	USA	Radiology
C Crum MD	Professor of Pathology Harvard Medical School	**Support AIUM**	USA	Pathology
J Dodge MD	Assistant Professor University of Toronto	**Society of Gynecologic Oncology of Canada**	USA	Gynecologic Oncology
D Levine MD	Professor of Radiology Harvard Medical School	**SRU**	USA	Radiology
E Pavlik MD, PhD	Associate Professor University of Kentucky	**Society of Gynecology Oncology**	USA	Gynecologic Oncology
D Timmerman MD, PhD	Professor, University Hospitals Leuven	**(IOTA)** and Flanders Ultrasound Society	Belgium	Gynecology
F Ueland MD	Professor ,Univ Kentucky	**ACOG**	USA	Gynecologic Oncology
W Wolfman MD	Professor, Univ Toronto	**SOGC**	Can	Gynecology

Group acknowledged

√Agreed that the consensus statement published by SRU in 2009/10 entitled “Management of Asymptomatic Ovarian and Adnexal Cysts Imaged at Ultrasound” remains relevant and appropriate

SRU Consensus Statement

- Agreed :

√ Pelvic US is still the primary imaging modality to evaluate adnexal masses

√ Morphologic features in combination with Doppler evaluation of vascularity, in the hands of an expert sonographer, can correctly characterize most adnexal masses, especially if their appearance is classic for that entity

***So why did we need another consensus statement? ***

*Levine D, Brown DL, Andreotti RF, Benacerraf B, Benson CB, Brewster WR, et al. Management of Asymptomatic Ovarian and Other Adnexal Cysts Imaged at US: Society of Radiologists in Ultrasound Consensus Conference Statement Radiology. **2010**;256(3):943-54.*

Why Another Consensus Conference?

Panelists all Agreed 2 main premises

1. Excess surgery for clearly benign masses

- *ACOG (2015)made this more likely when re-affirmed "with the exception of simple cysts on TVS most pelvic masses in postmenopausal women will require surgical intervention."*

- ~ 200,000 USA women undergo surgery for pelvic mass to find 21,290 women with ovarian cancer (0.1%)
  - **9.1** USA surgeries/malignancy
  - **2.3** (IOTA European oncology centers)
  - **5.9** (other European centers)

Why Another Consensus Conference?

Panelist all Agreed on 2 main premises

2, Too many women do not benefit from a gynecologic oncologic evaluation prior to surgical intervention

- Abundant data demonstrates women with ovarian malignancies have better long-term outcomes when treated by gynecologic oncologists
- Only 33% women with OC benefit from such a preoperative referral

Gynecologic Oncology Consult

- Most important factor for survival is stage at diagnosis.
- **After stage,** appropriate referral to a center **specialized in gynecological malignancy** is the important prognostic factor in improving patient survival
  - Gynecologic Oncologist for optimal surgery/therapy
  - Pathologist with specialized expertise
    - less risk over and underdiagnoses of ovarian malignancies, in particular of borderline ovarian tumors on frozen section

Why Another Consensus Conference?

Panelists all Agreed on 2 main premises

Panel mandate was to ***address*** the gap between current knowledge and the translation of this knowledge into practice

- Group recognized that an absolute distinction between all benign and malignant masses was unlikely

- However, a schema could be identified to stratify masses into 3 “buckets”

The 3 Buckets

Category	Management
Almost certainly benign	Variable but conservative
Indeterminate*	Second stage testing
Suspicious for malignancy	Proceed to surgical evaluation involving gynecology-oncology

*Defined unable to unambiguously place into either the benign or malignant category after US

Ovarian Cancer (OC): Not a Monolithic Entity

- **Epithelial OC (EOC)2 types** : Morphology & genetics
  - **Type 1**: Slow growth, good prognosis
    - low grade serous, mucinous, endometriod, clear cell, Brenner, borderline
  - **Type 2**: 75% all OC and 90% deaths
    - p53 mutation in 80%
    - Precursor in situ lesion “serous intraepithelial tubal carcinoma” or STIC which resembles high grade ovarian serous carcinoma
    - Majority Type2 EOC arise from STIC in fimbriated end FT ie majority are of Mullerian rather than mesothelial origin

Discussion Points
Malignant Potential Simple Cysts

- No documented relationship between serous cystadenomas & HGSC
- Mutation evidence is supportive above
- All linkages are via retrospective data

The long term risk of malignancy following a diagnosis of serous cystadenoma is similar to that of the general population

Discussion Points – Trials – Risk Malignancy Unilocular Cystic Tumors <10cm

University of Kentucky Ovarian Screen Trial:

- 15,106 women > 50yr underwent annual TV
  - if positive finding repeat at 4-6wks
- 70% resolved spontaneously (2/3 within 3 months)
- 133 surgically excised unilocular cystic masses
  - 52% serous cystadenomas versus 12% serous cystadenofibromas, 8% mucinous cystadenoma

No malignant or borderline unilocular cysts < 10 cm

Modesitt SC, Pavlik EJ, Ueland FR, et al. Risk of malignancy in unilocular ovarian cystic tumors < 10 centimeters in diameter. O&G. 2003;102(3):6.

Pawlik, Ueland et al. Frequency & Disposition of Ovarian Abnormalities followed with Serial TVUS Ob & Gyn 2013

Discussion Points – Trials –
Risk Malignancy Unilocular Cystic Tumors <10cm
University of Kentucky Ovarian Screen Trial:

- Overall risk malignancy < 0.1%, thus permit serial F/U
  - 10 women diagnosed with invasive cancer
  - 7 demonstrated morphological change (solid/papillary)
  - 2 after cyst had resolved
  - 1 in other ovary

  - Final conclusion: potential shift in stage distribution and mortality reduction however no control group and mixed risk population with 23% FH OC

Modesitt SC, Pavlik EJ, Ueland FR, et al. Risk of malignancy in unilocular ovarian cystic tumors < 10 centimeters in diameter. O&G. 2003;102(3):6. Pawlik, Ueland et al. Frequency & Disposition of Ovarian Abnormalities followed with Serial TVUS Ob & Gyn 2013

Discussion Points - Trials

Malignant Potential Simple Cysts

Prostate, Lung, Colorectal, and Ovarian cancer screening trial (PLCO)

- 4 year F/U TVS & Ca125
  - **RCT** 78,216 women age 55-74
- Single trigger to recommend surgery=large # FP
  - Although did not improve cancer mortality there was increase in adverse health effects primarily due increase surgery (FP) and associated surgical/medical harm
    - 15% surgical group experienced major complication
  - Concluded simple cyst(s), single or multiple, did not increase risk subsequent invasive OC

Greenlee et al. Prevalence, incidence, and natural history of simple ovarian cysts among women >55 years old in a large cancer screening trial. AJOG. 2010;202(4):9. (American)

Discussion Points : Trials

Malignant Potential Simple Cysts

United Kingdom Collaborative Trial : OC Screen US in PMW

- **RCT** cohort study: 2,531/48,053 women had unilocular cysts
  - Within 3 years: 5 BOT & 4 Type 2 EOC
  - Absolute risk malignancy 0.4% (4/1,000)
    - Subgroup unilocular or multilocular cyst with no solid elements at initial scan
    - Authors comment "there was a change in morphology in the few women with initial unilocular cyst who later developed EOC"
  - Thus simple or unilocular cysts no rush to surgery but some interval F/U appropriate

Sharma et al. ***Risk of epithelial ovarian cancer in asymptomatic women with US-detected ovarian masses: a prospective cohort study UK collaborative trial of ovarian cancer screening (UKCTOCS).*** *UOG. 2012;40(3):7*

Discussion Points

Risk with Septations

- Kentucky Group :1,319 women multilocular cysts (no solid elements) followed TVS US at 4- to 6-month intervals for an average of 77 months
  - Majority serous or mucinous cystadenomas (surgery), 1 BOT
  - No correlation OC with septal number or width, No OC
  - Consider malignancy in a multiseptated cyst with smooth inner walls unlikely
- PCLO : multiseptated cysts not associated > OC
  - Mutilocular cysts > association with BOT or Stage 1 EOC

Ueland FR, et al. Risk of malignancy in sonographically confirmed septated cystic ovarian tumors. Gynecol Oncol. 2010;118(3):278-82.
Timmerman D, Testa AC, Bourne T, Ameye L, Jurkovic D, Van Holsbeke C, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. Ultrasound Obstet Gynecol. 2008;31(6):681-90.

Discussion Point
Malignant Potential Mucinous Cystadenomas

- Limited data
  - Mucinous BOT typically ≥10cm, > 10 locules, no solid elements
  - If a cyst is clearly mucinous by US, a different index of suspicion for surveillance rather than surgical removal may be prudent.
    - *Similar k-ras mutations in Stage I intestinal type cancers to adjacent normal mucinous epithelium in 6/20*
- *Descriptors: Thin walled, multiple locules, mucin appears as fluid with low level echogenicity or "Onion skin" appearance of concentric layering of mucin content or "mosaic" sign if different locules have varying echogenicity or heterogenous scattered low level echoes*

Discussion Points – **Malignant Potential**
Mature Cystic Teratomas & Endometriomas

- Low association with malignancy, < 0.9%
- Prudent to follow over time
  - Growth or develop solid vascular elements
- Risk increase larger endometriomas (> 9cm) and older women (> 45 years)
  - No definitive data on endometriotic implants excision associated with reduced risk malignancy

Park J-Y et al Malignant transformation of mature cystic teratoma of the ovary: experience at a single institution. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2008;141(2):173-8. ** Comerci et al. Mature cystic teratoma: a clinicopathologic evaluation of 517 cases and review of the literature. Obstetrics & Gynecology. 1994;84(1):22-8. Kobayashi et al. Risk of developing ovarian cancer among women with ovarian endometrioma: a cohort study. International J of Gynecological Cancer 2007. Johnson et al Consensus on current management of endometriosis Human Reproduction. Van Holsbeke et al. Endometriomas: their ultrasound characteristics. UOG 2010

Role of CDS

- Interrogate all septations or solid areas
  - Meta-analysis of 46 publications concluded that the combination of US morphological assessment with CDS of tumor vascularity performed significantly better in ovarian mass characterization than either technique individually*
- No discriminatory value of spectral Doppler to reliably distinguish malignant vs benign
  - > greater degree of vascularity > concern for potential malignancy
  - Central intratumoral vascularity > predictive value for malignancy whereas the absence of intratumoral vascularity has a high negative predictive value
    - although malignancy can occur without measurable flow
- THUS, Doppler cannot be used as an isolated feature to determine the risk of malignancy

*Kinkel et al. US characterization of ovarian masses: A meta-analysis. Radiology. 2000;217(3):9.

Approach

Role General Gynecologist

- Front-line to decide monitor or surgery
- Foremost consideration risk malignancy
- Secondary considerations of impact on fertility, hormonal status and premature menopause, complications of surgery

Two Key Approaches To Adnexal Masses Incidental' Discovered on Ultrasound

1. Risk Assessment based on pattern recognition
   - Best utilized by practionners with experience/expertise

2. Risk prediction models – Emphasis on IOTA Simple Rules.
   - Could be successfully utilized by practionners with less expertise

The 3 Buckets

Category	Management
Almost certainly benign	Variable but conservative
Indeterminate*	Second stage testing
Suspicious for malignancy	Proceed to surgical evaluation involving gynecology-oncology

*Defined unable to unambiguously place into either the benign or malignant category after US

Mass Characterization

Bucket 1: Almost certainly benign

- Simple or unilocular cyst
- Classic hemorrhagic cyst, including hemorrhagic corpora lutea
- Classic endometriomas
- Classic dermoids
- Classic Ovarian fibromas

Levine D, Brown DL, Andreotti RF, Benacerraf B, Benson CB, Brewster WR, et al. Management of Asymptomatic Ovarian and Other Adnexal Cysts Imaged at US: Society of Radiologists in Ultrasound Consensus Conference Statement 1. Radiology. 2010;256(3):943-54.

Mass Characterization

Bucket 2: Indeterminate

- Unable to unambiguously place bucket 1 or 3

- Recognition, what may be confidently interpreted as “almost certainly benign” in the hands of one examiner may well be ”indeterminate” for another.

Next Steps: Indeterminate

- Serial ultrasound or referral to an “expert” ultrasound consultant
- Application of established risk-prediction models
- Correlation with MRI imaging
- Referral to gynecologic oncologist further evaluation
- Correlation with serum biomarkers.

The decision which to use will in part reside with the experience and comfort of the clinician and local resource availability

Next Steps: Referral to Expert

- Despite extensive research into various risk prediction models, subjective assessment in the hands of an expert remains as accurate as any technique
  - Excellent discrimination benign vs malignant
    - Sensitivity up to 96.7%, FN 1/30, correct specific dx ~42%

- BUT, skills are not easily transferable thus consider referral to an expert

Next Steps: Serial US

- Most adnexal masses spontaneously resolve over time
- Provide opportunity improve the prediction of ovarian malignancy while decreasing # of operations performed for benign abnormalities *
  - *Monitor for growth/morphology change/solid elements*
  - *Monitor stability, decrease in size or resolution*
  - **Recent review suggested low-risk abnormalities can undergo initial 3 month F/U
    - If stable or decreasing in size repeat annually x 5 years

* Elder et al.Gynecol Oncol 2014; 135:8–12 **van Nagell JR, Miller RW. Obstet Gynecol 2016; 127:848–858

Next Step: Risk Prediction Models
International Ovarian Tumor Analysis (IOTA)

- > 10,000 patients in > 20 centers, multiple countries, academic/non-academic centers with consistent results suggest data is robust/generalizable.
- IOTA Simple Rules
  - simple to use thus simple to implement
  - permit US practionners with varying degrees expertise to quickly use uniform terminology and arrive at similar results
- IOTA simple rules classify ~75% benign or malignant.
  - Triage point: to experienced imager for ~25% inconclusive

Improving strategies for diagnosing ovarian cancer: a summary of the IOTA studies. UOG. Volume 41, Issue 1,p9–20, 2013

Next Steps:
Risk Prediction Model: IOTA Simple Rules

- The rules work well for characteristic lesions
  - Endometrioma, dermoid cysts, simple cysts and advanced invasive malignancies
- Rules work less well in tumors that tend to be more difficult to classify sonographically

- In their **surgical** population
  - ~ 40% of inconclusive masses were malignant thus "possibly malignant" in inconclusive is not unreasonable conclusion

https://itunes.apple.com/us/app/iotamodels/id637567054; http://www.iotagroup.org

Next Steps:
Risk Prediction Models

- A recent systematic review of the literature examining **different risk-prediction models** recommended incorporating the use of the IOTA Simple Rules or the prediction model LR2 for preoperative characterization of ovarian masses, particularly in premenopausal women.

Kaijser, et al. *Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis* Human Reproduction Update. 2013

Next Steps:
Risk Prediction Models: IOTA Simple Rules

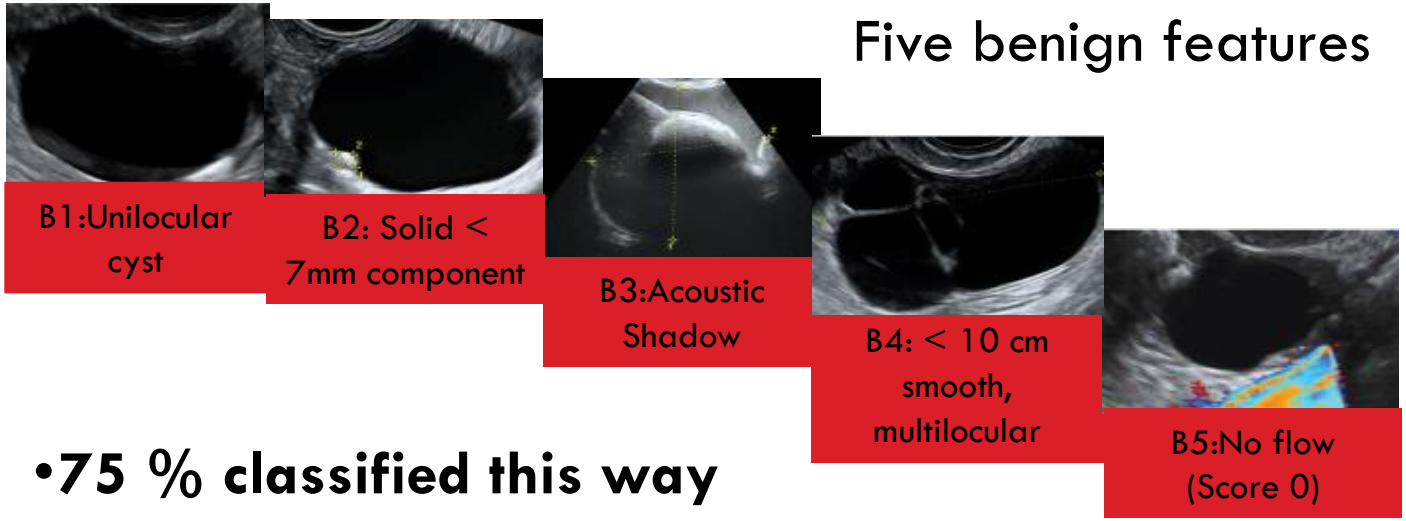
M- Rules	B- Rules
M1 Irregular solid tumor	B1 Unilocular
M2 Ascites	B2Solid component < 7mm
M3 ≥4 papillary projections	B3 Acoustic shadows
M4 Irregular multilocular solid > 10 cm	B4 Multilocular smooth inner wall < 10 cm
M5 Strong blood flow	B5 Avascular

https://itunes.apple.com/us/app/iotamodels/id637567054; http://www.iotagroup.org

IOTA "SIMPLE RULES"

- If ≥ 1M-rulew apply in absence of a B-rule, classified as malignant.
- If ≥ 1B-rules apply in absence of a M-rule, classified as benign.
- Unclassifiable:
  - If both M-rules and B-rules apply or no rule applies

IOTA Simple Rules

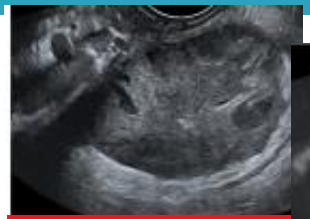


- **75 % classified this way**

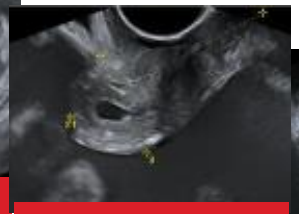
Simple ultrasound-based rules for the diagnosis of ovarian cancer. Timmerman et al. UOG, 2008 (31) 681-690

IOTA Simple Rules

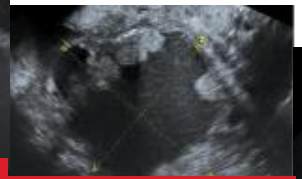
Five Malignant Features



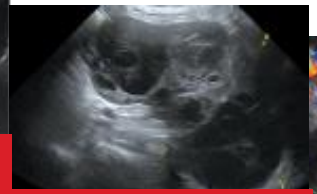
M1:Irregular solid



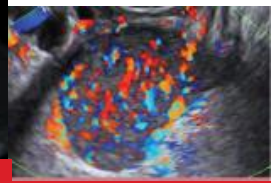
M2: Ascites



M3: ≥ 4 papillary nodules



M4: > 10 cm irregular solid multilocular



M5: Strong blood flow (Score 4)

- **75 % classified**

Simple ultrasound-based rules for diagnosis ovarian cancer. Timmerman et al. UOG, 2008 681-690

Next Steps: Indeterminate Mass Referral for MRI

- MRI with contrast enhancement provides the highest post-test probability of ovarian cancer detection for indeterminate masses (US, CT, PET)

- The key contribution - increased specificity permits confident diagnosis of many benign adnexal lesions
  - Also highly sensitive/specific in diagnosis malignancy

Next Steps:
Referral Gynecologic-Oncologist

- Indeterminate mass then referral to a gynecological oncologist is appropriate next step option
  - not necessarily for prompt surgical exploration, but for utilization of their expertise

Next Steps: Referral Biomarkers

- Role of serum biomarkers, whether in isolation or as part of an algorithm is not yet clearly established
  - *Ca-125 low sensitivity in early stage EOC*
  - *OVA1 and the Risk of Malignancy Algorithm (ROMA) are only FDA-cleared tests for preoperative evaluation ovarian tumor*
  - *ROMA and OVA1: no RCT or direct comparisons*
    - *OVA1 may be >sensitive (early-stage malignancy & premenopausal*
  - *Role best if indeterminate malignant risk*
    - *Help decide if refer to a gynecologic oncologist*
  - *Neither HE4 nor CA125 should be used as individual diagnostic tests in the preoperative evaluation of an adnexal mass.*

Mass Characterization

Bucket 3: Suspicious for Malignancy

- No ultrasound is perfect at discriminating benign from malignant, nor is any algorithm a replacement for sound clinical judgement

- Nonetheless there are some features which should trigger concern for potential malignancy within an adnexal mass.

Feature	Comment
Solid component	In general solid component worrisome for malignancy, however typical hyperechoic shadowing of lesions with fat (mature cystic dermoids) or classic hypoechoic lesion with strong acoustic shadowing (fibromas) are solid benign lesions.
Blood Flow	Central vascularity >concerning than peripheral. > degree of vascularity > concern.
Septations	Thin ≤ 2- 3mm avascular incomplete septations are considered benign Thicker septations (≥3mm), multiple, irregular or vascular may be more worrisome

Feature	Comment
Papillary Projections	≥ 4 papillary projections, or involvement of more than half the wall with papillary projections of any size is worrisome
Ascites	Complex pelvic fluid extends beyond the pelvis is > worrisome than simple fluid not extend beyond
Interim growth	No convincing data to determine amount of growth which is worrisome.
Change in Morphology	A change in sonomorphology, in particular the development of solid or vascular features is concerning.

Consensus Statements

- Simple ovarian cysts are not precursor lesions to malignant ovarian cancer
  - There is very low risk that these simple or even unilocular cysts can progress to malignancy thus some degree of follow-up may be prudent.
  - Crucial to perform high quality US prior to designate as simple
- Majority of ovarian lesions are benign
  - IF US suggests benign patient may be followed rather than having urgent surgical removal.

Consensus Statements

- If an ovarian lesion is indeterminate on initial scan (appropriate clinical evaluation) then "second-step".
  - Serial ultrasound or referral to a specialized ultrasound consultant
  - Application of established risk-prediction models
  - Correlation with MRI imaging
  - Referral to a gynecologic oncologist for further evaluation
  - *Correlation with serum biomarkers.*

Consensus Recommendations

- The group did not come to consensus on length or timing of follow-up
  - Not enough data
- Group recognized less surgical intervention may well result in an increase in ultrasound surveillance

Summary

- Panel mandate was to ***address*** the gap between current knowledge and the translation of this knowledge into practice to enhance patient care by:
  - Current approaches to improve initial assessment
    - Include both risk algorithms(less experienced) such as IOTA simple rules and pattern recognition(more experienced)
  - Enable concept of referrals to expert sonologists
  - Provide evidence based recommendations to enable conservative management of more benign lesions
  - Disseminate knowledge to aid in improved referral rates to gynecology-oncologist when malignancy suspected

Thank you

Thank you to AIUM for unrestricted educational grant used to support face-face meeting

Please look out for publication 2017 JUM

- In the United States approximately how many surgery for pelvic mass are performed to identify 1 malignancy.

a. 9
b. 7
c. 6
d. 2

The correct answer is A. In the United States there are approximately 9.1 surgeries per ovarian malignancy* as compared to the European International Ovarian Tumor Analysis trial centers where the rate is only 2.3 in dedicated oncology centers and 5.6 in other centers**.

* Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J. Clin 2015; 65:5–29.

**Timmerman D, Van Calster B, Testa A, et al. Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis (IOTA) group. Am J Obstet Gynecol 2016; 214:424–437.

Ultrasound feature which are typically associated with malignancy include which of the following:

A. Solid hyperechoic with acoustic shadowing component.
B. Solid hypoechoic with acoustic shadowing component
C. Multiple papillary projections.
D. 2-3mm thick septations.

The correct answer is C. A solid hyperechoic shadowing component is typically associated with fat as in a dermoid lesion. A solid hypoechoic with strong acoustic shadowing component is typically associated with an ovarian fibroma or fibroma-thecomatous lesions. Septations which are ≤ 2-3mm in diameter are considered benign findings whereas thicker, irregular or vascular septations are concerning for malignancy. A papillary projection is defined as a solid projection whose height > 3mm and projects along the inner of the mass or less commonly along the septae or outer wall of the mass (exophytic papillary projection). It is considered that ≥ 4 papillary projections or involvement of more than half the wall with papillary projections of any size is worrisome.

References :

Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol* 2008; 31:681-690

Hassen K, Ghossain MA, Rousset P, et al. Characterization of papillary projections in benign versus borderline and malignant ovarian masses on conventional and color Doppler ultrasound. *AJR Am J Roentgenol* 2011; 196:1444-1449

High grade serous ovarian malignancy generally originates from which of the following:

A. Simple cyst
B. Serous cystadenoma.
C. Ovarian parenchyma
D. Fallopian tube

- The correct answer is D, Most pelvic high-grade serous carcinomas originate from the fallopian tube rather than the ovary, thus accounting for the high incidence of peritoneal spread at the time of diagnosis. Neither simple cysts nor serous cystadenomas are considered a precursor lesion for malignancy.

Reference: Salvador S, Gilks B, Köbel M, Huntsman D, Rosen B, Miller D. The fallopian tube: primary site of most pelvic high-grade serous carcinomas. International Journal of Gynecological Cancer 2009; 19:58-64

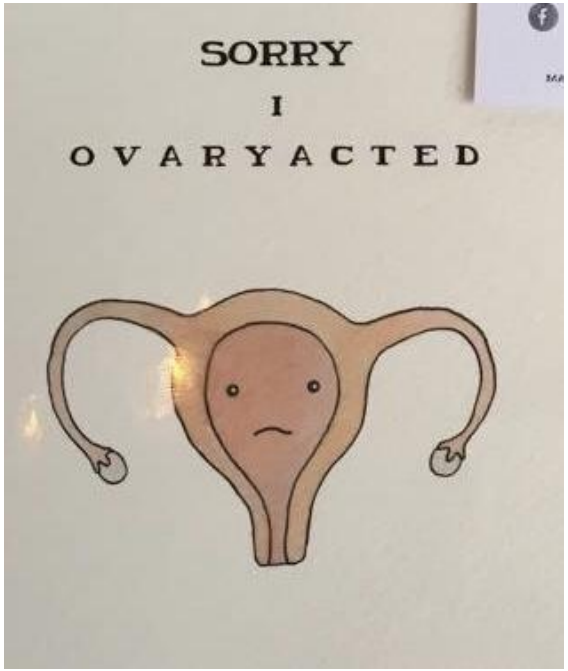
How many surgeries are performed to find one ovarian malignancy in the United States?

- 3
- 9
- 12
- 15

The correct answer is B. There are approximately 9.1 surgeries per malignancy in the United States as compared to 2.3 in European Oncology Centers and 5.9 in other European Centers.

Timmerman D, Van Calster B, Testa A, Savelli L, Fischerova D, Froyman W, et al. Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis (IOTA) group. American journal of obstetrics and gynecology. 2016.

Thank you all very much for your time and attention



Handouts are available @ phyllisglanc.com