Adnexal Masses:
Borderline Ovarian Tumors of Low Malignant Potential
Can we define them more reliably?

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Description of the lecture

• In the tile of the lecture I ask if we can, or could define adnexal masses more clearly, more accurately
• Unless my previous, more general, teaching lectures on adnexal masses, this talk is entirely different
• I will try to share my attempt to present a deeper insight of a restricted number of entities rather than repeat discussing a large number of issues in a broad manner
• This lecture is dedicated to sonographers and sonologists who want to understand more about some important selected entities

Learning Objectives

After the presentation, attendees will be able…

• ….to understand, and more importantly, apply the available scanning strategies, diagnostic rules, US tools, simple maneuvers and effectively use them, not only to characterize, but also to fine-tune certain features of adnexal findings leading to accurate clinical diagnoses.
• ….to apply some of the scanning techniques to be able to recognize the sonographic features of borderline ovarian tumors and their differential diagnoses

1. Scanning strategies

1. Imperative (MD & RDMS!!) : obtain good history, ask patient, review chart, call referring doctor and/or NP
2. Use primarily transvaginal scanning route. Always add transabdominal, and, if needed, transrectal scan.
3. Use the highest frequency transvaginal US probe
4. LEARN AND USE 3D US TECHNIQUES
5. Be familiar with scoring systems (e.g. IOTA)
6. Read the literature and follow new clinical information and new technical developments with new applications
7. Attend relevant courses. Listen/watch webinars
8. If possible ask if you can shadow someone who can teach you a new way to improve your skills

Disclosures
Ilan E. Timor-Tritsch

I have no relevant financial relationships
Scanning for adnexal pathologies

• US should be the almost always the 1st line imaging before CT & MRI
• You MUST arrive at a conclusion!
• Therefore use all available US tools:
  – primarily transvaginal sonography (TVS), combine it with
  – transabdominal sonography (TAS)
  – Use a variety of transducers for frequency, depth, color and power Doppler, employ 3D as needed….

Menstrual Hx.: Important!!

• In the reproductive years, physiologic as well as pathologic processes are driven by the menstrual cycle or by (therapeutic or pathologic) hormonal stimulation.
• Know your patients’ first day of her cycle.

Is this an ovarian malignancy?

How about this?

2. General and basic information follow the message of the talk
First:
We have to be familiar with appearances of ovarian masses

Know what to look for?
- Appearance:
  - “Bizarre shapes”
  - Mixed components
  - Size
  - Is it uni- or bilateral?
  - Ascites
  - Motion tenderness
  - Vessels
  - Mobility: sliding/fixed?

When these are documented, the next step is: LOOK AT THE VASCULARITY.

Look for these or similar images
- General appearance
  - Solid
    - Hyperechoic
    - Hypoechoic
  - Cystic:
    - without solid component
    - With solid component
  - Unilocular, Multilocular

Look for details
- Internal echo structure:
  - Anechoic/hypoechoic
  - Echogenic (solid)
  - Low-level echoes (ground glass appearance)
  - Mixed echogenicity
  - Reticular, etc

Examine inner wall structure
- Wall structure:
  - Thickness
  - Inner, mural papillae

If inner wall papilla/e or nodules are seen, apply power [not color] Doppler with the highest sensitivity to detect blood vessels.

Second:
We should be familiar of scoring systems and how to apply them to better differentiate between benign and malignant ovarian masses
What do scoring systems do?

- They translate macroscopic, pathologic features to sonographically recognizable features.
- All are based upon the same building blocks:
  - Wall thickness
  - Septations
  - Echogenicity
  - Papillary formations
  - Solid components
  - Blood supply (vascularity)
- Some systems add: size, ascites, age, etc…

Several scientifically proven set of articles suggest that subjective evaluation of adnexal masses is almost as good as the evaluation based upon strict scoring systems.

One may use Morphology Scoring Systems: they are out there.

- Sassone M, Timor-Tritsch et al, AJOG 1991
- Kentucky, DePriest et al, Gynecol Oncol 1997
- 1993; Osmers, AJOG 1994
- Bromley et al, Obstet Gynecol 1994
- Lerner JP, Timor-Tritsch al, AJOG 1994
- Kurjak, UOG 1994
- Ferazzi, UOG 1998

The most tested for accuracy is the IOTA system (Timmerman, UOG 1999-2016).

However, they do not have to be applied to the letter. Just understand their basic idea to differentiate a benign tumor & from a suspicious or a malignant one.

The IOTA scoring system

The simple rules by the IOTA group

I= international
O= ovarian
T= tumor
A= analysis

IOTA simple rules

Benign features

- B1 feature: unilocular cyst with thin, few, or incomplete septations or wall nodularity of ≤3 mm. There may be internal echoes.
- B2: presence of a solid component of ≤ 7 mm in largest diameter.
- B3: acoustic shadowing
- B4: smooth multilocular tumor of with a largest diameter ≤10 cm
- B5: no detectable Doppler flow

Malignant features

- M1: irregular solid tumor.
- M2: presence of ascites.
- M3: at least 4 papillary structures within a cystic lesion.
- M4: irregular multilocular solid tumor with a largest diameter of ≥10 cm
- M5: very high color contenton color Doppler examination.
IOTA color score

Subjective assessment of blood flow

1. Color score of 1 is given when no blood flow within the septa, cyst walls, or solid tumor areas.
2. Color score of 2 is given when only minimal flow can be detected.
3. Color score of 3 is given when moderate flow is present.
4. Color score of 4 is given when the adnexal mass appears highly vascular with marked blood flow.

3. My first subject: nodules and papillae in ovaries

My plan

• I will devote the first part of this talk to discuss internal wall nodules and papillae in ovarian or paraovarian cysts as well as some new ways to assess ovarian cysts.
• The second part of this talk will share some technical skills to improve the diagnosis.

Be forewarned! Be informed!

Almost everybody I know uses the terms “papilla” and “nodule” interchangeably.
So does the literature.
I have different definitions for them.

My definition of nodule & papilla

Nodule

- Hyperechoic mostly shadowing, subcentimeter, avascular inner wall structure in ovarian or paraovarian cysts & at times on septae

Papilla (plural: papillae)

- Hypoechoic, mostly non-shadowing, subcentimeter, irregularly shaped, vascular inner wall structure in ovarian or paraovarian cysts

Does the finding of papillae in adnexal cysts increase the risk of ovarian cancer?
**The significance of papillary formations in ovarian cysts**

- Agreement in EUROPE and the USA:
  - Cysts with “Small”, hyperechoic papilae *without* blood vessels are benign and can be followed by periodic imaging

**The significance of papillary formations in ovarian masses**

- Agreement in EUROPE and the USA:
  - Cysts containing papilae *with* blood vessels are suspicious for malignancy and should be removed

**The questions are:**

- How do we make distinguish between a nodule and a papilla?
- Are they different histologically?
- How do we use color or power Doppler?
- Are there any characteristic US features that help sorting them out?
- And if we sort them out, does it mean the we will be able to predict or rule out malignancy?

**Papillary projections within ovarian or other cysts**

- Thought to be sensitive markers of malignancy
- If found, more work has to be done
  - 1. Measure them
  - 2. Determine shape and echogenicity
  - 3. Look for vessels in it
  - 4. Examine their signature texture

**How to measure the papilla?**

![Image](Timmmerman D: The IOTA group UOG 2000;16:500)

**The kinds of papillary projections**

![Image](Timmmerman D: The IOTA group UOG 2000;16:500)
Papillae: general appearance

Three kinds of nodules/papillae

Three kinds of nodules/papillae

Nodule: usually benign (cystadenofibroma)

Three kinds of nodules/papillae

Three kinds of nodules/papillae

I present 3 kinds of nodules/papillae and point out the subtle features to help in defining them and in an attempt to get as close as possible the correct diagnosis.

First: papillae in an endometrioma

An example:
Imperative (MD & RDMS!!) : obtain good history, ask patient, review chart, call referring doctor and or NP

• You scan a 31 y.o. patient at 12 weeks for NT in the right adnexa this is the TVS finding:

Benign or malignant?
Benign: CL? or malignant? or “other”?

Scenario #1
• Ask patient: have you had any Hx. of pelvic disease? A: No
• Any problems getting pregnant? A: No
• Any pelvic imaging (US, CT, MRI) in the last years? A: US for pregnancy 2 y ago: NL
• Your Diff. Dx: CL vs E-oma vs ov. malignancy (BOT/LMP)?
Call MD/Gyn Onc→ Rescan PRN

No change → Probably removal @16w

Scenario #2
• Ask patient: have you had any Hx. of pelvic disease? A: Yes
• Any problems getting pregnant? A: Yes, 4y infertility Rx
• Any pelvic imaging (US, CT, MRI) in the last years? A: US- one endometrioma ?side?
Your Diff. Dx now: CL vs most probably: decidualized E-oma
Call MD → F/U and rescan as needed

What is a decidualized endometrioma?
It is a subset of endometriomas with a characteristic appearance seen in pregnancy

Here is the science behind the lesions

Histology
• Under the influence of progesterone during pregnancy the uterine endometrium transforms into decidua; vessels enter the decidual lining.
• The same is happening in the decidua lining the inner wall of the endometrioma

The point of the matter
• With decidualization the sonographic appearance of endometriomas can become more heterogeneous with papillary excresences and increased vascularization
The point of the matter

- And... since a richly vascularized ovarian lesion is considered malignant unless proven otherwise
- And... since the proof is usually surgical exploration, that may lead to pregnancy loss or premature labor......

It is therefore of great importance to correctly differentiate between a decidualized E-oma and ovarian malignancy.

Watch the difference between a papilla in a decidualized endometrioma and that of a BOT

- Shallow, mostly smooth, rounded papillae protruding from a thick inner surface “lining”
- Moderate amount of vessels in papillae
- As pregnancy progresses picture returns to the basic character of the preexisting EOMa

Make everything possible to obtain reliable history, previous US images, laparoscopy results etc. A proven diagnosis of endometriosis by the above saves surgery during pregnancy!!

“DIAGNOSTIC POINTERS“

Decidualized Endometrioma vs Ovarian Cancer

- Shallow, rounded papillae versus large irregular (cauliflower shaped) papillae protruding from the inner surface

Several ovarian cysts with nodules

What do they have in common?

- They have echogenic, shadowing nodules

An example:
What next?

Apply power Doppler!!

The ultimate proof:
following is a series of ovarian
cysts with nodules with their
histology
All the above were histologically proven benign cystadenofibromas.

Question: do they undergo changes in appearance and/or size?
**Is there another variety of benign fibromas in the ovary?**

Answer: not really!

**Non-neoplastic ovarian cysts**
These are by far the most common cysts.

**Ovarian fibroma**
- Benign ovarian tumor

**Cystic**
- Hyperechoic, shadowing mural papilla/e
- Avascular papillae
- Anechoic fluid
- Mostly unilocular
- Thin wall, thin septae
- Slow rate of growth

**Solid**
- Hypoechoic mass with strong acoustic shadowing
- Myometrium-like stroma
- They tend to have minimal vascularity interrogated with color Doppler US
- Almost certainly benign
- Slow rate of growth

**Solid Fibroma Ovarii**
- Hypoechoic
- Shadowing
- Poor vessel content

**Finally, the secret to the Dx.**
- Turn on POWER Doppler NOT Color Doppler (Power Doppler is more sensitive)
- Use the smallest possible ROI for the Doppler search
- Use the lowest possible PRF, just before artifacts start to appear.
Third: papillae in a cyst

An example:

Papilla with blood flow

Let us analyze this image

Paraovarian cyst with papilla

Attention: paraovarian cysts may have papillae. If they do, look for blood vessels. If they have, it may be a reason to remove them

Diagnosis

- Paraovarian/paratubal cyst (you were right)
- Low Malignant potential changes in the papilla
- Remember: paraovarian cysts may have LMP areas
Which leads me into the borderline tumors of LMP

In a significant number of cases, mostly in reproductive age women, cysts with vascular papillae are borderline ovarian tumors of low malignant potential

Why is it important to mention this kind of ovarian tumor?

Only two “word slides”.....

General

- Borderline Ovarian Tumors (BOT) or tumors of Low Malignant Potential (LMP) are:
  - epithelial tumors (serous=50%; mucinous= 46%)
  - have a slow growth & low invasive potential
  - are often diagnosed at an earlier stage than invasive Ca.
  - have good prognosis, present as: Stage I=70%; Stage II=10%;
  - tend to occur in younger women
  - 5 y. survival rate is ≈95%
- Because of all the above, fertility sparing conservative treatments have been proposed
- Some suggest endoscopic approach after surgical staging

Conclusions

- Although the correlation of stage with survival was mixed, performing staging procedures for low malignant potential ovarian tumors is not supported by the best available evidence. Guidelines in support of staging based their recommendations on a few regional studies and conflict with better-quality data that do not support staging procedures. An international consensus statement is needed to standardize the surgical management of low malignant potential ovarian tumors.
This study systematically reviews the literature for the accuracy of TVUS, MRI and CT in the diagnostic of BOTs.

- Search in PubMed/Medline of articles in English from the last 5 years and included 14 studies for systematic review, 9 of them meta-analysis.
- The pooled sensitivity and specificity was respectively:
  - 77.0% and 83.0% for TVUS (5 studies) and
  - 85% and 74% for MRI (4 studies) in differentiating benign from malignant BOTs.
- 4 CT studies have also shown a high accuracy in differentiating BOTs from malignant ovarian cancers.

**METHODS**

**OBJECTIVE**

To determine if there are any features that can help discriminate between benign and malignant BOTs.

**MATERIAL AND METHODS**

- A historical cohort study of consecutive borderline ovarian tumors cases treated at a single institution over 30 years (1981–2011).
- Data on surgical approach (fertility sparing or otherwise), disease stage, CA125 levels, histological features, adjuvant treatment and follow-up data were collected.
- RESULTS: 213 patients were included.
- Of 132 women age 40 years and below at diagnosis, 112 (85%) had fertility-preserving procedures (90% had conservation of an ovary.
- Fifty patients (24%) developed recurrences; (hazard ratio = 2.57; 95% confidence interval 1.1–6.0) and advanced stage (hazard ratio = 4.15; 95% confidence interval 2.3–7.6 p < 0.001) were independently associated with recurrence on multivariate analysis.
- Eleven (5%) patients died of their disease.
- Fertility preservation was not associated with compromised survival.
- CONCLUSIONS: Borderline ovarian tumors carry a good prognosis overall.
- Fertility preservation is associated with a higher risk of disease relapse; however, most relapses are localized and may be salvaged with surgical treatment.
- Overall survival is not compromised.

**OBJECTIVES**

- Fertility preservation in women with borderline ovarian tumors - how does it impact disease outcome? A cohort study.

**MATERIAL AND METHODS**

- 204 masses included, of which:
  - 131 (64%) were benign,
  - 42 (20.5%) were borderline tumors,
  - 31 (15%) primary invasive and
  - one (0.5%) was a metastasis.

**RESULTS**

- Multivariate logistic regression analysis showed the following US features to be independently associated with malignancy:
  - the height of the largest papillations
  - blood flow in papillations.
  - papillation confluence or papillation dissemination, and
  - shadows behind papillations.

**CONCLUSIONS**

- We have identified US features that can help discriminate between benign and malignant unilocular solid cysts with papillations but no other solid components.
- Our results need to be confirmed in prospective studies.
What are the sonographic characteristics of BOTs?

Exacoustos C et al, Sonographic appearance of borderline ovarian tumors.

- The most frequent diagnostic feature on imaging BOT is the presence of papillae within the cyst. However, neither papillae nor other sonographic features constituted highly sensitive sonographic markers of BOT. (Doppler was NOT used)


Alfuhaid TR et al. Low malignant potential tumor of the ovary: Sonographic features with clinicopathologic correlation in 41 patients

Shape and size variations

Morphologic variations

- Wide variety of morphologies
- Only 35.3% had a unique appearance—a cyst within the ovary of small to medium size with vascular mural

Our NEW observation regarding US characteristics of BOT of LMP

- Low-power microscopic, histology pictures were obtained of 71 ovarian masses with proven BOT-LMP
- Before surgery TV-US performed by 5-9 MHz probes
- US images were juxtaposed and compared to the microscopic pictures
- Histologic diagnosis of 10 ovaries was BOT, however 1-5% of their areas demonstrated features of epithelial cancer, these were analyzed separately, therefore…
- …61 US/histology pairs were analyzed for US features of adnexal masses applying the IOTA “simple rules”

New observation regarding US characteristics of BOT of LMP

- 61 BOT c. LMP with histologic confirmation
- Unilocular 31 (50.8%)
- Multilocular 30 (49.1%)
- Septae 44 (72.1%)
- Solid component present 52 (83.8%)
- Papilla/e ≤7mm 31 (50.8%)
- Microcystic appearance 51 (83.8%)

What are these “microcysts”? and how do they look?

A new sonographic descriptor of Borderline ovarian tumors of low malignant potential

- As we evaluated the sonographic appearance of the 61 histologically proven BOT with LMPs a unique feature became increasingly evident.
- A number of the papillae, solid components of different sizes demonstrated a microcystic texture.
- These microcysts measured between 1 and 3mm.

One more observation

Do I have false positives? Yes I do!
Here is one:

Histologic Dx: Benign cystadenofibroma

Morale: 1. Pay MORE attention to the sono characteristics
2. If in doubt rescan in 1-2 months
Technical aspects: Here to help!

Again: the most efficient pelvic evaluation is by using high frequency transvaginal probes.

For structures 6-7 cm away use 5-8/5-9MHz probes.
If they are small and only 4-7 cm away, it is worth the trouble to plug in a higher frequency probe (use 6-12MHz). You will be rewarded by clearer images!

Technical aspects
Use the “Sliding organs sign”

Generated by the intermittent pressure of the vaginal probe moving the cervix, ovaries, uterus back and forth to evaluate their movement relative to the pelvic floor and/or each other. Useful to diagnose or rule out pelvic adhesions.

Timor-Tritsch IE and Rottem S Elsevier Science Publishing Co. New York 1988; Pages 24,35,52,55,72,84

Sliding organs sign

Important in patients with infertility, endometriosis or suspect for a frozen pelvis

Positive sliding organs sign (normal):

Uterus and cul-de-sac

Test for pain with the transvaginal probe

- Every fifth patient scanned by us is referred for “pelvic pain” or a combination of pain and something else
- Touch and press against the ovaries, adnexae and cervix while watching the patient’s face for a possible pain reaction and asking her if “this is the pain” for which she has the scan


Positive sliding organs sign (normal):

Normal right ovary Normal left ovary

At the same time also test for pain (Endometriosis? Torsion?)

Timor-Tritsch IE and Rottem S Elsevier Science Publishing Co. New York 1988; Pages 24,35,52,55,72,84
Record the mobility or fixed nature of pelvic organs

- Add credibility to your report!
- Acquire and save “sweeps” of the adnexae

The “jiggling” blood clot in a hemorrhagic CL

Most common mistake: calling it suspicious for malignancy. Solution: scan patients between days 5-9 of their period!!

Advise to find postmenopausal ovaries

- Harder to find (no, or rare follicles as markers).
- Linger on the adnexae & look for hypoechoic, 1-3 cm structures amidst constantly moving bowel.

Steroid cell tumors

- Rare, found usually by their clinical presentation & laboratory tests

7. The Fallopian tube

The normal and abnormal Fallopian tube

- A normal Fallopian tube is almost impossible to detect sonographically, unless it is surrounded by pelvic fluid, or, fluid is injected in it (hydrosonography)
- However, tubal pathologies can be detected and diagnosed by gray scale and color Doppler transvaginal US

7.2. Tubal carcinoma

- Primary fallopian tube cancer is the rarest among female genital tract cancers.
- It accounts for 0.3% to 1.8% of these cancers.
- Papillary serous adeno-carcinoma represents more than 90% of these cancers [2, 3].
- Other less common types include clear cell carcinoma, endometroid cancer, germ cell cancers, and sarcoma.
Tubal carcinoma

8. Additional sites to check

Look at the cul-de-sac

Postoperative peritoneal inclusion cysts in loculated pelvic fluid

- The Dx should be suspected in the right clinical setting.
- Dx depends on the presence of filmy, undulating strings of adhesions within surrounding loculated fluid confined to the intra-peritoneal space.


Cul-de-sac/pelvic peritoneum

Tumor seedings
The New Consensus Panel Recommendations

The AIUM convened a group of experts as well representatives of the involved and pertinent professional governing bodies to hold a consensus conference on the subject of imaging and managing adnexal masses.

The content of the following slides show the results of the agreed upon features of the adnexa/e

Adnexal Mass Consensus Recommendations

1. Pelvic sonography should include the transvaginal approach with Doppler imaging as indicated.

2. Simple ovarian cysts are not precursor lesions to malignant ovarian cancer; however, it is crucial to perform a high-quality examination to ensure the absence of any solid/papillary structures before designating it a simple cyst. The risk of progression to malignancy is extremely low; thus, a degree of follow-up is prudent.

3. Real-time pattern recognition sonography in the hands of an experienced imager is currently the most accurate method of characterizing an ovarian mass.

4. Initial mass characterization could be performed either by pattern recognition or via a risk model such as the IOTA Simple Rules.

5. When an ovarian lesion is considered benign, the patient may be followed conservatively, or if indicated, surgery can be performed by a general gynecologist.

6. Serial sonography is a beneficial strategy, but there are limited prospective data to support an exact interval and duration.

7. Fewer surgical interventions may well result in an increase in sonographic surveillance.

8. When an ovarian lesion is considered indeterminate on initial sonography, and after appropriate clinical evaluation, a "second-step" evaluation may include: referral to an expert sonologist, serial sonography, application of established risk prediction models, correlation with serum biomarkers, correlation with MRI, or referral to gynecologic oncologist for further evaluation.

9. Summary and conclusions
Summary and conclusions

- Most of the time adnexal masses carry defined sono characteristics and pathognomonic features (markers)
- The major, refined sono-markers of adnexal masses were described to enable a better recognition of their possible histology
- Where applicable, relevant articles from the contemporary literature were quoted

Conclusions

- Most adnexal masses can be assessed subjectively using:
  - Hi frequency TV-US probes (TA if large mass)
  - An enhanced basic US knowledge
  - Liberal use of power Doppler
  - IOTA simple rules: **Benign and malignant US markers**
- For my friends in radiology:
  - If you like to use the term: "complex mass", please describe it in terms of their sonographic character (based on the new consensus data or IOTA "simple rules")
  - You help the gyn by focusing on minimal # of Diff. Dx-ese

Avoid the word “cyst” referring to follicles or corpora lutea: Define them!!

Be attuned to the issues of nodules/papillae in a cyst (size, shape, echogenicity, shadowing, blood vessels in it)

Avoid the sentence: “…malignancy can not be ruled out”! It sentences patients to surgery!!

Use: "My suspicion of the structure to be malignant is: high, moderate, low, none or can not classify" ADD: "I favor xyz..diagnosis"

Ask for MRI or Gyn Onc only if really needed

Key References

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- John R van Nagell Jr, Miller, RW. Management of Asymptomatic Ovarian Tumors Obstet Gynecol 2016;127:848-58
- Fruscella E et al. Sonographic features of decidualized ovarian endometriosis suspicious for malignancy. JOG 2004; 58:1-3