Approach to Patients with an Adnexal Masses

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Background

Prevalence of specific adnexal mass pathologies in patients in the International Ovarian Tumor Analysis group (IOTA) study (n = 4848)

All benign pathologies	**3183 (65.7)**
Endometrioma	845 (17.4)
Benign teratoma (dermoid)	512 (10.6)
Simple/parasalpingeal cyst	285 (5.9)
Functional cyst	128 (2.6)
Hydrosalpinx	112 (2.3)
Peritoneal pseudocyst	34 (0.7)
Abscess	45 (0.9)
Fibroma	245 (5.1)
Serous cystadenoma	543 (11.2)
Mucinous cystadenoma	359 (7.4)
Rare benign pathologies	75 (1.5)

All malignant pathologies	**1665 (34.3)**
Primary invasive stage I	222 (4.6)
Primary invasive stage II	82 (1.7)
Primary invasive stage III	658 (13.6)
Primary invasive stage IV	102 (2.1)
Rare primary invasive pathologies*	113 (2.3)
Borderline stage I	249 (5.1)
Borderline stage II	9 (0.2)
Borderline stage III	25 (0.5)
Borderline stage IV	1 (0.02)
Secondary metastatic cancer	204 (4.2)

Presentation

- Incidental finding
- Symptoms
  - Pain (pelvic area, often unilateral)
  - Fullness
  - Early satiety, nausea, vomiting
  - Constipation
  - Changes in bladder habits (frequent urination, difficulty urinating)
  - AUB, PMB
  - Dyspareunia
  - Weight loss
  - Fever

Work Up - History

- Medical history
- Gynecologic history
  - Menstrual history
  - Characteristics of pelvic pain
  - Sexual history
  - Presence /absence of infertility
- Family history
  - Ovarian, breast, endometrial, colon cancer or genetic syndromes
- Social history
  - Smoking
- All in consideration with pt age

Risk factors for ovarian cancer

	Relative risk	Lifetime probability (%)[1]
General population	1.0	1.3[1]
***BRCA1* gene mutation**		35 to 46[2,3]
***BRCA2* gene mutation**		13 to 23[2,3]
Lynch syndrome (hereditary nonpolyposis colon cancer)		3 to 14[4,5]
Other gene mutations		
BRIP1		5.8[6]
RAD51C		5.2[7]
RAD51D		12[7]
Family history of ovarian or fallopian tube cancer (with negative testing for a familial ovarian cancer syndrome)	Uncertain[8]	
Infertility	2.67[9]	
Endometriosis (increase in risk of clear cell, endometrioid, or low-grade serous carcinomas)	2.04 to 3.05[10]	
Cigarette smoking (increase in risk of mucinous carcinoma)	2.1[11]	
Intrauterine device	0.68[12]	
Past use of oral contraceptives	0.73[13]	
Past breastfeeding (for >12 months)	0.72[14]	
Tubal ligation	0.69[15]	
Previous pregnancy	0.71[16]	

Work Up - Physical Exam

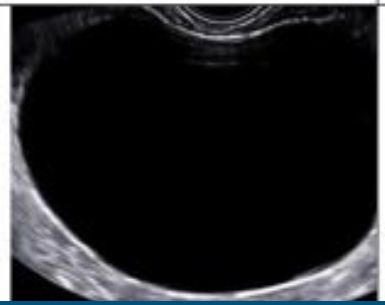
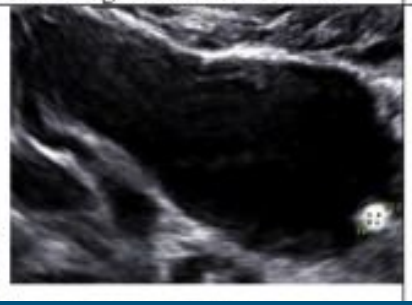
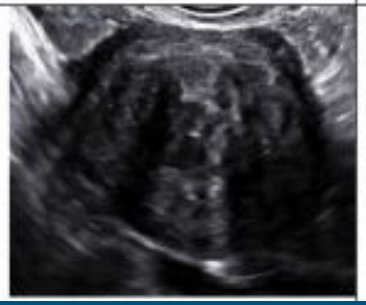
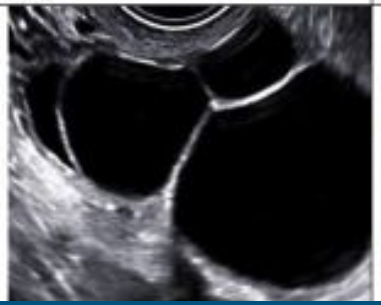
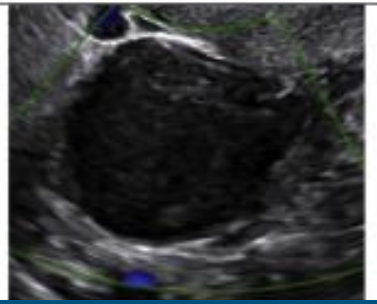
- General appearance
- Cardiopulmonary auscultation
- Abdominal exam
  - Note distention, ascites, masses
- Assess for signs of hormonal ovarian mass
  - Virilization (facial hair, male-pattern baldness, acne, deeper voice, enlarged clitoris, irregular menstruation) or elevated estrogen (ex vaginal bleeding from endometrial hyperplasia)
- Lymph nodes
  - Cervical, supraclavicular, axillary, and groin
- Pelvic exam
  - Assess size, consistency (firmness, nodularity, irregularity), and mobility of mass if palpable
  - Examine other pelvic structures (perineum, cervix, vagina, uterus)

Work Up - Imaging

- TVUS
  - Pelvic exam shown to have limited ability to identify an adnexal mass in BMI>30, any suspicion confirmed with imaging
  - Asses size and composition of mass (cystic, solid, mixed), laterality, presence/absence of septations, mural nodules, papillary projections, free fluid in pelvis
  - Color doppler US to assess vascular characteristics
- CT, MRI, PET not recommended as first line
  - MRI can help differentiate origin of mass if unclear or if mass has indeterminate features on ultrasound
  - CT can help evaluate abdomen for mets (noninvasive staging), peritoneal implants, pelvic or paraaortic lymph node involvement, ascites, obstructive uropathy, and possibly detect alternate primary cancer site

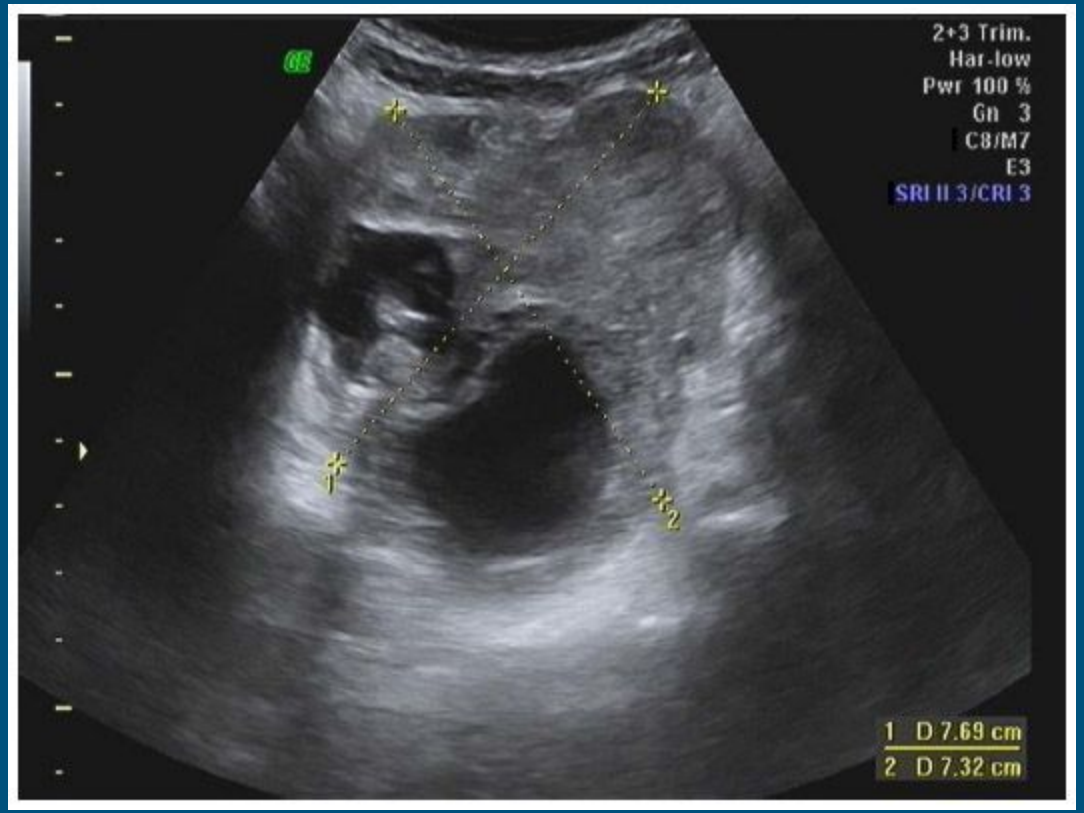
TVUS - Benign Features

- Simple appearance: thin, smooth walls
- Sonolucent/hypoechoic
- Absence of solid components, septations or solid components with diameter <7mm, thin septations
- Absence of internal blood flow on color doppler

B1 Unilocular cyst	B2 Presence of solid components where the largest solid component has a largest diameter < 7 mm	B3 Presence of acoustic shadows	B4 Smooth multilocular tumor with largest diameter < 100 mm	B5 No blood flow (color score 1)
				

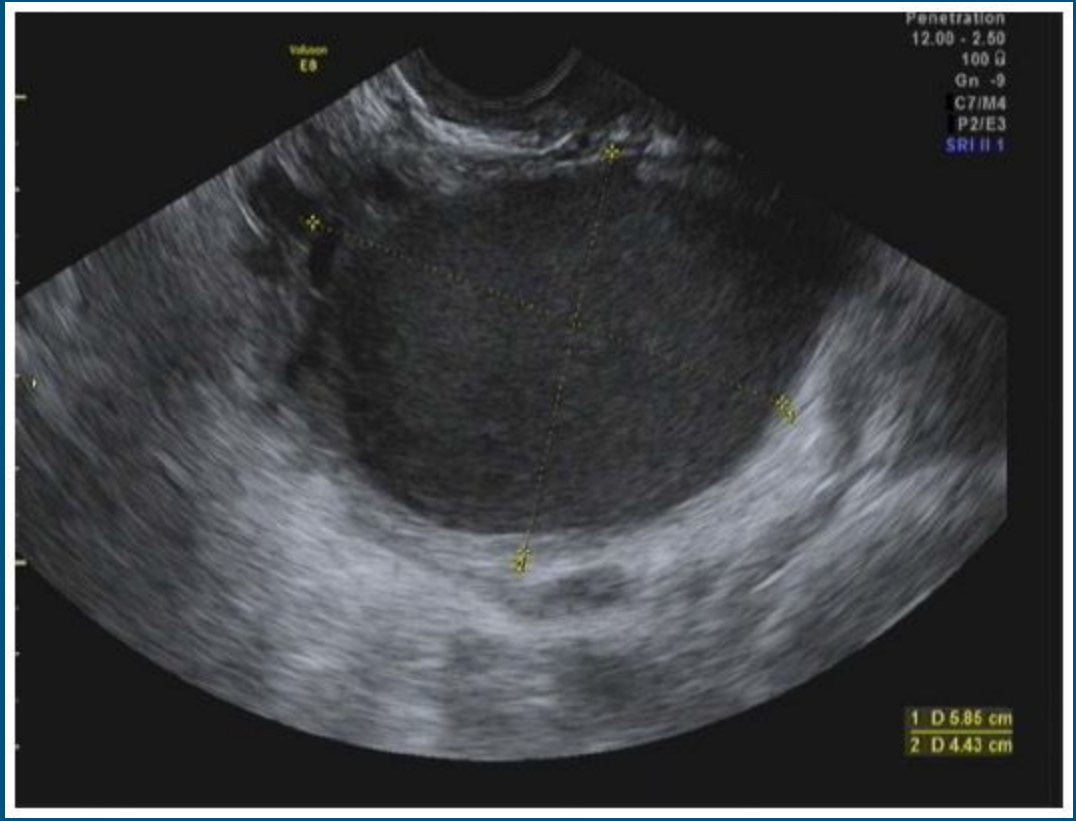
Benign cystic teratoma

- Hypoechoic attenuating component with multiple small homogeneous interfaces→ mature teratoma (58% sensitivity and 99% specificity)



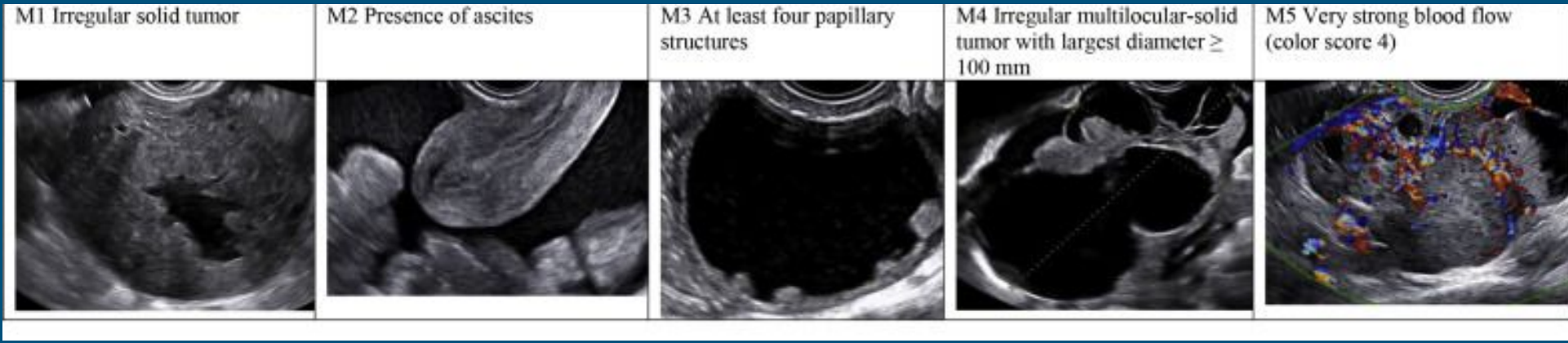
Endometrioma

- Round homogenous-appearing cyst with low-level echoes within the ovary→ endometrioma (83% sensitivity and 89% specificity)

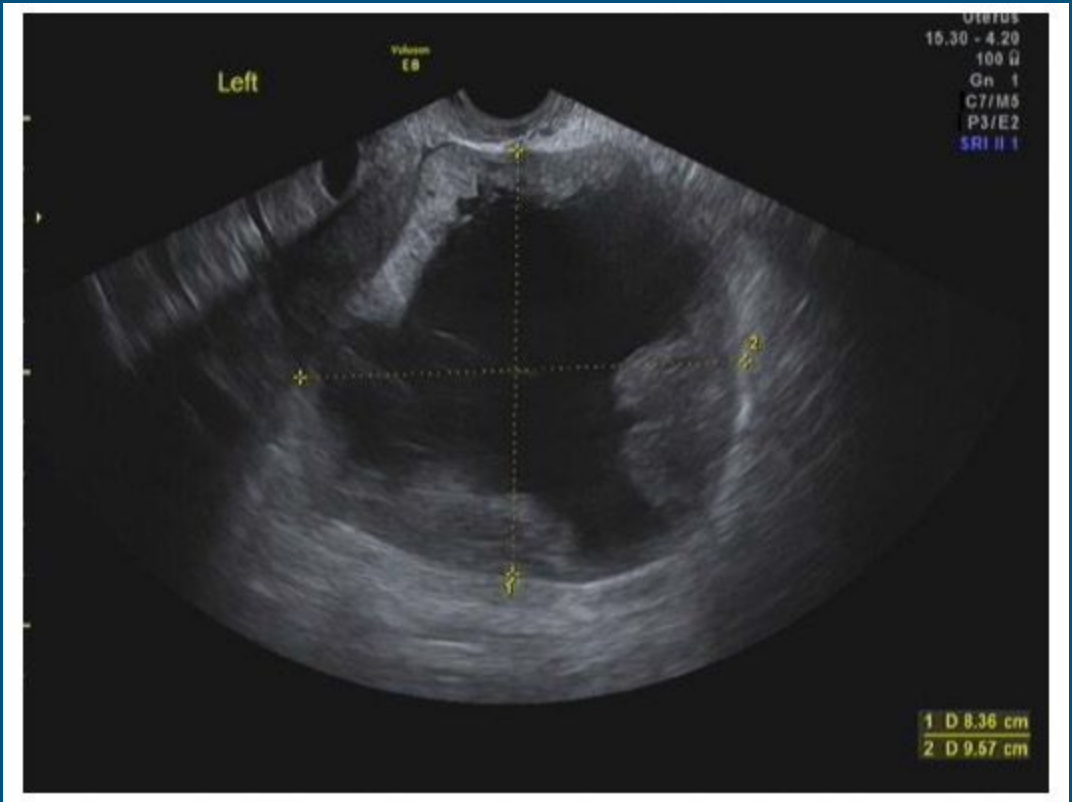


TVUS - Malignant features

- Thick septations (>2-3mm)
- Papillary or solid components
- Irregular shape
- Greater than 10 cm in diameter
- Cyst wall thickening
- Ascites
- High color doppler flow
- Poorly defined margins



Adenocarcinoma of ovary



International Ovarian Tumor Analysis (IOTA) Simple Rules

- If ovarian lesion has at least one benign feature and no malignant features, it can be considered benign
- If ovarian lesion has at least one malignant feature and no benign features, it can be confidently considered malignant

Emerging Classification System for American College of Radiology (O-RADS)

O-RADs risk stratification and management system

O-RADS score	Risk category (IOTA model)	Lexicon descriptors		Management	
				Pre-menopausal	Post-menopausal
0	Incomplete evaluation (N/A)	N/A		Repeat study or alternate study	
1	Normal ovary (N/A)	Follicle defined as a simple cyst ≤3 cm		None	N/A
		Corpus luteum ≤3 cm			
2	Almost certainly benign (<1%)	Simple cyst	≤3 cm	N/A	None
			>3 to 5 cm	None	Follow up in 1 year*
			>5 cm but <10 cm	Follow up in 8 to 12 weeks	
		Classic benign lesions	Refer to figure 3¶ for separate descriptors	Refer to figure 3¶ for management strategies	
		Non-simple unilocular cyst, smooth inner margin	≤3 cm	None	Follow up in 1 year If concerning, US specialist or MRI
			>3 cm but <10 cm	Follow-up in 8 to 12 weeks If concerning, US specialist	US specialist or MRI
3	Low risk malignancy (1 to <10%)	Unilocular cyst ≥10 cm (simple or non-simple)		US specialist or MRI	
		Typical dermoid cysts, endometriomas, hemorrhagic cysts ≥10 cm		Management by gynecologist	
		Unilocular cyst, any size with irregular inner wall <3 mm height			
		Multilocular cyst <10 cm, smooth inner wall, CS = 1 to 3			
		Solid smooth, any size, CS = 1			
4	Intermediate risk (10 to <50%)	Multilocular cyst, no solid component	≥10 cm, smooth inner wall, CS = 1 to 3	US specialist or MRI Management by gynecologist with GYN-oncologist consultation or solely by GYN-oncologist	
			Any size, smooth inner wall, CS = 4		
			Any size, irregular inner wall and/or irregular septation, any color score		
		Unilocular cyst with solid component	Any size, 0 to 3 papillary projections, CS = any		
		Multilocular cyst with solid component	Any size, CS = 1 to 2		
		Solid	Smooth, any size, CS = 2 to 3		
5	High risk (≥50%)	Unilocular cyst, any size, ≥4 papillary projections, CS = any		GYN-oncologist	
		Mullilocular cyst with solid component, any size, CS = 3 to 4			
		Solid smooth, any size, CS = 4			
		Solid irregular, any size, CS = any			
		Ascites and/or peritoneal nodules$^{\Delta}$			

Graphic shows O-RADS US risk stratification and management system.

Work Up - Labs

- Pregnancy test in reproductive age women
- CBC
  - Especially if febrile or infectious etiology is suspected
  - Hgb if having bleeding or to know baseline if surgery is possible
- Serum biomarkers

Work Up - Serum Biomarkers

- **Useful to monitor disease response to treatment**
- **CA 125**
  - Associated with epithelial ovarian malignancies
  - Endometriosis, leiomyoma, pregnancy, PID, cervical adenocarcinoma, cholangiocarcinoma, lymphomas (NHL), medical disorders with inflammatory component (SLE, IBDs)
- Human epididymis protein 4 (HE4)
  - Epithelial ovarian malignancies
- b-hCG, AFP, LDH, T, DHEA, AMH, inhibin, E2,
  - If germ cell/ sex cord stromal tumors are suspected (androgen or estrogen excess)
- CA 19-9, CEA
  - Mucinous ovarian tumors
  - Metastatic GI tumors

Work Up - Multimodal Tests (Epithelial Ovarian Cancer)

- **Risk of Ovarian Malignancy Algorithm (ROMA)**
  - CA 125, HE4, menopausal status
  - Algorithm not proprietary and may be determined with calculator, through websites, or on apps
    - **Premenopausal: high risk ≥13.1%**
    - **Postmenopausal: high risk ≥27.7%**
  - Note: ROMA has similar diagnostic performance compared with either CA 125 or HE4 alone for diagnoses of epithelial ovarian cancer
- **Multivariate Index Assay/ OVA1**
  - CA 125 II, beta 2 microglobulin upregulated
  - Transferrin, transthyretin (prealbumin), apolipoprotein A-1 downregulated
  - Utilizes algorithm to generate ovarian malignancy risk score (0-10)
    - **Premenopausal: OVA1 <5 low probability of malignancy, ≥5 high probability**
    - **Postmenupausal: OVA1 <4.4 low probability, ≥4.4 high probability**
  - Note: OVA1 appears to have better sensitivity for diagnosis of EOC but decrease in specificity
- **Overa/OVA2**
  - CA 125 II, human epididymis protein 4 (HE4), apolipoprotein A-1, FSH, transferrin
  - With FSH, determining menopausal satus is not required
  - Test uses same proprietary software as OVA1 and scoring (0-10)
    - **Low risk of malignancy <5, high risk ≥5**
  - Note: OVA2 has better test performance than OVA1 (similar sensitivity, higher specificity

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“Serum biomarker panels may be used as an alternative to CA 125 level alone in **determining the need for referral to or consultation with a gynecologic oncologist when an adnexal mass requires surgery**. These biomarker panels are **not recommended for use in the initial evaluation** of an adnexal mass, but may be helpful in assessing which women would benefit from referral to a gynecologic oncologist.”

When to Observe

- US suggests benign disease
- Normal CA 125 level and no suspicious US findings
- <10 cm simple cysts (even if postmenopausal, can be observed with repeat imaging)
- Benign disease
    - Endometriomas, mature teratomas, hydrosalpinx

When to Refer to Gyn Onc

- Postmenopausal with elevated CA 125 and suspicious ultrasound or clinical findings
- Premenopausal with very elevated CA 125 level and suspicious US or clinical findings
- Premenopausal or postmenopausal with elevated score on formal biomarker risk assessment test or US-based scoring systems from IOTA group

Sources

https://www.uptodate.com/contents/approach-to-the-patient-with-an-adnexal-mass?search=adnexal%20mass&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H2623255221

https://journals.lww.com/greenjournal/Fulltext/2016/11000/Practice_Bulletin_No__174__Evaluation_and.52.aspx

https://radiopaedia.org/articles/iota-ultrasound-rules-for-ovarian-masses?lang=us

https://www.ajog.org/article/S0002-9378%2817%2930861-X/fulltext

https://creogsovercoffee.com/notes/2019/8/11/adnexal-masses-part-1-imaging

https://www.iotagroup.org/research/iota-models-software/iota-simple-rules-and-srrisk-calculator-diagnose-ovarian-cancer

https://www.dovepress.com/assessment-of-adnexal-masses-using-ultrasound-a-practical-review-peer-reviewed-fulltext-article-IJWH

https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/jog.14427#:~:text=Serum%20CEA%20is%20also%20commonly,in%20mucinous%20epithelial%20ovarian%20tumor.&text=This%20study%20evaluated%20these%203,malignancy%20in%20mucinous%20ovarian%20tumors.

https://academic.oup.com/oncolo/article/9/4/417/6387584