Evidence Based Guidelines-Evaluation of adnexal mass

INTRODUCTION

Adnexal masses can be benign or malignant and their spectrum ranges from simple functional cysts to ovarian carcinomas. The clinical challenge lies in distinguishing between benign and malignant lesions to ensure timely intervention while avoiding unnecessary surgery.

## Purpose and scope

This guideline has been produced to provide information, based on clinical evidence, to assist clinicians with the initial assessment and appropriate management of suspected ovarian masses.

Evaluation of Adnexal mass

Evaluation involves a combination of history, physical examination, imaging techniques (especially ultrasound), and tumor markers. Management strategies depend on factors such as patients age, menopausal status, clinical presentation, and risk of malignancy.

Many ovarian masses in the premenopausal women can be managed conservatively. Functional or simple ovarian cysts (thin walled cysts without internal structures) which are less than 50 mm maximum diameter usually resolve over 2-3 menstrual cycles without the need for intervention.

# Types of adnexal masses

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| Benign ovarian Functional cysts  Endometriomas  Serous cystadenoma  Mucinous cystadenoma  Mature teratoma |
| Benign non ovarian Para tubal cyst  Hydro salpinges  Tubo-ovarian abscess  Peritoneal pseudocysts  Appendiceal abscess  Diverticular abscess  Pelvic kidney |
| Primary malignant ovarian Germ cell tumor  Epithelial carcinoma  Sex-cord tumor |
| Secondary malignant ovarian Predominantly breast and gastrointestinal |

A thorough medical history with specific attention to risk factors or protective factors for ovarian malignancy and a family history of ovarian or breast cancer.

A careful physical examination is essential and should include abdominal and vaginal examination and the presence or absence of local lymphadenopathy. In the acute presentation with pain the diagnosis of accident to the ovarian cyst should be considered (torsion, rupture, hemorrhage).

Although clinical examination has poor sensitivity in the detection of ovarian masses (15-51%) its importance lies in the evaluation of mass tenderness, mobility, nodularity and ascites.

# A Pelvic ultrasound is the single most effective way of evaluating an ovarian mass with transvaginal ultrasonography being preferable due to its increased sensitivity over transabdominal ultrasound.

At present the Risk of Malignancy Index (RMI) is the most widely used model but recent studies have shown a specific model of ultrasound parameters, the ultrasound rules derived from the International Ovarian Tumor Analysis(IOTA) Group,O-RADS to have increased sensitivity and specificity.

# Risk Of Malignancy Index

The RMI is simple to use and reproducible, but its utility is negatively affected in the premenopausal woman. This is primarily because of the incidence of endometriomas, borderline ovarian tumors, non-epithelial ovarian tumors and other pathologies increasing the level of CA-125 in this group.

# RMI sensitivity 78%, specificity 87%

# IMAGING

There are simple ultrasound rules derived from the IOTA Group. The use of specific ultrasound morphological findings without CA-125 has been shown to have high sensitivity, specificity and likelihood ratios.

If not clearly classifiable from these rules, further investigation by a specialist in gynaecological ultrasound is appropriate.

Simple ultrasound rules were developed to help classify masses as benign (B-rules) or malignant (M-rules). Using these rules the reported sensitivity was 95%, specificity 91%, positive likelihood ratio of 10.37 and negative likelihood ratio of 0.06.

# IOTA Simple Rules

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| Rules for predicting a malignant tumor (M-rules) | Rules for predicting a benign tumor (B-rules) |
| M1- Irregular solid tumor | B1- Unilocular cyst |
| M2- Presence of ascites | B2- Presence of solid component where largest solid component is less than 7mm in largest diameter |
| M3- At least 4 papillary structure | B3- Presence of acoustic shadows |
| M4- Irregular multilocular solid tumor with largest diameter greater 100mm | B4- Smooth multilocular tumor with largest diameter less than 100mm |
| M5- Very strong blood flow (color score 4) | B5- No blood flow (color score1) |

# IOTA LR1(Logistic Regression)-more sensitive

# Input Variables:

* The LR1 model has 12 specific variables. E.g. personal history of ovarian cancer, hormonal therapy use, lesion size, presence of blood flow.

# Calculation:

* These variables are fed into a formula that calculates a probability of malignancy.

# Outcome:

* A probability score is generated, which is then used to classify the mass as likely benign or malignant.

# IOTA LR2(Logistic Regression)-more specific

# Input Variables:

* The model considers AGE and five USG features.

# Predictive Power:

* It calculates a score that indicates the likelihood of the tumor being malignant.

# Purpose:

* LR2 helps classify adnexal masses as benign or malignant and can be used by non-expert examiners.

# The ADNEX Model

* Assessment of different neoplasias in the adnexa.
* The ADNEX Model was developed in 2014 by the IOTA group.
* To differentiate between benign, borderline tumors, stage1 invasive, stage 2-4 invasive ovarian cancer and secondary metastatic cancer.
* The model uses nine different predictors, three clinical and six ultrasound variables.

# Clinical variable

* Age
* Serum CA-125 level
* The type of center (oncology centers vs other hospitals)

# Ultrasound predictors

* Maximum diameter of the lesion
* The proportion of solid tissue
* More than ten cyst locules
* Number of papillary projections
* Acoustic shadows
* Ascites

# Comparisons of various model

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| Variable | RMI | IOTA-Simple Rules | IOTA-LR1 & LR2 | IOTA-ADNEX |
| Year Developed | 1990 | 2008 | 2013 | 2014 |
| Use | Used for discriminating benign and malignant adnexal masses | Use to predict malignancy peri-operatively | Use to predict likelihood of malignancy | Use to discriminate benign and malignant and also suggest stage of malignancy |
| System | RMI1, RMI2, RMI3, RMI4 | No different scoring system | LR1 and LR2 | Calculation is done with or without Serum CA-125 marker |
| Algorithm | The equation used is: the product of the menopausal status score(M), ultrasonographic score (U), and an absolute value of Serum CA-125 | The Simple Rules consist of five features typical for benign tumors(B-features) and five features typical for malignant tumors(M-features) | LR1 consists of 12 selected variables.A simpler version (LR2) uses six selected variables | The IOTA-ADNEX model uses three clinical features and six ultrasound parameters with or without Serum CA-125 marker |
| Results Interpretation | More than 200: high risk,25-200: intermediate risk, less than 25: low risk | Benign: Only B-features apply, Malignant: Only M-features apply, Inconclusive: No features apply or both B and M-features apply |  | Benign tumors, borderline tumors, early-stage primary cancers, late-stage primary cancers(stage 2-4), and secondary metastatic cancers |

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**O-RADS(Ovarian -Adnexal Reporting and Data System)**

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| * + **O-RADS** | * + **Risk category** | * + **Lexicon description** |
| * + **0** |  | * + **Incomplete evaluation** |
| * + **1** | * + **Normal ovary** | * + **Follicle≤ 3cm,corpus ≤3cm** |
| * + **2** | * + **Almost certainly benign(<1%)** | * + **1.Simple cyst<10cm**   + **2.Classic benign lesions:hemorrhagic (<10cm),mature teratoma (<10cm),endometrioma (<10cm ),paraovarian cyst (any size),peritoneal inclusion cyst(any size)hydrosalpinx(any size)**   + **3.Non -simple unilocular(smooth inner margin <10cm** |
| * + **3** | * + **Low risk malignancy(1%-10%)** | * + **1. Unilocular cyst≥10cm**   + **2.Typical dermoid cyst,endometriomas,hemorrhagic cyst≥10cm**   + **3. Unilocular cyst,any size,irregular inner wall(thickness<3mm)**   + **4.Multilocular cyst<10cm,smooth inner wall,CS=1-3**   + **5. Solid smooth, any size,CS=1** |
| * + **4** | * + **Intermediate risk(10%-50%)\_** | * + **1. Multilocular cyst with no solid component(≥10cm,smooth inner wall,CS=1-3;any size,smooth inner wall,CS=4;any size ,irregular inner wall and/ or irregular seoatation,any colour score)**   + **2.Unilocular cyst with solid component,any size,0-3 papillary projection(height>3mm),any colour score**   + **3Multilocular cyst with solid component,any size,CS=1-2**   + **4.Solid ,smooth, any size, CS=2-3** |
| * + **5** | * + **High risk(>50%)** | * + **1.Unilocular cyst, any size,≥ papillary projection, any color score**   + **2.Multilocular cyst with solid component, any size, CS=3-4**   + **3.Solid,smooth,any size, CS=4**   + **4.Solid irregular, any size, any color score**   + **5.Ascites and/or peritoneal deposits** |

# MRI

* Conventional MRI
* sensitivity of 92%(89-94%)
* Specificity of 88%(84-92%)

**O-RADS MR Scoring**

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| SCORE 1 |

No ovarian mass/extra-ovarian mass

Physiological findings in premenopausal women:Follicle <3cm,Haemorrhagic cyst <3cm or Corpus luteum <3cm

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| SCORE 2 | SCORE 3 | SCORE 4 | SCORE 5 |
| Simple unilocular cyst  Unilocular endometriotic cyst  Lesion with fat with out solid tissue except Rokitansky nodule  Solid dark-dark lesion  Hydrosalpinx  Paraovarian cyst | Proteinaceous,haemorrhagic, or mucinous unilocular cyst  Multilocular cyst of any type  Lesion with solid tissue showing low-risk uptake curve (TYPE 1)  Pyosalpinx  Haematosalpinx | Any lesion with solid tissue and intermediate risk uptake curve (TYPE 2)  If there is no dynamic study, solid tissue uptake less than the myometrium at 30-40 s  Lesion with fat,but with solid tissue (not Rokitansky nodule) | Any lesion with solid tissue and high risk uptake curve (TYPE 3)  If there is no dynamic study, solid tissue uptake greater than the mymetrium at 30-40 s  Peritoneal carcinomatosis |
| Cystic Lesions Dark-Dark Solid Mass | Cystic Lesions Solid Tissue With Low-Risk Curve | Solid Component With Intermediate Risk Curve | Solid Component With High Risk Curve  Carcinomatosis |

# Comparison of USG and MRI

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| Feature | Ultrasound | MRI |
| Primary role | First line imaging | Problem solving for indeterminate masses |
| Overall accuracy | Good to moderate performance using standardized models | High accuracy, superior to US for difficult cases |
| Strengths | Widely available, low cost, no ionizing radiation | Excellent soft tissue contrast, high specificity |
| Weaknesses | Operator dependent, lower specificity for indeterminate lesions | More expensive, less accessible, requires contrast for optimal characterization |
| Reporting system | IOTA models, O-RADS US | ADNEX MRI, O-RADS MRI |
| Decision making | Guides initial management, indicates need for advanced imaging | Confirms benignity or high suspicion of malignancy to guide surgical planning |

# Clinical Implication

# A structured, multi-step imaging approach is optimal for evaluating adnexal masses.

1. Initial US: The initial evaluation should be a TVS/TAS using a standardized reporting system like the IOTA-ADNEX or O-RADS US.
2. Referral for MRI: Masses that remain indeterminate after US, or those with features of malignancy, should be referred for MRI. This increases diagnostic confidence and can help avoid unnecessary surgery for benign lesions.
3. Referral to oncology: Patients with a high probability of malignancy based on US and MRI findings should be referred to a gynecologic oncologist for specialized management.

# TUMOR MARKERS:

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* A serum CA-125 assay is not necessary when a clear ultrasonographic diagnosis of a simple ovarian cyst has been made.
* If serum CA-125 assay more than 200 units/ml, discussion with a gynaecological oncologists is recommended.
* When serum CA-125 levels are raised, serial monitoring of CA-125 may be helpful as rapidly rising levels are more likely to be associated with malignancy than high levels which remain static.
* Lactate dehydrogenase (LDH), AFP and hCG should be measured in all women under age 40 with a complex ovarian mass because of the possibility of germ cell tumors.
* HE4 is a serum biomarker that can be elevated in epithelial ovarian cancer,particularly in serous and endometrioid subtypes.

It has higher specificity than CA-125, especially in distinguishing ovarian cancer from benign gynaecological conditions such as endometriosis fibriods.

## ROCA-Risk of Cancer Algorithm

* CA125 in women without ovarian cancer static or decreased with time whereas with malignancy level rises
* Low risk: Repeat CA125 after one year
* Intermediate risk: Repeat CA125 in 6-8 weeks
* Elevated risk: Referred for TVS

## ROMA-Risk of Ovarian Malignancy Algorithm

* CA-125 and HE4 along with menopausal status
* To assess the likelihood of epithelial ovarian cancer in women with adnexal masses.
* Sensitivity:89% and Specificity:75%

## CONCLUSION

Ovarian cancer evaluation emphasizes a multidisciplinary approach, using the Risk of Malignancy Index (RMI) combining CA125 levels, menopausal status, and transvaginal ultrasound for risk stratification.

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