

Pre-operative assessment of adnexal mass

Abstract

Adnexal masses are tumors which may be located either in the ovary or the fallopian tubes or the surrounding connective tissue, i.e. mesosalpinx, the mesovarian section and the broad ligament. It is a common gynecological issue. Thus a previous determination of the benignity or malignancy risk is essential for a subsequently careful management. There is a variety of radiological approaches, biomarkers or clinically pre-surgical procedures and predictive models studied and validated all over the world in order to differentiate the etiology of adnexal masses. Dr. J. Kaijser and his clinical research team conducted a systematic review and meta-analysis over the use of mathematically predictive models of diagnosis beforehand of adnexal masses. Nowadays the analysis of different studies and systematic reviews prove that both IOTA LR2 and *Simple Rules* are the best diagnostic approaches available in the preoperatively differentiation of both benign and malignant adnexal masses. Such disquisition is vitally important for women of reproductive age, as it deals with fertility preservation. Furthermore, having obtained predictive outcomes over benign diseases, women are more likely to be treated by obstetrician-gynecologists (OB-GYN) or in general hospitals and patients given a diagnostically suspected malignancy would be referred to and treated by gynecologic oncologists.

Keywords: Adnexal mass, predictive model, ovarian cancer

Introduction

Adnexal masses are tumors which may be located either in the ovary or the fallopian tubes or the surrounding connective tissue, i.e. mesosalpinx, mesovarian section and broad ligament, being a relatively common gynecological issue. When a woman is diagnosed with an adnexal mass adnexal, it is very important for doctors to define whether they are dealing with a benign illness, i.e. endometriosis, cystadenomas -among others- or an ovary cancer since the illness treatment and prognosis drastically change in both cases. According to the last 2010-2012 Metropolitan Lima Cancer Record, the ovary cancer is placed ninth among the most common tumors affecting female population in Peru, with a 7.73 Standardized Age Rate out of 100,000 women and a 3.57 Mortality Rate out of 100,000 women.¹ Women diagnosed with ovary cancer have subtle and unspecified symptoms such as abdominal pain, polaquiuria, intestinal discomfort, which makes ovary cancer diagnosis difficult.^{2,3}

In the last few years in many countries clinical guides to cancer treatment recommend that patients with adnexal masses and posing a high malignancy risk are to be referred to a gynecologic oncologist.⁴ A wide variety of radiological procedures, biomarkers or clinically pre-surgical procedures have been studied and validated worldwide in order to differentiate benign adnexal masses from those in suspicious cancer.⁵ Different studies have proven that survival rates for patients with initially ovarian cancer are better when the surgery is carried out by a gynecologic oncologist.⁶⁻¹⁰

Different predictive models of diagnosis help doctors to make a suitable triage in order to decide on the best treatment. However, neither of them has been universally accepted by clinically everyday practice. In fact, clinical guides of the National Institute of Clinical Excellence and Royal College of Obstetrics and Gynecology suggest utilizing the Risk of Malignancy Index (RMI) as a primarily diagnostic tool in the United Kingdom. Whereas in other countries, the use of biomarkers in combination with algorithms is strongly recommended such as the ROMA -Risk of Ovarian Malignancy Algorithm- one in

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clinical practice. Other guides suggest utilizing ultrasound screening and clinical models, i.e. IOTA - LR2.^{11,12}

The aim of the article herein is to update different diagnostic approaches for the pre-surgical assessment of adnexal masses.

Ultrasound screening- MRI and CA 125

Results suggest that the 3D-ultrasound screening has better sensitivity and specificity in relation to that of the 2D one.¹³ The adnexal mass assessment by performing a color Doppler study does not have a bigger sensitivity or specificity than that of simple ultrasonography. Furthermore, an exact diagnosis only based on Doppler studies may derive on distortion of the results due to superimposition of vascular parameters between malign and benign masses.¹⁴

Of all imaging methods, MRI has the best results, however with no significant difference in relation to CAT scan technology. On the other hand, the CA 125 screening measurement is the least reliable among the different assessment methods due to variations shown in pre- and post-menopausal women even if they are suffering from malign or benign illnesses.^{15,16}

Predictive models

Dr. J. Kaijser and his clinical research team conducted a systematic review and meta-analysis over the use of mathematically predictive models of presurgical diagnosis of adnexal masses (Table 1).¹⁷ All predictive models were classified on the basis of type of model, i.e. morphologically scoring systems, Risk of Malignancy Index -RMI, logistical regression as well as ultrasound ruling and biomarking-ROMA. Table 2 below shows sensitivity and specificity of the various models with their different cut sections and a 95%-confidence interval. Unlike other models, ROMA takes account of different cut sections for pre- and post-menopausal patients. In addition, such values change by being subject to the type of kit utilized in the measurement of serum CA125 and HE4 levels (Chart 3).

Table I Prediction Models

Model^a	Model type	Variables	Cut level	Number of validation studies^b	Number of adnexal masses
Tailor	Logistical Regression	(i) Papillas, (ii) age (iii) time average of maximum speed in tumor vessels	50%	6	2527
LRa	Logistical Regression	(ii) Color scoring, (ii) CA125 (iii) papillas (iv) menopause scoring	25%	3	1888
LRb	Logistical Regression	(i) Papillas, (ii) inner wall (iii) unilocular cyst (iv) ascites (v) bilateralism (vi) menopause (vii) CA125 scoring	60%	5	2155
Jokubkiene	Logistical Regression	(i) Lesion size (3-diameter average) (ii) biggest solid part size (3-diameter average) (iii) any irregularity	12%	2	2043
Prompeler	Logistical Regression	(i) Ascites, (ii) shadowless solid lesion (iii) a 30%-solid-part cyst (iv) lesion diameter (v) multilocularity (vi) cyst surface	10%	2	1236
IOTA LR2	Logistical Regression	(i) Age (ii) ascites (iii) blood flow inside a papillary projection (iv) maximal diameter of biggest solid part (contained in 50 mm) (v) irregular inner cystic wallacoustic (vi) acoustic shadows	10%	3	1356
Ferrazzi	Morphologic Score	(i) Wall structure (ii) septum (iii) vegetation (iv) echogenicity	9	9	1814
Depriest	Morphologic score	(i) Cyst volume (ii)wall structure (iii) septal structure	5	10	1957
Lerner	Morphologic Score	(i) Wall structure (ii) acoustic shadows (iii) septum (iv) echogenicity	3	10	3035
Sassone	Morphologic Score	(i) Inner wall structure (ii) wall thickness (iii) septum (iv) echogenicity	9	21	2981
RMI I	Multimodal Scoring System	(i) menopausal state (ii) CA125 (iii) multilocular cyst (iv) solid areas (v) metastasis (vi) ascites (vii) bilaterality	200	35	9597
RMI II	Multimodal Scoring System	(i) Similar to RMI I	200	18	4772
RMI III	Multimodal Scoring System	(i) Similar to RMI I	200	14	5169
RMI IV	Multimodal Scoring System	(i) Menopausal state (ii) CA125 (iii) multilocular cyst (iv) solid areas (v) metastasis (vi) ascites (vii) bilaterality (viii) biggest lesion diameter	450	5	2191
ANN1	Artificial Neural Network	(i) Papillas, (ii) color score (iii) menopausal (iv) CA125	45%	3	1976
ANN2	Artificial Neural Network	(i) Papillas, (ii) smooth surface (iii) unilocularity(iv) ascites (v) bilaterality (vi) menopausal state (vii) CA125	60%	4	2055
Simple Rulesc	Ultrasound Rules	Criterion M: (irregular solid mass, 4-score colo, irregularly multilocular solid mass ≥100 mm, ascites, at least 4 papillary structures); criterion B: (unilocular cyst, 1-color score, multilocular smooth cyst with a bigger diameter than 100 mm, acoustic shadow presence, solid part presence where the biggest solid parthas a diameter bigger than 7mm)	n/a	5	2315
ROMAd	Bioscoring Algorithm	(i) CA125 (ii) HE4 (iii) menopausal state	n/a	18	5116
OVA-1e	Bioscoring Algorithm	(i) CA125 (ii) transferrin (iii) transthyretin (pre-albumin) (iv) A1 protei apolyp (v) beta- 2 microglobulin	n/a	2	1018

LRa, logistical regression model a; LRb, logistical regression model b; IOTA LR2, logistical regression model 2 of the International ovarian tumor analysis Stud; RMI, risk of malignancy index; ANN, artificial neural networkl; ROMA, risk of ovarian malignancy algorithm

a Original Model Publicatio.

b Included in the quantitative data synthesis.

c For Simple Rules, slightly conclusive cases are categorized as malign.

d The cut value is independent of the utilized test type.

e The cut value is different for pre- and post-menopausal women.

Obtained from: <http://humupd.oxfordjournals.org/>at Aston University on January 26th, 2014

Table 2 Summary of Contained (Sensitivity and Specificity) Estimates and 95%-Confidence Intervals

Model	Cut	Study(n)	Centers^a (n)	Sensitivity	Specificity
Morphological Punctuation Systems					
Sassone	9	19	19	0.85 [0.77;0.90]	0.80 [0.73;0.86]
Lerner	3	9	17	0.80 [0.70;0.86]	0.61 [0.53;0.68]
Depriest	5	8	8	0.90 [0.81;0.95]	0.68 [0.57;0.77]
Ferrazzi	9	7	7	0.86 [0.77;0.91]	0.80 [0.66;0.89]
Ultrasound Rules					
Simple Rules	n/a ^b	5	17	0.93 [0.89;0.95]	0.81 [0.76;0.85]
Risk of Malignancy Indexes (RMI)					
RMI I	200	23	41	0.72 [0.67;0.76]	0.92 [0.89;0.93]
RMI II	200	15	32	0.75 [0.69;0.80]	0.87 [0.84;0.90]
RMI III	200	9	19	0.70 [0.60;0.78]	0.91 [0.88;0.93]
RMI IV	450	3	13	0.68 [0.59;0.76]	0.94 [0.91;0.96]
Logistical Regression Models					
Tailor	50%	6	24	0.35 [0.24;0.49]	0.96 [0.94;0.98]
LRa	25%	3	20	0.76 [0.70;0.81]	0.87 [0.82;0.90]
LRb	60%	4	21	0.82 [0.77;0.86]	0.78 [0.73;0.83]
Prompeler	10%	2	10	0.61 [0.46;0.74]	0.81 [0.70;0.89]
Jokubkiene	12%	2	20	0.77 [0.71;0.82]	0.87 [0.83;0.89]
IOTA LR2	10%	3	13	0.92 [0.88;0.95]	0.83 [0.77;0.88]
Artificial Neural Network					
ANN1	45%	3	20	0.77 [0.71;0.82]	0.86 [0.80;0.90]
ANN2	60%	4	21	0.97 [0.95;0.98]	0.37 [0.31;0.44]

^aFor outcomes per specific center, herein are only shown centers on multicenter studies which contributed with at least 3 benign cases and 3 malign cases.

^bFor simple rules, slightly conclusive cases were categorized as malign.

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The *Simple Rules* ultrasound study and the IOTA LR2 logistical regression had the best results over sensitivity and specificity. Subjectivity and dependence on the ultrasound operators experience and skill are part of the criticisms leveled at the transvaginal ultrasonography as a diagnostic approach to women with adnexal masses. Thus the International Ovarian Tumor Analysis -IOTA- was aimed at solving such issue apart from developing models and rules

that enable less experienced operators to copy the “experts” results. The IOTA study developed simple rules and mathematical models based on logistical regression (LR 1-2), which are very easy to utilize in clinical practice in order to assess the malignancy risk of adnexal masses.¹⁸ Such models have been externally and exploratively validated by achieving extremely good outcomes, that is to say, close to those obtained by an expert ultrasound operator (Table 3).

Table 3 Roma Study

Roma study	Masses	Sensitivity	Limit of inferior confidence	Limit of superior confidence	Specificity	Limit of inferior confidence	Limit of superior confidence
Anton 2012	128	0.76	0.63	0.86	0.82	0.7	0.9
Jacob 2011	127	0.86	0.74	0.94	0.87	0.77	0.94
Lenhard 2011	427	0.77	0.69	0.83	0.95	0.92	0.97
Moore 2009	531	0.86	0.8	0.91	0.74	0.7	0.79
Moore 2011	472	0.81	0.71	0.88	0.75	0.7	0.79
Pitta 2013	176	0.57	0.43	0.69	0.88	0.81	0.93
Presl J 2012	552	0.8	0.61	0.92	0.85	0.82	0.88
VanGorp 2011	389	0.85	0.79	0.9	0.8	0.74	0.85

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IOTA assessment model

(<http://www.iotagroup.org/adnexmodel/site%20iota.html>)

1. Age of patient (years)
2. Referral Oncology Center
3. Maximal diameter of lesion (mm)
4. Maximum diameter of solid part (mm)
5. More than 10 locules
6. Number of papillary projections
7. Acoustic shadows present
8. Ascites
9. CA125 (U/ml)

All required data are input to a calculator and the following risks are detected: Chance of Benign Tumor

Risk of Malignancy:

- a. Risk of Borderline
- b. Risk of EC I Ovary Cancer
- c. Risk of EC II, IV Ovary Cancer
- d. Risk of Metastasis

It is worth mentioning that almost all existing diagnosis approaches -including IOTA LR2 and *Simple Rules*- are based on patients scheduled for surgical treatment and they utilize the final histological outcome as their reference standard. There is no information available in relation to the group of women who were conservatively observed or managed and the final outcome of likely complications or malign transformation of the adnexal mass such as rupture, twisting, hemorrhage, etc.

Conclusion

Nowadays the review of different studies and systematic research prove that both IOTA LR2 and *Simple Rules* are the best diagnosis approaches available in order to differentiate benign and malign adnexal masses beforehand. Such disquisition is vitally important

for women of reproductive age, as it deals with fertility preservation. Furthermore, having obtained predictive outcomes over benign diseases, women are more likely to be treated by obstetrician-gynecologists (OB-GYN) or in general hospitals and patients given a diagnostically suspected malignancy would be referred to and treated by gynecologic oncologists.

Acknowledgments

None.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Registro de Cáncer de Lima Metropolitana. 2012.
2. Scottish Intercollegiate Guidelines Network (SIGN). Epithelial ovarian cancer, a national clinical guideline. Edinburgh, Scotland: SIGN; 2003.
3. Myers ER, Bastian LA, Havrilesky LJ, et al. Management of Adnexal Mass. *Evid Rep Technol Assess (Full Rep)*. 2006;(130):1–145.
4. Le T, Giede C, Salem S, et al. Initial evaluation and referral guidelines for management of pelvic/ovarian masses. *J Obstet Gynaecol Can*. 2009;31(7):668–680.
5. Dodge JE, Covens A, Lacchetti C, et al. Preoperative identification of a suspicious adnexal mass: A systematic review and meta-analysis. *Gynecol Oncol*. 2012;126(1):157–166.
6. Nguyen H, Averette H, Hoskins W, et al. National survey of ovarian carcinoma. Part V. The impact of physician's specialty on patients' survival. *Cancer*. 1993;72(12):3663–3670.
7. Mayer AR, Chambers SK, Graves E, et al. Ovarian cancer staging: does it require a gynecologic oncologist? *Gynecol Oncol*. 1992;47(2):223–227.
8. Chan JK, Chan JK, Shin JY, et al. Influence of the gynaecologic oncologist on the survival of ovarian cancer patients. *Obstet Gynecol*. 2007;109(6):1342–1350.
9. Earle CC, Schrag D, Neville BA, et al. Effect of surgeon specialty on processes of care and outcomes for ovarian cancer patients. *J Natl Cancer Inst*. 2006;98(3):172–180.
10. Engelen MK, Kas H, Willemse P, et al. Surgery by consultant gynecologic oncologist improves survival in patients with ovarian carcinoma. *Cancer*. 2005;106(3):589–598.

11. Liu J, Xu Y, Wang J. Ultrasonography, computed tomography and magnetic resonance imaging for diagnosis of ovarian carcinoma. *Eur J Radiol.* 2007;62(3):328–334.
12. Geomini P, Kruitwagen R, Bremer GL, et al. The accuracy of risk scores in predicting ovarian malignancy: a systematic review. *Obstet Gynecol.* 2009;113(2 Pt 1):384–394.
13. Geomini P, Kluivers K, Moret E, et al. Evaluation of adnexal masses with three-dimensional ultrasonography. *Obstet Gynecol.* 2006;108(5):1167–1175.
14. Laban M, Metawee H, Elyan A, et al. Three-dimensional ultrasound and three-dimensional power Doppler in the assessment of ovarian tumors. *Int J Gynaecol Obstet.* 2007;99(3):201–205.
15. Valentin L. Gray scale sonography, subjective evaluation of the color Doppler image and measurement of blood flow velocity for distinguishing benign and malignant tumors of suspected adnexal origin. *Eur J Obstet Gynecol Reprod Biol.* 1997;72(1):63–72.
16. Van Calster B, Timmerman D, Bourne T, et al. Discrimination between benign and malignant adnexal masses by specialist ultrasound examination versus serum CA-125. *J Natl Cancer Inst.* 2007;99(22):1706–1714.
17. Kaijser J, Ahmad Sayasneh A, Van Hoorde K, et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis. *Hum Reprod Update.* 2014;20(3):449–462.
18. Timmerman D, Testa AC, Bourne T, et al. International ovarian tumor analysis group. logistic regression model to distinguish between the benign and malignant adnexal mass before surgery: a multicenter study by the International ovarian tumor analysis group. *J Clin Oncol.* 2005;23(34):8794–8801.