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RESEARCH ARTICLE

ULTRASOUND IN ADNEXAL TUMOR: NEW CONCEPT

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ABSTRACT

Background: For pre-surgical assessment of an adnexal mass, the International Ovarian Tumor Analysis (IOTA) ADNEX model can be used by medical doctors to diagnose ovarian cancer in women who have at least one persistent adnexal and estimates the probability that an adnexal tumor is benign or malignant. **Objective:** To study the value of the international ovarian tumor analysis (IOTA) in differentiation between malignant and benign ovarian tumor. **Patients and methods:** Fifty one patients presented with suspicious adnexal mass to the radiological department in Baghdad teaching hospital in medical city complex in the period from February 2016 till the end of December 2016. U/S was performed to confirm & characterize the adnexal mass. CA-125 tumor marker was measured. All patients underwent surgery to remove the mass and the masses were sent for histopathological study. **Results:** the IOTA score was calculated and compared, and shows that IOTA score was efficient in the determination of benign or malignant. The sensitivity of the IOTA score system was 92% and specificity was 98% in detection the malignant at cut off point 49.25%. **Conclusion:** the IOTA score (ADNEX model) was highly sensitive (92%) and highly specific (98%) in detection of benign or malignant at score of 49.25.

INTRODUCTION

Ovarian cancer has the highest fatality-to-case ratio (70.3%) and is the most challenging of the gynecological cancers (Jemal et al., 2011).

Types of ovarian tumors: Approximately 90% of ovarian cancers are epithelial ovarian carcinomas. Epithelial malignancies are adenocarcinomas. In this type of cancer, a malignant tumor originates in the surface epithelium tissue, which is the lining on the outside of the ovary (Seidman et al., 2003).

Clinical features: The suspicion of malignancy must be particularly high in a postmenopausal female with a symptomatic and palpable pelvic mass. Most women with early ovarian cancer are asymptomatic. In very advanced disease, patients may have symptoms related to the presence of ascites or metastatic disease, which may include abdominal distention, abdominal pain, bloating, constipation, nausea, emesis, weight loss, anorexia, reflux, or early satiety (Goff et al., 2004).

Imaging diagnosis: For pre-surgical assessment of an adnexal mass, transvaginal ultrasonography (US) combined with Doppler techniques is the first-line and best imaging technique (Rosemarie et al., 2016). When a lesion is large or extends

beyond the field of view of transvaginal US, complementary transabdominal US should be performed according to the 2013 American College of Radiology appropriateness criteria. MRI is usually considered as complementary problem-solving modality (Spencer et al., 2010). Integration of additional clinical features (e.g., menopausal status) and serum biomarkers (CA-125) allow further risk stratification, e.g., as in the widely used risk of malignancy index (RMI). The value of gray scale and color Doppler US has been extensively analyzed by the International Ovarian Tumor Analysis (IOTA) group. The pattern recognition of specific ultrasound findings and assignment into categories of diagnostic certainty of malignancy is well established (Valentin et al., 2011).

IOTA Scoring system: In 2008, the International Ovarian Tumor Analysis (IOTA) group proposed simple ultrasound-based rules for the diagnosis of ovarian malignancy. These rules are based on the simple identification of certain findings on ultrasound examination, some of which are characteristic of malignant lesions (malignant or M-features) and others of benign lesions (benign or B-features). A prospective internal validation from the IOTA group showed that these rules can be applied to 77% of adnexal masses and that, when applied, the diagnostic performance is high (AlcaZar et al., 2013). The examiner analyzed the mass according to the IOTA simple rules to determine whether there were malignant (M) features

(M1, irregular solid tumor; M2, presence of ascites; M3, at least four papillary projections; M4, irregular multilocular solid tumor with largest diameter ≥ 100 mm; M5, very strong blood flow (IOTA color score 4)) or benign (B) features (B1, unilocular tumor; B2, presence of solid components with solid component largest diameter < 7 mm; B3, presence of acoustic shadows; B4, smooth multilocular tumor with largest diameter < 100 mm; B5, no blood flow (IOTA color score 1)) (Timmerman *et al.*, 2008). At the end of the examination, a diagnosis of benign, malignant or inconclusive was provided. The mass was classified as benign if one or more B-features were present in the absence of M-features. The mass was classified as malignant if one or more M-features were present in the absence of B-features. If both B- and M-features were present, or none was present, the mass was classified as inconclusive (Timmerman *et al.*, 2010). The ADNEX risk model can be used by medical doctors to diagnose ovarian cancer in women who have at least one persistent adnexal (ovarian, para-ovarian, and tubal) tumor and are considered to require surgery. ADNEX estimates the probability that an adnexal tumor is benign, borderline, stage I cancer, stage II-IV cancer, or secondary metastatic cancer (i.e. metastasis of non-adnexal cancer to the ovary). The model was developed by clinicians and statisticians from the International Ovarian Tumor Analysis (IOTA) group, and is based on clinical and ultrasound data from almost 6000 women recruited at 24 centers in 10 countries (Italy, Belgium, Sweden, Czech Republic, Poland, France, UK, China, Spain, and Canada) (Epstein *et al.*, 2016). The ADNEX model uses nine predictors. There are three clinical variables, age, serum CA-125 level, and type of center (oncology referral center vs other), and six ultrasound variables, maximal diameter of lesion, proportion of solid tissue, more than 10 cyst locules, number of papillary projections, acoustic shadows, and ascites. All patients included required surgery as judged by a local clinician. As with all current diagnostic models for adnexal tumors (e.g. IOTA models, RMI, ROMA) it implies that patients selected for expectant management were excluded when creating the model. As a consequence ADNEX cannot be applied to conservatively treated adnexal tumors (Epstein *et al.*, 2016).

Objectives: To study the value of the international ovarian tumor analysis (IOTA) in differentiation between malignant and benign ovarian tumor.

MATERIALS AND METHODS

This is a prospective study performed in radiological department in Baghdad teaching hospital in medical city complex in the period from February 2016 till the end of December 2016. Fifty one adult women patients with clinical suspicion of adnexal masses were enrolled in this study. Informed consent was obtained from the patients to participate in this study,

Exclusion criteria:

1. Patients who don't have definite histopathological results
2. Any patient with non ovarian lesion (e.g: pendunculated fibroid, paratubal cyst).

A grey scale and color Doppler ultrasound examination was performed (Transabdominal evaluation using a curved array 3 – 5 MHz transducer) and (Transvaginal high frequency 5 – 10 MHz transducer) to obtain morphological and blood flow

variables to characterize each adnexal mass. A hospital type ultrasound equipment (Voluson, GE Healthcare Austria) or (Philips HD11 XE Netherland) were used. Then the mass was stated likely to be malignant or benign on the basis of subjective evaluation of ultrasonic findings (“subjective assessment”). The risk of malignancy was calculated using the IOTA logistic regression models ADNEX. The IOTA model uses nine predictors. There are three clinical variables, age, serum CA-125 level, and type of center, and six ultrasound variables, maximal diameter of lesion, proportion of solid tissue, more than 10 cyst locules, number of papillary projections, acoustic shadows, and ascites (Epstein *et al.*, 2016). Results of CA 125 marker was recorded. All patients underwent surgery, and the mass was removed and sent for histopathological study. The IOTA score was calculated by application by entering the data as shown in Figure 3.

Statistical analysis

- Analysis of data was carried out using the available statistical package of SPSS-22 (Statistical Packages for Social Sciences- version 22).
- The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means.
- The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2 -test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.
- Reliability tests (Sensitivity and specificity) and critical cut-off points were calculated using receiver operator curve (ROC).

RESULTS

In this study, the mean age for the malignant cases according to the histopathology were 49.7 years old (ranging from 14 to 75 years) and the mean age for the benign patient was 38.7 years old (ranging from 16 to 70 years), but this difference show no statistical significant between the determination of histopathological type (whether benign or malignant). The following ultrasound signs were assessed; the diameter of the lesion, the maximum diameter of the largest solid mass, number of the locules, number of the papillary projections, the presence of acoustic shadow, presence of ascites and vascularity of the lesion,. It has been found that the largest lesion is the most common to have a malignancy (as the mean maximum diameter of the largest solid mass in the malignancy was 73.3 mm while the benign was 41.3 mm). It has been found that when the more number of locules, the incidence of malignancy was more (in malignancy the mean number of locules was 8.9 while in benign lesions, it was 5.3). The presence of acoustic shadow was seen in 2 patients (15%) with malignancy from 13, and 27 of benign (71%) from 38, so presence of acoustic shadow was seen more frequently in malignancy. Ascites was seen in 10 cases (7 cases were malignant (53% of malignant cases), while 3 were benign (7.9% of benign cases)). So ascites was seen in malignancy more than benign cases. The presence of vascularity was seen in 10 cases (7 cases were malignant (representing 53% of malignant cases) while 3 cases were benign (representing 7.9% of benign cases)).

Table 1. Ultrasound features in the study sample

Ultrasound features:		Malignant		Benign		P value
		No	%	No	%	
US diameter lesion (mm)	Mean± SD (Range)	116.8±53.43 (55.0-250.0)		98.5±46.43 (40.0-274.0)		0.243
US maximum diameter of the largest mass (mm)	Mean± SD (Range)	73.3±39.59 (18.0-160.0)		41.3±22.34 (15.0-90.0)		0.015*
Number of locules	Mean± SD (Range)	8.9±2.43 (4.0-10.0)		5.3±3.73 (1.0-10.0)		0.004*
Number of papillary	Mean± SD (Range)	3.3±2.06 (1.0-6.0)		-		-
Shadow	Yes	2	15.4	27	71.1	0.0001*
	No	11	84.6	11	28.9	
Ascites	Yes	7	53.8	3	7.9	0.0001*
	No	6	46.2	35	92.1	
Vascularity	Yes	7	53.8	3	7.9	0.0001*
	No	6	46.2	35	92.1	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level

Table 2. IOTA score between the malignant and benign patients

Type of tumor	IOTA score	P value
Benign	8.44 + 9.04 (0.3 -38.5)	0.0001*
Malignancy	78.68±14.8 (60.0-97.1)	

*Significant difference between two independent means using Students-t-test at 0.05 level

Table 3. Histopathology in the study groups

Histopathology	No	%
Benign		
Functional Cyst	2	5.26%
Dermoid	9	23.68%
Endometrioma	3	7.89%
Hemorrhagic corpus luteal cyst	7	18.42%
Mucinous cyst	3	7.89%
Papillary serouscystadenofibroma	2	5.26%
Seromucinous tumor	1	2.63%
Serous cystadenoma	8	21.05%
Serouscystadenofibroma	2	5.26%
Sex cord stroma	1	2.63%
Fibromatosis	1	7.69%
Malignant		
Immature cystic teratoma	2	15.38%
Metastasis	2	15.38%
Mucinous cystadenocarcinoma	4	30.77%
Papillary serous adenocarcinoma	1	7.69%
Serous and mucinous tumor	1	7.69%
Serouscystadenocarcinoma	1	7.69%
Transitional cell carcinoma	1	7.69%

Figure 1: IOTA score calculation application



Figure 2. Acoustic shadow in an ovarian mass, suggesting dermoid, benign score IOTA 8.64



Figure 3. Multilocular complex ovarian cystic lesion with solid component, malignant IOTA score 76.1 indicating malignancy

In analysis of the CA 125 marker, the mean CA 125 marker seen in the malignancy was 69.6 u/ml, while the mean CA 125 marker seen in the benign was 30.6 u/ml. The IOTA score was calculated and analyzed, and shows that IOTA score was efficient in differentiation of benign from malignant ovarian tumors, The IOTA score in histopathologically proved malignant cases was 78.7 while in benign cases, it was 8.2 with a p value was 0.0001 which was statistically significant. There were 38 cases with benign according to histopathology (37 of them was benign according to the IOTA score and 1 was malignant), and there was 13 patients with malignant according to histopathology (12 of them was malignant according to IOTA score and 1 was benign). The sensitivity of the IOTA score system was 92% and specificity of the IOTA was 98% in detection of malignancy. The most common benign tumor was dermoid (9 cases (23% of the benign cases)), while the most common malignant tumor was mucinous cystadenocarcinoma (4 cases (30% of the malignant patients), the other histopathology seen in the study groups were listed in the Table 3.

DISCUSSION

The clinical impact of defining whether an adnexal mass is benign or malignant is enormous. Thus, predictive models have been developed to triage women presenting with adnexal masses to an appropriate treatment regimen (Rosemarie Forstner *et al.*, 2016). In analysis of our study data the patients grouped into two groups according to their final diagnosis whether benign or malignant depending on the histopathological results. There were no statistical significant difference had been noticed between the two groups in relevant to the age at time of presentation, which means that the age was not considered to be a predictor in determining the mass to be benign or malignant. This finding, when compared with other study shows that the incidence of the cancer increased with age but not the type of the tumor, and this was mentioned in Sassone et al (USA 1991) (Margherita Sassone *et al.*, 1991) while in the Brown et al (USA 2010) (Douglas *et al.*, 2010). In this study, IOTA score when calculated depend on the ultrasound parameter with ca 125 marker and recorded, the percentage of the malignancy and the benign was calculated, and found that the IOTA score in detecting the malignancy was 92% sensitive and 98% specific if the score was 49.2%. Abbas et al (Egypt 2014) (Ahmed Mohamed Abbas *et al.*, 2014) shows that the benign was more than the malignant and the main benign tumor was endometriotic cyst 27% followed by simple cyst 16% while the malignant tumor was mainly mucinous cystadenocarcinoma 4.4% but they use only 3d ultrasound and they found it 3D ultrasound MSV can be helpful in the morphological assessment of adnexal masses especially in detection of papillary projections in adnexal cysts, and this was compatible with our study. In brown *et al* (Douglas *et al.*, 2010) they showed that the overwhelming majority of adnexal masses are benign and most can be recognized on the basis of characteristic US features. Malignancy, while infrequent, is likewise usually identifiable by a different set of distinguishing US features. Accordingly, in most cases the report should reflect a reasonably confident diagnosis of a benign or malignant entity. Clear communication of the US results will assist in proper patient care and should include a sufficient description and/or conclusion regarding the most likely diagnosis. Fischerova, Zikan, Dundr *et al.* (Czech 2012) (Daniela Fischerova *et al.*, 2012) showed that ovarian tumors represent a wide spectrum of tumors with different biological potential and uncertain malignant potential. No precise prognostic or predictive markers exist to clearly distinguish between tumors of purely benign behavior and those with risk of malignant transformation into carcinomas. Therefore, the oncologic safety must be always balanced against less radical treatment, and this was incompatible to our results because they did not depend on the IOTA score as we did. Forstner *et al* (Portugal 2016) (Rosemarie *et al.*, 2016), they conclude that the Imaging is integral in various aspects in assessing ovarian cancer. It is not only used as a diagnostic tool but is also a major determinant in triaging to personalized treatment. Sonography is an excellent modality to predict malignancy in adnexal masses and thus assists in reducing unnecessary surgeries, and this was more to be compatible with our study but they used the U/S and MRI with FIGO score to determine these results. In Andrade Neto *et al.* (Austria 2011) they shows that The correct sonographic identification of adnexal masses is fundamental both for screening of benign conditions and for the early diagnosis and better follow-up of malignant lesions. The sonographer must, therefore, be well prepared and aware of the different usual presentations of adnexal masses, in order

to be able to interact with the assisting physician with the purpose of proposing strategies that may best guide the specific therapy for the patient, and this support our study results.

Conclusion

1. The IOTA scoring system (ADNEX model) was sensitive and specific for the detection of the malignancy before surgery.
2. The age was not a predictor for the type of ovarian tumor (benign or malignant).

Recommendation

Installation of the mobile phone application (IOTA score calculator) is recommended to assist in evaluation of ovarian masses by ultrasound and calculated according to IOTA score (ADNEX model) to exclude malignancy

Abbreviation list

CT	computed tomography
HU	Hounsfield unit
IOTA	International Ovarian Tumor Analysis
IUP	Intrauterine pregnancy
LH	luteinizing hormone
Mm	Millimeter
MRI	Magnetic resonance imaging
MSV	MultiSlice View
P value	Predicted value
PMP	Postmenopausal
U	Unit
U/S	Ultrasound

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