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Original paper

A new scoring model for characterization of adnexal masses based on two-dimensional gray-scale and colour Doppler sonographic features

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Abstract

Objective: **To determine the most discriminating two-dimensional gray-scale and colour Doppler sonographic features that allow differentiation between malignant and benign adnexal masses, and to develop a scoring model that would enable more accurate diagnosis with those features.**
Methods: **A cross sectional prospective study was conducted on patients scheduled for surgery due to presence of adnexal masses at Woman's Health Center, Assiut University, Egypt between October 2012 and October 2013. All patients were evaluated by 2D ultrasound for morphological features of the masses combined with colour Doppler examination of their vessels. The final diagnosis, based on histopathological analysis, was used as a gold standard.**
Results: **One hundred forty-six patients were recruited, 104 with benign masses, 42 with malignant masses. Features that allowed statistically significant discrimination of benignity from malignancy were; volume of mass, type of mass, presence and thickness of septae, presence and length of papillary projections, location of vessels at colour Doppler and colour score. A scoring model was formulated combining these features together; Assiut Scoring Model (ASM). The cut-off level with the highest accuracy in detection of malignancy, was ≥6, had a sensitivity of 93.5% and specificity of 92.2%.**
Conclusion: **Our Scoring Model; a multiparameter scoring using four gray-scale ultrasound and two colour Doppler features, had shown a high sensitivity and specificity for prediction of malignancy in adnexal masses compared with previous scoring systems.**

Key words: **2D US, adnexal mass, Doppler, ovary, ovarian cancer, scoring system.**

Introduction

Adnexal masses are considered one of the most common disorders in gynaecology. Ovarian tumours, alone represent two thirds of these cases. They represent an increasing challenge to the gynaecologists, and ovarian cancer being the most lethal of all gynaecological cancers, characterized by late presentation and poor response to treatment (Gaughan et al., 2006).

Adnexal masses can be present in patients being evaluated for a gynaecological complaint or in asymptomatic patients. Most of patients with ovarian cancer stay asymptomatic for long time. When symptoms develop, they are usually nonspecific. In early-stage disease, patients commonly suffer from lower abdominal pain or non-specific gastrointestinal complaints. Irregular uterine bleeding is rarely present. Moreover, in advanced-stage disease, patients may have symptoms related to the presence of ascites or intestinal metastases (Olson et al., 2004).

Preoperative suggestion of ovarian cancer can conduct the physician to refer women with doubtful adnexal masses to a skilled gynaecological oncologist for appropriate therapy and optimized debulking, while patients with benign adnexal masses can undergo more conservative surgical treatment (Yazbek et al., 2008).

No single diagnostic tool (ultrasonography, magnetic resonance imaging, and computerized tomography) is good enough in preoperative determination of malignancy, but there is an agreement that ultrasound assessment of adnexal mass morphology by an experienced sonographer

can properly estimate the risk of malignancy (Yazbek et al., 2008).

Doppler ultrasound is usually combined with 2D ultrasound evaluation aiming to predict malignancy more appropriately through obtaining intratumoural blood flow velocity waveforms to calculate the Resistance and Pulsatility indices. Also, evaluation of gray-scale ultrasound morphology with colour Doppler findings of an adnexal mass is highly accurate in predicting its nature (Van Calster et al., 2007).

Prediction models have been developed to assist clinicians to triage patients to appropriate treatment pathways; however, none has gained universal acceptance in routine daily practice. The International Ovarian Tumour Analysis (IOTA) group has developed and validated two ultrasound-based logistic regression models (LR1 and LR2) that estimate the risk of malignancy in adnexal masses (Timmerman et al., 2005), but the performance of such models was tested by expert sonographers not less experienced ones besides the need of a computer for risk estimation using an EXCEL file that cannot be present in most hospitals and clinics in developing countries (Van Calster et al., 2012). So, there was a need for a prediction model that has a high sensitivity and specificity combined with simplicity and low cost to be valid for application in developing countries for triaging patients with adnexal masses.

The aim of our study was to determine the best two-dimensional and Doppler sonographic features that allow distinction between benign and malignant adnexal masses and to develop a scoring model enables accurate triaging of patients with malignancy using those features.

Patients and Methods

The study period was one year starting from the 1st of October 2012 till the 30th of September 2013, 146 women diagnosed as having an adnexal mass and scheduled for surgical management at Woman's Health Center, Assiut University, Egypt, were included in this prospective study.

The study was approved by the Ethical Review Board of Assiut faculty of medicine and all women gave written informed consent. Diagnostic work-up included a complete medical history, physical examination, 2D ultrasound and Doppler examination.

2D Ultrasound and Doppler evaluation was done using a Sono-Ace X8 machine (Medison, Korea) with multifrequency transabdominal and trans-vaginal volumetric probes. All ultrasound scans were done by the same sonographer (level II experience).

First, the volume of the mass was calculated from the three diameters obtained in the two perpendicular planes. Then, morphological evaluation was performed according to the International Ovarian Tumour Analysis (IOTA) protocol (Timmerman et al., 2000) attending the following features:

- Bilaterality
- Type of mass (All masses were classified into one of five categories: unilocular cyst, unilocular-solid cyst, multilocular cyst, multilocular-solid cyst, and solid mass)
- Internal wall (smooth or with papillae < 3 mm or ≥ 3 mm length)
- Septae (not present, incomplete, complete; thin < 3 mm or thick ≥ 3 mm)
- Echogenicity (anechoic, low-level echogenic, 'ground glass' appearance, haemorrhagic or mixed echogenic)
- Presence of internal shadows
- Presence of free fluid in Douglas pouch

After 2DUS evaluation was performed, the colour Doppler gate was activated to assess tumour vascularization. A subjective semi quantitative assessment of the amount of blood flow within the examined lesion (colour score) was made according to the IOTA protocol (Timmerman et al., 2000).

The amount of blood flow within the mass was scored as follows: if there is no blood flow detected in the lesion, a score of 1 was given; if minimal blood flow could be detected, a score of 2 was given; a score of 3 was given when moderate flow was present, and a score of 4 was given when the adnexal mass appeared highly vascularized with marked blood flow. A colour score ≥ 3 was considered suggestive of malignancy.

The area distribution of visualized vessels in the adnexal mass was also recorded as in the centre of the mass, in the septum, in the papillae, at tumour wall or peri-tumour areas. Malignancy was suspected if the penetrating vessels were visualized within papillary projections, solid areas, or central areas of a solid tumour.

Spectral pulsed wave Doppler analysis was done after that, Resistance index (RI) and Pulsatility index (PI) were calculated for each mass. When no blood flow was detectable within the tumour, a signal was recorded from peripheral areas or the adnexal branch of the ovarian artery.

The Doppler variables used for diagnosing malignant adnexal mass was RI ≤ 0.42 and PI ≤ 1.0 obtained from papillary projections, thick septa, solid parts or cystic walls (Weiner et al., 1992).

All surgically removed masses were examined histopathologically to assess their nature as the final diagnosis was based on histopathological reports.

In our study, we chose the 2D sonographic and Doppler features of adnexal masses that are best fitted to predict the pathological outcome of benignity or malignancy. Then we combined those features together to develop a new scoring model, *Assiut Scoring Model (ASM)*.

Analysis of data was done using SPSS Inc., Chicago, IL, USA, version 21. Qualitative variables were expressed as percentages and compared by Fisher's exact test. Quantitative variables were presented in terms of mean, standard deviation and range, compared by "Mann-Whitney test" for non-parametric data and "Student's T-test" for parametric data.

Sensitivity, specificity, positive and negative predictive values were calculated for 2DUS and Doppler evaluation, and finally for the new scoring model. P-value < 0.05 was considered as statistically significant.

Results

The mean (± SD) age of patients included in the study was 35.2 ± 13.9 years (range 12-70 years). One hundred twenty-nine patients (88.4%) were in the reproductive age, 13 were postmenopausal (8.9%), and 4 of them (2.7%) were in the premenarche period. Forty-five patients (30.8%) were nulliparous.

Overall, 104 patients (71.2%) confirmed to have benign masses, and 42 patients (28.8%) with malignant masses according to their final histopathological analysis. Number of the evaluated masses was 161 masses (due to bilaterality of masses in 15 patients); 115 proved to be benign and

Table I. — 2D ultrasound features of benign and malignant masses.

	Benign masses (n = 115)	Malignant masses (n = 46)	P-value
Tumor Volume/ml (Mean ± SD)	269.5 ± 595.4	659.1 ± 791.6	**< 0.01**
Maximum diameter/cm (Mean ± SD)	7.6 ± 3.7	10.9 ± 4.3	**< 0.001**
Type of mass			
• **Unilocular**	69 (60%)	1 (2.2%)	**< 0.001**
• **Unilocular-solid**	7 (6.1%)	7 (15.2%)	
• **Multilocular**	14 (12.2%)	11 (23.9%)	
• **Multilocular-solid**	2 (1.7%)	14 (30.4%)	
• **Solid**	23 (20%)	13 (28.3%)	
Internal shadows	35 (38%)	17 (51.5%)	> 0.05
Fluid in DP	10 (8.7%)	10 (21.7%)	**< 0.05**
Fluid measurement/mm Mean (range)	17.2 (9-32)	24.5 (8-44)	**< 0.05**
Echogenicity of the cyst *			
• **Anechoic**	29 (31.5%)	24 (72.7%)	**< 0.001**
• **Low level echogenicity**	19 (20.7%)	5 (15.2%)	
• **Ground glass**	27 (29.4%)	3 (9.1%)	
• **Hemorrhagic**	12 (13%)	1 (3%)	
• **Mixed**	5 (5.4%)	0	
Septae inside the cyst *			
• **Complete**	16 (17.4%)	25 (75.8%)	**< 0.001**
• **Incomplete**	5 (5.4%)	0	
• **Thin Septum < 3 mm**	15 (93.7%)	8 (32%)	**< 0.001**
• **Thick Septum ≥ 3 mm**	1 (6.3%)	17 (68%)	
Cyst wall *			
• **Smooth**	89 (95.7%)	19 (57.6%)	**< 0.001**
• **Papillae < 3 mm**	3 (4.3%)	2 (6.1%)	
• **Papillae ≥ 3 mm**	0	12 (36.3%)	

*(n = 92) in benign masses, (n = 33) in malignant masses; SD, standard deviation; DP, Douglas pouch.

Table II. — Doppler findings of the benign and malignant adnexal masses.

	Benign masses (n = 115)	Malignant masses (n = 46)	P-value
PI (Mean ± SD)	1.66 ± 0.56	0.82 ± 0.28	
• **Range**	(0.46 – 2.93)	(0.41 – 1.64)	
• **> 1.5**	71 (61.7%)	1 (2.2%)	**< 0.001**
• **1 - 1.5**	26 (22.6%)	8 (17.4%)	
• **< 1**	18 (15.7%)	37 (80.4%)	
RI (Mean ± SD)	0.79 ± 0.18	0.50 ± 0.20	
• **Range**	(0.36 – 1.00)	(0.29 – 1.00)	**< 0.001**
• **> 0.42**	113 (98.3%)	24 (52.2%)	
• **≤ 0.42**	2 (1.7%)	22 (47.8%)	
Colour score			
• **Score 1**	20 (17.4%)	1 (2.2%)	
• **Score 2**	87 (75.6%)	16 (34.8%)	**< 0.001**
• **Score 3**	8 (7%)	19 (41.3%)	
• **Score 4**	0	10 (21.7%)	
Vessel Localization			
• **Central**	10 (8.7%)	16 (34.8%)	
• **In the wall**	80 (69.6%)	6 (13%)	
• **In Septae**	5 (4.3%)	18 (39.1%)	**< 0.001**
• **In Papillae**	0	5 (10.9%)	
• **Peritumour**	20 (17.4%)	1 (2.2%)	

SD, standard deviation; PI, Pulsatility index; RI, Resistance index; PSV, Peak systolic velocity; cm/sec, centimetre/second.

46 malignant. Almost all of the evaluated 2D ultrasound features differed significantly between benign and malignant masses except presence of internal shadows (Table I).

Doppler examination revealed that the mean PI and RI values of arteries in malignant masses were significantly lower than benign masses. High vascularity was found mainly in malignant masses. Blood flow signals commonly obtained from papillary projections, septae or central parts of the malignant masses (Table II).

Assiut scoring model, a new model evaluated four gray-scale sonographic features used to predict the adnexal mass status: volume of the mass, type, presence and thickness of septae, and presence and length of papillary projections. Also, there are two colour Doppler features; location of vessels and colour score. The different features were rated on a scale from 0 to 3 points depending upon the degree of expression observed for the individual characteristics (Table III).

The total score obtained is the basis for differentiation of the adnexal mass. The highest value of reliability in differentiation of malignant and benign adnexal masses was attaining score 6 or more (Fig. 1, 2). All parameters of the score showed significant *P*-values, thus demonstrating a statistically significant correlation between score point numbers and histological findings.

Discussion

Although ovarian cancer is the second most common female genital cancer, preceded only by cancer body of the uterus, more women die from ovarian cancers. It is the most lethal of all the gynaecologic cancers, killing more women each year than both of cervical and endometrial cancers (Zoorob et al., 2001).

Good preoperative discrimination between benign and malignant ovarian tumours results in more women being correctly referred for gynaecologic oncology care and more women with benign masses undergoing conservative management (Yazbek et al., 2008).

In the study conducted by Jokubkiene et al. (2007) on 106 patients with adnexal masses, they concluded that almost all ultrasound features differed significantly between benign and malignant masses except presence of papillary projections, internal shadows, thick septae and bilaterality of masses. Our results agreed with them regarding presence of internal shadows and bilaterality, but differed in presence of papillary projections and

Table III. — Assiut Scoring Model for differentiation of adnexal masses into benign and malignant.

Score	0	1	2	3
2DUS features				
Tumour volume	0 – 50 ml	50-500 ml	> 500 ml	
Type of mass	Unilocular	Multilocular	Unilocular-solid Multilocular-solid solid	
Papillary projections	No	Length < 3 mm	----------	≥ 3 mm
Septae	No	Thin < 3 mm	----------	Thick ≥ 3 mm
Doppler features				
Vessel location	Peri-tumour	Peripheral	Central or septal	
Colour score	1	2	3	4
A score ≥ 6 was considered as suspicious of malignancy.				

thick septae. The malignant cystic masses were often had papillary projections (42.4% vs. 4.3%, P < 0.001), and thick septae (68% vs. 6.3%, P < 0.001) than benign masses.

In the light of our results, multilocular-solid mass was the most common pattern of ovarian malignancy (30.4%) followed by solid mass (28.3%). This was consistent with the results of Timmerman et al. (2005) who found that multilocular-solid masses represent 43.6% of ovarian malignancy followed by solid masses (31.6%). Also we agreed with Jokubkiene et al. (2007) who found that multi-locaular-solid and solid masses represented 52% and 41% respectively of malignant ovarian masses.

Regarding the echogenicity of cyst fluid in malignant masses, our results showed that most of them were anechoic (72.2%) followed by low level echogenicity; 15.2%. This keeps with the results of Timmerman et al. (2005), malignant cysts were anechoic in 40.2% of masses followed by low level echogenicity; 22.6%. Also in Jokubkiene et al. (2007) series; anechoic pattern was found in 67% of masses.

As regards to Doppler indices in the present study, RI and PI values were calculated for each mass. The mean value of RI was 0.79 for benign masses and 0.50 for malignant masses, while the mean value of PI was 1.66 for benign masses and 0.82 for malignant masses.

These values, in correlation to various studies using "0.42" and "1" values for RI and PI respectively as a cut-off value for prediction of malignancy reflected that, RI had a sensitivity of 44% and a specificity of 99%, while PI had a sensitivity of 80% and a specificity of 84%. P-value was < 0.001 for both RI and PI among both groups,

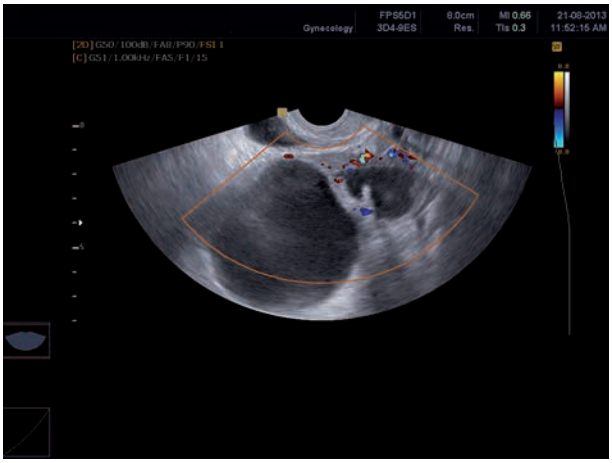

Fig. 1. — An adnexal mass showing the following criteria: multilocular (score 1), volume 487 ml (score 1), thick septum 3.4 mm (score 3), septal blood vessels (score 2), color score 2 (score 1). Total score according to Assiut scoring model is 8. Histopathological examination revealed mucinous cystadeno-carcinoma.

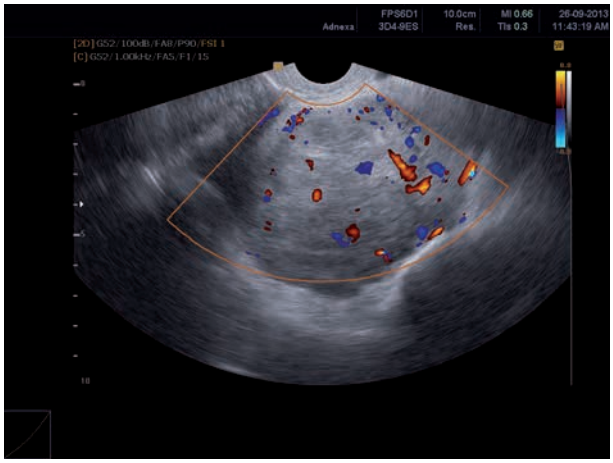

Fig. 2. — An adnexal mass showing the following criteria: solid (score 2), volume 327 ml (score 1), central blood vessels (score 2), color score 3 (score 2). Total score according to Assiut scoring model is 7. Histopathological examination revealed dysgerminoma.

being of significant value in predicting malignancy of adnexal masses.

In the previous studies, some authors suggested the existence of clear cut-off values for RI and PI of benign and malignant tumours; Timor-Tritsch et al. (1993) reported the RI value of 0.4 had sensitivity 93.8% and specificity of 98.7%. Alcázar and Jurado (1998) preferred 0.45. Laban et al. (2007) also reported that the best RI cut-off value was < 0.48 giving a sensitivity, specificity, and accuracy of 90%, 89%, and 90%. Medeiros et al. (2009) in their systematic review showed that Doppler can detect malignant masses when the RI was < 0.50.

Ueland et al. (2003) reported sensitivity and specificity of 52.8% and 77.6% respectively using cut-off value of PI < 1. In spite that we found that low PI < 1 was an important feature of malignancy (80.4 %) but PI < 1 was also found in 15.7% of benign masses. So PI alone cannot be a reliable feature to detect malignancy.

Out of 115 benign masses, colour Doppler study could diagnose 107 masses as benign (colour score ≤ 2) but labelled eight masses as malignant that were actually benign, while out of 46 malignant masses, only 29 masses were diagnosed as malignant (colour score > 3). Our study showed a sensitivity of 61% and specificity 96%. The IOTA study results published by Timmerman et al. (2005) showed that colour score sensitivity and specificity were 80% and 66.6%, respectively.

Colour Doppler results showed predominantly peripheral localization of vessels in benign masses (69.6%) and predominantly central or septal vessel localization (39.1% and 34.8%) was observed in malignant masses. There were 20 benign masses showed absence of blood flow (17.4%), on the other hand nearly all the malignant masses showed vascularity (97.8%). This keeps with the results of Jokubkiene et al. (2007) who found that 57% of benign masses showed peripheral vascularization versus 70% of malignant masses showed central vascularization.

There have been several different sonographic scoring systems developed for evaluation of particular characteristics of ovarian tumours in order to classify malignant diseases in the most objective way.

Sassone et al. (1991) stated a scale for morphological features, including inner wall structure, wall thickness, presence of septa and echogenicity of the mass, and were able to differentiate benign from malignant masses with specificity of 83%, sensitivity of 100%.

Depriest et al. (1993) used the weighted sum of tumour volume, wall structure, and septal structure. The weighted sum of these three features varied between 0 and 12, with the cut-off point set at 5. At this cut-off point, sensitivity was 91%, specificity 69%. Both of the previous two scoring systems had a low specificity besides of not using Doppler features in their models

In 1994, Lerner et al. tried to simplify the scoring system by excluding the parameter of wall thickness from Sassone scoring system and added another one; shadowing in order to discriminate dermoid cysts from malignant adnexal masses. Lerner scoring system using a cut-off at score 3 was reported to have 96.8% sensitivity and 77% specificity.

Twickler et al. (1999) integrated the patient's age, ovarian volume, Doppler velocimetry and vessel location, and echogenic predominance of the mass with the morphology scale of Sassone to calculate the ovarian tumour index, a calculated probability of malignancy based on the weighting of each of the previous features.

When we applied our new scoring model on the evaluated masses in the study we found that 43 out of 46 malignant and 106 out of 115 benign masses were accurately identified.

The preliminary results of application of our scoring model are promising showing a sensitivity of 93.5%, specificity 92.2%, PPV 82.7% and NPV 97.3% with overall accuracy 92.6%, but a larger prospective study is a must to validate our new scoring model.

Based on the results of our score, patients with masses score < 4 can be managed in gynaecological unit by a gynaecologist; either conservatively or surgically according to their features. Patients with masses score ≥ 8 must be referred to gynaecological oncologist and to be managed in specialized oncology centres. Patients with masses score 4-8 are suspicious with high possibility of malignancy if score ≥ 6 so further investigations may be ordered as MRI or CA-125.

In conclusion, Assiut Scoring Model (ASM) is simple, non time consuming, easy to applied and interpreted with reasonable accuracy and high sensitivity and specificity, so less experienced sonographers should be trained on its application and further studies should be conducted to test its validity to be incorporated in hospitals guidelines of work for accurate identification of ovarian malignancy and appropriate referral to gynaecologic oncologists.

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