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International Ovarian Tumor Analysis (IOTA) the Malignancy Risk Index, Morphologic Index, and the Ultrasonographically Determined Tumor Size in the Assessment of Adnexal Masses and the Correlation of the Relevance of the Results in the with Malignancy

Adneksiyal Kitlelerin Kriterleri, International Ovarian Tumor Analysis (IOTA) Malignite Risk İndeksi, Morfolojik İndeks ve Sadece Ultrasonografide Tümör Boyutu ile Değerlendirilmesi ve Bulguların Malignite ile İlişkisinin Karşılaştırılması

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ÖZ

Amaç: Bu çalışmanın amacı adneksiyal kitlesi olan premenapozal ve postmenapozal hastalarda preoperative dönemde malignite riskini değerlendirmek ve benign ve malign adneksiyal kitle ayırımını öngörmede tekniklerin etkilerini karşılaştırmaktır.

Gereç ve Yöntemler: Ankara Dr Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi Jinekoloji ve Onkoloji polikliniğine başvuran adneksiyal kitlesi olan, perimenapozal veya postmenapozal dönemde olan 160 hasta çalışmaya dahil edildi. Hastalar 4 gruba ayrılarak IOTA kriterleri, malignite risk indeksi,morfolojik indeks ve ultrasonografide tümör boyutu ile değerlendirildi. Bu prospektif değerlendirmelerin sonuçları postoperatif patoloji sonuçlarıyla karşılaştırıldı. Istatistiksel analizlerde modele dahil edilme olasılığı 0,05, çıkarılma olasılığı 0,10 olarak kabul edildi. Odds oranı (OR) lojistik regresyon analizinden elde edildi ve güven aralığı %95 olarak belirlendi. Gebeliği olan ve yapılan ultrasonografi tarihinden itibaren 3 ay içinde opere olmayan hastalar çalışmaya dahil edilmedi.

Bulgular: Preoperatif olarak malignite indekslerinden elde ettiğimiz sensitivite ve spesifite oranları sırasıyla IOTA'nın sensitivitesi %85.7, spesifitesi %80.8; malignite risk indeksin sensitivitesi %50, spesifitesi %94.1; morfolojik indeksin sensitivitesi %23.5, spesifitesi %94.1; ultrasonografide tümör boyutu değerlendirmesinin sensitivitesi %100, spesifitesi %31.3 olarak bulundu.

Sonuç: Sonuç olarak geniş popülasyonlar üzerinde yapılan çalışmalarla tanı doğruluğu kanıtlanmış ve bizim çalışmamızda da tanı doğruluğu (%85,7) en yüksek saptanan IOTA modelleri ile hastanın preoperatif malignite riski tahmin edilebilecek ve hastanın operasyonu bu doğrultuda planlanabilecektir.

Anahtar Kelimeler: Adneksiyal kitle, malignite, skorlama sistemi, ultrason, menapoz

ABSTRACT

Aim: This study aims to assess the malignancy risk in the pre-operative period and compare the effectiveness of the methods used in predicting the discrimination between benign and malignant adnexal masses in perimenopausal and postmenopausal patients presenting with an adnexal mass.

Material and Methods: Presenting to Ankara Dr. Zekai Tahir Burak Women Health Educational and Research Hospital Gynecology and Oncology Outpatient Clinics, a total of 160 patients who were either in the perimenopausal or postmenopausal period and who were diagnosed with adnexal masses were included in the study. The patients were assigned into four respective groups and to be evaluated with IOTA (International Ovarian Tumor Analysis), malignancy risk index, morphological index, and the tumor size as determined by the ultrasound. The results of these prospective assessments were then compared with the postoperative histopathological results. In the statistical analysis, the probability of being included in the model was accepted to be 0.05, while, the probability of exclusion from the model was accepted to be 0.10. The Odds Ratios (OR) were derived from the logistic regression, and the level of confidence was determined to be 95%. Patients who hadn't undergone the operation after 120 days from ultrasound and pregnants excluded from the study.

Results: Preoperatively yielded sensitivity and specificity rates of malignancy indexes for predicting a malignancy were found to be 85.7% and 80.8% for IOTA; 50% and 94.1% for the malignancy risk index; 23.5% and 94% for the morphological index; and 100% and 31.3% for the tumor size as determined by the ultrasound respectively.

Conclusion: Owing to the highest level of sensitivity of about 85.7% obtained by the IOTA models as proven also by large population-based studies, the risk of malignancy can be predicted and the surgical approaches can be planned accordingly in the pre-operative period.

Keywords: Adnexal mass, malignancy, scoring system, ultrasound, menopause

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INTRODUCTION

Adnexal masses constitute a common gynecologic problem. They develop due to functional, congenital, inflammatory, and neoplastic processes in the adnexes consisting of the fallopian tubes, ovaries, and the broad ligament (1). According to the data in the literature, it is reported that approximately 300.000 women are hospitalized every year in the United States due to adnexal masses (1). Besides, it is also reported in the literature that 5-10% of women had undergone surgical interventions in their lifetime due to a suspicion of an ovarian neoplasm (1). Ovarian cancer is the seventh frequent cancer according to the data from the United States. However, among all types of cancer in women, it is the fifth common type of cancer-causing death (2). Ovarian cancer is the most lethal gynecologic cancer and 90% of ovarian cancers arise from the surface epithelium (3). It is reported that, at the time of diagnosis, 70% of the patients are at the advanced stages of the disease. The 5-year survival is 86.9% at the stage 1a, however, it is 11% at stage 4 (4). The frequency of ovarian cancer increases with age and the average age at the time of diagnosis is 63(5). The annual incidence of the disease is 17/100.000 and the lifetime total risk of developing ovarian cancer is 1.4% (5). Early diagnosis is crucial for reducing the mortality, increasing the quality of life the patients, and decreasing the costs of treatment (5).

To perform an evaluation of adnexal mass for diagnosis in the pre-operative period, it is necessary to obtain a detailed history from the patient, perform a detailed physical examination, and utilize imaging methods, and perform the relevant tests with appropriate tumor markers. Many malignancy risk indexes have recently been introduced into the clinical practice to discriminate between benign and malignant masses. These indexes provide calculations to predict the risk of malignancy of an adnexal mass based on the ultrasound and doppler findings, tumor markers, and the menopausal status of the patient. Among these tools; IOTA, RMI, and De Priest MI (Morphological Index) have been chosen for this present study. IOTA (International Ovarian Tumor Analysis) models provide a tool to predict the malignancy risk of adnexal masses. These models are based on ultrasound findings (septation, papillary projections, presence of acoustic shadows, and ascites); doppler imaging of adnexal masses; the menopausal status, age, and the family history of the patient, the status of current hormonal therapies, presence of pain; and RMI (Risk of Malignancy Index). RMI uses data on the multilocularity of the adnexal mass, the presence of a solid component, the bilaterality of the masses, the presence of ascites along with the evidence of metastasis, the menopausal status of the patient, and serum CA 125 levels. De Priest MI (Morphological Index) is based on the tumor volume, the structure of the cyst wall, and the structure of septa. In this study, we aimed to define the characteristics of the masses with ultrasound by using the criteria defined by IOTA, RMI, and De Priest MI in perimenopausal and postmenopausal patients with adnexal masses. The results will then be compared with the postoperative findings of the histopathological examinations to investigate the effectiveness of these criteria in determining the malignancy risk of adnexal masses.

We aimed in this study that to assess the malignancy risk in the pre-operative period and compare the effectiveness of the methods used in predicting the discrimination between benign and malignant adnexal masses in perimenopausal and postmenopausal patients presenting with an adnexal mass.

MATERIAL AND METHODS

This study was planned prospectively to compare the postoperative histopathologic findings with the pre-operatively evaluated malignancy risk of patients who underwent surgical interventions due to the identified of adnexal masses. After obtaining the approval of Ankara Dr Zekai Tahir Burak Women Health Educational and Research Hospital Education and Planning and Coordination Committee, 160 of 180 patients, who were admitted to Ankara Dr Zekai Tahir Burak Women Health Educational and Research Hospital Gynecology and Oncology Outpatient Clinics with diagnoses of adnexal masses between 30.10.2013 -15.08.2014, were included in the study. It was ensured that all patients included in the study signed the informed consent forms. 20 patients were excluded from the study because they didn't undergo any operations during 120 days after the ultrasound examination. In patients with more than one adnexal mass, the characteristic features of the larger mass were taken into the evaluation. The patients included in the study were assigned into four groups randomly as IOTA, RMI, MI, and ultrasound groups. Each group consisted of 40 patients. Patients who were pregnant and who were not operated in the three months after the ultrasonography were excluded.

The pelvic and physical examinations were performed in all patients included in the study. The age, obstetric history, family history, and the personal medical histories of the patients were documented and the status of their hormonal therapies was recorded.

The menopause process was defined for the patients as having at least one year of amenorrhea, having undergone a hysterectomy previously, and being over 50 years old.

The findings observed during the operation were documented. The specimens collected from the patients were submitted for histopathologic evaluation after the surgical intervention and the results were compiled. The histopathologic diagnosis was accepted as the golden standard. Toshiba Aplio 500, 3.5 Mhz convex abdominal probe and 7.5 Mhz vaginal probes were used in ultrasonography. The abdominal ultrasonography method was used during the evaluation of the virgin patients and for the patients who had adnexal masses larger than 8 cm. Bilaterality, locularity, the structure of the wall and thickness of the mass, the presence and thickness of septa, the presence of solid components, acoustic shadows, ascites, any presence of metastasis, the volume and the maximal diameter of the mass, any presence of papillary projections, the presence of any blood flow in papillary projections, the maximal diameter of the largest solid component (bounded at 50mm), irregularities of the internal cyst wall, and the score of the intratumoral blood flow obtained from the colour doppler ultrasound were evaluated. In the estimation of the mass volume, the ellipsoid formula (V = A x B x C x 0.523) was used. IOTA and MI scores were obtained by using these parameters.

Patients in the IOTA group were scored by using the following parameters including (1) the personal medical history of the ovarian cancer (yes = 1 or no= 0), (2) the status of current hormonal therapies (yes = 1 or no = 0), (3) the age of the patient (in years), (4) the maximum diameter of the lesion (in millimeters), (5) the presence of pain during the examination (yes = 1 or no= 0), (6) the presence of ascites (yes = 1 or no = 0), (7) the presence of blood flow within a solid papillary projection (yes= 1or no= 0), (8) the presence of a purely solid tumor (yes = 1or no = 0), (9) the maximal diameter of the solid component (expressed in millimeters, but not larger than > 50 mm), (10) the presence of irregular internal cyst walls (yes = 1 or no= 0), (11) the presence of acoustic shadows (yes= 1or no= 0), and (12) the color score (1, 2, 3, or 4). The formula is presented below, where "e" is the mathematical constant and base value of natural logarithms:

$$y=1/(1+e-z)$$

$$z=-6.7468+1.5985*(1)-0.9983*(2)+0.0326(3)+0.00841*(4)-0.8577*(5)+1.5513*(6)+1.1737*(7)+0.9281*(8)+0.0496(9)+1.1421*(10)-2.3550*(11)+0.4916*(12)$$

A score of over 10% was accepted to be malignant and a lesion with a score lower than 10% was accepted to be benign.

Bilaterality and locularity of the mass; the presence of solid components, ascites, and metastases; the menopausal status, and the levels of serum CA-125 were used to calculate RMI. RMI scores were calculated by using the ultrasound score (U), menopause score (M), serum CA-125 levels, and by the [U] x [M] x [CA-125] formula. A score (M) of 1 was assigned to premenopausal women and 3 to postmenopausal women. The level of serum CA-125 was directly added to the formula. To be incorporated in the ultrasound score (U), the following five parameters obtained from the ultrasonographic examination were suggestive of cancer including the multilocularity, solid areas, bilateral masses, ascites, and the evidence of metastases. For each ultrasonographic feature, an additional 1 point was added. When the score of RMI was equal to or over 200, it was accepted to be a malignant lesion. When it was lower than 200, the lesion was accepted to be benign (6).

Table 1: DePriest morphologic scoring system (7)

	0	1	2	3	4
Volume	<10 cm^3	10-50 cm^3	>50-200 cm^3	>200-500cm^3	>500 cm^3
Wall	Regular<3mm	Regular>3mm	Papillary projection <3mm	Papillary projection ≥3mm	Predominantly solid
Septa	No	Thin <3mm	Thickness 3mm-10mm	Solid area ≥10mm	Predominantly solid

The patients in the MI group were scored according to Table 1. The scores equal to or over 5 were accepted to be indicative of a malignant lesion. On the other hand, the scores lower than 5 were accepted to be indicative of a benign lesion (8).

In the patient group, where only the size of the tumor determined in the ultrasonographic examination was taken into the evaluation; the tumor sizes over or equal to 80 mm were accepted to be indicative of a malignant nature while the tumor sizes lower than 80 mm were accepted to be benign in the perimenopausal patients. On the other hand, in the postmenopausal patients, the sizes over or equal to 50 mm were accepted as malignant and the sizes below 50 mm were accepted as benign (2).

STATISTICAL ANALYSIS

For statistical analysis and calculations, IBM SPSS Statistics 21.0 (SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp., released in 2012) and MS-Excel 2007 programs were used.

The presence of solid components, papillary projections, ascites, the structure of the cyst wall, multiloculation, and bilaterality were taken as independent variables, whereas, the histopathologic results were taken as dependent variables in the logistic regression model set by using the Backward method. By using this model, the factors which could be involved in the results of the pathological examination were attempted to be detected. The probability value for being included in the model was taken as 0.05 and the probability value for exclusion from the model was accepted to be 0.10. Using the Odds Ratio (OR) levels obtained from the logistic regression model, 95% confidence intervals were determined.

To compare the IOTA, MI, and RMI data and the USG (ultrasonography) scores with the pathology results, the Mc Nemar test was used. To evaluate the correlation of these scoring systems to the pathology results, kapa co-efficient was used. To evaluate the diagnostic performances of the four scoring systems used in this present study in determining the malignant characteristics of the lesion; the sensitivity and specificity values; the positive predictive values, the negative predictive values, the accuracy rates, and Youden indexes were calculated.

RESULTS

The average age of the patients included in the study was 54.4±9.0 years. The median of the maximal diameters of the lesions was 78 mm. The pathology results revealed malignant lesions in forty-eight (30%) patients, whereas, the lesions were benign in 112 (70%) patients. Fifty-nine (36.9%) patients were in the perimenopausal period and 101 (63%) patients were in the postmenopausal period. In the patients with benign lesions, the average serum CA-125 level was 62.62 mU/L and it was 126.2 mU/L in the patients with malignant lesions. The data of the age, serum CA-125 levels, and the maximal diameter of the lesions were distributed homogeneously in the groups. Of 160 patients included in the study, thirty-six (22.5%) patients were diagnosed with malignant lesions, 112 (70%) patients were diagnosed with benign lesions, and 12 (7.5%) patients were diagnosed with borderline lesions (Table 2).

Table 2: Distribution of pathology results

Pathology results	n	%		n	%		n	%
Malign			**Borderline**			**Benign**		
Clear Cell carcinoma	1	0.6	Borderline Brenner tumour	1	0.6	Brenner tumour	1	0.6
Endometrioid carcinoma	9	5.6	Borderline mucinous tumour	4	2.5	Angioleiomyom	1	0.6
Serous+transitional carcinoma	1	0.6	Borderline serous tumour	7	4.4	Endometrioma	9	5.6
Serous Papillary carcinoma	1	0.6				Fibroma	11	6.9
Serous carcinoma	13	8.1				Follicle cyst	1	0.6
Peritoneal serous carcinoma	1	0.6				Hemorrhagic cyst	2	1.3
Mucinous carcinoma	1	0.6				Hydrosalpix	2	1.3
Mixt epithelial carcinoma	2	1.3				Ceratinöz cyst	1	0.6
Malign tumour with unknown origin	1	0.6				Corpus luteum cyst	3	1.9
Malign mixt mullerian tumour	1	0.6				Leiomyolipoma	1	0.6
Kruckenberg tumour	1	0.6				Mature cystic teratoma	6	3.8
Metastasis of adenocarcinoma	2	1.3				Mucinous cystadenoma	17	10.6
Sertoli leydig cell tumour	2	1.3				Myoma uteri	4	2.5
						Paraovarian cyst	2	1.3
						Peritoneal cyst	2	1.2
						Rete cystadenoma	2	1.3
						Serou cystadenoma	44	27.5
						Struma ovarii	1	0.6
						Tubo Ovarian abscess	2	1.3
Total malign	36	22.5	Total borderline	12	7.5	Total benign	112	70
Total	160	100						

The patients in the study underwent (76 patients; 47.5%) TAH+BSO (Total Abdominal Hysterectomy

and Bilaterally Salpingo Oophorectomy) most frequently. 44 (7.5%) patients in the study underwent a staging surgery (TAH+BSO+Omentectomy+Appendectomy+Bilaterally Pelvic Paraaortic Lymph Node Dissection), 20 (12.5%) patients underwent USO (Unilaterally Salpingo Oophorectomy), 15 (9.4%) patients underwent cystectomy, 3 (1.8%) patients underwent BSO (Bilaterally Salpingo Oophorectomy), and 2 (1.3%) patients underwent oophorectomy (Table 3).

Table 3: Surgery types

Surgery types	%	n
Staging surgery	27.5	44
Oophorectomy	1.3	2
TAH+BSO	47.5	76
BSO	1.8	3
USO	12.5	20
Cystectomy	9.4	15
Total	100	160

TAH: total abdominal hysterectomy BSO: bilateral salpingo-oophorectomy
USO: unilateral salpingo-oophorectomy

When the other variables were kept constant, the patients with solid areas in their adnexal masses were found to have a malignancy risk of 4,65 folds higher (Odds Ratio was 4,65) (95% CI= 1.60 – 13.52; p= 0.005). The patients with papillary projections had a malignancy risk with an OR of 6.49 (95% CI= 1.59 – 26.46; p=0.009). The patients with ascites had an OR of 5.23 (95% CI= 2.00 – 13.65; p=0.001) and the patients with multiloculated lesions had an OR of 4.95 (95% CI= 1.80 – 13.62; p=0.002), signifying their risk of having a malignant lesion (Table 4).

Table 4: The result of logistic regression analysis showing the roles of the indicated variables in predicting the results of the pathologic examinations

Variable	**Co-efficient (β)**	**Standard Error**	**Wald 2**	**p**	**Odds Ratio (OR)**	**% 95 Confidence Interval (CI) for OR**
Presence of solid area	1.54	0.55	7.962	**0.005**	4.65	1.60 – 13.52
Presence of papillary projections	1.87	0.72	6.802	**0.009**	6.49	1.59 – 26.46
Presence of ascites	1.65	0.49	11.416	**0.001**	5.23	2.00 – 13.65
Multiloculation	1.60	0.52	9.608	**0.002**	4.95	1.80 – 13.62
Constant	-3.43	0.53	41.796	**<0.001**	0.03	-

It was determined that there was not a statistically significant difference between the IOTA scoring results and pathology results (p=0.453; Table 5). Kappa coefficient value of IOTA was found to be 0.634 (p<0.001). This value reveals that there is a significant correlation between the IOTA scores and pathology results. A statistically significant difference was found between the values derived from the MI and USG results and pathologic examination results (p=0.007; p<0.001 respectively).

RMI scoring results and pathology results were compatible with each other in general (=0.474; p=0.003).

Table 5: Comparison of the indicated scoring system and pathology results

Presence of ascites	1.65	0.49	11.416	**0.001**	5.23	2.00 – 13.65
Multiloculation	1.60	0.52	9.608	**0.002**	4.95	1.80 – 13.62
Constant	-3.43	0.53	41.796	**<0.001**	0.03	-

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Table 5: Comparison of the indicated scoring system and pathology results

Scoring systems and results		Pathology result		Mc Nemar	Kappa Co-efficient
Benign n(%)		Malign n(%)	p		
IOTA	**Benign**	21 (80.8)	2 (14.3)	0.453	0.634
	Malign	5 (19.2)	12 (85.7)		
MI	**Benign**	21 (91.3)	13 (76.5)	**0.007**	0.162
	Malign	2 (8.7)	4 (23.5)		
RMI	**Benign**	32 (94.1)	3 (50.0)	1.000	0.474
	Malign	2 (5.9)	3 (50.0)		
USG	**Benign**	10 (31.3)	0 (0.0)	**<0.001**	0.154
	Malign	22 (68.8)	8 (100.0)		

When associations between the four respective scoring systems and pathology results were analyzed, it was seen that only IOTA and RMI results were correlated with the pathologic examination results.

The psychometric values calculated for all scoring systems are shown in Table 6. The sensitivity of IOTA was 85.7% and its specificity was 80.8%. The positive predictive value was 70.6% and the negative predictive value was %91.3 (Table 6). The sensitivity of RMI was 50% and its specificity was 94.1%. By using the IOTA scoring system which is one of the major scoring systems with a relatively higher Youden index in predicting the results of the pathologic examination, it may be suggested that malignancies could be detected more accurately.

Table 6: Psychometric values of IOTA, MI, RMI ve USG scoring systems

Scoring system	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy Rate (%)	Youden index
IOTA	85.7	80.8	70.6	91.3	82.5	66.5
MI	23.5	91.3	66.7	61.8	62.5	14.8
RMI	50.0	94.1	60.0	91.4	87.5	44.1
USG	100.0	31.3	26.7	100.0	45.0	31.3

DISCUSSION

Ovarian masses constitute a great proportion of adnexal masses and their diagnoses in the pre-operative period are difficult due to the histopathologic variabilities and the dynamic changes occurring during the menstruation. In the literature, the correlation between the ultrasound imaging findings and the morphology of the macroscopic materials obtained by the surgical resection has been reported to be between 78-99% (9). Regardless of the menopausal situation, the prevalence of malignancies in the patients who underwent surgery due to adnexal masses varies between 5.7-57.5%, whereas, the prevalence of the borderline and benign tumours, vary between 1.4-11.2% and 40-100% respectively. In our study, while the prevalence of malignant adnexal masses was 22.5%, the prevalence of borderline and benign tumours were 7.5% and 70% respectively.

Shalev et al. (10) treated 55 patients who did not have complex cysts and whose Ca-125 levels were normal by using operative laparoscopy. They found that all cysts had a benign nature according to the results of the pathologic examinations(10). In the same period, 75 patients with complex cysts and with higher than normal Ca-125 levels underwent laparotomies and the authors reported that of those patients, 23 were identified to have a malignant tumour (10). As a result, derived from these studies, it has been reported that the cyst size in postmenopausal patients is an essential marker for predicting the malignancy potential(11). In postmenopausal patients, the cysts smaller than 5 cm have been reported to be rarely malignant, however, the cysts larger than 5 cm have been reported to be associated with a relatively higher risk of malignancy (11). In our study, when we accepted the cut off value of the tumour size as 5 cm and 8 cm in the postmenopausal and perimenopausal patients respectively, we found that the sensitivity of predicting a malignancy was 100%. Its specificity was 31.3%, the PPV (positive predictive value) was 26.5%, the NPV (negative predictive value) was 100%, the accuracy rate was 45%, and the Youden index was 31.3.

Because neither the imaging methods nor the tumour markers are not efficient diagnostic tools when used alone, the sensitivity and specificity values of these tests were attempted to be calculating involving the RMI scoring, which is calculated with the data of the menopausal status, ultrasound scores, and the CA 125 levels of patients (12).

Jacobs et al. recommended a cut off level of 200 for RMI. By using this cut off level, discriminating against the benign masses from the malignant ones could be made possible with an 85% sensitivity and 97% specificity(13). While the risk of having developed an ovarian cancer is 42 folds higher in patients with RMI>200 compared to the normal population, in patients with RMI>200, the risk is only 0.15 folds higher compared to the normal population(13). In our study, in order to calculate the RMI scores, we used the menopausal scores (M) (1, if the patient was premenopausal or 3, if the patient was postmenopausal), the CA-125 levels (directly added to scoring formula), and the ultrasound scores (we added 1 point to the score for each finding identified among the 5 major findings of the ultrasound examination). Patients whose RMI scores were above or equal to 200 were accepted to have a malignant lesion. If their RMI scores were lower than 200, those lesions were accepted to have a benign nature. The sensitivity of RMI was found to be 50%, the specificity was 94.1%, the PPV was 50%, the NPV was 91.4%, the accuracy rate was 81.5%, and the Youden index was 44.1.

De Priest and colleagues suggested a modified morphologic scoring system evaluating the tumour volume and the morphologic appearance of the mass. A morphologic index was calculated by using the tumour volume and the structures of the wall and septa (7). Between the years 1987-1992, a transvaginal ultrasound was applied preoperatively to all patients with ovarian tumours smaller than 15 cm(7). A score was determined and this result was compared with the results of the histologic examinations (7). 108 of the 121 patients had benign ovarian lesions and 13 patients had malignancies. While the average morphologic index for benign tumours was 3.64 ± 2.98, it was 8.46 ± 2.48 for malignant tumors (p<0.001)(7). When the threshold of this new scoring system was accepted to be ≥ 5, the sensitivity was found to be 89% and the PPV was found to be 45% (7). In our study, we took the cut off level as 5 and we found the sensitivity as 23.5%, specificity as 91.3%, PPV as 66.7%, NPV as 61.8%, and diagnostic accuracy as 62.5%.

Sassone et al., devised a scale for characterization of the ovarian masses, involving the following factors including the inner wall structure, the presence of septa, the thickness of the cyst wall, and the echogenicity of the mass(14). The authors were able to distinguish benign lesions from malignant masses with 83% specificity, 37% sensitivity, 37% positive predictive value, and 100% negative predictive value (14).

In our study, we found a statistically significant correlation between the malignancy and some morphologic characteristics in ultrasonography. These morphological characteristics found in the ultrasonographic examination were the presence of solid areas, papillary projections, the thickness of the cyst walls, multiloculation, and bilaterality. When the other variables were kept constant, in our study, the malignancy risk of an adnexal mass had an OR of 4.6 folds higher (p: 0.009) in patients who had solid areas in their masses. The malignancy risk was higher in the patients with masses containing papillary projections with an OR ratio of 6.49 (p: 0.001) and higher in patients with multiloculated lesions with an OR ratio of 4.95 (p: 0.002).

Pattern recognition in the diagnoses of pelvic masses by gray-scale ultrasound imaging has already been confirmed (15). Therefore, the contribution of an experienced radiologist in ultrasound will serve remarkably in the discrimination between the benign and malignant lesions. In fact, in a large multicenter study, the pattern recognition was found to be superior to serum CA-125 levels as regards to the diagnostic efficiency of discriminating the benign and malignant adnexal masses (15).

The major drawback of these scoring systems was proposed that validation

studies in different populations were not available to determine their performances as each was developed in their respective institutions. Then, in 1999, a prospective, multicenter study was started including study sites from five European countries. The purpose of this IOTA study was to minimize the limitations of previous research by prospectively collecting the demographic and sonographic data from more than 1000 patients with persistent adnexal masses by following a standardized protocol stating the terms, definitions and qualitative and quantitative endpoints to be used in defining the characteristics of the ultrasound images of the adnexal tumors (16). Using this data, a mathematic model was developed to calculate the risk of malignancy in an adnexal mass, with an area under the ROC value of 0.96 (16). Currently, there are numerous scoring systems, logistic regression models, neural networks, and relevance vector machines to aid in the preoperative diagnosis of an adnexal mass (17).

In Phase 1 of the International Ovarian Tumor Analysis study (1999-2002), the ultrasound data from 1066 non-pregnant women with at least one persistent adnexal mass were collected from nine clinical study sites from five countries (16). A training set derived from 754 patients (70.7%) was used for model development, and a test set derived from the remaining 312 patients was used to test the internal validity of the models (16). Between 2002 and 2005, another IOTA study (IOTA Phase 1) recruited 507 new consecutive patients from three sites which had already participated the Phase 1 to perform a prospective temporal validation of the models which were demonstrated to provide best performances as regards to the internal validation in the Phase 1 study (17). Recruiting further 997 patients at 12 new study sites, which did not participate the Phase 1 study, the aim of the IOTA Phase 2 (2205-2007) study was to externally validate the models for temporal validation (18).

Initially, 11 prediction models were derived from the IOTA 1 dataset. Scoring systems, simple rules developed for ultrasound imaging, logistic regression analysis, artificial neural network models (ANN), and kernel methods, such as support vector machine models, were developed (19). It was found that more complex statistical modelings did not improve the diagnostic performance more remarkably compared to simpler statistical approaches, such as logistic regression. Following these findings, two relatively simple logistic regression models, logistic regression model 1 (LR1) and logistic regression model 2 (LR2) were developed. Both of these models provided appreciable diagnostic performances on both the training and test data and their accuracy was found to be stable when tested for prospective temporal validation in three clinical study centers using the IOTA1b dataset (18). The IOTA study has been emphasized that a good sensitivity value is more important than specificity. However, interpreting the indexes of diagnostic performance depends on the prevalence of pathology in the studied population. According to the IOTA study, a 28% overall prevalence of cancer implies a fixed specificity level of 75% with a sensitivity of 90% indicating that for every five patients who undergo a surgical intervention due to a mass suspected of being malignant, only two of these patients will be diagnosed with a benign lesion confirmed by histology(18).

In the study conducted by Timmerman et al., including 1970 patients, the RMI and IOTA LR 2 models were compared, finding the sensitivity of RMI to be 92.8% and its specificity to be 62.1%. The sensitivity and specificity of IOTA were reported to be 94.3% and 71.1%, respectively. In this study, it was emphasized that the IOTA protocol provided more accurate results compared to RMI in discriminating the malignant or benign adnexal masses (20). According to our study results, it can be suggested that, in predicting the malignancy potential of adnexal masses, IOTA criteria are more successful compared to RMI, morphologic index, and tumor size measurement in ultrasound imaging.

The limitations of the study are; the sample size was limited, the study was conducted in only one center (hospital) and not all the patient's ultrasound evaluation was performed by radiologists, some were performed by gynecologists.

In conclusion, with proven diagnostic accuracies derived from large population-based studies and with the highest value of sensitivity among the other tools and methods used in our study (85.7%), the use of IOTA models will induce a coordination between respective departments and will allow deciding on the type of incision and planning of the preoperative frozen section evaluation in the pre-operative period and will provide means for the maintenance of the optimally efficient plans for the patient management.

There is no conflict of interest.

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