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ORIGINAL ARTICLE

# Utilization of ultrasound as a diagnostic tool in the preoperative assessment of patients with adnexal masses

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## *Summary*

***Purpose:*** *To evaluate the reliability of ultrasound scan (US) findings in the preoperative assessment of the nature of adnexal masses in females.*

***Methods:*** *After detailed history, a preoperative US examination was performed in all women. Tumor diameter, localization, the presence of solid, cystic and multilocular components, excrescences, metastasis and free fluid were assessed. Doppler scan was done and pulsatility (PI) and resistance indices (RI) were determined. These data were compared with postoperatively obtained histopathological findings and statistically analyzed.*

***Results:*** *The study included 609 women out of which 20.7% had malignant, 73.7% benign, and 5.6% borderline tumors. Patients with malignant tumors were oldest (p<0.001). There were significantly more positive US parameters in malignant than in benign tumors (p<0.001). Also, there were significant differences (p<0.001) between malignant, benign and borderline tumors regarding all examined US and Doppler parameters except tumor multilocularity. RI had sensitivity 75%, specificity 61.2%, positive predictive value (PPV) 42.70% and negative predictive value (NPV) 96.16%. PI had sensitivity 50%, specificity 35.3%, PPV 8.37% and NPV 25.93%. Sensitivity of US characteristics was 94.34%, specificity 30.62%, PPV 22.27% and NPV 96.25%.*

***Conclusions:*** *US pattern characteristics and Doppler parameters were found to be moderately reliable in discriminating malignant, benign and borderline adnexal tumors. Tumor of solid or mixed consistency, presence of ascites and excrescences were the best predictors of malignancy.*

***Key words:*** *adnexal masses, Doppler, malignancy, ultrasound, ultrasound pattern recognition*

## Introduction

Appropriate oncologic approach to patients with adnexal masses depends predominantly on adequate preoperative discrimination between benign and malignant ovarian tumors [1,2]. No single diagnostic tool is reliable enough in this determination [3]. Therefore, malignant ovarian tumors are usually diagnosed at an advanced stage and are associated with the highest mortality figures of all gynecological malignancies [4]. There were suggestions that appropriate malignancy risk estimation could be achieved by US assessment of tumor's echomorphology (wall thickness, presence of papillary projections and septas, solid/cystic components, etc) with sensitivity and specificity higher than 90% [3,5]. However, due to a wide variation in patient populations, diagnostic abilities of imaging techniques, and interpretation of US scans, establishing a correct preoperative

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**Table 1.** Baseline characteristics of the patients in the two groups

| *US parameters* | *Circle the mark* | | |
|---|---|---|---|
| | *Present* | | *Absent* |
| Multilocularity | 1 | | 0 |
| Solid parts | 1 | | 0 |
| Mixed consistency | 1 | | 0 |
| Excrescences | 1 | | 0 |
| Bilaterality | 1 | | 0 |
| Septa | 1 | | 0 |
| Ascites | 1 | | 0 |
| Us score | Maximal 7 | / | Minimal 0 |

Each of US parameters was estimated as present or absent and the overall finding was calculated as a summary of all positive ultrasound parameters

diagnosis is still more complicated than it might be expected. Doppler scan has not been found consistent in the diagnosis of malignancy [1].

The aim of this study was to evaluate the reliability of US pattern recognition with Doppler assessment in the discrimination between benign and malignant adnexal masses, and to determine which US data could preoperatively the most consistently predict the nature of the tumor.

## Methods

The study included all consecutive patients with adnexal masses hospitalized at the Clinic of Obstetrics and Gynecology, Clinical Center of Serbia, during a period of 36 months, starting from January 2010. The study was approved by the Clinics Ethics Committee. Written informed consent for all diagnostic and therapeutic procedures was signed by all participants on admission to the Clinic.

Preoperatively, basic epidemiological data and gynecological history (age, presence of symptoms, etc.) were registered. After clinical examination transvaginal US scan of pelvic organs was performed in all women. Tumor diameters were measured and categorized as: <5cm, 5-10cm, and >10cm. Additionally, tumor features such as localization, solid/cystic or multilocular components, excrescences, metastasis and ascites presence were ultrasonographicaly assessed. Doppler scan was done and PI and RI indexes were determined for the largest central tumor blood vessels. US scan was performed separately by two experienced ultrasonographers on Philips HDI 5000, Sono CT and Xres, with endovaginal-V8–4MHz (V) probe and its associated software.

After surgery (laparotomy and staging surgery - salpingooophorectomy for younger patients and expected benign tumors; total abdominal hysterectomy with bilateral salpingooophorectomy, omentectomy, lymphadectomy and appendicectomy in case of suspected malignancy), the histopathological findings (HP) were examined in order to make the final diagnosis and the stage of disease. Tumors were categorized as benign, malignant and borderline, while malignant tumors were also divided according to FIGO stages. All these findings were compared to US scan findings. Finally, we have scored the presence of all examined US parameters as one and absence as zero, and created an US score as an algorithm that connected all single tumor characteristics (Table 1).

*Statistics*

For statistical analyses we used methods of descriptive and analytical statistics (percents, mean values, confidence intervals and standard deviation). For data analysis SPSS 15 (SPSS Inc, Chicago, Ill) computer software was used. Of the methods for testing significance of differences of the evaluated US parameters in different groups of HP findings we applied ANOVA, Kruskal–Wallis nonparametric ANOVA test and $x^2$ test. Moreover, we performed Spearman's nonparametric correlation and discriminant analysis in order to examine which data obtained by US could predict the HP nature of adnexal masses.

Discriminant analysis helps determine which parameters separate two or more groups i.e. categories of the dependent variable. In the analysis, functions that discriminate between groups are constructed. Group centroids are used for evaluation of the obtained significant functions. Centroids are means of discriminant function scores by the group (in our case, tumor type) for each calculated function. The obtained function is an adequate predictor of the group with highest values of centroids. If an evaluated parameter is significantly correlated with the function, it means that it contributes to the discrimination between groups and is a good predictor to which group a case belongs [6].

Finally, we used a receiver operator characteristics curve (ROC) for Doppler characteristics of tumors and patient age, as well as all single tumor features. The curve is created by plotting the true positive rate against the false positive rate for different cut-off points of a parameter. The area under the curve is a measure of how well a parameter can distinguish between two

**Table 2.** Distribution of obtained histopathological diagnoses

| *Histopathological diagnoses* | *Patients* | |
|---|---|---|
| | *N* | *%* |
| Malignant tumors | | |
| Serous adenocarcinoma | 23 | 3.8 |
| Mucinous adenocarcinoma | 16 | 2.6 |
| Endometrioid carcinoma | 25 | 4.1 |
| Clear cell carcinoma | 11 | 1.8 |
| Other malignant tumors | 5 | 0.8 |
| Metastatic tumors | 16 | 2.6 |
| Mixed Mullerian tumors | 6 | 1.0 |
| Papillary adenocarcinoma | 24 | 3.9 |
| Borderline tumors | | |
| Cyst simplex | 94 | 15.4 |
| Endometrioma | 121 | 19.9 |
| Hemorrhagic cyst | 61 | 10.0 |
| Benign tumors | | |
| Benign teratoma | 59 | 9.7 |
| Benign cystadenoma | 75 | 12.3 |
| Fibrothecoma | 31 | 5.1 |
| Other benign tumors | 8 | 1.3 |
| Total | 609 | 100.0 |

examined groups (in our case, tumor types) [6]. Finally, based on the standard formulae, we determined the sensitivity, specificity, positive and negative predictive value of the calculated US score.

## Results

The study included 609 women out of which 126 (20.7%) had malignant, 449 (73.7%) benign and 34 (5.6%) borderline tumors (Table 1). The age of patients ranged from 17 to 87 years (mean 45.11±15.63;median 43). Significantly more women did not have any symptom. Still, malignant tumors of higher FIGO stage were mostly accompanied with pelvic and abdominal pain as well as urinary obstruction (Table 2).

The incidence of various histopathological diagnoses of adnexal masses is listed in Table 1, while descriptive data of parameters that were investigated are presented in Table 3.

*Differences between tumor types in relation with the parameters*

There were significant differences between malignant, benign and borderline tumors regarding all examined parameters except tumor multilocularity. Women with malignant tumors were the oldest with mean age of 57.40 years. Most patients with malignant tumors had ascites. Malignant tumors usually were of mixed consistency or had solid parts and with diameter greater than 5cm. There were significant differences in mean Doppler RI and PI of patients with malignant, benign and borderline tumors (Table 3).

There were significantly more positive US parameters of US score in malignant than in benign tumors (Table 3). The majority of all patients (N=189) had two positive US findings suggestive of malignancy (31%), while only one (with malignant tumor) had all 7 assessed positive findings ($x^2$=444.386; p<0.001). Women with benign tumors mostly had less than 3 positive US parameters and none of them had more than 5 positive US parameters.

According to HP findings, the majority (N=40) of malignant tumors were diagnosed at FIGO stage IIIc ($x^2$=148.990; p<0.001). There were significant differences between borderline and malignant tumors in FIGO stage I regarding the presence of symptoms and excrescences as well as lower RI values that were all more frequently registered in malignant tumors. In FIGO stages II-IV malignant tumors were more often bilateral, with solid parts, ascites and had lower values of RI and higher US score than borderline tumors of the same stage (Table 4).

*ROC analysis*

Reliability of RI, PI and VS scores in the prediction of malignant adnexal masses is presented in Table 5. RI (cut off level 0.88) explained 71.8 % of malignant cases, PI (cut off level 0.56) 29.8% and age 66.3%. Age with cut off level of 45.5 years had sensitivity of 87.5% and specificity of 56.9%, and explained 78.2% of the malignancies (Figure 1).

Moreover, when we made ROC for ultrasonographic characteristics of tumors, multilocularity explained 54.9% of malignant cases, solid tumors 54.4%, mixed consistency 64.1%, excrescences 57.1%, bilaterality 58.2%, presence of septas 53.9% and ascites 69.7 % of malignant cases. Tumor diameter adequately predicted 61.6% of malignant cases and showed very satisfactory sensitivity and NPV.

US score (present ≥3 of the examined risk factors for malignancy) showed excellent sensitivity and NPV that were higher than 90%. Still, specificity and PPV were low. On the other hand, US score had only 6 false-negative findings (4.76%) (borderline or malignancies with

**Table 3.** Descriptive data and differences of the examined parameters between tumor types

| *Parameter* | *Category* | *Benign* | *Borderline* | *Malignant stage I* | *Malignant stage II-IV* | *KWx² or F* | *p value* |
|---|---|---|---|---|---|---|---|
| Age (years) | mean | 41.01 | 53.71 | 57.80 | 57.28 | 49.157 | <0.001 |
| | SD | 14.04 | 17.70 | 12.52 | 13.02 | | |
| Symptoms | no | 354 | 21 | 11 | 43 | 11.591 | <0.001 |
| | yes | 95 | 13 | 19 | 53 | | |
| Diameter (cm) | < 5 | 185 | 7 | 10 | 12 | 22.302 | <0.001 |
| | 5-10 | 237 | 18 | 12 | 57 | | |
| | > 10 | 26 | 9 | 8 | 27 | | |
| Multilocularity | no | 226 | 11 | 15 | 39 | 2.157 | 0.092 |
| | yes | 223 | 23 | 15 | 57 | | |
| Solid parts | no | 180 | 19 | 14 | 17 | 7.995 | <0.001 |
| | yes | 269 | 15 | 16 | 79 | | |
| Mixed consistency | no | 409 | 23 | 19 | 73 | 61.816 | <0.001 |
| | yes | 40 | 11 | 11 | 23 | | |
| Excrescences | no | 443 | 32 | 22 | 81 | 23.724 | <0.001 |
| | yes | 6 | 2 | 8 | 15 | | |
| Bilaterality | no | 354 | 27 | 23 | 50 | 10.593 | <0.001 |
| | yes | 95 | 7 | 7 | 46 | | |
| Septa | no | 397 | 26 | 21 | 82 | 3.825 | 0.010 |
| | yes | 52 | 8 | 9 | 14 | | |
| Ascites | no | 387 | 23 | 19 | 33 | 49.603 | <0.001 |
| | yes | 62 | 11 | 11 | 63 | | |
| RI | mean | 0.87 | 0.78 | 0.58 | 0.54 | 1322.905 | <0.001 |
| | SD | 0.03 | 0.10 | 0.08 | 0.08 | | |
| PI | mean | 0.66 | 0.32 | 0.31 | 0.32 | 228.718 | <0.001 |
| | SD | 0.16 | 0.07 | 0.06 | 0.07 | | |
| US score | mean | 1.87 | 2.26 | 2.74 | 3.37 | 28.150 | <0.001 |
| | SD | 0.23 | 0.35 | 0.12 | 0.31 | | |

RI: resistance index, PI: pulsatility index, KW: Kruskal-Wallis test, F: ANOVA

**Table 4.** Differences in the examined parameters between malignant and borderline tumors

| *Parameter* | *Borderline – Malignant stage I* | | *Borderline – Malignant stage II - IV* | |
|---|---|---|---|---|
| | *KWx² or F* | *p value* | *KWx² or F* | *p value* |
| Age | 0.968 | 0.329 | 1.553 | 0.215 |
| Symptoms | 4.873 | 0.031 | 0.161 | 0.689 |
| Diameter | 0.253 | 0.617 | 0.581 | 0.447 |
| Multilocularity | 1.649 | 0.204 | 0.719 | 0.398 |
| Solid parts | 0.354 | 0.554 | 20.934 | <0.001 |
| Mixed consistency | 0.208 | 0.650 | 0.908 | 0.342 |
| Excrescences | 5.859 | 0.018 | 2.098 | 0.150 |
| Bilaterality | 0.001 | 0.992 | 8.132 | 0.005 |
| Septa | 0.436 | 0.511 | 1.423 | 0.235 |
| Ascites | 0.208 | 0.650 | 12.227 | 0.001 |
| RI | 83.675 | <0.001 | 194.495 | <0.001 |
| PI | 0.808 | 0.372 | 0.092 | 0.762 |
| US score | 0.308 | 0.740 | 4.269 | 0.032 |

RI: resistance index, PI: pulsatility index, KW: Kruskal-Wallis test, F: ANOVA

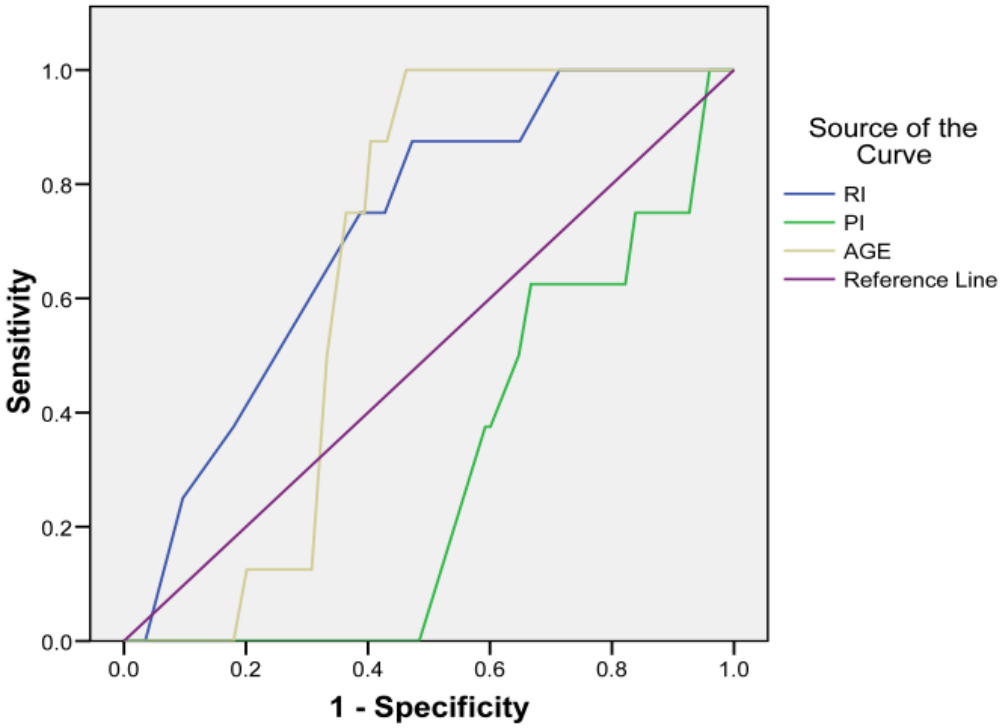


**Figure 1.** Receiver Operator Curve for patient's age and tumor Doppler characteristics, showing that RI and age are good predictors of the nature of adnexal tumors. PI : pulsatility index, RI : resistance index

zero US score).

*US scan in the prediction of tumor's nature*

When we tested which US parameters are the best for the preoperative estimation of tumors' nature, two statistically significant functions ($x^2$=1349.600; p=0.000; % of variance=97.6 and $x^2$=56.805; p=0.000; % of variance=2.4) were obtained. From the largest group centroids for significant function, it can be concluded that patient's age, presence of ascites and excrescences discriminated well malignant tumors from other tumor types, while all other examined US parameters could be successfully used for discrimination of borderline tumors from other tumor types (Table 6).

## Discussion

In this research almost one quarter of malignant tumors were diagnosed at FIGO stage IIIc, emphasizing the significance of early diagnosis on primary health care level. US parameters in our study were proven good predictors of tumors' nature. There were highly significant differences between malignant, benign and borderline tumors regarding all examined parameters except tumor multilocularity. Doppler RI was more reliable than PI for predicting malignancy. Parameters like older age, presence of ascites and excrescences were the best for revealing malignant tumors. According to our results, scoring systems have high sensitivity and can give important additional information about the tumors' nature.

US examination of adnexal masses is based on the detection of changes in size and architecture of the adnexal structures that might precede the manifestation of the disease [7]. Using US scan an adnexal mass can be depicted and characterized at the same time. In addition, this examination is not expensive, easily accessible, and without any harm to the patient. Therefore, US is nowadays accepted as the primary imaging technique in the evaluation of ovarian masses and the main triage method prior to treatment [8,9]. Magnetic resonance imaging (MRI) and computerized tomography (CT) improve accuracy in the characterization of adnexal masses, but are significantly more expensive [10,11]. Additionally, CT has lower sensitivity for small adnexal masses and a physiological corpus luteum can therefore mimic

**Table 5.** Reliability of the examined parameters in the prediction of malignant adnexal masses

| *Parameters* | *Sensitivity* % | *Specificity* % | *Positive predictive value* % | *Negative predictive value* % |
|---|---|---|---|---|
| PI | 50 | 35.3 | 8.37 | 25.93 |
| RI | 75 | 61.2 | 42.70 | 96.16 |
| US score | 94.34 | 30.62 | 22.27 | 96.25 |
| Tumor diameter (5cm) | 86.45 | 33.25 | 41.29 | 81.88 |

PI: pulsatility index, RI: resistance index

**Table 6.** Correlation coefficients between discriminating variables and standardized canonical discriminant function and group centroids of discriminant function

| *Parameters* | | *Function* | |
|---|---|---|---|
| | | *1* | *2* |
| Examined US parameters | Ascites | 0.389* | -0.302 |
| | Age | 0.307* | 0.098 |
| | Excrescences | 0.213* | 0.061 |
| | PI | 0.360 | -0.620 |
| | RI | -0.447 | 0.462* |
| | Mixed consistency | 0.315 | 0.367* |
| | Solid parts | 0.053 | -0.317* |
| | Bilaterality | 0.062 | -0.278* |
| | Septa | 0.136 | 0.205* |
| | Diameter | 0.153 | 0.186* |
| | Multilocularity | 0.031 | 0.177* |
| | Symptoms | -0.019 | -0.087 |
| Functions at group centroids | Malignant | 2.865 | -0.166 |
| | Benign | -0.784 | -0.020 |
| | Borderline | 1.648 | 0.994 |

Function 1 : significant, Function 2 : significant, PI: pulsatility index, RI: resistance index *Largest absolute correlation between each variable and any discriminant function. Functions in the centroid group are the means of the discriminant function scores by group for each function calculated. The function explains satisfactorily the tumor nature with the highest value of centroids

an aggressive malignancy. Compared to US, MRI has lower accuracy for borderline ovarian tumors [6,7]. Thus, transvaginal ultrasonography, should be the initial modality of choice in the identification and characterization of ovarian masses [12].

About 90% of adnexal masses can be evaluated only with US [13]. Transvaginal US has demonstrated considerable advantage over conventional transabdominal US, which is still useful mainly in large tumors [12,13]. Scoring systems help differentiate benign from malignant masses [14-17] and can determine with greater certainty whether the patient will be followed up or referred to alternative imaging method or surgery. Only by performing US examination for every patient is possible to reduce unnecessary procedures or act in a proper manner [18]. This study also proved that scoring and taking into consideration all tumor features together can reach good reliability of preoperative tumor assessment.

When used as the only screening test, US is sensitive, but has low PPV [18]. Current data from large international studies that evaluated subjective assessment of US findings also reached excellent diagnostic performance of this method, obtaining both sensitivity and specificity of US scan higher than 90% [19]. We found that malignant tumors had more positive US parameters than

benign ones. Women with benign tumors usually had less than 3 positive US parameters. US in our study had very high sensitivity but rather low specificity. This is in accordance with other literature data [11]. Furthermore, obtaining two statistically significant functions in this study, we concluded that the examined US tumor parameters can adequately distinguish factors between different types of adnexal masses. Parameters like older age, presence of ascites and excrescences are the best for revealing malignant tumors.

Doppler examination of intratumoral blood flow velocity waveforms is usually added on gray-scale imaging with intention to more correct prediction of malignancy [20]. Doppler examination raises confidence in achieving the correct diagnosis mostly in stage I ovarian carcinoma (83%) [19]. Although most ovarian tumors are well vascularized, advanced epithelial ovarian malignancy has more solid tissue, making it even more vascularized [21]. Malignant tumors show increased flow signals both at the periphery and in the central parts of the mass as well as in septa and in the solid areas [21]. In our study the obtained sensitivity of Doppler scan was similar to literature data. Still, based on the results of ROC curve, RI and age were more reliable for the preoperative prediction of malignancy, while PI was not so reliable.

In future gynecologic oncology research, 3D US may be an important modality in the clinical evaluation of adnexal tumors [22].

In conclusion, US parameters are appropriate predictors of the tumor's nature. Optimal characterization could be obtained through the combination of gray-scale US morphology and color Doppler flow imaging evaluation. Parameters like US-diagnosed presence of ascites and excrescences are the best for characterizing malignant tumors. Tumor's solid and mixed consistency found on US scan are also consistent markers of malignancy. Doppler RI is more reliable than PI for predicting malignancy. US tumor features' score had sensitivity and NPV higher than 90%. As almost 1/4 of malignant tumors are diagnosed at FIGO stage IIIc, there is a need for early diagnosis of disease on primary health care level. Therefore, detailed US examination with Doppler scan and the use of scoring systems should always be performed in all patients with adnexal masses.

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