ROLE OF COMBINING COLOUR DOPPLER AND GREY SCALE ULTRASOUND IN DIFFERENTIATING BENIGN FROM MALIGNANT OVARIAN MASSES

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ULOGA KOMBINOVANE COLOR-DOPPLER I GRAY-SCALE ULTRAZVUČNE METODE U DIFERENCIJACIJI BENIGNIH OD MALIGNIH OVARIJALNIH PROMENA

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ABSTRACT

The aim of this study was to evaluate ovarian masses with conventional grey scale ultrasonography and colour Doppler flow imaging and to assess the diagnostic reliability of these methods in differentiating benign and malignant ovarian masses.

We assessed 56 patients with an ovarian mass. Morphological characterisation of the mass was performed utilising the Sassone score. Colour Doppler parameters were recorded for each patient, and the Caruso vascular score was also applied. The results were compared with surgical/pathological and/or follow-up scans.

Using the Sassone score, overall reliability in differentiating ovarian masses had a sensitivity of 89.5% and a specificity of 78.4%. Using the Caruso score alone, we found a sensitivity of 89.5% and a specificity of 86.5%. Using the Sassone and Caruso scores together, we found a sensitivity of 94.7% and a specificity of 89.1%.

Combining both morphological and colour Doppler scores in the evaluation of ovarian masses obtained higher specificity, sensitivity, and accuracy than was obtained using a single score only.

Keywords: *Ovarian mass, Ultrasonography, Vascular score, Malignant, Benign.*

SAŽETAK

Cilj ove studije bila je evaluacija ovarijalnih tumora konvencionalnom crno-belom ultrasonografijom kao i kolor-dopler metodom sa ciljem diferentovanja benignih i malignih osobina tumora.

Uključili smo 56 pacijenata sa tumorima ovarijuma. Morfološka karakterizacija tumora je urađena pomoću Sasson skora. Za svakog pacijenta određeni su parametri pomoću kolor-dopler metode kao i Karuzo vaskularni skor. Ovi rezultati su upoređivani sa hirurškim i/ili patološkim nalazima.

Korišćenjem Sasson skora, opšta pouzdanost u proceni vrste ovarijalnih tumora ima senzitivnost od 89,5% i specifičnost od 78,4%. Korišćenjem Karuzo skora, pronašli smo senzitivnost od 89,5% i specifičnost od 86,5%. Upotrebom oba skora, Sassone i Karuzo, senzitivnost je bila 94,7% a specifičnost čak 89,1%.

Kombinovanjem morfoloških i kolor-dopler skorova u evaluaciji i dijagnostici ovarijalnih tumora dobijamo veću specifičnost, senzitivnost i tačnost dijagnoze u odnosu na pojedinačno upotrebljene metode.

Ključne reči: *Ovarijalni tumor, ultrasonografija, vaskularni skor, maligni, benigni*

INTRODUCTION

The diagnosis of ovarian masses is a frequent dilemma in clinical work. Most ovarian masses are benign (1,2). The most crucial step following identification of the ovarian mass is the perception of a level of malignancy; determining the level of malignancy will have a great impact on patient survival. It is the danger of malignancy that drives us to reliable and immediate diagnosis to decrease morbidity and mortality. Ovarian cancer represents a principle surgical difficulty in that it requires exhaustive and usually complicated therapies, and it greatly affects the patient's psychological and physical state. It has the greatest case fatality rate of all the gynaecological malignan-

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Table 1. Criteria used in Sassone score for sonomorphological characterisation (7)

Inner wall structure	Smooth	Irregularity less than 3 mm	Papillarities more than 3 mm	Not applicable	-
Septae	No septa	Thin less than 3 mm	Thick more than 3 mm	-	-
Wall thickness	Thin less than 3 mm	Thick more than 3 mm	Not applicable mostly solid	-	-
Echogenicity	Sonolucent	Low echogenic	Low echogenic with echogenic core	Mixed echogenicity	High echogenicity

Benign: <9; Malignant: ≥ 9

cies (3). Therefore, it is necessary to have a diagnostic tool for its immediate discovery and conventional treatment and to increase survival. Therefore, we want diagnostic means that allow proper classification of ovarian masses before surgery; hence, it is essential to identify the nature of the tumour before surgery. Ultrasonography (USG) is regarded as the basic imaging modality for recognising the nature of the ovarian mass as benign or malignant (4). USG morphologic assessment is still the most common modality for detecting ovarian cancer (5). USG relates morphologic images with gross macroscopic pathologic characteristics of ovarian masses. However, when morphologic characteristics only are used to predict the ovarian malignancy, there is a tendency to over-diagnose malignant tumours because of a large overlap between malignant and benign masses. Accordingly, the addition of colour Doppler imaging with pulsed Doppler spectral analysis enhances the characterisation of ovarian masses by means of quantitative blood flow measurements obtained from tumour vessels and thus improves sensitivity and specificity of the characterisation of ovarian masses (1-4). High operator dependence and extreme variability in the characteristics of ovarian tumours make a definite diagnosis still difficult. To overcome these limitations, applying scoring systems has been promoted. These scoring systems, joining various parameters of USG and colour Doppler, raise the sensitivity and specificity of diagnosis with excellent accuracy (6).

The purpose of this study was to evaluate the ovarian masses with conventional grey scale and colour Doppler flow imaging and to assess the diagnostic reliability of these methods in differentiating benign and malignant ovarian masses.

MATERIALS AND METHODS

This prospective study was carried out between August 2015 and January 2017. The study included 56 patients who were clinically suspected to have ovarian neoplasm and referred for USG and Doppler examinations. Ethical clearance for the study was obtained from our local institutional scientific and ethics committee with approval number 32 / 2015 before the commencement of the study. Informed consent for all participating patients was obtained. All patients were examined on GE Voluson E6 Color Doppler Machine with 3.5–5 MHz convex and 7.5 MHz transvaginal transducers and with grey scale, power, and spectral Doppler. The detailed history of all patients was studied, and complete examination was performed. USG preferably was performed during the proliferative phase of the menstrual cycle in premenopausal women. The same radiologist evaluated all the cases. Scanning was performed in the supine position. The whole of the abdominal cavity was scanned in longitudinal and axial plane with particular reference to the pelvic cavity. The ovaries were recognised. Ovarian masses in either ovary, if seen, were assessed. In uncertain cases of ovarian masses on transabdominal USG, transvaginal USG was done to exclude extra-ovarian masses. The Sassone scoring system on the basis of morphological parameters was applied where a score ≥9 is considered to be probably malignant. Table 1 shows the Sassone scoring system, which is based on the visualisation of the inner wall structure, wall thickness, septae and solid part echogenicity. Subsequently, power and Doppler flow imaging and spectral analysis were performed. Doppler parameters were optimised for detection of flow and calculation of impedance indices. Flow results were recorded as being absent or present and further characterised as normal or increased. Normal flow was characterised by fine branching vessels, no evidence of "hot-spots"/aliasing, and presence of peripheral flow. The flow was classified as increased if di-

Table 2. Criteria used in Caruso score (8)

Vessels location	Absent	0
	Present	1
	Peripheral	0
	Septal	1
	Central	2
Arrangement of vessels	Regular	0
	Random	2
Waveform pattern	Sharp with diastolic notch	0
	Smooth without notch	2
Lowest RI	More than 0.43	0
	Less than 0.43	2

*Benign: <5; Malignant: ≥ 5. RI: Resistive index

Table 3. Distribution of ovarian masses according to age and parity.

		Histopathology		
		Malignant %	Benign %	P value
Age	<30	21.1	29.7	0.287
	30---39	15.8	32.4	
	40---49	15.8	13.5	
	=>50	47.4	24.3	
	Mean±SD (Range)	45.0±15.5(20-67)	38.2±12.2(20-67)	
Parity	Nulliparous	26.3	16.2	0.016
	P1	10.5	37.8	
	P2	10.5	29.7	
	P3	26.3	10.8	
	P4 & more	26.3	5.4	
	Mean±SD (Range)	2.3±1.8(0-5)	1.5±1.1(0-4)	

SD: Standard deviation, P: Para.

lated prominent parenchyma vessels were present; "hot-spots" and aliasing were seen in colour flow mapping. The vessel location (peripheral, central, and septal), arrangement (regular/random) and morphology (normal-fine tapering vessels versus abnormal dilated prominent vessels, focal stenosis, aneurysms, blind-ending lakes and dichotomous branching) were also noted. Spectral Doppler study including RI (Resistivity index), PI (Pulsatility index), PSV (Peak systolic velocity) and presence or absence of dicrotic notch were recorded in each patient. Caruso score (Table 2) was applied for further characterisation of the mass where a score ≥5 was supposed indicative of malignancy. Benign and malignant classification of the ovarian masses was done depending upon the grey scale and colour Doppler USG. The results were correlated with the histopathological findings.

Table 4. The histopathological diagnosis of the studied ovarian masses.

	Histopathological diagnosis	No. (%)
Benign	Serous cystadenoma	8 (14.29)
	Mucinous cystadenoma	4 (7.14)
	Mature teratoma	13 (23.21)
	Haemorrhagic cyst	5 (8.93)
	Fibrothecoma	2 (3.57)
	Serous cystadenofibroma	2 (3.57)
	Endometriosis	2 (3.57)
	Epidermoid cyst	1 (1.79)
	Total	37(66.07)
Malignant	Serous cystadenocarcinoma	5 (8.93)
	Mucinous cystadenocarcinoma	3 (5.35)
	Endometroid adenocarcinoma	2 (3.57)
	Immature teratoma	7 (12.50)
	Brenner cell	1(1.79)
	Fibrosarcoma	1(1.79)
	Total	19 (33.93)

Statistical analysis

Statistical Package for the Social Sciences version 20 (SPSS 20) was used for both data entry and data analysis. Discrete variables were displayed as a number (%). Chi-square test (or Fisher's exact test when appropriate) was used to test the significance of the relationship for the discrete variable. P-value of < 0.05 was regarded as significant.

RESULTS

Fifty-six patients were included in this study. Thirty-eight (68%) patients were pre-menopausal, and 18 (32%) were postmenopausal women. The mean (± SD) age of patients included in the study was 45.0 ±15.5 years (range 20-67 years) for malignant masses and 38.2±12.2 years (range 20-67 years) for benign masses. In correlation with the parity, the malignant masses were significantly noted more among nulliparous and para 3 women, while the benign masses were more among para 1 women. Table 3 shows the distribution of the ovarian masses according to age and parity. Table 4 summarises the histopathological diagnosis of 56 ovarian masses studied where 37 (66.07%) were benign and 19 (33.93%) were malignant.

Table 5 shows the distribution of 56 patients according to the Sassone, Caruso and combined scoring systems and its correlation to the finally confirmed histopathological diagnosis. Out of 37 benign cases, the Sassone scoring system alone was able to diagnose 29 (78.3%) cases, the Caruso scoring system alone was able to identify 32 (86.4%) cases, and the combined scoring system was able to identify 33 (89.1%) cases. Out of 19 malignant cases, the Sassone scoring system alone was able to diagnose 17 (89.4%) cases, the Caruso scoring system alone was able to diagnose 17 (89.4%) cases, and the combined scoring system was able to diagnose 18 (94.7%) cases. These findings, regarding the Sassone scoring system alone, had a sensitivity of 89.5%, a specificity of 78.4%, a positive predictive value (PPV) of

Table 5. Comparison between Sassone, Caruso and combined scoring systems and histopathology

	Benign	Malignant	Total
Sassone score			
Benign (0-8)	29	2	31
Malignant (≥9)	8	17	25
	37	19	
Caruso score			
Benign (<5)	32	2	34
Malignant (≥5)	5	17	22
	37	19	
Combined score			
Benign	33	1	34
Malignant	4	18	22
	37	19	

86.0%, a negative predictive value (NPV) of 93.5% and an accuracy of 82.1%; the findings of the Caruso scoring system alone had a sensitivity of 89.5%, a specificity of 86.5%, a PPV of 77.3%, an NPV 94.1% and an accuracy of 87.5%. Using both the Sassone and Caruso scores together, we found a sensitivity of 94.7%, a specificity of 89.1%, a PPV of 81.8%, an NPV of 97.0% and an accuracy of 91.0%.

Table 6 gives comparative efficacy of Sassone, Caruso, and combined scoring systems in differentiating benign from malignant ovarian masses and shows that the combined scoring system is a better performing scoring system.

DISCUSSION

Today, the commonly applied means for distinguishing between malignant and benign ovarian masses are the physical examination, serum tumour markers, and grey scale and colour Doppler USG (9). Colour and pulsed Doppler can improve preoperative diagnosis of ovarian tumours when compared to transvaginal sonography alone or tumour marker assessment (10). Although grey scale USG is sensitive in identifying ovarian carcinoma, its reliability has not been enough to preclude further invasive methods, such as laparoscopy and laparotomy. Colour Doppler imaging and spectral Doppler imaging have been reviewed as potential means of increasing the specificity of grey-scale USG in differentiating benign from malignant masses (11,12).

Timmerman D et al.(13) in their prospective validation study, which was conducted in 19 USG centres in

Table 6. Statistical comparison between two scoring systems

Statistical parameter	Sassone scoring system %	Caruso scoring system %	Combined scoring system %
Sensitivity	89.5	89.5	94.7
Specificity	78.4	86.5	89.1
PPV	68.0	77.3	81.8
NPV	93.5	94.1	97.0
Accuracy	82.1	87.5	91.0

PPV: Positive predictive value, NPV: Negative predictive value

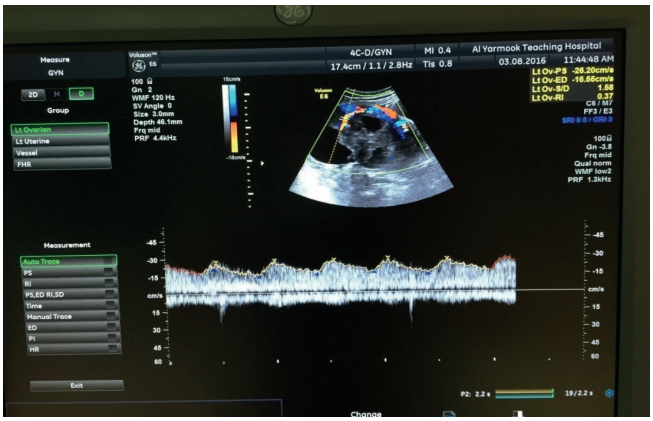

Figure 1. Spectral Doppler USG of 47 year-old patient shows complex ovarian mass with internal vascularity and low RI=0.37 diagnosed as serous cyst adenocarcinoma on histopathology

eight countries, concluded that the use of the simple USG rules (shape, size, solidity, and results of colour Doppler examination) to distinguish benign from malignant ovarian masses has the potential to improve the management of women with an ovarian mass.

Characteristics that raise the suspicion of malignancy in USG include the presence of thick septa, papillary projections, heterogeneous echotexture, and septa greater than 3 mm in thickness or which have flow on colour Doppler USG (14,15). Neovascularisation in the tumour always offers lower resistance to blood flow in malignant neoplasms (Fig 1).

Benign tumours have been characterised as being unilocular, with thin septae, homogenous iso echogenicity and thin wall capsule (16).

In our study, using only a grey scale Sassone scoring system, out of 37 benign tumours, 29 were correctly diagnosed and 8 were misdiagnosed. Out of 19 malignant tumours, 17 were correctly diagnosed as malignant and 2 were misdiagnosed as benign. Using Caruso scoring system, out of 19 malignant masses, 17 were correctly diagnosed. Using the combination of both scoring systems, out of 19 malignant cases 18 were correctly diagnosed. The only case, which was not diagnosed, was of immature teratoma. In this case, the tumour was of mixed echogenicity without solid mass or vascularisation. Accordingly, out of 37 benign masses, 33 were correctly diagnosed as benign and 4 were misdiagnosed as malignant; these were 2 cases of fibrothecoma and 2 cases of serous cystadenofibroma. In these cases, the tumours were encountered as unilocular cysts with solid areas and central flow.

In our study, Colour Doppler results showed predominantly peripheral localisation of vessels in benign masses (65%) and predominantly central or septal vessel localisation (81.8%) in malignant masses. This agrees with the results of Jokubkiene et al. (17) who found that 57% of benign masses showed peripheral vascularisation versus 70% of malignant masses that showed central vascularisation.

In our study, the RI alone was an insufficient discriminating parameter, as there was overlap between benign and

malignant masses. The RI cut-off value of <0.43 used had a significant p-value (<0.0005). Pulsatility index <1.0 had a sensitivity of 73.6% and a specificity of 64.9%, and there was a significant overlap between malignant and benign masses. Ueland et al. (16) reported sensitivity and specificity of 52.8% and 77.6%, respectively, using the cut-off value of PI < 1. In spite of that, Abbas et al. (18) reported that PI < 1 was an important feature of malignancy (80.4%), but PI < 1 was also found in 15.7% of benign masses. Thus PI alone cannot be a reliable parameter to detect malignancy. Shah D et al. (19) reported sensitivity (97.5 %) and specificity (84.1 %) with *PI* and *RI* values of <1.0 and <0.6, respectively, in their multi-parameter analysis utilising B-mode USG along with Colour Doppler and Spectral Doppler to differentiate between malignant and benign ovarian tumours. These findings are correlated with our result.

In the present study, B mode USG along with Doppler showed a sensitivity of 94.7%, a specificity of 89.1%, a PPV of 81.8%, an NPV of 97.0% and an accuracy of 91.0%. These results agreed with those of Abbas et al. (18) who were using a new scoring model (Assiut Scoring Model {ASM}), in which they used two-dimensional USG and Doppler features and showed a sensitivity of 93.5%, a specificity of 92.2%, a PPV of 82.7% and an NPV of 97.3%, with overall accuracy of 92.6%. Our results also agree with the results of Dhwani et al. (20), who conclude that using the combination of both grey scale and colour Doppler in differentiating benign from malignant ovarian masses gives results with more accuracy. Furthermore, our results agree with those of Malhotra A et al. (21), who conclude that grey scale USG combined with Colour and Spectral Doppler is superior to grey scale USG alone in differentiating benign and malignant adnexal masses. Gagandeep et al. (22) evaluated 30 patients with ovarian mass in their study, and they showed a sensitivity of 91.7% and a specificity of 77.7% when using the Sassone score alone, a sensitivity of 83.3% and a specificity of 88.9% when using Caruso score alone, and a sensitivity of 90.9% and a specificity of 93.3% when using both scores together. These findings are well correlated with our results.

Based on the results of our study, patients with masses score < 5 can be managed in the gynaecological unit by a gynaecologist, either conservatively or surgically, according to their features. Patients with masses score ≥ 8 must be referred to a gynaecological oncologist and be managed in specialised oncology centres. Patients with masses score 4-6 are suspicious with high possibility of malignancy if score ≥ 6, so further investigations may be ordered such as MRI.

CONCLUSION

There is significant overlap in the morphologic features of different ovarian masses. The combination of grey scale USG with colour and spectral Doppler is recommended as the leading diagnostic modality in patients with an ovarian tumour. This combination gives better diagnostic achievement than an individual method and accordingly will establish the definite diagnosis of malignancy early in the course of the disease.

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