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Evaluation of gray-scale and color Doppler sonography accuracy in discrimination between benign and malignant adnexal tumors

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Abstract

Introduction: Adnexal tumors are third common neoplasms in female reproductive ages and the fifth cause of death in women.
Objectives: The aim of the study was to evaluate sonography accuracy in discrimination between adnexal malignancies.
Patients and Methods: This is a retrospective study in women with adnexal masses. Sonography findings were compared with histopathology diagnoses.
Results: Around 67 masses were involved in the study and accuracy of sonography was 92%.
Conclusion: The accuracy of gray-scale and color Doppler sonography in discrimination between malignant and benign adnexal masses were high and proved to be valuable diagnostic tools.

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Introduction

An adnexal tumor may be found in women presenting with gynecological complaints or it may be an incidental finding. The finding of an adnexal mass usually raises anxiety because of the possibility of malignancy. Accurate discrimination between benign and malignant adnexal masses is the essential starting point for optimal management. Most women with an adnexal mass do not have cancer (1). Identifying women with benign pathology is important in order to avoid unnecessary morbidity as well as unnecessary costs. Conversely, recognizing cancer means that treatment is not delayed and appropriate staging can be carried out in specialized surgical centers (2).

Nowadays, three primary tests are common for diagnosis of adnexal masses; pelvic physical examination, CA125 tumor marker serum level measurement and ultrasound examination. Ultrasonography is currently considered as the primary imaging modality for identifying and characterizing adnexal masses (3).

Key point

In a study on 67 adnexal masses, we found the accuracy of gray-scale and color Doppler sonography in discrimination between malignant and benign adnexal masses were high and proved to be valuable diagnostic tools.

Ultrasound imaging is almost always used to determine the nature of a mass. In the hands of an experienced ultrasound examiner subjective evaluation of ultrasound findings, i.e. pattern recognition, is an excellent method for discrimination between benign and malignant masses (1). Sonography is a fast, non-invasive, repeatable, inexpensive and accessible diagnostic modality.

Objectives

It is necessary to find the accuracy of ultrasonography findings for determination of approach and avoidance of unnecessary invasive or expensive diagnostic methods. The aim of this study was to determine the accuracy of gray-scale and color Doppler

ultrasound in the diagnosis of malignancy in adnexal masses.

Patients and Methods

Study protocol

This cross-sectional analytical study was designed to retrospectively collect data from 2013 to 2014 by non-probability purposive sampling technique. Women were included if they were referred for an ultrasound examination in the radiology department of Imam Khomeini teaching hospital in Ahvaz. Pre- and post-menopausal women having both ultrasound and histopathology records of ovarian masses were recruited in the study. Medical records (histopathology and ultrasound reports) for ovarian masses were collected during the study period. Although a mass was diagnosed on ultrasound, there was no histopathology report on it, thus it was excluded from the study.

After permission from research departmental heads of tertiary care hospitals; data collection process was commenced. Confidentiality of patients' records was assured and maintained throughout the study. Ultrasound reports from medical records of patients with proven ovarian masses on histopathology were analyzed. Final diagnosis was confirmed with histopathology considered as a gold standard.

Ethical issues

The research followed the tenets of the Declaration of Helsinki and this study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran (Ethical code# ajums.REC.1393.37).

Statistical analysis

For sample size calculation, we separately calculated P-sensitivity and P-specificity of ovarian carcinoma (0.88 and 0.96 respectively) (4). The sample size was based on the maximum amounts. Confidence interval was set at 95%, bound on error of 9%, and calculated sample size N=67. $[N=Z_{\alpha/2}{}^{2}P(1-P)/d^{2}]$.

Data were entered and analyzed using SPSS software. Frequencies were generated and proportions reported for qualitative variables. Mean and standard deviation computed for quantitative variables such as age. Sensitivity and specificity of the ultrasound for were calculated for ovarian masses. Positive and negative predictive values (NPVs) were also computed.

Results

Around 67 women characterized by (mean age 40.72 years, range 20-64) entered the study. Of these, 43 (65%) were premenopausal and 24 (35%) were postmenopausal. After gray-scale ultrasound image evaluation and supplementation of Doppler evaluation, there were 58 (86%) benign tumors and 9 (14%) malignancies. Mean age was 41.16 years and 37.89 years respectively in benign and malignant pathologies ($P=0.79$). The histological diagnosis is shown in Table 1. Comparison of sonography and histopathology results in the differential diagnosis of malignant adnexal masses is shown in Table 2.

Subjective evaluation of gray-scale and color Doppler correctly predicted benignity in 96% of tumors and malignancy in 77% of them. It missed out on two of 9 malignant and three of 58 benign tumors. False positive cases are shown in Table 3.

Premenopausal women had 36(53%) benign and 7 (10%) malignant pathology and postmenopausal women had 22 (32.8%) benign and 2 (2.9%) malignant pathology ($P=0.360$). Premenopausal women had 36 (53%) and 7 (10.4%) benign and malignant ultrasound diagnosis respectively and the postmenopausal women had 21 (31.3%) and 3 (4.4%) benign and malignant ultrasound diagnosis respectively ($P=0.677$).

The sensitivity, specificity, positive predictive value (PPV) and NPV of gray-scale and color Doppler sonography in the characterization of benign and malignant ovarian masses are shown in Table 4.

The women with low levels of serum CA125 had 54 (80.5%) benign pathology and 4 (5.9%) malignant pathology. Accordingly, the women with high levels of serum CA125 had 4 (5.9%) benign pathology and 5 (7.4%) malignant pathology ($P<0.001$). Around 15 (22.3%) of masses had solid components of which 7 (10.4%) masses were benign and 8 (11.9%) were malignant. Furthermore, 52 (77.6%) of masses did not have solid components. Of which 51 (76.1%) of masses were benign and one (1.4%) were malignant ($P<0.001$). Only one case had ascites that were malignant but were not significant ($P=0.533$). Moreover, 5 masses had papillary projections, two of which were dermoid cyst and three were malignant ($P=0.002$). Additionally, 4 masses were cystic with wall thickness more than 3 mm, three of which were malignant and one

Table 1. Histopathological diagnoses of tumors

Histological diagnosis	No.	%
Serous cystadenoma	4	6
Cystadenofibroma	4	6
Mucinous cystadenoma	8	11.9
Follicular cyst	8	11.9
Malignant	9	13.4
Dermoid cyst	14	20.9
Hemorrhagic cyst	18	26.9
Endometrioma	2	3
Total	67	100

Table 2. Sonography and pathology results crosstab; frequency and percentage per row

	Benign Pathology	Malignant Pathology	Total
Benign sonography (%)	55 (96.49%)	2 (3.50%)	57
Malignant sonography (%)	3 (30%)	7 (70%)	10
Total	58	9	67

Table 3. False positive cases

Pathology	Menopause	CA125	Volume (cc)	Gray-scale	Doppler
Endometrioma	post-menopause	High	943.9	Solid mass	No findings
Endometrioma	post-menopause	High	60.7	Solid mass	No findings
Hemorrhagic cyst	pre-menopause	Low	106.6	Heterogeneous echo with solid components	No findings

Table 4. Sensitivity, specificity, PPV and NPV of gray-scale and color Doppler sonography in discrimination of adnexal malignancies

Population		Sensitivity	Specificity	PPV	NPV	Accuracy
All Patients	Gray-scale	77.7%	94.8%	70.0%	96.4%	92.5%
	Gray-scale +color Doppler	77.7%	94.8%	70.0%	96.4%	92.5%
Pre-menopause	Gray-scale	85.7%	97.2%	85.7%	97.2%	95.3%
	Gray-scale +color Doppler	85.7%	97.2%	85.7%	97.2%	95.3%
Post-menopause	Gray-scale	50.0%	90.9%	33.3%	95.2%	87.5%
	Gray-scale +color Doppler	50.0%	90.9%	33.3%	95.2%	87.5%

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

was cystadenofibroma ($P<0.001$). In addition, 21 masses had internal echogenicity, of which 6 were dermoid cysts, 4 mucinous cysts, 4 hemorrhagic cysts, 2 endometriomas and 5 malignant tumors ($P=0.057$). Likewise, 5 masses had a thick septum (more than 3 mm) one of which was dermoid cyst, 1 mucinous cyst, 1 hemorrhagic cyst and 2 malignant tumors ($P=0.070$). The accuracy, sensitivity, specificity, NPV and PPV of gray-scale sonography parameters and CA125 serum level are shown in Table 5.

From 9 malignant tumors, color Doppler sonography showed low color flow in 4 cases, high color flow in 3 cases and no color flow in 2 cases. Six masses were suggestive of malignancy by color Doppler resistance index of (RI<0.4) and 5 were suggestive of malignancy by pulsatility index of (PI<1.0). The results were not statistically significant. We had no benign tumor suggestive of malignancy by use of color Doppler findings. Mean volume of masses in pathology findings are shown in Table 6.

Discussion

Adnexal masses are common complications in clinical practice. Sonography is considered the first-line imaging technique for discriminating between malignant and benign lesions, and it has been shown to be useful for determining optimal treatment (5).

Masses felt to be benign can be managed expectantly or with minimal-access surgery. Malignant pathology will require referral to an appropriately trained gynecological oncologist (6).

The studies that evaluate the sensitivity of sonography in discriminating between benign and malignant adnexal tumors have shown sonography to be a high sensitive modality. They reported 88-100 percentage sensitivity for gray-scale sonography (4). However, 100 percentage sensitivity seems to be due to technical problems, because there are many reports about false positive and false negative cases (7).

Guerriero and colleagues obtained sensitivity and specificity of 98 and 89 percentages respectively, by joint sonography and Doppler findings in a study with more than 2000 pelvic masses (8). In our study, we obtained 77.7% sensitivity and 94.8% specificity which did not change after adding color Doppler findings.

This means that all of the detected malignant tumors had gray-scale findings suggestive of malignancy whereas malignant tumors with no gray-scale findings, neither had any color Doppler findings suggestive of malignancy. However, this result can be due to few malignant tumor cases in our study (7 malignant tumors in ultimate sonography diagnosis). Nevertheless, Valentin et al (4) in a study with 173 adnexal masses also could only find one case from incorrect sonography confident diagnosis cases and obtained a correct diagnosis by adding color Doppler findings. This evidence suggests Doppler findings play a small role in discriminating between benign and malignant adnexal masses. However it can help to confirm grayscale findings and identify vascular characteristics of these masses.

Table 5. Accuracy, sensitivity, specificity, PPV and NPV of gray-scale sonography parameters and CA125 serum level

	Sensitivity	Specificity	PPV	NPV	Accuracy
CA125	55.5%	93.1%	55.5%	93.1%	88.0%
Solid components	88.8%	87.9%	53.3%	98.0%	88.0%
Papillary projections	33.3%	96.5%	60.0%	90.3%	88.0%
Wall thickness	33.3%	98.2%	75.0%	90.4%	89.5%
Echogenicity	55.5%	72.4%	23.8%	91.3%	70.1%
Septation	22.2%	94.8%	40.0%	88.7%	85.0%

Table 6. Mean volume of masses in pathology samples

Histological diagnosis	Mean volume	Range
Serous cystadenoma	18.67 ± 3.86	5.7-38.9
Cystadenofibroma	61.67 ± 4.99	30.0-87.2
Mucinous cystadenoma	508.48±126.59	30.8-1568.9
Follicular cyst	31.22 ± 20.81	9.3-87.9
Malignant	76.62 ± 55.76	12.7-201.6
Hemorrhagic cyst	132.34 ± 140.76	11.4-723.1
Dermoid cyst	167.45 ± 315.27	11.2-974.5
Endometrioma	502.30 ± 151.06	60.7-943.9
Total	165.07± 569.41	5.7-1568.9

In the study by Guerriero et al (8) 81% of malignant tumors were correctly classified in the premenopausal population in comparison to 92% in the postmenopausal population. Conversely, there are studies that have reported higher specificity for discrimination between benign and malignant adnexal tumors in postmenopausal population. Additionally, our study accuracy, sensitivity, specificity, PPV and NPV in the premenopausal population were higher than the postmenopausal state. The greatest difference was in PPV. As Menopausal phase is identified as a malignancy risk factor, it can have an effect on the mind of the sonographer and raise the false positive rate. In our study, also 2 from 3 false positive cases were postmenopausal. It can be due to low PPV. Regarding hormonal changes in the premenopausal phase and structural changes in pelvic structure, anatomical variations are greater and based on day of menstrual cycle, are predictable. On the other hand, despite structural stability in the postmenopausal phase, the prevalence of atypical pelvic pathologies are higher and false negative or false positive rate is more common.

In past studies, tumor morphology in gray-scale features reported poor diagnostic test with a false positive rate of 63% (4).

In our study the PPV's of gray-scale findings were 23.8%-75% that show each of them alone had low value for adnexal malignancies diagnosis. Most specific gray-scale findings were wall thickness (98.2%) and most sensitive was solid components (88.8%).

We had three false positive cases. Two cases of endometrioma and one hemorrhagic cyst. Endometrioma cases were in postmenopausal women with high CA125 (>35 U/mL) and high volume mass (60.7 and 943.9 cc) that were solid masses without any blood flow in Doppler sonography. Typically an endometrioma is a unilocular tumor and has low-level echogenicity representing old blood in the cyst cavity. Endometriomas may also have atypical features, and frequently had debris within the cyst and may give the impression that it is a unilocular-solid lesion with solid papillary projections. In postmenopausal women the appearance of an atypical endometrioma should be examined very carefully as there is a significant risk of malignancy within such lesions in this age group (9). In our study, also, demographic and laboratory data may have had potential effects on the misdiagnosis of patients.

Another false positive case was a mass in a premenopausal woman with a mixed Solid Cystic Echogenicity in gray-scale without any blood flow in color Doppler sonography with hemorrhagic cyst in pathology diagnosis. Some corpus luteum cysts may show areas of internal hemorrhage. They can frequently show different features including blood clots within the cyst resembling solid components. Doppler examination may be useful in these circumstances as the blood clots will have no blood flow (9). In this case also Doppler sonography showed loss of blood flow. This case shows the importance of supplemental findings of Doppler sonography.

In the evaluation of adnexal tumor volume, mean volume in malignant tumors was 76.6 cc which was low compared with cases reported in the European population studies (7). Sonography is considered an inexpensive and accessible diagnostic tool in our country. It may be a reason for early detection of adnexal masses and reason for the difference in tumor mean volumes.

The sensitivity of serum CA125 was low (55.5%) that showed the low level of CA125 (<35 U/mL) is not reliable. Severi and colleagues showed adding CA125 level to sonography findings, did not raise the diagnostic accuracy of sonography in discrimination between benign and malignant adnexal masses (6). Likewise, Guerriero et al also did not support routine evaluation of CA125 in all women who refer with an adnexal mass. They showed the CA125 level can raise false positive and negative rates (8). In our study also 2 of 3 false positive cases had the high level of CA125 and from 9 cases with the high level of CA125, 4 cases had benign pathology.

Conclusion

The accuracy of gray-scale and color Doppler sonography in discrimination between adnexal malignancies are high (92.5%) and these are valuable diagnostic tools.

Limitations of our study

The major limitations of our study include a small sample size and no long-term follow-up assessments.

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Authors' contribution

MM and ND: search for subjects and data, analysis and interpretation of data and preparation of the manuscript. ZM and SA: study's concept and design, search for subjects and data and preparation of the manuscript. MB and MD: study's concept and design, statistical analysis, interpretation of data and critical review of the manuscript for important intellectual content.

Conflicts of interest

The authors declare that they have no competing interest.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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