Role of Ultrasound & Ovarian Artery Duplexversus Histopathology in Diagnosing Ovarian Mass

ELsayed ELdesouky[1], M. A. Abd El-Latif[2], Mohamed Yousef [3] and Mahmoud Abd Ellatif Hashish[4]

[1] Department Obstetric and Gynecology, Faculty of Medicine, Al-Azhar University, Egypt.
[2] Department of Diagnostic radiology, Faculty of Medicine, Al-Azhar University, Egypt.
[3]Department of Pathology, Faculty of Medicine, Al-Azhar University, Egypt.
[4]Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Egypt.
dr_zidan666@yahoo.com

Abstract: Background: Ovarian masses are common among women of all ages and two thirds of ovarian tumors are encountered during reproductive years; of those the risk of malignancy in an ovarian mass in patients above 40 years is remarkably high although the premenarchal lesions are usually malignant. **Aim of the Work:** The aim of this study is to evaluate the efficacy of ultrasonography and Duplex in discrimination of benign and malignant ovarian tumors and to correlate the imaging finding with postoperative histopathological results. **Patients and Method**: A prospective study was conducted at the Obstetrics and Gynecology Department of Al-Azhar University Hospitals (El-Hussein and Saied Galal), starting form May 2014 to May 2016. The study included 50 patients with age ranges (35-60) years who had a preliminary diagnosis of adnexal masses clinically and/or sonographically. Regard less the patients' complaint, or parity. Spectral analysis of intramural flow was performed on at least 3 hot spots, the lowest PI and the lowest RI were electronically calculated. **Results:** The color Doppler indices showed that there was highly statistically significant difference in the mean (RI) between benign and malignant tumors. The mean (RI) of the benign tumors was 0.57 ± 0.078, while the mean RI of the malignant tumors was 0.39 ± 0.077. (RI) ≤ 0.49 was taken as the cut-off value for detection of malignant masses. **Conclusion:** The combination of the 2D ultrasound with color Doppler scanning showed highly statistically significant difference between the benign and the malignant tumors, with (80%) of agreement, with ≤ 6 as the best cut off value for detection of malignancy.
[ELsayed ELdesouky, M. A. Abd El-Latif, Mohamed Yousef and Mahmoud Abd Ellatif Hashish. **Role of Ultrasound & Ovarian Artery Duplexversus Histopathology in Diagnosing Ovarian Mass.** *Life Sci J* 2017;14(12):7-12]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 2. doi:10.7537/marslsj141217.02.

Keywords: ultrasound & ovarian, artery duplexversus histopathology, diagnosing ovarian mass

1. Introduction

Neoplasm of the ovary presents an increasing challenge to the physician. They are the cause of more deaths than any other female genital tract tumors. Approximately (4-24%) of adnexal masses in premenopausal women and (39-68%) in postmenopausal women are malignant ***(Hata et al., 2013).*** Most women with ovarian masses (cancer) have no symptoms for long periods of time. Several factors may hinder the diagnosis, even for an experienced gynecologist such as virginity, obesity, associated pregnancy, ascites and pelvic tenderness ***(Roman et al., 2013).*** The ultrasound describes the characteristics of ovarian and adnexal masses and predict the ovarian cancer based on these characteristics and clinical parameters. ***(*Emoto et al., *2013).*** The observations made in the late 1989 indicated that the transvaginal color Doppler ultrasonography can be used in the detection of ovarian cancer and has generated a stream of clinical trials **(Folknian et al 1989)**. However, the conflicting results of numerous publications have led to major controversy. Transvaginal color Doppler ultrasonography saves times and increases the accuracy of measurements, though masses over 10 cm in size are bets evaluated using conventional transabdominal sonography ***(Miyazaki, 2012).***

Studies that compared color Doppler ultrasonography with paraffin-embedded sections parameters for the diagnosis of ovarian tumors concluded that ultrasonography with color Doppler is a useful preoperative test for predicting the diagnosis of pelvic masses ***(*Marret*et al., 2013).*** One study concludes that TV-CDS is a useful imaging diagnostic modality in preoperative discrimination of benign and malignant ovarian tumors due to its excellent characterization of tumors neovascularization ***(*Benjapibal., et al*, 2013).***

Aim of the work:

The aim of this study is to evaluate the efficacy of ultrasonography and color Doppler in discrimination of benign and malignant ovarian tumors and to correlate the imaging finding with postoperative histopathological findings.

2. Patients and Methods

A prospective study was conducted at the Obstetrics and Gynecology Department of Al-Azhar

University Hospitals (El-Hussein and Saied Galal), starting form May 2014 to May 2016. The study included 50 patients with age ranges (35-60) years who had a preliminary diagnosis of adnexal masses clinically and/or sonographically. Regardless the patients' complaint, or parity.

All patients were subjected to the following after taking a written consent from each patient:

1. Detailed history taking.
2. Comprehensive clinical examination for all patients.

Clinical evaluation of patient:

The following findings were used with the suspicion of malignancy particularly if several of them were found in the same patient:

- Is there is family history of breast, ovarian or colon cancer.
- Nulliparity, history of infertility and endometriosis.
- Old age "over 40 years".
- Ovarian tumors in childhood are usually malignant.
- Bad general condition especially cachexia.
- Varicosities or edema of the legs particularly if unilateral.
- Rapid abdominal enlargement.
- Presence of dyspareunia, dysmenorrhe, abdominal pain
- Uterine bleeding especially postmenopausal.
- Bilaterality of adnexal mass.
- Solidity or solid areas in cystic tumors.
- Fixed lesion of the tumor.
- Tenderness over tumor.
- Gastrointestinal symptoms: nausea, vomiting and dyspepsia.
- Ascites.
- Hard nodules in the Douglas Pouch.
- Signs of distant metastasis.
- Breast examination.

3. Abdominal and/or transvaginal ultrasound for the assessment of the mass, uterus and ovaries according to the size. Using 2D ultrasonography.
4. Colored Doppler imaging of the ovarian tissue to detect neovascularization. Spectral Doppler analysis using the resistance index and/or pulsatility index was done.
5. Quantitative assessment of serum level of (CA-125-CEA-Inhibin.
6. On laparotomy: The pelvis will be explored, the mass will be described as before and the presence of ascites or metastases, para-aortic lymph nodes and the liver will be evaluated in all cases.
7. The Histopathological examination of the specimens of all masses by cross and microscopic examination.
8. The results will be obtained tabulated and statistically analysed.

2D U/S for morphological score, the scoring system described by ***Sassonect al (1991)*** for the prediction of malignant lesion was applied as follows

On the Doppler Flow Imaging:

Tumors without, detectable flow were considered benign while tumors with detectable flow were subjected to further analysis. Spectral analysis of intramural flow was performed on at least 3 hot spots, the lowest PI and the lowest RI were electronically calculated. Malignancy was predicted according to the following criteria:

a. Presence of high flow that was central rather than peripheral.

b. Spectral broadening and increased diastolic flow.

All the studied group (50 patients) underwent either laparoscopy or laparotomy. The patients were examined under anesthesia, Surgical staging was performed as usual procedure. All removed masses and peritoneal fluid aspirate were sent for histopathological and cytological examination. Data were tabulated and presented in terms of range, /mean, standard deviation and percentages. Accuracy was presented using terms of sensitivity, specificity +ve predictive value, -ve predictive value and overall accuracy.

3. Results

The study population included 50 patients.

Table (1): Distribution of patients according to their age

Age group	Number	Percent
30 – 35 years	18	36.00%
35 – 40 years	15	30.00%
40 – 50 years	10	20.00
50 – 60 years	7	14.00
Total	50	100%

Table (2): Distribution of nature of ovarian masses in relation to age group

	Number/percentage	≤45	>45
Benign	35 (70%)	32 (91.5%)	3 (8.5%)
Malignant	15 (30%)	6 (40%)	9 (60%)
Total	50 (100%)	38 (76%)	12 (24%)

Table (3): Morphological criteria of tumor wall on US

	Number	Percent
Smooth irregularities	21	42%
Irregularity (≤3mm)	32	46%
Capillarities (> 3mm)	1	2%
Solid	5	10%
Total	50	100%

Table (4): Coloured Doppler flow mapping in relation to tumor pathologic type

Color flow mapping	Benign masses		Malignant masses		P value
	No.	%	No.	%	
No flow (n= 16)	16	100.00	0	0.00	< 0.001*
Peripheral (n= 23)	23	100.00	0	0.00	
Papillary or septal (n=7)	3	40	4	60	
Mainly central (n =14)	0	0.00	14	100.00	

Doppler Analysis of Study Population:

1- Resistance index:

In benign masses showing vascular flow, the RI varied from 0.48 to 1.3 (mean of 0.78±0.12) while in malignant masses, the RI varied from 0.29 to 0.85 (mean of 0.56±0.14) (Fig 2).

2- Pulsitility index:

In benign masses showing vascular flow, the PI varied from 0.83 to 4.4 (mean 2.4±0.9) while in malignant masses, the PI varied from 0.59 to 1.6 (mean of 1.3 ±0.6).

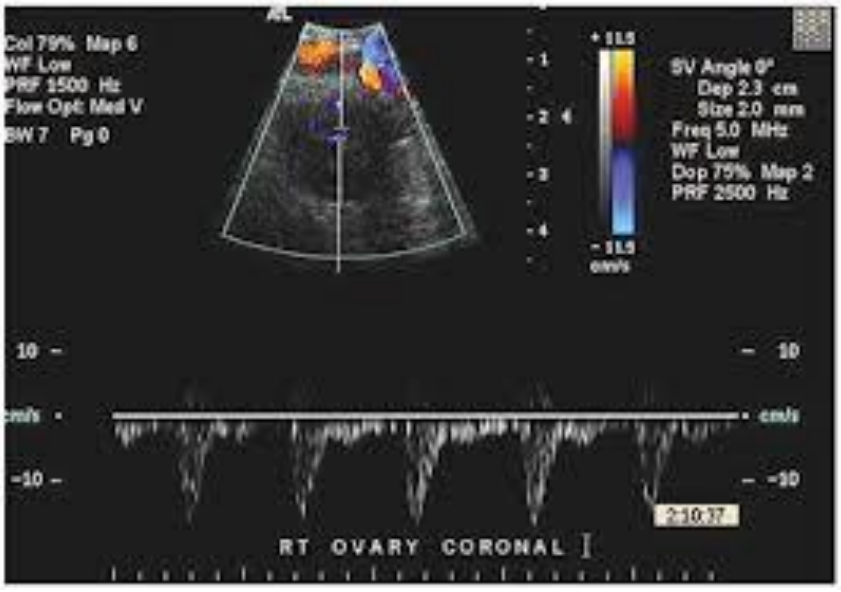

Fig 1: Spectral Doppler image of benign ovarian cyst shows high resistive and pulsatility indices.

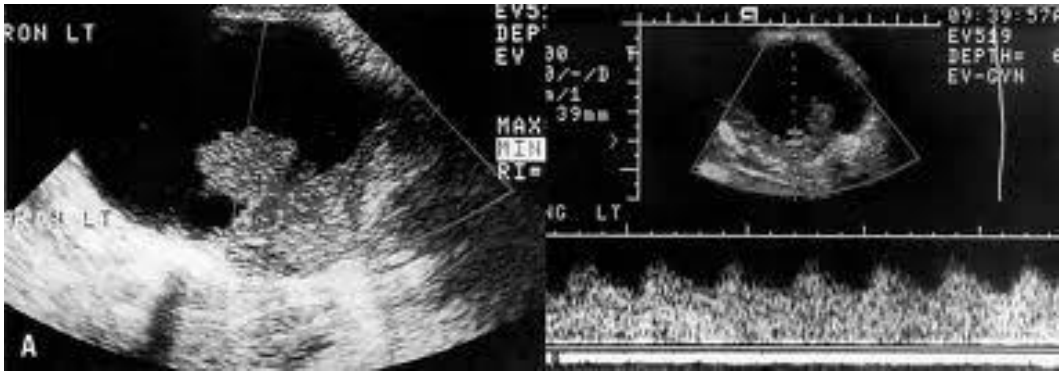

Fig 2: B mode and Spectral Doppler images of malignant ovarian cystic lesion shows low resistive and pulsatility indices.

Table (5): Mean PI and RI ± SD according to the pathological nature of the masses with detectable flow.

Type	RI	PI
Endometrioma (n = 6)	0.8 ±0.12	2.3 ±0.4
Simple serous cystadenoma (n = 8)	0.92+0.3	2.4+0.87
Papillary serous cystadenoma (n = 2)	1.01+0.3	2.3±0.8
Mucinous cystadenoma (n = 4)	0.76+0.2	1.9 ±0.4
Benign cystic teratorna (n = 5)	0.83+0.2	1.7±0.3
Papillary serous cystadenocarcinoma (n = 4)	0.32+0.1	0.92+0.4
Granulosa cell tumor (n = 3)	0.47+0.06	1.1+0.2
Thecoma (n = 2)	0.6	1.2
Mucinous cystadenocarcinoma (n = 2)	0.45	0.71
Clear cell adenocarcinoma (n = 2)	0.42	0.68
Hgic corpus luteal cyst (n = 8)	0.92 ± 0.4	2.8 ± 087
Liomyosarcoma (n = 2)	0.3 ± 0.2	0.92 ± 0.6
Krukenberg tumor (n = 2)	0.50 ± 0.1	0.9 ± 0.4

Table (6): The sensitivity and specificity of Doppler studies in the diagnosis of malignant adnexal tumour.

Cut off	Sensitivity	Specificity	PPV	NPV
Central flow	77	100	100	88
PI-1	46.15	95.65	85.7	75.86
RI = 0.45	38.46	100	100	74.91
Combined	92	94	86	93

Table (7): Postoperative pathological diagnosis

	No. of Cases	Percentage
Endometrioma	6	12%
Benign serum cyst	10	20%
Mature teratoma	5	10%
Mucinous cystodenoma	4	8%
Cystadenocarinoma	4	8%
Clear cell carcinoma	2	4%
Granulosa cell tumor	3	6%
Fibroma thecoma	2	4%
HgC. Corpus luteal gsb	8	16%
Krukenberg tumor	2	4%
Mucinous cyst adenocarcinoma	2	4%
Leiomyosarcoma	2	4%
Total	50	100%

On comparing that histopathological results to ultrasonographic finding we found:

- The ten cases diagnosed by ultrasound as endometrioma were confirmed histopathologically in six cases while the other two were dermoid cyst and two hemorrhagic cyst.
- All benign serous cysts were confirmed histopathologically as diagnosed before by ultrasound.
- Ultrasonographic diagnosis of dermoid cysts were totally confirmed by histopathology and some cases three were ultrasonographically diagnosed as endometrioma and mucinous cyst but the histopathology confirmed the dermoid nature of the tumor.
- Four cases of the previous diagnosed by ultrasound as mucinous cyst were confirmed histopathologically.
- Granulosa cell tumor can be mistaken by ovarian fibroma and broad ligamentarymyoma.

4. Discussion

The diagnostic accuracy of pelvic examination in cases with ovarian mass varied in different series between 50% and 90%. It is affected by several variables, including the experience of the gynecologist, the type of the patient and the characteristics of the mass. Several factors may hinder the diagnosis, even for an experienced gynecologist. Virginity, obesity, associated pregnancy, ascites and pelvic tenderness ***(Fleisher et al, 2011).*** In that study ***Buy et al. (2010)*** there was also a significant difference in the age of patients regarding benign and malignant masses (mean age 39 years versus 45 years in benign and malignant lesions respectively), which agree with the results of the present study. In the present study, there was a direct relation between the age of patients and the presence of malignant masses. Malignant masses were found in older group than benign masses (mean age 39.02 ± 9 in benign and 44.9 ± 11.7 in malignant masses). These results coincided a with those of ***Lerner et al. (2010)*** who found that the mean age of patients with benign lesions was 48.9 and for those with malignant masses 55.7 years.

In the present study, distribution of patients (76%) premenopausal and 24% postmenopauasal patients with ovarian masses. This is in agreement with ***Cohen et al. (2009)*** who revealed that (56.3%) of the patients with ovarian masses were premenopausal and 43.7% were postmenopausal.

Sonography is a well established technique for examining the female pelvis. Advances in sonographic technology such as additional use of color Doppler imaging has increased the diagnostic accuracy in differentiation of benign from malignant adnexal masses, by classification of the tumors on the basis of their sonomorphologic appearance and location ***(Alczzar and Castillo, 2005).***

In the present study, there was no significant statistical difference between clinical examination and ultrasound as regard the diagnosis of benign ovarian tumors. While in determining the exact pathological type of those benign tumors ultrasound was superior to clinical examination.

This result emphasized the value of ultrasound in the assessment of benign ovarian cysts as it can show what is inside the cyst. However, this value is questionable in cases of mixed or solid benign tumors because of their high sonographic score.

Based on the theory of neovascularization by ***Folknian (1989)*** in fast growing vessels which is an obligatory event in the development of malignant tumors together with the lack of smooth muscles in their walls, blood flow with low impedance in malignant rumors would be expected ***(Emoto et al., 2012).*** The results of the present study revealed that the transvaginal Doppler flow imaging allowed the diagnosis and differential diagnosis of the majority of ovarian tumors, particularly in part of ovarian carcinoma at early stages, with (92%), and (94%) accuracy. This was agreed with the results reported by ***Guerriero et al (2012)*** who showed (100%) sensitivity, (84%) accuracy.

The present study revealed a cut off value (0.45) with a sensitivity of (38.46%), NPV of (74.91%), specificity of (100%) and PPV of (100%). The mean RI varied significantly between benign and malignant masses being 0.45 and 0.8 in malignant and benign lesions respectively (P value >0.05). However, there was a considerable overlap between benign and malignant lesions. ***Maly et al (2013),*** revealed a cut off value of 0.6 for RI with a sensitivity of (67%), specificity of (53%), PPV of (22%) and NPV of (87%); ***Ebrashy and Ezzat (2000),*** found RI of 0.45 to be of 86% sensitivity while ***Marret et al (2010),*** reported a cut off value of 0.53 for RI with a specificity of 93%. ***Benjapibal et al. (2013)*** revealed a cut off points of 1.0 for PI with a sensitivity ranging between (58%) to (71%) and a specificity ranging between (66%) to (95%) in the discrimination between benign and malignant lesions in their studies.

The present study revealed a cut off value of 1.0 for PI with a sensitivity (46.15%), specificity (95.65%), PPV (85.71%) and NPV (75.86%). The PI varied significantly between benign and malignant masses benign 1.1 and 2.06 in malignant and benign masses respectively (P value >0.05). In general, both indices tended to be lower in malignant masses than in benign masses ***(Flesicher et al., 2011 and Brown et al., 2009;),*** but the increasing evidence that both indices demonstrate considerable overlap between malignant and benign ovarian masses limits the

usefulness of pulsed Doppler ultrasound in differentiating these lesions ***(Benjapibal et al., 2013).*** On the contrary to the present study, ***Daskalakis et al. (2012)*** showed lower sensitivity of Doppler study (87.5%), which may be due to the lower number of malignant cases included in the that study. Also ***Marret et al (2012)*** disagreed with the present study by showing a higher specificity (97.4%), as their study included higher number of benign cases (73 out of 96 cases).

Statistical analysis of central flow as a Doppler variable showed (77%) sensitivity, (100%) specificity, (100%) PPV and (88%) NPV in the, discrimination between benign and malignant ovarian tumors. In the present study, color Doppler correctly diagnosed the false positive cases of both ultrasound and clinical evaluation by detecting peripheral flow with high Doppler indices. So, when combined with both modalities, Doppler increased their specificity and diagnostic accuracy. This proves that the color Doppler should be used as a complementary tool in the diagnosis of ovarian tumors.

Conclusions and Recommendations

- 2D U/S and power Doppler are potentially helpful in the diagnosis of ovarian masses.
- Every woman at average risk should have a periodic pelvic examination, pelvic ultrasound and CA125 test to make sure she does not harbor an occult ovarian cancer.
- Further large-scale studies are needed to refine and test the scores used to differentiate benign from malignant lesions.

References:

1. Alcazar JL and Castillo G (2005): Comparison of 2-dimensional and 3-dimensional power-Doppler imaging in complex adnexal masses for the prediction of ovarian cancer. Am JObstet Gynecol.;192(3):807-812.
2. Benjapibal M, Sunsancevitayakul Pand Borboonhirunsarn D (2013): Color Doppler ultrasonography for prediction of malignant ovarian tumours. J Med Assoc Thai; 85 (6): 709-715.
3. Brown DL, Zou KH and Tempany CM (2009): Primary versus secondary ovarian malignancy: imaging findings of adnexal masses in the Radiology Diagnostic Oncology.
4. Group Study. Radiology; 219:213-218.
5. Buy JN, Ghossain MA, Hugol D, Hassen K and Sciot C (2010): Characterization of adnexal masses: combination of color Doppler and conventional sonographycompred with spectral Doppler analysis alone and conventional sonography alone AJR, 166: 385-.
6. Lerner JP, Timor-Tritsch IE, Federman A and Abramovich G (2010): Transvaginalultrasonographic characterization of ovarian masses with an improved weighted system. Am. J. Obstet. Gynecol; 170: 81-85.393.
7. Cohen LS, Escobar PF, Schann C, Glimco B and Fishman DA (2009): Three-dimensional power Doppler ultrasound improves the diagnostic accuracy for ovarian cancer prediction. Gynecol Oncol; 82 (1): 40-48.
8. Daskalakis G, Kalmantis K, Skartados N, Thoinakosy V.
9. Hatziioannou L and Antsaklis A (2012): Assessment of ovarian tumours using transvaginal power Doppler ultrasonography. Ear J Gynaecol Oncoi; 25(5):594-596.
10. Ebrashy A and Ezzat E (2000): Adding color flow Doppler measurements to the morphological scoring system in the ultrasound evaluation of adnexal masses. Does it really help? Egy J Fertl Steril; Vol. (4) 41-48.
11. Emoto M, Iwasaki H and Mimura K (2012): Difference in the angiogenesis of benign and malignant ovarian tumours, demonstrated by analyses of color Doppler ultrasound, immunohistochemistry, and micro vessel density. Cancer; 80: 899-907.
12. Fleischer AC, Milam MR, Crispens MA and Shappell HW (2011): Sonographic depiction of intratumoural vascularity with 2- and 3-dimensional color Doppler techniques. J Ultrasound Med.;24(4):533-537.
13. Fleishcher AC, Cullinan JA, Kepple DM and Williams LL (2011): Conventional and color Doppler transvaginalsonography of pelvic masses: A comparison of relative histologic specificities. J Ultrasound Med; 12: 705-712.
14. Folknian J, Waltson K, Ingber D and Hanahan D (1989): Induction of angiogenesis during the transition from hyperplasia to neoplasia. Nature; 339: 58-62.
15. Guerriero S, Ajossa S and Melis GB (2012): Is three-dimensional power Doppler ultrasound better than two-dimensional'Power Doppler. Gynecol Oncol.;84:352-353.
16. Hata K, Miyazaki K and Hanahan D (2013): Color Doppler imaging and angiogenesis in ovarian tumours. Med Electron Microsc.;36(3): 127-130.
17. Maly Z, Riss P and Deutinger J (2013): Localization of blood vessels and quantitative assessment of blood flow in ovarian tumours. Obstet Gyencol; 85: 33-36.
18. Marret H, Ecochard R and Giraudeau B (2012): Color Doppler energy prediction of malignancy in adnexal masses using logistic regression models. Ultrasound Obstet Gynecol; 20 (6): 597-604.
19. Marret H, Sauget S, Giraudeau B, Body G and Tranquart F (2010): Power Doppler vascularity index for predicting malignancy of adnexal masses. Ultrasound Obstet Gynecoi.;25(5): 508-513.
20. Miyazaki K (2012): Color Doppler imaging and angiogenesis in ovarian tumours. Med Electron Micros; 36 (3): 127-30.
21. Roman LD, I. aila IM, Stein S. M, Barin I. S, Susan G and Mattow PC (2013): Pelvic examination, tumour marker level, gray scale and Doppler sonography in the prediction of pelvic cancer. Obstet. Gvnecol.; 89(4): 193-500.
22. Sassone M, Timor-Tritsch I, Arter A (1991): Transvaginalsonographic characterization of ovarian disease: Evaluation of a new scoring system to predict ovarian malignancy. Obstet. Gynecol.;78: 70-76.