ORIGINAL RESEARCH

Correlation of Clinical, Doppler Study and Histopathological Features of Ovarian Tumors

Sindhu Kodali[1], Sangeeta Shah[2], Lakshmi D Sundari,[3] Disha Shah[4]

Abstract

Aims and objectives: The aim of the study were: (1) to study the correlation between clinical, sonological, and histopathological features of ovarian tumors; (2) to assess accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of color Doppler in differentiating benign and malignant ovarian pathologies; and (3) to study the epidemiology of ovarian tumors.

Materials and methods: This is a prospective study conducted between March 2018 and September 2019.

Inclusion criteria: All women who presented with adnexal masses (premenopausal: >5 cm, postmenopausal: any size) were included in this study.

Exclusion criteria: Known case of ovarian tumors who came for second-look surgery. Anechoic unilocular cyst <5 cm in ovary that resolves on follow-up. Clinical presentation data such as age, parity, menstrual history, and per abdominal and per vaginal examination findings are collected. Ultrasound Doppler findings such as resistivity index (RI) and pulsatility index (PI) are calculated and correlated with histopathology postsurgery. Statistical analysis was done by Pearson's "R" correlation coefficient, sensitivity, specificity, accuracy, PPV, and NPV.

Results: With RI (0.4) and PI (1), Doppler was able to differentiate 94.4% of the histopathological examination (HPE) benign cases and 97.1% of the HPE malignant cases. (Pearson's "R" for RI and HPE: 0.6925, Pearson's "R" for PI and HPE: 0.4215), the sensitivity and specificity of color Doppler 78.5 and 94.4%, respectively. The PPV was 84.6% and NPV was 91.8%. Diagnostic accuracy of color Doppler was 90.0%.

Conclusion: Doppler with the prescribed RI and PI values has to be incorporated into screening of ovarian tumors as they have a high degree of sensitivity and specificity for malignant masses.

Clinical significance: Doppler study is a cost-effective, noninvasive, diagnostic method and can be a useful tool for differentiating benign from malignant ovarian tumors.

Keywords: Clinical features, Doppler sonography, Ovarian tumors, Pulsatility index, Resistivity index.

Journal of South Asian Federation of Obstetrics and Gynaecology (2022): 10.5005/jp-journals-10006-2024

Introduction

Among females, cancer of the ovary is the seventh most common cause of cancer and the fifth leading cause of cancer-related mortality. It usually manifests in an advanced stage with extensive spread due to its asymptomatic nature, leading to delay in diagnosis and increased fatality rate. High fatality rates can also be explained by high rates of recurrence and resistance to chemotherapy. The five-year survival rate is poor. Hence, early diagnosis and appropriate treatment are necessary for a better outcome. The lifetime risk of being diagnosed with ovarian cancer is 1–1.5% and of dying from ovarian cancer is almost 0.5%.[1] Hence, there is an urgent need for discovering novel methods for screening and early diagnosis, prognostication, and therapy. Benign and malignant lesions of ovary can be differentiated by the use of color Doppler sonography. Angiogenesis and neovascularization in malignant tumors lead to low resistance flow in blood vessels making Doppler a useful tool for detecting malignancy.[2–5]

Aims and Objectives

- To study the correlation between clinical, sonological, and histopathological features of ovarian tumors.
- To assess accuracy, sensitivity, specificity, PPV, and NPV of color Doppler in differentiating benign and malignant ovarian pathologies.
- To study the epidemiology of ovarian tumors.

[1–3]Department of Obstetrics and Gynaecology, Gandhi Medical College, Hyderabad, Telangana, India

[4]Department of Radio Diagnosis, Gandhi Medical College, Hyderabad, Telangana, India

Corresponding Author: Sangeeta Shah, Department of Obstetrics and Gynaecology, Gandhi Medical College, Hyderabad, Telangana, India, Phone: +91 9849323877, e-mail: drsshah19@yahoo.com

How to cite this article: Kodali S, Shah S, Sundari LD, *et al*. Correlation of Clinical, Doppler Study and Histopathological Features of Ovarian Tumors. J South Asian Feder Obst Gynae 2022;14(3):257–260.

Source of support: Nil

Conflict of interest: None

Materials and Methods

A cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Gandhi Hospital, Secunderabad, between October 2018 and April 2019, over a period of 18 months. During the study period, 50 patients with an ovarian tumor confirmed by transabdominal ultrasound examination were enrolled into the study group. The investigations done are surgical profile that includes complete blood count, blood grouping and typing, renal function tests, liver function test, thyroid profile, bleeding time, clotting time, serum electrolytes, chest X-ray posteroanterior view (PA) view, ECG, upper gastro intestinal (GI)

endoscopy, and colonoscopy. Ovarian Doppler was done and RI and PI were measured. Relevant tumor markers were done, and histopathological examination of each surgically removed tumor was done and classified according to the World Health Organization (WHO) system of ovarian tumors.

Inclusion Criteria

Females diagnosed with adnexal mass [premenopausal (>5 cm), postmenopausal group (any size)] were included.

Exclusion Criteria

- History of ovarian tumor admitted for second-look surgery.
- Simple ovarian cyst <5 cm that resolves on follow-up.
- Endometrioma.

Statistical Analysis

Data entry was done by Microsoft Excel 2010 version. Data were presented in percentages and proportions. Numerical data were expressed as the mean ± SD (standard deviation) and range. Correlation between numerical data was done using Pearson's correlation coefficient. The sensitivity, specificity, PPV, NPV, and accuracy of ovarian Doppler in differentiating benign and malignant ovarian tumors were calculated. Area under the receiver operating characteristic (ROC) curve represents accuracy. A perfect test gives an area under the curve (AUC) of 1; a failed test gives an AUC of 0.5. The measurements of ROC curve are: 0.90–1 = excellent (A), 0.80–0.90 = good (B), 0.70–0.80 = fair (C), 0.60–0.70 = poor (D), and 0.50–0.60 = fail (F).

Results

Study population included 50 cases, among which 34 (68%) were benign, 14 (28%) were malignant, and 2 (4%) were borderline. Mean age of presentation was 41.6, 42.5, and 44.5 years for benign, borderline, and malignant, respectively. Ovarian tumors were common in females with parity 4 and above which constitutes 35.3% benign and 35.7% malignant tumors. Among nulliparous women, benign and malignant tumors were 20.6 and 7.1%, respectively. One case (2%) was ovarian tumor complicating pregnancy. Clinical presentation varies among the individuals as noted in Table 1. Most patients presented with pain abdomen which included 55.8% benign and 78.5% malignant cases. About 73.5% of the benign tumors were cystic in consistency and 35.7% of the malignant tumors were firm. Most ovarian tumors were unilateral which accounted for 85.3% benign and 78.5% malignant tumors. In the current study, epithelial tumors constituted 74% (37) of the cases followed by germ cell tumors 14% (7) as listed in Table 2.

Table 3 depicts that the number of true-positive cases was 13 (97.1%), false positives 2 (5.6%), true negatives 34 (94.4%), and false negatives 1 (2.9%). The AUC for RI was 0.941 and PI was 0.912 which were significant as noted in Figure 1.

With RI and PI data from Figure 1, color Doppler had a sensitivity of 78.5%, specificity of 94.4%, NPV of 91.8%, PPV of 84.6%, and an accuracy of 90%.

Discussion

A wide variety of clinical, morphological, histopathological features are manifested in ovarian tumors that may be misdiagnosed for other neoplastic and non-neoplastic conditions. In the current study, incidence of benign tumors is 68% which is less than the incidence reported by Chandra and Arora,[6] Modepalli et al.,[7] but more than that observed by Agrawal et al.[4] similar to Valamarthy and Hema.[5] In the current study, benign tumors were common between 21 and 30 years of age (29.4%). Similar incidence was seen in the study by Agrawal et al.[4] which constitute 33.7%. A total of 42.8% of malignant tumors were seen in between 41 and 50 years which is comparable to Chandra and Arora[6] (31.6%) and Agrawal et al.[4] (33.75%). In studies reported by Modepalli et al.,[7] the peak incidence was between age group 21 and 30 (31%), 52.4% presented with mass per abdomen, and 33% cases had pain abdomen. In this study, 62% of ovarian tumors present with pain abdomen and 18% cases had mass per abdomen. Similar incidence was found in Chandra and Arora[6] study.

Menstrual disturbances were caused by hormone-producing tumors. Four percent of cases had menstrual disturbances and one case had postmenopausal bleeding. In Chandanwale et al.,[8] 6% of cases had menstrual irregularities. However, in Modepalli et al.[7] and Chandra and Arora[6] studies, 16 and 54.2%, respectively, had menstrual disturbances as presenting feature.

A total of 84% of benign tumors were cystic and 23% of malignant tumors were hard according to Modepalli et al.[7] In this study, cystic consistency seen in 73.5% of benign tumors and 42.8% of malignant masses. About 35.7% of malignant tumors were firm in consistency.

Table 1: Clinical presentation

	Number of cases							
	Benign		*Borderline*		*Malignant*		*Total cases*	
Mode of presentation	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Mass per abdomen	8	23.5	1	50	—	—	9	18
Pain	19	55.8	1	50	11	78.5	31	62
Menstrual disturbance	—	—	—	—	2	14.2	2	4
Postmenopausal bleeding	—	—	—	—	1	7.2	1	2
Distention	7	20.5	1	50	5	35.7	13	24
Urinary symptoms	1	2.9	—	—	—	—	1	2
White discharge	1	2.9	—	—	—	—	1	2
Constipation	2	5.8	—	—	1	7.2	3	6
Vomiting	2	5.8	—	—	—	—	1	2
Total	34*	100	2*	100	14*	100	50*	100

*There was more than one presentation in these cases

Table 2: Incidence of various subtypes of ovarian tumors

	Cases	
Tumor type	*No.*	*%*
Epithelial tumors		
Serous tumors	23	46
• Benign serous cystadenoma	18	78.2
• Benign papillary serous cystadenofibroma	—	—
• Borderline serous papillary cystadenoma	1	4.4
• Serous cystadenocarcinoma	—	—
• Papillary serous cystadenocarcinoma	4	17.4
Mucinous tumor	11	22
• Benign mucinous cystadenoma	9	81.8
• Borderline mucinous cystadenoma	1	9.1
• Mucinous cystadenocarcinoma	1	9.1
• Papillary mucinous cystadenocarcinoma	—	—
Endometrioid tumor	—	—
• Benign		
Brenner tumor	—	—
• Malignant		
Undifferentiated tumor	3	6
• Poorly differentiated papillary carcinoma	1	33.3
• Poorly differentiated carcinoma	—	—
• Adenocarcinoma	2	66.7
Mixed tumor	—	—
• Benign papillary seromucinous cystadenoma		
Germ cell tumors		
Teratoma	7	14
• Immature	—	—
• Mature (cystic dermoid)	7	14
Sex cord stromal tumor	**5**	**10**
• Granulosa cell tumors malignant	3	60
• Fibrothecoma	2	40
Metastatic carcinoma	**1**	**2**
• Krukenberg tumor		
Soft tissue tumors not specific to the ovary (leiomyosarcoma)	—	—
Total	50	100

Multicentric origin of the tumors is represented by bilaterality. In this study, bilaterality seen in 14.7% of benign and 21.5% of malignant tumors. Unilateral involvement seen in 85.3% benign and 21.5% malignant tumors. In Agrawal et al.'s[4] study, bilateral involvement seen in 30.2% of malignant masses. In this study, 82% of cases were found to have unilateral involvement that was similar to studies conducted by Chandra and Arora.[6]

Of all the tumors, 74% constitute surface epithelial tumors among which 46% were serous tumors followed by 22% mucinous tumors. Thirty-six percent cases were serous cystadenoma. Four cases were serous tumors with malignancy, of which three were presented unilaterally and one was bilateral. Three were cystic in consistency and one was firm.

Table 3: Correlation of Doppler with histopathology

		Histopathology		
		Benign	*Malignant*	*Total*
Doppler	**Benign (*n*)**	34 (TN)	1 (FN)	35
	% within HPE	94.4%	2.9%	70.0%
	% of total	68%	2%	70.0%
	Malignant (*n*)	2 (FP)	13 (TP)	15
	% within HPE	5.6%	97.1%	30.0%
	% of total	4.0%	26%	30.0%
TP: True positive	**Total count**	36	14	50
FP: False positive	% within HPE	100.0%	100.0%	100.0%
TN: True negative	% of total	72%	28.0%	100.0%
FN: False negative				

Among 11 mucinous tumors, 9 were mucinous cystadenoma, 1 was borderline mucinous tumor, and 1 was mucinous cystadenocarcinoma. Germ cell tumors were common next to epithelial ovarian tumors.14% of ovarian tumors were mature benign cystic teratoma (dermoid cyst) which were more common among germ cell tumors and occurred in the age group of 28–60 years. Of all the germ cell tumors, three cases had menstrual disturbances and were firm. One case of Krukenberg tumor with a history of stomach carcinoma 3 years back was presented with the complaint of abdominal pain and constipation. Of the two cases of fibrothecoma, one was presented with distention and the other was presented with pain abdomen. Grossly one was hard in consistency and other was cystic and both were unilateral.[9]

In the study conducted by Subash et al.,[10] 150 women were screened using ultrasonography, which had sensitivity of 78.94%, specificity of 98.47%, and diagnostic accuracy of 88.23%.

Studies conducted by Zhou et al.[11] in 2019 reported 89.08, 86.67, and 87.95% of sensitivity, specificity, and accuracy, respectively, by computed tomography (CT) scan to detect malignancy. Sensitivity of about 86.32% and specificity of 70.5% were observed with RI value of 0.4. In the current study, sensitivity was 71.4% and specificity was 94.4% with the cutoff of RI 0.4.

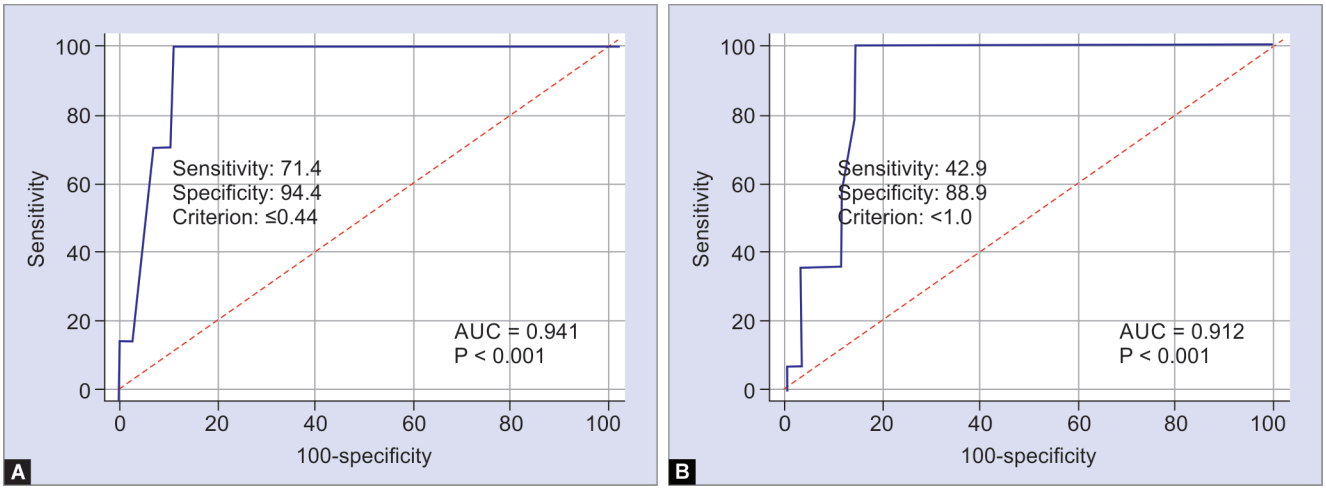
With the PI value cutoff 1.0, there were 42.8% and 88.8% sensitivity and specificity, respectively. Similar observations were found in Eldesouky et al.'s[9] study, in which sensitivity was 46.15% and specificity was 95.6%.

Moses et al.[3,12] first described the ROC methodology that was applied in this study, which is shown in Figure 1. AUC was 0.942 for RI with cutoff of <0.4 with *p*-value <0.001, 0.905 for PI with cutoff of <1.0 with *p*-value <0.001.

With the correlation coefficients shown in Table 4, it was observed that there is a positive correlation between Doppler indices and histopathological findings.

Conclusion and Clinical Significance

Color Doppler is a valuable diagnostic modality to differentiate between benign and malignant lesions. As most ovarian cancers are asymptomatic in the early stages, Doppler with the prescribed RI and PI values has to be incorporated into screening of ovarian tumors as they have a high degree of sensitivity and specificity to detect malignancy obliterating the need for further imaging, especially in centers, where higher modalities are not available. Early referral to a higher center for early intervention improves overall survival.



Figs 1A and B: ROC interpretation of Doppler indices (RI and PI)

Table 4: Correlation coefficients for histopathology and Doppler indices

	Pearson's correlation coefficient (R) (R = 0: no association R = 0 to +1: perfect positive linear correlation R = 0 to −1: perfect negative correlation)		*Spearman's rank correlation coefficient (rho) (rho = 0: no association rho = 0 to +1: perfect positive linear correlation rho = 0 to −1: perfect negative correlation)*	
	For RI and HPE	*For PI and HPE*	*For RI and HPE*	*For PI and HPE*
Sample size	50	50	50	50
Correlation coefficient	0.6925	0.4215	0.693	0.422
Significance level	$p < 0.0001$	$p = 0.0023$	$p < 0.0001$	$p = 0.0023$
95% confidence interval	0.5131–0.8140	0.1622–0.6264	0.513–0.814	0.162–0.626

Orcid

Sindhu Kodali https://orcid.org/0000-0002-4828-8184
Sangeeta Shah https://orcid.org/0000-0003-2075-5980

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