Diagnostic Accuracy of Color Doppler Indices for Differentiation of Benign and Malignant Ovarian Tumors

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ABSTRACT

Background: Ovarian malignancy is an abnormal growth of cells which involves the ovary. With the progression of the malignancy, the symptoms become overt. Ultrasonography is the most popular method to investigate the female reproductive tract tumors. A few studies are available about the ultrasonography appearance of ovarian tumors. Objective: To assess the diagnostic accuracy of color Doppler indices for differentiation of benign and malignant ovarian tumors in females taking histopathology as a gold standard. **Methods:** It was a cross sectional study conducted at Gynecology Unit 4, Lady Aitchison Hospital, and Lahore from January 2020 to July 2020. 200 cases fulfilling inclusion criteria were enrolled in study after taking Informed consent. Non Probability consecutive sampling was used. Demographic details were noted. All the females were examined by the same operator using a special ultrasound (USG) equipment. Resistance Index (RI) and Pulsitility Index (PI) were noted. Then patients were labeled as positive or negative (as per operational definition) depending on RI and PI values. The females, then underwent Dilatation and Curettage (D&C) under spinal anesthesia by the same gynecologist. Endometrial biopsy samples were obtained and sent for histopathological assessment of the type of lesion. Reports were assessed and patients were confirmed as positive or negative (as per operational definition). All the collected data was entered and analyzed using SPSS version 20. **Results:** The mean age of patients was 42.27±10.61 years, the mean BMI of patients was 29.38±5.81kg/m^2. The sensitivity, specificity, and diagnostic accuracy of RI Doppler was 98.33%, 91.25%, & 95.5% respectively and the sensitivity, specificity, and diagnostic accuracy of PI Doppler was 99.17%, 96.25%, & 98.00% respectively. **Conclusion:** Color Doppler indices including PI and RI are effective and reliable for differentiation of benign and malignant ovarian tumors taking histopathology as gold standard.

Keywords: Ovarian Tumors, Malignant, Histopathology, Pulsitility Index, Resistance Index.

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INTRODUCTION

Reproductive organs are one of the most common site for female tumors, only second to breast cancer. Ovarian masses are a frequent cause of gynecological consultation and usually detected during imaging or surgery for evaluation of pelvic or abdominal pain syndromes. With more than two million new cases reported annually, ovarian malignancy represents the fourth commonest cause of cancer related deaths globally. Ovarian cancer has the highest mortality rate amongst gynecologic cancers. Because most ovarian cancer is diagnosed in the advanced stage of the disease, five-year survival rate is very poor. In a local study, the overall incidence of malignant ovarian tumors was found to be 23.4% in Pakistan. Ultrasonography is one of the first line methods in the investigation of the female pelvic pathologies. Three-dimensional Pelvic Doppler (PD) vascular indices can be helpful in decreasing the false-positive rate in cystic-solid and solid adnexal masses with increased vascularity.[1-7]

Sonography is usually the first line investigation for defining the ovarian masses. However, only a very few studies explain the monographic findings of ovarian tumors, and no specific findings help in the diagnosis of tumors. Various blood velocity measurements are used to show the low impedance of blood circulation in ovarian malignancy. Although favorable results of Doppler scan in differentiating benign from malignant tumors have been reported, there are others who have obtained less encouraging results. One study has reported the sensitivity and specificity of RI, to be lower as compared to sensitivity and specificity of PI. While another study indicated that the sensitivity and specificity of RI was 83% and 93%, respectively while the sensitivity and specificity of PI i.e. 87.5% and 95.4%, respectively.[8-11]

Color Doppler Ultrasound is now used in many centers as a baseline modality as well as for distinguishing malignant and benign lesions of ovarian masses. In routine, RI is usually preferred as a diagnostic index. But literature review indicates that PI is more accurate in comparison to RI. But contradictory evidence is also available in the literature. Moreover, we did not find any local evidence which can help us in making use of more sensitive method. The rationale for this study is to

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observe the diagnostic accuracy of Color Doppler Indices in our local setup for differentiating benign and malignant ovarian tumors. We will also get local evidence and will be able to implement the use of PI instead of relying on the value of RI.

Objective:

To assess the diagnostic accuracy of color Doppler indices (RI & PI) for differentiation of benign and malignant ovarian tumors in females taking histopathology as gold standard

Operational Definitions

Ovarian Tumors: On color Doppler, if RI≤0.5, then lesion was categorized as malignant but if RI>0.5, it was considered benign. On color Doppler, if PI≤1.0, then lesion was labeled as malignant but if PI>1.0, it was labeled as benign. On histopathology, lesion was labeled as malignant if there were cystic and solid components, cellular atypia, necrosis, appearance of tubular glands, and strong resemblance to the endometrium and was labeled as benign in case of normal cell growth and presence of palpable mass and cyst .

For RI:

True positive (TP): When RI≤0.5 and malignant lesion present on histopathology

True negative (TN): When RI>0.5 and benign lesion present on histopathology

False positive (FP): When RI≤0.5 but lesion was benign on histopathology

False negative (FN): When RI>0.5 but lesion was malignant on histopathology

For PI:

True positive: When PI<1.0 and malignant lesion present on histopathology

True negative: When PI≥1.0 and benign lesion present on histopathology

False positive: When PI<1.0 but lesion was benign on histopathology

False negative: When PI≥1.0 but lesion was malignant on histopathology

Sensitivity: TP/(TP+FN)

Specificity: TN/ (TN+FP)

Positive Predictive Value (PPV): TP/(TP+FP)

Negative Predictive Value (NPV): TN/(TN+FN)

MATERIALS & METHODS

Study Design: Cross sectional study.

Setting: Gynecology Unit 4, Lady Aitchison Hospital, Lahore.

Duration of Study: Six months from January 2020 to July 2020.

Sample Size: Sample size of 200 was calculated with 95% confidence level, taking expected percentage of ovarian malignancy i.e. 23.4% and sensitivity of RI i.e. 78.3% with 12% margin of error and specificity of RI i.e. 83.1%10 with 10% margin of error taking histopathology as gold standard.

Sampling Technique: Non-probability consecutive sampling.

Selection Criteria
Inclusion Criteria

Patients from 20-60 years of age with various complaints like abnormal vaginal bleeding, amenorrhea, lower abdominal pain and ovarian mass (on gray USG) scheduled to undergo D&C were included in the study.

Exclusion Criteria

Patients having pelvic mass of uterine origin diagnosed either per-operatively or on histopathology report.

Patients having ovarian fluid areas (cysts, follicles) and dermoid cysts with avascular areas (on USG). Pregnant patients.

Data Collection Procedure

200 cases fulfilling inclusion criteria were enrolled in the study from Outpatient Department of Obstetrics & Gynecology, Lady Aitchison Hospital, Lahore. Informed consent was taken. Demographic data (including name, age, parity presenting complaint, duration of symptoms & BMI) was recorded. Then patients underwent Doppler indices assessment. All the females were examined by the same operator (S.S.) using a 5–8-MHz transvaginal ultrasound transducer and Technos MPX EsaoteTM equipment for color Doppler and power Doppler ultrasonography was done using (ESAOTE Inc., Florence, Italy). RI and PI were noted. Then patient were labeled as positive or negative (as per operational definition) on both RI and PI values. Then females underwent D&C under spinal anesthesia by a single gynecologist having 4 years of residency experience. Samples were obtained and sent for histopathological assessment of type of lesion to Pathology department. Reports were assessed and patients were confirmed as positive or negative (as per operational definition). All the information was collected on a specially designed proforma.

Data Analysis Procedure

All the collected data was entered and analyzed through SPSS version 20. Quantitative data like age and duration of symptoms were presented as mean and Standard Deviation. Qualitative data like pathology (malignant or benign) on PI, RI and histopathology were presented as frequency and percentage. Parity was also presented as frequency. 2x2 table was generated to calculate sensitivity, specificity, PPV, NPV and diagnostic accuracy of RI and PI on Doppler USG taking histopathology as gold standard. Data was stratified for age, parity, duration of symptoms and BMI. Post-stratification, 2x2 table was generated to calculate sensitivity, specificity,

PPV, NPV and diagnostic accuracy of RI and PI on Doppler USG taking histopathology as gold standard.

RESULTS

In this present study total 200 cases were enrolled. The mean age of the patients was 42.27±10.61 years with minimum and maximum ages of 25 & 60 years respectively [Table 1]. The mean BMI of the patients was 29.38±5.81 kg/m^2 with minimum and maximum BMI of 19.50&40.07 kg/m^2 respectively [Table 2]. The parity status of the patients in this study is depicted in [Figure 1].

Table 1: Descriptive statistics of age (years)

Age (years)	N	200
	Mean	42.27
	standard Deviation	10.61
	Minimum	25
	Maximum	60

Table 2: Descriptive statistics of BMI (Kg/m^2)

BMI (Kg/m^2)	N	200
	Mean	29.38
	standard Deviation	5.81
	Minimum	19.50
	Maximum	40.07

Table 3: Frequency distribution of RI Doppler

		Frequency	Percent
RI Doppler	Positive	125	62.5
	Negative	75	37.5
	Total	200	100.0

The ovarian tumor was diagnosed positive by RI Doppler in 125(62.5%) patients and negative in 75(37.5%) patients [Table 3].The ovarian tumor was diagnosed positive by PI Doppler in 122(61.0%) patients and negative in 78 (39.0%) patients [Table 4]. The ovarian tumor was diagnosed positive by histopathology among 120(60.0%) patients and negative in 80(40.0%) patients [Figure 2]. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of RI Doppler is shown in [Table 5]. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of PI Doppler taking histopathology as gold standard [Table 6].
In patients ≤40 years, the sensitivity, specificity and diagnostic accuracy of RI was 100%, 94.44% & 97.8% respectively. In patients >40 years, the sensitivity, specificity and diagnostic accuracy of RI was 96.92%, 88.64% & 93.58% respectively. In patients ≤40 years, the sensitivity, specificity and diagnostic accuracy of PI was 100%, 97.22% & 98.9% respectively. In patients >40 years, the sensitivity, specificity and diagnostic accuracy of RI was 98.44%, 95.45% & 97.25% respectively taking histopathology as gold standard [Table 7].
In patients with normal BMI the sensitivity, specificity and diagnostic accuracy of RI was 100%, 70.0% & 94.64% respectively. In patients with abnormal BMI the sensitivity, specificity and

diagnostic accuracy of RI was 97.3%, 94.29% & 95.83% respectively. In patients with normal BMI the sensitivity, specificity and diagnostic accuracy of PI was 97.83%, 90.0% & 96.43% respectively. In patients with abnormal BMI the sensitivity, specificity and diagnostic accuracy of RI was 100%, 97.14% & 98.61% respectively taking histopathology as gold standard [Table 8].
In primiparous patients, the sensitivity, specificity and diagnostic accuracy of RI was 100%, 83.33% & 94.12% respectively. In multiparous patients, the sensitivity, specificity and diagnostic accuracy of RI was 98.17%, 91.89% & 95.63% respectively. In primiparous patients, the sensitivity, specificity and diagnostic accuracy of PI was 100%, 100% & 100% respectively. In multiparous patients, the sensitivity, specificity and diagnostic accuracy of RI was 97.3%, 98.61% & 97.81% respectively taking histopathology as gold standard [Table 9].
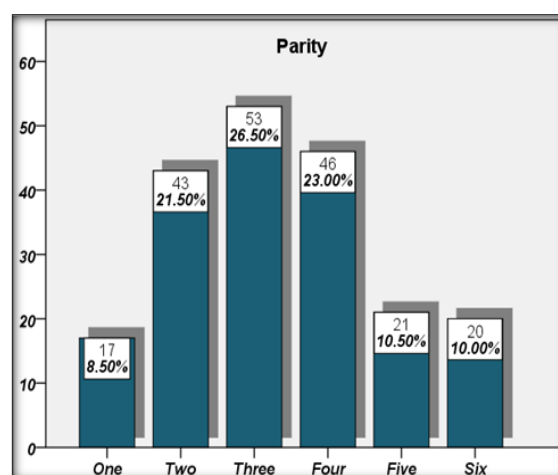

Figure 1: Frequency distribution of parity

Table 4: Frequency distribution of PI Doppler

		Frequency	Percent
PI Doppler	Positive	122	61.0
	Negative	78	39.0
	Total	200	100.0

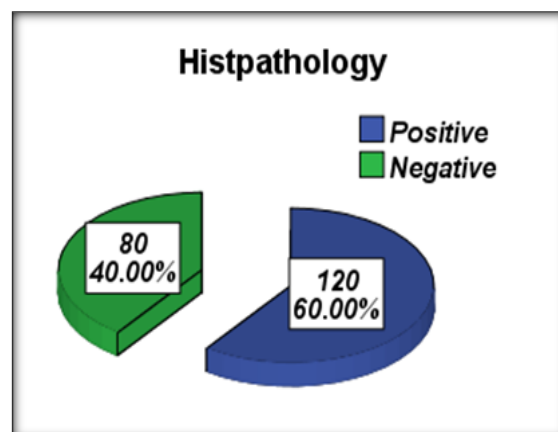**Figure 2: Frequency distribution of histopathology**
Table 5: Validity of RI Doppler taking histopathology as gold standard

		Histopathology		Total
		Positive	Negative	
RI Doppler	Positive	118	7	125
	Negative	2	73	75
Total		120	80	200

Sensitivity	98.33%
Specificity	91.25%
PPV	94.4%
NPV	97.33%
Diagnostic Accuracy	95

Table 6: Validity of PI Doppler taking histopathology as gold standard

		Histopathology		Total
		Positive	Negative	
PI Doppler	Positive	119	3	122
	Negative	1	77	78
Total		120	80	200

Sensitivity	99.17%
Specificity	96.25%
PPV	97.54%
NPV	98.72%
Diagnostic Accuracy	98.00%

Table 7: Validity of RI & PI Doppler taking histopathology as gold standard stratified by age

Age (years)	RI Doppler	Histopathology		PI Doppler	Histopathology	
		Positive	Negative		Positive	Negative
≤ 40	Positive	55	2	Positive	55	1
	Negative	0	34	Negative	0	35
> 40	Positive	63	5	Positive	64	2
	Negative	2	39	Negative	1	42

	RI		PI	
	Age (years)			
	≤ 40	> 40	≤ 40	> 40
Sensitivity	100%	96.92%	100%	98.46%
Specificity	94.44%	88.64%	97.22%	95.45%
PPV	96.49%	92.65%	98.21%	96.97%
NPV	100%	95.12%	100%	97.67%
Diagnostic Accuracy	97.8%	93.58%	98.9%	97.25%

Table 8: Validity of RI & PI Doppler taking histopathology as gold standard stratified by BMI

BMI	RI Doppler	Histopathology		PI Doppler	Histopathology	
		Positive	Negative		Positive	Negative
Normal	Positive	46	3	Positive	45	1
	Negative	0	7	Negative	1	9
Abnormal	Positive	72	4	Positive	74	2
	Negative	2	66	Negative	0	68

	RI		PI	
	BMI			
	Normal	Abnormal	Normal	Abnormal
Sensitivity	100%	97.3%	97.83%	100%
Specificity	70%	94.29%	90%	97.14%
PPV	93.88%	94.74%	97.83%	97.37%
NPV	100%	97.06%	90%	100%
Diagnostic Accuracy	94.64%	95.83%	96.43%	98.61%

Table 9: Validity of RI & PI Doppler taking histopathology as gold standard stratified by parity

Parity	RI Doppler	Histopathology		PI Doppler	Histopathology	
		Positive	Negative		Positive	Negative
Primary	Positive	11	1	Positive	11	0
	Negative	0	5	Negative	0	6
Multiple	Positive	107	6	Positive	108	3
	Negative	2	68	Negative	1	71

	RI		PI	
	Parity			
	Primary	Multiple	Primary	Multiple
Sensitivity	100%	98.17%	100%	97.3%
Specificity	83.33%	91.89%	100%	98.61%
PPV	91.67%	94.69%	100%	99.08%
NPV	100%	97.14%	100%	95.95%
Diagnostic Accuracy	94.12%	95.63%	100%	97.81%

DISCUSSION

Ovarian malignancy is usually detected late once after it has reached an advanced stage. This makes it imperative to diagnose it in earlier stages. The ovarian malignancy is the third leading cause of cancer in females (8%) as seen in PAECCR, Lahore Registry Data comprising thirty years of cancer incidence from 1984- 2014. Therefore early diagnosis and management of ovarian tumors has significant clinical impact. Effective evaluation of ovarian malignancy using Color and Spectral Doppler has

been a subject of interest in the recent years. Color Doppler with spectral analysis using indices such as PI and RI is very valuable in revealing better characterization of ovarian tumors.[12,13]

In this study the sensitivity, specificity, PPV, NPV and diagnostic accuracy of RI Doppler was 98.33%, 91.25%, 94.4%, 97.33% & 95.5% respectively taking histopathology as gold standard. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of PI Doppler was 99.17%, 96.25%, 97.54%, 98.72% & 98.00% respectively taking histopathology as gold standard.

A study by Dharita Shah et al documented that a good specificity (84.1 %) and sensitivity (97.5 %) with PI and RI values of <1.0 and <0.6, respectively, was achieved which is very impressive finding in differentiating between malignant and benign ovarian neoplasms. 87.5 % of malignant tumors had PI less than 0.8 in contrast to only 4.54 % of benign tumors. Similarly, majority of malignant tumors had RI less than that of benign tumors.[14]

Hossain F et al stated that the Resistance Index was capable of detecting 92% of malignant cases and 89% of benign cases accurately which translates into an impressive accuracy in the diagnosis of ovarian tumors. Predictive values for positive (84.6) and negative (94.1) tests were also found to be quite high. Pulsitility index was found to be of moderate accuracy (63.3%).[15]

One study has reported that the sensitivity and specificity of RI were low as compared to sensitivity and specificity of PI. While another study showed that the sensitivity and specificity of RI were 83% and 93%, respectively while the sensitivity and specificity of PI i.e. 87.5% and 95.4%, respectively.[10,11]

On the contrary a study by Stein SM et al concluded that the PI and RI values were significantly lower in malignant masses in comparison to benign masses. For a PI of less than 1.0, sensitivity was 67%, specificity was 66%, NPV was 83%, and PPV was 46%. For an RI of less than 0.4, sensitivity was 24%, specificity was 90%, NPV was 73%, and PPV was 50%.[16]

Another study by Antonić J et al casted a doubt on use of RI and PI values to differentiate between benign and malignant ovarian tumors in women more than 34 years of age. The use of CA 125 serum level in identification of ovarian cancer in women over 35 years of age is more helpful. CA 125 under 35 U/ml together with the lack of detectable color flow in the tumor, can exclude ovarian malignancy reliably, in women over 35 years of age (NPV = 100%).[17]

One more study by Ueland et al demonstrated that PI 1.0 indicated malignancy and was associated with: sensitivity 0.528, specificity 0.776, PPV 0.288, NPV 0.906. On the other hand RI 0.4 as indicative of malignancy was associated with: sensitivity 0.222, specificity 0.867, PPV 0.222, and NPV 0.867.[18]

From a study done by Prasad and colleagues in Bihar, India it was inferred that PI and RI both correlate with malignancy and support the fact that tumors have morphologically abnormal vessels. PI was found to be more accurate that RI which supports our claim as well.

CONCLUSION

According to this study both RI and PI color Doppler indices are reliable and effective for differentiation of benign and malignant ovarian tumors in females taking histopathology as gold standard. More studies are required on the subject over a large sample to strengthen the findings of this study.

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