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Original Article

Validity of E-Flow Colour Doppler Indices in Differentiating Benign and Malignant Ovarian Tumours

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Abstract

Background: To determine the validity of Pulsatility and Resistive index of trans-abdominal Doppler ultrasound(e-flow) in distinguishing between benign and malignant adnexal masses keeping histopathology as gold standard.

Methods: In this cross sectional study patients scheduled for elective surgery due to adenaxal masses were included. All patients were sonographically evaluated for Pulsatility and Resistance indices aided with colour e-flow Doppler before the elective surgery of lesions. The performing radiologist had no information on the patients, to differentiate between benign and malignant adnexal masses based on Doppler indices. The final diagnoses were based on pathological and operative findings, keeping histopathology as gold standard.

Results: Two hundred and twenty-nine patients were recruited out of which 18 were excluded, since the masses were finally not proven to be adnexal. Of the remaining 211 cases available for analysis, 163 were benign and 48 were malignant. The sensitivity and specificity of the Pulsatility index for distinction were 89.57% and 85.42% and values for the Resistance index were 89.57% and 89.58% respectively.

Conclusions: Pulsatility and resistance indices with trans-abdominal Doppler ultrasound (e-flow) have high accuracy in differentiating between benign and malignant adnexal masses.

Key Words: Adnexal mass, Pulsatility index,Resistance index,Doppler ultrasound,Ovarian tumours.

Introduction

To differentiate between benign and malignant adnexal masses is of great value as therapeutic approach is markedly different between the two entities. [1] Benign lesions like benign ovarian masses or functional changes need more conservative approach like either close observation or laparoscopic surgery, whereas malignant tumours require urgent laparotomy and in most of cases patient is being referred for further chemotherapy or radiotherapy by involving oncologists.[2] Several attempts have been made to distinguish between the conditions in the past but with the availability of high-resolution ultrasound machines, colour doppler ultrasound is a possible technique for differentiation of benign from malignant adnexal masses as well as for early diagnosis of ovarian carcinoma for several years. [3,4] Some reports also showed the superiority of this technique in screening ovarian cancer while there are some other reports favouring its ability in differentiating benign from malignant tumours preoperatively. [5,6]However, colour Doppler application in such previous reports was often needed via transvaginal approach and this might be inconvenient to some patients. [7] Currently, high-resolution colour Doppler with extended flow (e-flow) has been developed, resulting in higher sensitivity in detection of blood flow in minute vessels even during trans abdominal examination. [8,9]Therefore, the purpose of the present study was to determine the sensitivity and specificity of Pulsatility index (PI) and resistance index (RI), derived from trans-abdominal colour Doppler e-flow, in differentiating benign from malignant ovarian tumours.

Patients and Methods

This cross-sectional validation study was done at Department of Gynecology and Radiology at Fauji Foundation Hospital Rawalpindi from January 2014 to December 2014.Two hundred and eleven patients of ovarian masses were included in the study with non-probability purposive sampling. All patients referred by gynecologist with suspected ovarian mass for diagnostic workup and who are going to be operated from indoor and outdoor department were included in the study. Patients with disseminated disease and with severe co-morbid conditions and declared inoperable, patients with known diagnoses of ovarian malignancy which was scheduled for a second look operation and patients with past history of major pelvic surgery for non-ovarian pathological fibrosis or vascular changes

were excluded from study.Doppler ultrasonography was performed using a Curvilinear probe of Aloka SSD 5500 in dimly lit room with comfortable temperature (22-24C) in supine position and Resistive and Pulsatility indices were calculated. Both Pulsatility index (PI) and resistance index (RI) were calculated. The value of each artery was calculated from a curve fitted to the average waveform over three cardiac cycles. The formulas used for PI and RI were PI = (S-D)/ mean and RI = (S-D)/S respectively, when S is the peak Doppler frequency shift and D is the minimum. Signals from various areas within the tumour were determined but the lowest PI and RI were considered for data analysis. The area distribution of visualized vessels in the adnexal masses was also categorized and recorded as center of the mass, in the septum, in the papillae, at tumour wall or peri-tumor areas The final diagnosis as gold standard was based on either pathological findings or intraoperative findings in case of no pathological specimen. All of adnexal masses were divided into 2 groups as benign and malignant adnexal masses. The sensitivity and specificity of various cut-off levels of PI and RI were calculated and all data were analyzed using SPSS software version 16.0.

Resistive Index (RI) is calculated as RI = [peak systolic velocity - end diastolic velocity]/peak systolic velocity. Value should be less than 4 for malignant mass.Pulsatility Index (PI) is defined as the difference between the maximum flow and the minimum flow divided by the mean and value should be less than 1 for malignant lesion. Lesions were categorized as simple cyst (anechoic with a thin wall and acoustic enhancement, with or without a single thin septations), dermoid cyst(fluid layer or echogenic mural nodule with shadowing), or an endometrioma (cyst with diffuse low-level echoes with one or two thin septations and a thin wall).Atypical features such as a thick wall or multiple irregular septations, lesions having nodules or solid elements.Histopathological features of malignant tumours include nuclear atypia and degree of mitoses (> 12 per 10 high-power fields) p53, BRCA1/2 genes and other genetic mutations, solid and cystic areas, extensive haemorrhage and necrosis and degree of micro-invasion.

Results

Between January 2014 to December 2014, 229 patients initially diagnosed as ovarian tumours were recruited to undergo e-flow colour trans-abdominal, doppler ultrasound examinations. Out of these eighteen patients were excluded because of pathological diagnoses of non-ovarian tumour including subserous myoma, hydrosalpinx and patients who lost follow up due to domestic reasons etc. The remaining 211 patients were analyzed. Mean age (yrs) of 211 female patients was 45.29$\pm$10.51 with ranges from 20 to 80 years.Histopathological examinations revealed 163 patients (77.25%) having benign tumours and 48 patients (22.75%) having malignant tumours.Out of 211 patients, there were 151 patients who you were found benign (RI < 0.5) by doppler ultrasound, in which 146 patients were benign and 05 patients were found malignant histopathologically. Similarly, out of 211 patients, there were 60 patients who you were found malignant (RI $\geq$ 0.5) by doppler ultrasound, in which 17 patients were benign and 43 patients were found malignant histopathologically. So the sensitivity, specificity, PPV and NPV of doppler ultrasound measurements (Resistive Index) was 89.57%, 89.58%, 96.69%, 71.67% respectively (Table 1). Out of 211 patients, there were 153 patients who were found Benign (PI < 1) by doppler ultrasound, in which 146patients were benign and 07 patients were found malignant histopathologically. Similarly, out of 211 patients, there were 58 patients who were found malignant (PI $\geq$ 1) by doppler ultrasound, in which 17 patients were benign and 41 patients were found malignant histopathologically. Sensitivity, specificity, PPV and NPV of doppler ultrasound measurements (Pulsatility Index) was 89.57%, 85.42%, 95.42% and70.69% respectively(Table 2).

Table 1:Doppler USG (Resistive Index) with Histopathology

		Histopathology		Total
		Benign	Malignant	
Doppler Measurements (Resistive Index)	Benign	146	5	151
	Malignant	17	43	60
Total		163	48	211

Table 2:Doppler USG (Pulsatility Index) with Histopathology

		Histopathology		Total
		Benign	Malignant	
Doppler Measurements (Pulsatility Index)	Benign	146	7	153
	Malignant	17	41	58
Total		163	48	211

Discussion

Ovarian pathology is 5th most common malignancy and is characterized by few early nonspecific symptoms and signs.[10,11] The cure rate for disease at

early stage is 80-90 % and five-year relative survival rate for stage I is 95%. [12]Ultrasound abdomen is considered the best initial imaging technique while CT and MRI also play a role in the minority of cases where ultrasound is inconclusive. The sonographic examination includes trans-abdominal and transvaginal scans combined with colour and pulsed doppler images. [13] The trans-abdominal scans, in comparison with transvaginal approach, also provide assessment of ascites, adenopathy, hydronephrosis, and liver metastases. On trans-vaginal studies, the field of view is much smaller compared to the field of view on trans-abdominal scans and it is also difficult to assess a mass high in pelvis. [14] Many centers are now using colour doppler in early assessment of ovarian mass. Combination of both morphology and doppler is more accurate than either used alone but there is no agreement as to which doppler index is best and at which level the threshold should be set to distinguish between high and low impedance flow. [15] Considering the above mentioned limitations of trans-abdominal and endo-vaginal ultrasound we used to see the validity of E-flow colour doppler indices (Pulsatility and Resistive index) for detection of malignancy in ovarian tumours which were referred to radiology department for evaluation.

Differentiation of benign from malignant tumours is very important due to vast difference in mode of treatment and it might be achieved by several methods such as clinical signs and symptoms, serum CA 125 levels, and ultrasound.[16,17] Conventional ultrasound parameters for the differentiation of malignant from benign tumours are based merely on morphological features. The introduction of colour doppler ultrasound, especially high-resolution colour e-flow doppler with higher sensitivity in detection of blood flow in minute vessels, might allow a step forward from morphological to functional evaluation of the masses. The theoretical background comes from the observation that the new tumour vessels that grew as a result of angiogenesis differ from the normal vessels with respect to cellular composition, basement membrane structure and permeability. As a result, the haemodynamics of these vessels is changed. [18]

Considering angiogenesis as a neoplastic marker for malignancy, colour doppler ultrasound allows a better insight in the biological behaviour of the tumour and early diagnosis of cancer could become possible by detecting neo-vascularization in the tumour.[19] In previous studies, some authors suggested the existence of clear cut-off points of PI and RI of benign and malignant tumours; Kurjak et al reported only one false positive and two false negative results in a screening program involving 624 benign ovarian tumours and 56 malignant tumours by using a cut-off value of RI 0.4. [20] Sengoku et al reported sensitivity and specificity of 81.3% and 91.7% respectively when the cut- off value of PI 1.5 was used. [21] In the present study 54% of benign and 100% of malignant including borderline tumours had detectable arterial blood flow in the tumours using a colour doppler unit. This information may enable us to conclude that tumour without detectable blood flow is very unlikely to be malignant. Our cut-off PI value of 1.00, giving the sensitivity and specificity of 89.57% and 85.42%, respectively, was different from the study of Sengoku et al but was consistent with the data reported by Weiner et al.[22] The scanning approach (trans-vaginal or trans-abdominal) and frequency of the probes might partially explain inconsistent results reported previously by different authors (Zanetta et al). [23] Unlike previous reports in which they firstly used trans-abdominal probe and then trans-vaginal probe is performed if trans-abdominal examination was unable to visualize, our study with e-flow colour doppler we could identify the tumour in all cases. This may be the advantage of new high-resolution ultrasound technology permitting us avoiding the inconvenience of trans-vaginal approach. All authors agree that recognition of angiogenesis as a reference point for malignant changes within the ovary has proved to be a highly sensitive parameter.[24] Neovascularization is an obligate event in malignant change. This recognition enables to observe the earliest stages in ovarian oncongenesis. The signs of neo-vascularization tumours, considered benign by conventional ultrasound, can be missed by insufficient evaluation of the vascularity, whereas the tumours with suspicion of malignancy would be examined more thoroughly until the expected lowest PI and RI were found.[25] It is important to examine all arterial signals to find out the lowest ones in each case to reduce the bias described. The present study pertinently cater for it.

Conclusion

1. Trans-abdominal e-flow colour Doppler indices are a useful tool in preoperative diagnosis of ovarian tumours.

2.It is a objective sonological evaluation of the lesions and morphological features particularly those pointing to malignancy allows early detection and differentiation of benign and malignant tumours. Thus, it can help in timely referral of malignant cases to specialist care resulting in better outcome.

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