RESEARCH ARTICLE

Role of Ultrasound in Characterization of Ovarian Masses

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Abstract

Background: Ovarian cancer is the second most common malignancy in Pakistani women, accounting for 4% of all cancers in the female population. The aim of this study was to determine sensitivity, specificity, positive and negative predictive values and 95% confidence intervals for ultrasound in characterization of ovarian masses in patients presenting at public and private tertiary care hospitals in Karachi, Pakistan. Materials and Methods: We adopted a cross-sectional analytical study design to retrospectively collect data from January 2009-11 from medical records of two tertiary care hospitals. Using a non-probability purposive sampling technique, we recruited a sample of 86 women aged between 15 and 85 years fulfilling inclusion criteria with histopathologically proven ovarian masses presenting for an ultrasound examination in our radiology departments. Results: Our retrospective data depicted sensitivity and specificity of ultrasound to be 90.7%, 95%CI (0.77, 0.97) and 91.4%, 95%CI (0.76, 0.98) respectively. Positive predictive value was 93%, 95%CI (0.79, 0.98) and negative predictive value was 89%, 95%CI (0.73, 0.96). A total of 78 ovarian masses were detected, out of which 42 were malignant and 36 were benign. Conclusions: Results of our study further reinforce the conclusion that ultrasound should be used as an initial modality of choice in the workup of every woman suspected of having an ovarian mass. It not only results in decreasing the mortality but also avoids unnecessary surgical interventions.

Keywords: Ovarian masses - ultrasound characterization - Pakistan females

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Introduction

Ovarian cancer happens to be the second most common malignancy that accounts for 4% of all cancers in female population. Annually more than 190,000 new cases are diagnosed world over with the life time risk of developing ovarian cancer in India is 0.75% which vary considerably world over (Parkin et al., 2003; Jemal et al., 2008). However the mortality is the highest in comparison to the other gynecological cancers.

Different investigation tools such as serum CA-125 and pelvic examinations over a period of past many years have been tested and shown lower sensitivities in the diagnosis of ovarian masses. Owing to this and high mortality rate associated with ovarian malignancy, ultrasound has attained its role as the most important preliminary investigation of choice to rule out ovarian malignancies with sensitivity ranging from 80-100% (Kinkle et al., 2000; Van Calster et al., 2005; Arab et al., 2012).

Although, Doppler ultrasound allows detection of tumor flow. However, its role has not been found consistent in diagnosis of malignancy (Kinkle et al., 2005; Liu et al., 2007). Moreover, there exists a wide variation in patient population, imaging techniques, and results making things more complicated to precisely understand and assess the diagnostic ability of existing various imaging techniques.

Ultrasound features of malignant ovarian masses are (Ameye et al., 2009): Cysts with thickened and irregular walls, internal septae (>3 mm), vegetation or papillary projections, cystic lesions greater than 10 cm diameter, presence of solid components or completely solid lesions. Other associated signs include ascites or peritoneal deposits. Based on these features (Sassone et al., 1991) derived a scale which focused on the features such as echo pattern of the lesion, presence or absence of papillary projection and septae, and wall thickness. As a result they distinguished benign and malignant masses with sensitivity of 100%, and specificity of 83%. Similarly (Jacobs et al., 1990) showed 85% sensitivity and 97% specificity of ultrasound for the detection of malignancy. In 1999, International Ovarian Tumor Analysis Group performed a study which included multiple centers from five European countries. They collected relevant demographic and radiographic data of more than 1,000 patients presenting with persistent adnexal masses prospectively and developed a mathematic model so that the risk of risk of malignancy in an adnexal mass can be calculated, with an area under the receiver operating curve (ROC) of 0.96 (Timmerman et al., 2005).

In 2007, the same group reported sensitivity and

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specificity of morphologic features of ovarian masses on ultrasound to be 90% and 88% respectively.

The largest randomized controlled trial conducted by United Kingdom collaborative Trial of ovarian Cancer screening published their results of ovarian cancer screening in April 2009. They included more than 200,000 postmenopausal women in their study and reported ultrasound to be 84.9% sensitive for the detection of ovarian malignancy (Menon et al., 2009).

In spite of such an extensive research work and international data available with regards to the diagnostic accuracy of ultrasound in detection of both benign and malignant ovarian masses, to our surprise the literature from this part of the world appears scarce. No comprehensive study has been conducted in the recent past that emphasizes the significance of such a novel and yet effective investigative tool in detection of malignancy which is so fatal. We, therefore studied whether ultrasound is sensitive in characterization of ovarian masses in women (15-85 years) presenting at public and private tertiary care hospitals in Karachi? We hope that results of this study will encourage concerned personnel to expedite specific actions required to teach and train appropriate techniques to those who are routinely carrying out such ultrasounds as early detection and accurate staging will not only improve the disease prognosis but would also help avoiding excessive radiation examinations in those who would neither benefit nor require them.

Materials and Methods

A cross-sectional analytical study was designed to retrospectively collect data from Jan 2009-Jan 2011 by non-probability purposive sampling technique. Women aged between 15 and 85 years were included if referred/ presented for an ultrasound examination in radiology departments of two tertiary care hospitals in Karachi. 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 seen during this study period. They were excluded if diagnosed as ovarian mass on ultrasound but no histopathology report. They were also excluded if patients presented with histopathology positive for ovarian mass without ultrasound reports and if presented with recurrent or residual ovarian mass.After permission from radiology departmental heads of tertiary care hospitals and Ethical Review Committee exemption; 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 mass on histopathology were analyzed. All the ultrasounds were performed on NEMIO XG, TOSHIBA machines by a radiologist having at least 3 years of experience in performing pelvic ultrasounds. Trans abdominal scans were done using 3.5 MHz probe. Where ever required transvaginal scanning was also performed using 7.5 MHz frequency probe using the same machine in the single setting in both the centers. Data were collected in structured proforma which elicited information regarding patient's demographics and ultrasound characteristics of the ovarian mass. Final diagnosis was confirmed on histopathology taken as gold standard.

Sample size calculation

Calculated sensitivity of ultrasound for the detection of ovarian carcinoma is 80% (Jain, 1994; Jung et al., 2002) taking confidence interval of 95% , bound on error of 9%, the calculated sample size N=76. $n= [Z^2_{1-\alpha/2} - P (1-P)]/B^2$.

Plan of analysis

Data were entered and analyzed using SPSS windows package version 19.0. 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 ovarian masses was calculated and 95% Confidence Intervals (CI) reported. Positive and negative predictive values were also computed.

Results

Results gathered from our retrospective data depicted sensitivity and specificity of ultrasound to be 90.7%, 95%CI (0.77, 0.97) and 91.4%, 95%CI (0.76, 0.98) respectively in characterization of benign and malignant ovarian masses. The age range of patients was between 16-86 years with mean age of 40.95±SD 16.54. The mean tumor size was 7.6±4.03 x 6.1±3.13 in transverse and longitudinal axis respectively for the left ovary and 7.9±4.22 x 6.5±3.00 for the right ovary. Positive predictive value was 93%, 95%CI (0.79, 0.98) and negative predictive value was 89%, 95%CI (0.73, 0.96). Data were collected of 84 women with the diagnosis of ovarian masses over a period of two years from both hospital excluding six such cases for certain specific reasons. Reasons for exclusion were histopathologically inadequate sample in two and non-specific tissue in others. 49% of the tumors (42/78) were malignant, rest (36/78) were benign. The histopathological diagnoses of benign and malignant ovarian masses are shown in Table 2. Out of 42 malignant tumors diagnosed on ultrasound, 3 were histopathologically proven benign. Their final diagnoses were as follows: (n=1) serous cyst

Table 1. Historical Comparisons of Ultrasound and Clinical Criteria for Cancer Prediction

Study	No. of Patients	Characteristics	Accuracy
Sassone et al. 1991	143	Gray-scale characteristics score	Sensitivity, 100%; specificity 83%; PPV, 37%; NPV, 100%
Fleischer et al. 1993	50	Color and spectral Doppler characteristics	Pulsatility index; sensitivity, 100%; specificity, 82%; PPV, 73%; NPV, 100%
UKCTOCS, 2009	50,640	Multitechnique screening (ultrasound and serum CA-125)	Sensitivity, 89%; specificity, 99%; PPV, 35%; NPV, 99%
IOTA, 2005	1,573	Combined gray-scale and color mapping, age, and other clinical variables	AUC=0 0.96; pattern recognition: sensitivity, 90%; specificity, 88% and logistic regression: sensitivity, 95%; specificity, 74% and subgroup category: sensitivity, 88%, specificity 90%

Table 2. Histopathological Diagnoses of Tumors

Histopathological diagnoses		No. (%)
Benign:	Ovarian cyst	5 (12.8)
	Serous cyst adenoma	3 (3.84)
	Mucinous cyst adenoma	2 (2.5)
	Tubovarian inflammation	2 (2.5)
	Corpus albicantes	3 (3.84)
	Corpus haemorrhagicum	2 (2.5)
	Corpus luteal cyst	3 (3.8)
	Para tubal cyst	5 (6.4)
	Endometrioma	19 (24.4)
Malignant:	Adenocarcinoma	11(14.1)
	Ovarian carcinoma	3 (3.8)
	Clear cell carcinoma	1 (1.3)
	Endometriod carcinoma	4 (5.1)
	Mature cystic teratoma	3 (3.8)
	Papillary carcinoma	2 (2.5)
	Spindle cell tumor	2 (2.5)
	Serous cyst adenocarcinoma	2 (2.5)

Table 3. Sensitivity of Ultrasound in Differentiating between Benign and Malignant Ovarian Masses

Diagnosis	Sensitivity (%)
Malignancy	93 (39/42)
Endometriosis	90 (17/19)
Dermoid cyst	00 (0/1)
Para ovarian or Para tubal cyst	100 (3/3)
Tubo-ovarian abscess	100 (2/2)
Simple ovarian/hemorrhagic cyst	91 (10/11)

adenomas, (n=2) hemorrhagic cysts. Similarly, benign diagnosis was suggested in 36 tumors out of which 32 were found to be in concordance with histopathology. Those were: endometriomas (n=19), dermoid cyst (n=1), Para ovarian cyst (n=3), tubo-ovarian abscess (n=2), hemorrhagic cyst (n=6), simple ovarian cysts (n=5). The true positive rate of endometriosis was (17/19), of dermoid cyst (0/1), of tubo-ovarian abscess/inflammation disease (2/2), of Para ovarian cyst (3/3). The incorrect diagnoses of endometrioma represented one mucinous cystadenoma, one mature cystic teratoma; the one incorrect diagnoses of dermoid cyst comprised one mature cystic teratoma; the 1 incorrect diagnoses of ovarian hemorrhagic cyst represented ovarian endometriosis. Thus, ultrasound was able to make 39 correct specific malignant diagnosis and 32 of benign masses.

Discussion

Ultrasonography (US) has established and developed itself as the most important preliminary imaging tool in identification and characterization of the ovarian masses. This has eliminated unnecessary surgeries in those who will not get any benefit out of it. Both Trans abdominal and transvaginal techniques along with Doppler examination provides optimal visualization of ovarian masses (Fleicher et al., 1993). In the current study, mixture of both benign and malignant ovarian masses was present. Most of the benign lesions such as endometriomas, simple ovarian/ Para ovarian cysts, dermoid cysts, hemorrhagic cysts and tubo-ovarian infections were specifically diagnosed. However, malignancies and certain benign solid masses were not further sub classified into teratomas, sarcomas, ovarian fibromas, serous and mucinous cyst adenomas. As from a clinical perspective it has been found sufficient to suggest a benign solid ovarian tumor diagnosis rather than to be more specific (Jermy et al., 2001).

Therefore based on the sonological features and available clinical data we made a correct specific diagnosis of 91% of the tumors. This was very much in concordance with other international studies reporting the sensitivities and specificities between 85-100% (Buy et al., 1993; Nishat et al., 2011).

Despite the fact that endometriomas are known to exhibit certain classical sonographic features such as a '***ground glass***' appearance and low level internal echoes (Aleem et al.,1995) we came across both false-positives and false-negatives cases. One cases of ovarian mucinous cyst adenoma and one hemorrhagic cysts were inaccurately labeled as endometriotic cysts (false-positives). In the present series, therefore the true positive rate for this diagnosis is 90%.

Although such overlaps and confusions have also existed in the past in the literature as well between endometriomas and cyst adenomas, dermoid and hemorrhagic cysts on sonography. However, our results report true-positive rate of 90%. Guerriero et al (1995). has reported sensitivity as 83% (Guerriero et al., 1995).

Similarly one of the mature cystic teratoma was wrongly diagnosed as a dermoid cyst making the sensitivity of our imaging to be 0%. This figure does not depict the actual sensitivity and specificity as we had only a single case of dermoid. Reported sensitivity by Mais et al. (1995) ranged from 53-100% (Mais et al., 1995).

In the present series, there were no incorrect diagnoses of Para ovarian cyst. One hemorrhagic cyst was misjudged on imaging as an endometrioma (false-positive). There have been no reports of the specificity of ultrasound in the diagnosis of Para ovarian cysts or of the sensitivity and specificity of gray-scale imaging in the diagnosis of peritoneal cysts. We did not come across a peritoneal cyst in our collected data. Our present series of tumors included only two tubo-ovarian abscesses. One was correctly diagnosed; the other was misdiagnosed as an abscess originating from appendicitis (false-negative). Given the complex appearances and echo patterns of tubo-ovarian abscesses as well as absence of relevant clinical information, such confusions are not unexpected (Fleischer et al., 1992). No reports exist in the literature so far regarding the diagnostic accuracy of pelvic abscess. Only Fleischer et al have reported the diagnostic accuracy of ultrasound for diagnosing tubal disease as 83% sensitive and 73% specific.

Several studies define Doppler findings of endometriotic cysts, dermoid cysts, tubo-ovarian abscesses and other benign cysts (Aleem et al., 1995; Zalel et al., 1997; Pascual et al., 2000). However, none have proved to be consistent. In our series of patients, we used Doppler sonography wherever the radiologist would think its usefulness would greatly impact in making the diagnosis and at the same time not following any specified criteria.

However, the problem with both ultrasound and

Doppler examination is its operator as well as equipment dependency, and whether the results obtained from one type of equipment are pertinent to other system. Furthermore, we would have to perform multiple studies prospectively on a larger scale with larger patient population to assess the reliability of both forms of imaging, that is, color Doppler and grey scale imaging independently as well as concurrently with a predefined criteria in determining the diagnosis of ovarian masses (Van Nagell et al., 2007). Knowledge of the exact nature of a pelvic mass after ultrasound examination is also a prerequisite for effective management, surgical or non- surgical. Since this fact has been established well by literature that exclusion of ovarian malignancy with precise ultrasound information goes a long way in the future management and also helps avoiding needless surgical interventions not giving any benefit to them.

In conclusion, this study yielded the diagnostic accuracy of ultrasound to be 91% in the diagnosis of ovarian masses, thus increasing its reliability. Thus ultrasound seems to be an initial modality of choice in the workup of every woman suspected of having an ovarian mass. And, to rule out unnecessary surgical interventions in benign masses.

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