

SERUM CA-125 VERSUS ULTRASOUND EXAMINATION IN DIFFERENTIATING BETWEEN BENIGN AND MALIGNANT OVARIAN MASSES

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ABSTRACT

Objective: To differentiate between benign and malignant ovarian masses by using serum CA125 versus ultrasound examination.

Methodology: This descriptive study was conducted at Department of Obstetrics and Gynecology, Hayatabad Medical Complex from 1st January 2010 to 31st December 2010. Women fulfilling inclusion criteria were admitted. They underwent transabdominal gray-scale ultrasound examinations by an experienced examiner before surgery. Pattern recognition was used to classify a mass as benign or malignant. These women also had blood withdrawn preoperatively for measurement of serum CA-125 with cut off value of < 35 IU as normal. Results from both radiological finding and serum CA125 were then compared with histopathological findings which was used as gold standard.

Results: Pattern recognition by ultrasound correctly classified 69.64% of the tumors as benign or malignant. Serum CA-125 correctly classified at best 74.14% of the masses. Combining both parameters the diagnostic accuracy increased to 86.75% with sensitivity 80.36%, specificity 100%, positive predictive value 100% and negative predictive value of 71.05%.

Conclusion: Pattern recognition alone was inferior to serum CA-125. Combining both parameters for differentiating between benign and malignant ovarian masses further increased the diagnostic accuracy.

Key Words: CA125 levels, Ovarian mass, Ultrasound.

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INTRODUCTION

In 2008, around 6,500 women were diagnosed with ovarian cancer in the UK^{1,4}, making it the second most common gynecological cancer and the fifth most common cancer in women. It has been estimated that the life time risk of developing ovarian cancer is 1 in 54⁵. In Pakistan ovarian cancer is the fourth prevalent cause of cancer in women⁶.

The preoperative distinction between

benign and malignant ovarian mass is important as it directly affects surgical decisions and subspecialty referral and is therefore important for patient treatment. Although gray-scale US remains a mainstay of imaging detection of suspected ovarian masses, persisting controversies surround the optimal US techniques for subsequent characterization of the detected ovarian mass⁷.

Ultrasonography is a sensitive and noninvasive method for preoperative staging of suspected ovarian cancer regarding tumor size, ascites, invasion of adjacent organs and peritoneal carcinomatosis, but not for detection of malignant lymph nodes⁸. Transabdominal sonography has a sensitivity of 93%, a specificity of only 42%, positive predictive value of 39%, and a negative predictive value of 94%⁷.

CA125 is the gold standard tumor marker in the evaluation of pelvic masses, particularly in the ovarian epithelial cancer, elevated in over 90% of patients with advanced epithelial ovarian cancer and 40% of overall cases with advanced intra-abdominal malignancies with a cutoff value of more than 35 IU considered as malignant⁹. But it has been seen that elevated serum CA125

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(>35IU/ml) could be found in many benign condition such as menstruation, pregnancy, functional cyst, pelvic infection, and endometriosis^{9,10}. Therefore a standalone modality it has a low diagnostic accuracy of 60.8% with sensitivity of 83.1% when used to differentiate between benign and malignant ovarian masses¹¹.

In order to increase the accuracy in differentiating between benign and malignant ovarian masses combination of preoperative CA125 and ultrasonography is used. Finkler and colleagues¹² used the transabdominal ultrasound in combination with CA125 for ovarian cancer screening and found a sensitivity of 30% to 50% for stage 1 disease compared with 88% for advanced disease (stages 3 and 4)¹³.

METHODOLOGY

This descriptive study was conducted at Department of Obstetrics and Gynecology, Hayatabad Medical Complex from 1st January 2010 to 31st December 2010 after taking permission from the Hospital Ethical Committee. Eighty Three women with an ovarian mass who met the inclusion criteria out of 98, were recruited in the present study and 13 were excluded. Women with complex ovarian mass, symptomatic cysts and postmenopausal women with ovarian cysts >5cm were included in the study.

Patients with adnexal mass other than ovarian mass, pregnant women with ovarian mass, known case of prior malignancy, ovarian ectopic and recurrent ovarian cancer were excluded from the study.

Informed written consent was taken and they were included in the study. Detailed history regarding symptoms and clinical data like abdominal and vaginal examination of ovarian mass, consistency, mobility and tenderness was obtained and recorded for each individual. The records were reviewed for the age at presentation, presenting symptoms, diagnostic studies, operative approach, surgical procedure and pathology finding. Peripheral venous blood sample was drawn for CA125 levels performed by Architect 125 IInd generation Chemluminescent Microparticle Immunoassay (CMIA) from City Medical Laboratory, Peshawar within 1 week before the operation. Women with ovarian masses underwent transabdominal gray-scale ultrasound examinations only by an experienced radiologist before surgery. Pattern recognition was used to classify a mass as benign or malignant by using the International Ovarian Tumor Analysis (IOTA) Group which includes the cystic and solid tumor compositions as well as the presence and type of septations and papillations.

Results from both assays were then compared with histopathological findings which were used as gold standard. All women who entered into the present study underwent exploratory laparotomy and were followed up post operatively by histopathological analysis of all surgical specimens for gold standard or definite diagnosis of each case. The histopathology of all retrieved samples was performed by single gynecologic pathologist.

The accuracy of CA125 levels was assessed at levels more than 35U/ml in preoperative differentiation of ovarian cancer from benign ovarian disease in women who presented with an ovarian mass. The sensitivity, specificity, positive and negative predictive values were analyzed at 95% confidence interval.

RESULTS

Total 83 patients were assessed radiologically by abdominal ultrasound and serum CA125 levels before surgery. Out of these, 56 were suspected to be malignant on ultrasound, of which 39 patients were correctly diagnosed as malignant when followed by histopathology. Thus pattern recognition correctly classified tumors in 69.64% (Table 1).

Serum CA-125 correctly classified at best 43 patients as malignant out of 58 suspected malignant patients. Thus pattern recognition correctly classified tumors in 74.14% (Table 2).

Combining both parameters the diagnostic accuracy increased to 86.75% with sensitivity of 80.36% , specificity 100%, positive predictive value 100% and negative predictive value of 71.05% (Table 3).

DISCUSSION

Transabdominal sonography has a sensitivity of 93%, a specificity of only 42%, positive predictive value of 39%, and a negative predictive value of 94%⁷. but in our study it was able to identify correctly masses with sensitivity 69.64% a specificity of 100%, positive predictive value of 100%, and a negative predictive value of 61.36%. The reason for this low sensitivity and specificity may be absence of Doppler use in these patients.

The masses that were never misdiagnosed as malignant by ultrasound in this study were dermoid cyst, functional cysts and simple cysts which was also proved in study by Sokalaska¹⁰.

The diagnostic value of serum CA125 in distinguishing a benign from a malignant ovarian mass has been demonstrated in the literature with a sensitivity ranging from 56%-100% and a

Table 1: Diagnostic Test Evaluation of Radiological Findings

Histopathological Findings				
Radiological Findings		Positive	Negative	Total
	Positive	39	0	39
	Negative	17	27	44
		56	27	83

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	69.64%	(56.66, 80.1)
Specificity	100%	(87.54, 100)
Positive Predictive Value	100%	(91.03, 100)
Negative Predictive Value	61.36%	(46.62, 74.28)
Diagnostic Accuracy	79.52%	(69.62, 86.8)

Table 2: Diagnostic Test Evaluation of CA125 Levels

Histopathological Finding				
CA125 levels		Positive	Negative	Total
	Positive(>35)	43	2	45
	Negative(<35)	15	25	40
		58	27	85

Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	74.14%	(61.62, 83.65 ¹)	Wilson Score
Specificity	92.59%	(76.63, 97.94 ¹)	Wilson Score
Positive Predictive Value	95.56%	(85.17, 98.77 ¹)	Wilson Score
Negative Predictive Value	62.5%	(47.03, 75.78 ¹)	Wilson Score
Diagnostic Accuracy	80%	(70.28, 87.12 ¹)	Wilson Score

Table 3: Diagnostic Accuracy of Radiological and CA125 Test Evaluation

Histopathological Findings				
Ultrasound+CA125		Positive	Negative	Total
	Positive	45	0	45
	Negative	11	27	38
		56	27	83

Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	80.36%	(68.16, 88.66 ¹)	Wilson Score
Specificity	100%	(87.54, 100 ¹)	Wilson Score
Positive Predictive Value	100%	(92.13, 100 ¹)	Wilson Score
Negative Predictive Value	71.05%	(55.24, 83 ¹)	Wilson Score
Diagnostic Accuracy	86.75%	(77.81, 92.44 ¹)	Wilson Score

specificity ranging from 60%-92% according to the selected cutoff values (35IU/ml) and pre- or postmenopausal status of the patients^{15,16}. In this study at the cutoff value of 35iu/l of CA125 the sensitivity and specificity was 75% and 92.59%.

Thus in this study it is seen that as standalone modality ultrasound has low accuracy in differentiating between benign and malignant masses as compared to CA125. However addition of CA125 to ultrasound increases the diagnostic accuracy of 86.75% with sensitivity and specificity of 80.36% and 100% respectfully. It is seen in study by Lee EJ¹⁸ which showed that CA-125 is an additional help to radiological findings for differentiation borderline ovarian tumor from stage I carcinoma. Finkler and colleagues¹⁴ also used the transabdominal ultrasound in combination with CA125 for ovarian cancer screening and found similar results.

In number of trials examining CA-125 , with or without the use of sonography, in women with a pelvic mass, it has become increasingly clear that no one modality will be sufficient to predict accurately the presence of an ovarian malignancy. Many different tumor markers have been analyzed, but none has achieved the sensitivity or specificity to be clinically useful as an individual test¹⁷.

Thus the aim of this study is to create awareness among gynecologist to be alert in their diagnosis of ovarian mass as most of the cases may be missed by ultrasound as malignant, may actually be malignant . Addition of CA125 leads to a more accurate diagnosis and proper management.

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CONTRIBUTORS

F conceived the idea and planned the study. LH did the data collection and analyzed the study. Both the authors contributed significantly to the research that resulted in the submitted manuscript.