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A prospective study on 110 pelvic masses by clinical assessment, ultrasound scan and CA-125 – Prediction of malignancy

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ABSTRACT

Objective: To evaluate prospectively the accuracy, sensitivity and specificity of combined clinical assessment, grey scale abdominal ultrasound and serum CA 125 assay in predicting malignant status of pelvic masses in female patients preoperatively.
Design: A prospective study.
Patient: 110 female patients admitted to the University Hospital, Kuala Lumpur for laparoscopy and/or laparotomy for pelvic masses.
Intervention: Clinical assessment, grey scale abdominal ultrasound assessment and serum CA 125 assay.
Main outcome measure: Histopathological confirmation of malignancy.
Results: There were 13 (11.8%) malignancies in the 110 female patients evaluated. There were 10 patients with ovarian malignancies. There was poor correlation between clinical assessment findings alone and final diagnosis ($p = 0.27$). There were 41/110 (37.3%) patients who had ultrasound features suggestive of malignancy; of these only 9 patinets (22%) had malignant disease. This gave a sensitivity and specificity of 0.69 and 0.67 respectively for ultrasound alone. Absolute levels of serum CA 125 did not correlate significantly with malignancy although mean levels were positively correlated ($p < 0.05$). Diagnostic laparoscopy missed an adenocarcinoma of the colon (Duke's C) presenting as a pelvic mass. Ascites ($p < 0.05$), age above 45 years ($p = 0.011$) and postmenopausal status ($p = 0.002$) were positively correlated with the presence of malignancy but size was not.
Conclusion: In combination clinical assessment, grey scale abdominal ultrasound examination and serum CA 125 assay achieved an overall accuracy of 87.3% for a correct preoperative diagnosis of malignancy with a sensitivity and specificity of 0.54 and 0.92 respectively. The false positive and negative rates were respectiely 0.08 and 0.46.

Keywords: pelvic masses, serum CA 125, ultrasound.

INTRODUCTION

Ovarian cancer is currently the fourth leading cause of death among women in the United States and has the highest mortality rate of all gynaecological malignancies. It is imperative to detect ovarian malignancy early as survival is linked to early stage of diagnosis with more than 90% survival in Stage 1 disease[1]. Presently less than a third of primary ovarian malignancy is diagnosed when it is confined to the ovaries i.e. FIGO Stage 1a or 1b[2]. There is as yet no acceptable screening system that is sensitive, specific, acceptable and economical enough for implementation[3]. The potential cost-effectiveness of screening for ovarian cancer is limited by its lack of a preinvasive lesion, low prevalence and its rate of progression[4]. Test specificity would have to exceed 98% to be useful as a screening tool. This study attempts to evaluate the accuracy of preoperative diagnosis of pelvic masses whereby accurate diagnosis

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would optimize referral, surgery and staging in cancer centres for better survival[5] in a local setting. The combination of sonography and Doppler sonography although of high and reproducible diagnostic accuracy[6] is not widely available except in tertiary institutions in Malaysia.

MATERIALS AND METHODS

Female patients admitted to the University Hospital, Kuala Lumpur between July 1995 and February 1996 with a pelvic mass were randomly and prospectively selected into the study. All patients had clinical assessment, grey scale abdominal ultrasound evaluation and serum CA 125 assayed preoperatively. A preoperative diagnosis of malignant status was made based on these findings. (Computerized axial tomography was not routinely done and results were analysed separately where available).

Each patient's age, age of menarche, age of menopause, family history of malignancy and physical findings were noted. The normal values for serum CA 125 were 0 – 35 IU/ml. The abdominal ultrasound features were recorded by experienced ultrasonographers. Features suggestive of malignancy were solid components, multiseptated cysts, papillae, ascites, bilaterality and involvement of the ovarian capsule. If a surgical specimen was obtained at operation the histopathological diagnosis was taken as the final diagnosis. If no specimen was obtained the surgical diagnosis was taken as the final diagnosis (there was no surgical specimen in 6 patients).

STATISTICAL ANALYSIS

Normal convention of calculation was followed for sensitivity and specificity. Continuous data was tested with the student's t test. The Pearson Chi^2 test was utilized for paired data. The level of significance was taken as $p < 0.05$.

RESULTS

There were 92 premenopausal and 18 postmenopausal women with pelvic masses in the study. The mean age of the 110 patients was 42.11 years (range 12 – 74 years; SD 12.93 years). The mean age of menarche was 13.08 years (range 12 – 18 years; SD 1.87 years). The mean age of menopause was 48.67 years (range 38 – 56 years; SD 4.92 years).

There were 13 (11.8%) malignancies in the 110 patients evaluated. There were 10 (9.1%) malignant ovarian tumours the others being endometrial cancer (1), adenocarcinoma of the colon (1) and leiomyosarcoma (1). 2 of the thirteen patients with malignancy had a total abdominal hysterectomy with bilateral salpingo-oophorectomy and malignant disease was diagnosed on histopathology.

Benign pathology was found in 97 patients (88.2%): benign leiomyoma (19), benign cysts (9), benign cystic teratoma (9), adenomyosis (3), endometriotic cysts (28), serous cystadenoma (8), mucinous cystadenoma (5), ovarian fibroma (2), tubo-ovarian abscess (1), pelvic endometriosis with a broad ligament cyst (1), bizarre leiomyoma (1), corpus luteal cyst (1), hydrosalpinx (3), dysfunctional uterine bleeding with no cyst (1) and negative laparoscopy (7). One of the seven patients with a "normal laparoscopy" had a Duke's C adenocarcinoma of the colon diagnosed three months later when she presented with an acute abdomen.

Overall (utilising clinical assessment, grey scale abdominal ultrasound and serum CA 125) 44 out of the 110 patients (40%) had features suggestive of malignant disease preoperatively. Out of the 13 with malignant disease 4 (30.8%) were not felt to be so preoperatively. Seven of the thirteen women (53.9%) with malignant disease were premenopausal.

There were 9 epithelial ovarian cancers (serous cystadenocarcinoma in 4, endometriod adenocarcinoma in 2, clear cell adenocarcinoma in 1, mucinous adenocarcinoma in 1, papillary adenocarcinoma in 1) and 1 mixed germ cell tumour. Eight were diagnosed preoperatively. In the 2 misdiagnosed patients, ultrasound features in one was of a pedunculated fibroid with a large clear well encapsulated right ovarian cyst ($7.9 \times 8.0 \times 5.7$ cm.) and in the other of an endometriotic cyst (serum CA 125 2.0 IU/ml in the former and 12.0 IU/ml in the latter). Half of these (5/10) patients were postmenopausal.

There was poor correlation between clinical findings alone and final diagnosis ($p = 0.27$). Clinical ascites was correlated significantly with malignant status ($p < 0.05$). 5/13 (38.5%) of patients with malignancy had ascites. There were 41/110 (37.3%) patients who had ultrasound features suggestive of malignancy; of these only 9 patients (22%) had malignant disease. This gave a sensitivity and specificity of 0.69 and 0.67 respectively for ultrasound alone (Table 1). There was also no significant correlation between preoperative ultrasound features of malignancy and raised serum CA 125 and actual diagnosis of malignancy in these patients with pelvic masses (Table 2).

Postmenopausal status correlated significantly with the probability of malignancy ($p = 0.002$). 33.3% (6/18) of the postmenopausal patients had malignancy. The premenopausal group had a malignancy rate of 7.6% (7/92). The predominance of premenopausal patients in this study was not controlled for and age

TABLE 1
Overall analysis of sensitivity & specificity obtained in this study

	Sensitivity	Specificity	False (–)	False (+)	Overall Accuracy
Serum CA 125	0.615	0.701	0.385	0.300	0.691
Ultrasound	0.692	0.670	0.308	0.330	0.673
Both modalities	0.539	0.918	0.462	0.083	0.873

TABLE 2
The eight patients with ultrasound features of malignancy and serum CA 125 > 35 IU/ml with no malignancy histopathologically

Histopathology	Serum CA 125 (IU/ml)	Age (years)
Benign serous cyst of ovary	3767	70
Adenomyosis, left ovarian endometriosis	155	46
Endometriosis, broad ligament cyst	42	45
Bilateral ovarian fibroma	95	60
Bilateral endometriotic cyst	39	41
Bilateral endometriotic cyst	38	43
Right endometriotic cyst	96	42
Right endometriotic cyst	3089	21

above 45 years was also positively correlated with malignancy ($p = 0.011$). There were no patients with a family history (first degree or otherwise) of breast, ovarian or colonic malignancy.

Absolute levels of serum CA 125 (more than 35 IU/ml) did not correlate significantly with malignancy (29 patients with serum CA 125 more than 35 IU/ml had no malignant disease), although mean levels were positively correlated ($p < 0.05$). Increasing the cut-off value to 65 IU/ml did not improve accuracy. Patients with malignancy had a mean serum CA 125 level of 1557.31 IU/ml (range 2 – 14830) and in those with benign disease a mean value of 110.68 IU/ml (range 0 – 3767) ($p < 0.05$). There were 4 patients with benign disease with elevated serum CA 125 levels of 200 IU/ml (tuboovarian abscess), 864 IU/ml (endometriosis), 3089 IU/ml (endometriosis) and 3767 IU/ml (benign serous cyst of the ovary).

Overall the positive and negative predictive values were 0.46 and 0.93 respectively for a correct preoperative diagnosis. Ascites, age above 45 years and postmenopausal status was positively correlated with the presence of malignancy but size was not. The addition of Computerized Axial Tomography in 29 out of the 110 (26.4%) did not improve diagnostic accuracy ($p = 0.06$).

DISCUSSION

In this study consisting of patients with pelvic masses 97 out of 110 patients did not have malignancy. Ovarian cancer has a low incidence of 40 per 100,000 women aged 45 years and above. A test of 99.6% specificity with a 100% sensitivity would achieve a positive predictive value of 10%. This would mean a positive exploratory laparotomy in 1 out of every 10 screened patients[3].

Accurate preoperative diagnosis for pelvic masses would enable referral to cancer centres with adequate cytoreductive surgery and correct staging with better survival[5]. A thorough clinical examination although invaluable is of limited accuracy[7] in assessing malignant status as was found in this study. Accurate preoperative diagnosis would enable correct preoperative counselling and preparation of patient

expectations. Adequate blood and intensive care arrangements can be made beforehand especially for major debulking surgery.

Recend data[8] conclude that although various clinical and laboratory parameters are useful in the evaluation of pelvic masses, no combination of factors can be considered 100% accurate in predicting malignancy. The false positive rates for the detection of ovarian cancer with grey scale ultrasound is 1.2 – 2.5%; multimodal screening 0.1 – 0.6% and ultrasound with colour Doppler 0.3 – 0.7%. Ultrasound features of malignancy can be shared by benign pathology[9]. The absence of malignant features on ultrasound suggests a benign pathology but does not rule out malignancy.

Scoring systems[10,11] have been devised to aid correct preoperative diagnosis of pelvic masses. Newer developments[12] have assessed the use of artificial neural networks to determine scoring and status of the masses in question. Doppler assessment of the adnexal mass[13] has been advocated. In this study no expectant management or puncture and aspiration[14] was attempted. Follow up in selected patients was not advocated for women with simple ovarian cysts in another study[15].

Serum CA 125 alone has low predictive value in screening[16] and in the diagnosis of pelvic masses. Benign disease is also associated with raised serum levels. Serial serum levels have limited value[17]. The specificity of serum CA 125 is lower in premenopausal patients due to the higher prevalence of endometriosis in this age group. In one study[18] 14 out of 18 malignant adnexal masses were diagnosed preoperatively by a level exceeding 35 IU/ml. However only 14 out of 51 (27.5%) patients with elevated serum CA 125 had malignancy. Increasing the cut off level to 65 IU/ml did not improve accuracy. This study reaffirms this finding.

CONCLUSION

An overall accuracy of 87.3% for preoperative diagnosis was achieved in this study. The addition of CAT scan where it was done did not improve diagnostic accuracy. The enigma of the pelvic mass continues despite modern imaging and laboratory tests. As it stands even if proper evaluation was accurate, most ovarian or pelvic masses in the postmenopausal patient would still require surgical evaluation[8]; granted there is a higher incidence of benign/functional cysts in premenopausal women.

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