Stage I cancer ovary: Diagnostic modality in our locality

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Abstract

Objective:
The main objective was to evaluate the diagnostic tools used for diagnosis of stage I ovarian cancer.

Patients & methods:
This is a descriptive study was conducted during the period from 1999 to 2003 at Sohag University Hospital. 53 patients out of 212 had stage I ovarian cancer was included in the study. They subjected to thorough history taking, proper examination and routine investigations. Ultrasonography with Doppler flowmetry, CT, IVP and CA-125 were done for all patients. Surgical staging and histopathological examination of all specimens was carried out.

Results:
Ovarian cancer represented the most common type of genital tract malignancy 124(64.92%). 53(25%), 11(5.18%), 114 (53.77%) and 34(16.03%) cases were diagnosed as stage I, II, III and IV respectively. 27 patients (50%) with stage I ovarian cancer were symptomless at time of diagnosis. The most common symptoms in stage I ovarian cancer was abdominal swelling or fullness.

Conclusions:
Both of CT scan and Ultrasonography examination were found to be better than the clinical impression based on symptoms and signs in predicting the malignant nature of ovarian masses.

Key words:
Ovarian cancer, CT, Ultrasonography, Doppler.

Introduction
Ovarian cancer is the fourth leading cause of cancer related death in women. A causal relationship has been postulated between certain environmental and genetic factors and ovarian malignancy [1].

Few studies have examined the symptoms experienced by women before diagnosis of ovarian cancer. Information on symptoms might make women more aware of changes that are indicative of disease and lead to their seeking help more aggressively and might lead physicians to conduct appropriate exploratory tests when symptoms are present[2]. Most ovarian neoplasm cause symptoms by exerting pressure on the surrounding structures, as the tumor enlarges, abdominal swelling is a common symptom. Acute abdominal pain may occur secondary to hemorrhage, rupture or torsion. A combination of TVS and colored

Doppler technique will likely improve differentiation of benign from malignant ovarian and adenxal lesions [3].

Computed tomography is used mainly to assess the extent of the disease in patients before and after surgery [4]. The most useful tumor marker in ovarian cancer is still the antigen CA-125. However, the level of this marker is modified by peritoneal irritation from endometriosis and inflammatory disease. Further more, the level is not elevated in nearly half of the patients with stage I disease [5]. The surgical management of ovarian cancer presents one of the greatest technical and clinical challenges in surgical oncology. Although vast improvements have been made in the chemotherapy of ovarian cancer in the past 2 decades, surgery remains the cornerstone of treatment of the disease [6]

Aim of the work:
The aim of the study was to evaluate the diagnostic tools used for diagnosis of stage I ovarian cancer in our locality.

Patients & methods:

This was a descriptive prospective study conducted during a period from October 1999 to April 2003 and included all patients who were admitted to Sohag University Hospitals and diagnosed to have malignant ovarian tumors, on the ground of documented histopathological diagnosis, all patients were subjected to thorough history taking, detailed clinical presentation and proper systemic and pelvic examination. Routine investigations were done for each patient and included; urine analysis, complete blood count, random blood sugar, blood urea, X-ray chest and ECG. Specific investigations were done and included pelvic and abdominal ultrasonography with Doppler indices. IVP, CT pelvis and abdomen and CA-125 were done.

The exact surgical procedures done were reported; the type of incision used, findings on laparotomy and staging using FIGO staging procedures, then all the patients with stage I cancer ovary were selected. A standard check list was used to determine whether or not the examinations or procedures necessary for accurate staging and complete evaluation of the extent of ovarian cancer spread had been carried out according to the internationally accepted protocol for stage grouping of cancer of the ovary [7].

The specific examinations or procedures that were evaluated are:
Biopsy or removal of one or both ovaries, biopsy or removal of operator observed tumor on the uterus, tubes, bowel or pelvic peritoneal tissues, observation of the quantity of peritoneal fluid, its pathological appearance, and acquisition of a peritoneal fluid cytological specimen and visualization and palpation of the under surface of the diaphragm.

Statistics:

Odds ratio estimates together with their 95 percent confidence intervals were computed using an unmatched approach and, where appropriate, were tested for trend. Tests of significance were based on the usual X^2 value for comparison of proportions and student test for comparison of means. Differences were considered significant at $P < 0.05$.

Results:

The study included 212 patients with ovarian cancer, who were admitted to Sohag City hospitals during the period from October 1999 to April 2003. The control group consisted of 298 patients admitted to Sohag University Hospital and underwent a major gynecological operation during this period. Ovarian cancer represented the most common type of genital tract malignancies, representing (64.92%) of cases of malignancies of the female genital tract admitted to Sohag City Hospitals during the study period (Table I).

53 (25%), 11 (5.18%), 114 (53.77%) and 34 (16.03%) cases were diagnosed at stage I, II, III and IV respectively. 107 (86.29%) patients had malignant epithelia ovarian tumors, 10 (8.06%) patients had germ cell tumors and 7 (5.65%) patients had malignant granulosa cell tumors. Of the malignant epithelial ovarian tumor 78 (62.9%) patients were serous adenocarcinoma, 22 (17.74%) patients were Mucinous adenocarcinoma and 7 (5.65%) patients were endometroid carcinoma.

27 patients (50.49 %) with stage I ovarian cancer was symptomless at time of diagnosis. The most common presenting symptom in symptomatic patients was abdominal swelling or fullness in stage I ovarian cancer (Table III).

Table I: Prevalence of ovarian cancer among other malignancies of the female genital tract during the prospective part of the study.

Type of female genital tract malignancy	Number	%
Ovarian cancer	124	64.92
Fallopian tube cancer	0	0
Uterine corpus cancer	52	27.22
Uterine cervix cancer	10	5.24
Cancer vagina	2	1.05
Cancer vulva	3	1.57
Total	191	100

Table II: Epidemiological characteristics of women with malignant ovarian tumors and controls.

Patient characteristic	Malignant ovarian tumors (mean ± SD)	Controls (mean ± SD)
Age in years	51.47 ± 7.04	44.35 ± 8.38 *
Age at first pregnancy	16.57 ± 2.13	21.11 ± 3.06 *
Number of births	2.75 ± 2.40	5.85 ± 2.88 *
Duration since last delivery	17.53 ± 3.58	11.14 ± 4.05 *
Age at menarche	14.14 ± 5.06	13.78 ± 2.95 *
Age at menopause	49.83 ± 4.12	53.46 ± 3.72 *

* $P < 0.05$ (student test for comparison of means)

Table III: The presenting symptoms in cases of malignant and benign ovarian tumors and their distribution to the stage of the disease in cases with malignant ovarian tumors.

Presenting symptom	Benign N=328	Stage I N=53	Stage II N=11	Stage III N=114	Stage IV N=34
(symptomless)	182 (55.49%)	27 (50.49%)	4 (36.36%)	17 (14.91%)	2 (5.88%)
(Any symptoms)	146 (44.51%)	26 (49.06%)	7 (63.64%)	97 (85.09%)	32 (94.12
Abdominal swelling or sense of fullness /pressure in the abdomen or the pelvis.	54 (16.46%)	14 (26.42%)	3 (27.27%)	53 (46.94%)	17 (50.00%)
Abdominal or lower back pain.	40 (12.19%)	11 (20.75%)	3 (27.27%)	49 (42.98%)	15 (44.12%)
Vaginal bleeding.	36 (10.98%)	5 (9.43%)	1 (9.09%)	5 (4.39%)	2 (5.88%)
GIT symptoms.	16 (4.88%)	13 (24.53%)	3 (27.27%)	47 (41.23%)	15 (44.12%)
Lower limb swelling.	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (3.51%)	2 (5.88%)
Urination problems.	0 (0.00%)	3 (5.66%)	1 (9.09%)	21 (18.42%)	7 (20.59%)
Dyspnea.	0 (0.00%)	0 (0.00%)	0 (0.00%)	14 (12.28%)	5 (14.71%)
Easy fatigability.	0 (0.00%)	4 (7.55%)	2 (18.18%)	29 (25.44%)	9 (26.47%)

Table IV: shows assessment of the CT, U/S, and clinical impression findings according to the staging laporatomy findings, CT was found to be a highly specific diagnostic method for all diagnostic criteria.

Finding	TP	FP	TN	FN	Sens %	Spec %	PPV %	NPV %	ACC %
CT: 1. Growth is limited to the ovaries only	20	6	68	1	95.24	91.89	76.92	98.55	92.63
2. Abdominal and/or pelvic metastases									
>2cm	30	3	56	6	83.33	94.92	90.91	90.32	90.53
<2cm	35	1	56	3	92.11	98.25	97.22	94.92	95.78
3. Ascitis	52	0	43	0	100.0	100.0	100.0	100.0	100.0
Ultrasonography: 1. Growth is limited to the ovaries only	16	29	45	5	76.19	60.81	35.56	90.00	64.21
2. Abdominal and/or pelvic metastases									
>2cm	7	10	49	29	19.44	83.05	41.18	62.82	58.95
<2cm	25	8	49	13	65.79	85.96	75.76	79.03	77.89
3. Ascitis	41	2	41	11	78.85	95.35	95.35	78.85	86.32
Clinical impression: 1. Growth is limited to the ovaries only	13	54	20	8	61.90	27.03	19.40	71.43	34.74
2. Ascitis	37	8	35	15	71.15	81.40	82.22	70.00	75.78

TP = True positive   FP = False positive
TN = True negative   FN = False negative
Sens = Sensitivity   Spec = Specificity
PPV = positive predicative value   NPP = negative predicative value
Acc = Accuracy

Table V: shows the mean concentration of CA-125 was 291.45 ± 125.37 in stage I cancer ovary while 28.72 ± 26.12 in patients with benign ovarian tumors. There was a statistically difference between malignant and benign tumors as regards resistance and pulsatality.

	Malignant ovarian tumors	Benign ovarian tumors	P value
Resistance index	0.42 ± .018	0.79 ± 0.29	< 0.05
Pulsatality index	0.86 ± 0.75	1.84 ± 1.22	< 0.05
CA-125	291.45 ± 125.37	28.72 ± 26.12	< 0.01

Table VI: Distribution of malignant ovarian cases according to histopathological type stratified by stage of the disease.

Histopathological type	Stage I N=53	Stage II N=11	Stage III N=114	Stage IV N=34
Serous adenocarcinoma	20 (37.74%)	4 (36.36%)	82 (71.93%)	20 (58.82%)
Mucinous adenocarcinoma	7 (13.21%)	2 (18.18%)	16 (14.04%)	8 (14.71%)
Endometroid	6 (11.32%)	0 (0.00%)	11 (9.64%)	7 (20.59%)
Mesonephroid	0 (0.00%)	0 (0.00%)	2 (1.75%)	2 (5.88%)
Dysgerminoma	10 (18.87%)	3 (27.27%)	1 (0.88%)	0 (0.00%)
Malignant teratoma	2 (3.77%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malignant granulosa-cell tumors	8 (15.09%)	2 (18.18%)	2 (1.75%)	0 (0.00%)

Discussion:

In contrast to the advances in medicine over the last several decades, ovarian carcinoma is a disease where its overall survival has not significantly improved in the last 20 years and remains approximately 30% for 5 years survivals[8]. Unfortunately, the vast majority of these patients are first identified when their cancer has already reached stage III or IV. Five year survival in patients with stage I disease approaches 85% to 90%, therefore if timely identification of early disease can be achieved, a significant improvement in the outcome may occur [9].

There is a relative paucity of the epidemiological studies addressing the issue of ovarian tumors in Egypt, particularly in our locality. A study carried out in Ain Shams University, they found that ovarian cancer constitute 36.5% [10]. In this study we found that malignant ovarian tumors represented the commonest malignancy of the female genital tract (64.92%). The four stages of ovarian cancer were represented in this study. Stage I disease was found in 25% while stage III and IV in 70%. This may indicate that in our locality, most patients are seen at late stage of the disease. This is explained by the fact that the occult ovarian malignancy may asymptomatic disease. Moreover, it may indicate the low level of patient's awareness, lack of adequate screening system, and also insufficient referred system.

Malignant epithelial ovarian tumors represented 86.8% of cases while malignant germ cell tumors represented 7.55%, this was similar to the rates found in literature [11]. Symptoms of ovarian cancer are often described as non specific [12]. Some authors stated that ovarian cancer is asymptomatic in its early stages[13-14], a large proportion (49%) of women with stage I in this study reported symptoms in the months before diagnosis. This is consistent with the findings reported by other studies [11,15,2].

Preoperative clinical examination was of relative low sensitivity, specificity, positive and negative predictive values and accuracy. This is in agreement with the

work of Boente [16]. In detecting ovarian tumors limited to the ovaries, the sensitivity, specificity, positive and negative predictive values of CT were higher than U/S. The positive predictive values were 76.92% and 35.56% for CT and U/S respectively. However the considerably high negative predictive value of CT (98.55%) suggests that CT is a reliable method for diagnosis extra-ovarian extension of the tumor. These findings were in agreement with other studies [17,18].

In the present study, CT scan and U/S examinations are of great value in predicting the malignant nature of ovarian masses and in delineating the extent of ovarian cancer. Both of them were found to be better than the clinical impression based on symptoms and signs in predicting the malignant nature of ovarian masses. CT scan examination was more superior in terms of sensitivity, specificity, positive and negative predictive values and accuracy than U/S examination, but since U/S examination is cheaper, quicker and easier to perform, CT scan should be regarded as a complementary procedure to U/S examination rather than a competitive procedure.

Conclusions:
Both of CT scan and U/S examination were found to be better than the clinical impression based on symptoms and signs in predicting the malignant nature of ovarian masses.

Recommendations:
Since a good percentage of women with early stage ovarian cancer reported some symptoms in the months before diagnosis. Information on the symptoms should alert physicians to the possibility of malignant ovarian tumors.

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