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ULTRASOUND EVALUATION IN THE FOLLOW-UP OF OVARIAN CANCER TODAY

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Summary: From October 1982 through December 1986, standardized abdominal-pelvic sonography was performed on 257 patients with ovarian cancer scheduled to undergo surgery (laparoscopy, laparotomy). This U.S. test was evaluated by a gynaecologist who was informed of the clinical diagnosis and the findings of physical examination.

The Authors selected 110 patients with ovarian cancer, underwent a second look laparotomy, for both diagnostic and therapeutic purposes.

The sensitivity (53%), the specificity (68%), the predictive value (78%) and the accuracy 71.8%) of ultrasound for detecting disease have been evaluated to assess its usefulness as a non invasive diagnostic modality in these patients.

Key words: Ovarian Cancer, Ultrasound, Follow-up.

Since October 1982 the Authors started a clinical trial selecting the best ultrasonic parameters for the ovarian cancer follow-up. On this subject we used a correct form with some key-words to which answer for each patient studied with ultrasound (1).

In this investigation, we report, preliminarly, the results of our ultrasound management after 50 months of ovarian cancer follow-up, comparing the sensitivity, the specificity, the predictive value and the accuracy versus surgery.

MATERIAL AND METHODS

A series of 257 cases of ovarian cancer were collected at the Diagnostic Ultrasound Center of the Institute of Obstetrics and Gynaecology - University of Padua (Italy); these patients were referred to us from several surgical and medical divisions of the Padua area. We carried out 450 ultrasound examinations with a ratio echogram/patient equal 8:1. Tab. 1 shows the frequency of U.S. test repetition in our clinical trial,

Clin. Exp. Obst. Gyn. - ISSN: 0390-6663
XIV, n. 3, 1987

Table 1. — *Frequency of U.S. test repetition in our clinical trial (257 ovarian cancer).*

1	U.S. test	52 % (134/257)
2	U.S. tests	19 % (49/257)
3	U.S. tests	18.6% (48/257)
4	U.S. tests	5.4% (14/257)
>4	U.S. tests	4.6% (12/257)

Table 2. — *F.I.G.O. stage distribution of 257 ovarian cancer on trial up to date.*

Stage		Stage	
I	28% (72/257)	Iai	7 % (5/72)
II	10% (25/157)	Iaii	41.6% (30/72)
III	53% (137/257)	Ib	23.6% (17/72)
IV	9% (23/257)	Ic	27.8% (20/72)

while tab. 2 shows the F.I.G.O. stage distribution of 257 ovarian cancer on trial up to date.

The clinical criteria of assessment were previously described by our research group [2, 3, 4].

U.S.-Test

Each patient was prepared for this test by means of a variable bladder refilling (200-600 ml). We studied the patients in lateral, supine and Trendelemburg positions and we made vaginal inspection on real-time display by hand.

A gynaecologist with a special ultrasound training, made the examinations, using a linear array equipment on real time.

Surgery

The radical and/or debulking surgery modalities, the surgical second look and the chemotherapy have previously been reported [5, 6].

Overall Analysis

The sensitivity indicates the ability to detect disease and is calculated by dividing the number of true positives by true negatives and false negatives.

The specificity indicates how often a negative result correlates with cases and is calculated by dividing the true negatives by the true negatives and false positives.

The predictive value of the U.S. test is calculated by the sum of predictive value of false negatives (dividing the number of false positives by the true positives and false negatives) and the predictive value of false positives (dividing the number of false positives by false positives and true negatives).

The accuracy of a test is equal to the sum of true positives and true negatives divided by the sum of the true positives, true negatives, false positives and false negatives.

Ultrasound key words

In each ultrasound examination we evaluated the presence/absence of ascites, the presence of iliac-aortic nodes larger than 1.5 cm of ∅, the parietal peritoneal involvement, the profile of liver, the diaphragmatic pericolic recesses, the Douglas cul-de-sac, the gas artifacts, the faeces, the bowel movements, the intestinal anastomosis, the anus-praeter, the omentum or omental left-overs.

All sites and sizes of disease were noted from pathologic and surgical reports.

RESULTS

Tab. 3 shows the histologic type and the stage distribution in a series of 110 cases of ovarian cancer in follow-up up to date.

Stage I (28%) and stage II (10%) constitute about one third of the cases. Stage III (53%) is the series of most studied tumors. All patients followed a U.S. laparotomy second look procedure.

Tab. 4 shows the U.S. and the laparotomy agreed with 71.8% of the cases (28.2% real positives and 43.6% real negatives), while the U.S. had a 24.6% in-

Table 3. — *Histologic type and stage distribution in 110 ovarian cancers in follow-up today.*

FIGO stage	Serous 76/110 (69%)	Mucinous 20/110 (18%)	Endometrioid 3/110 (2.7%)	Other 11/110 (10%)	Total cases 110
I	22.3% (17/76)	50% (10/20)	—— ——	36.3% (4/11)	31/110 (28%)
II	9.2% (7/76)	15% (3/20)	33.3% (1/3)	—— ——	11/110 (10%)
III	59.2% (45/76)	25% (5/20)	66.6% (2/3)	54.5% (6/11)	58/110 (53%)
IV	9.2% (7/76)	10% (2/20)	—— ——	9.2% (1/11)	10/110 (9%)

Table 4. — *Comparison between U.S. test and laparotomic second-look in 110 patients with ovarian cancer.*

	Look +	Look −	Total
U.S. +	28.2% (31)	3.6% (4)	32% (35)
U.S. −	24.6% (27)	43.6% (48)	68% (75)
	52.7% (58)	47.3% (52)	(110)

cidence of false negatives compared to the pathologic staging; 3.6% of the cases had a false positive U.S. examination.

The statistical analysis showed a very interesting specificity (68%) of U.S. test with a sensitivity of 53%; the predictive value of ultrasound versus surgery was high (78.3%) reflecting the positive (32%) and the negative U.S. value (68%); finally the accuracy = 71.8%. Tab. 5 shows the correlations among U.S. and several sites of involvement. Fifty patients had a total of 17 nodal involvement. Only one false positive occurred in a fat patient.

The true nodes were localized in aortic area; the false negative nodes were at the level of the iliac external-internal bifurcation: the ascending-descending-sigmoid colon masks the nodes more than the ileum.

Seventy patients had a total of 21 omental involvements only 2 false positives in patients already operated were found. The false negatives U.S. patients had the least omentum involvement. No false positives or false negatives in ascites investigation were observed. Eight patients only were selected by U.S. at bowel-peritoneum level. In 52.5% of the cases the U.S. did not show the focal peritoneal involvement; 5 cases of false positives in patients who had undergone partial omentumectomy were noted.

DISCUSSION AND CONCLUSIONS

At the beginning of this clinical trial, we were conscious that the diagnostic ultrasound plays a very important role in

Table 5. — *Ultrasound findings compared with second-look laparotomy in patients with ovarian cancer.*

Second-look Laparotomy		
	Nodes (50 cases)	
	+	−
U.S. +	(10%) 5	(2%) 1
U.S. −	(24%) 12	(64%) 32
	Omentum (70 cases)	
	+	−
U.S. +	(5.7%) 4	(2.8%) 2
U.S. −	(24%) 17	(67%) 47
	Ascites (110 cases)	
	+	−
U.S. +	(25%) 28	——
U.S. −	——	(74%) 82
	Bowel-Peritoneum (80 cases)	
	+	−
U.S. +	(10%) 8	(6.2%) 5
U.S. −	(52%) 42	(31%) 25

Table 6. — *Technical criteria checked during ultrasonic management of ovarian cancer follow-up: advantages and disadvantages on U.S. tests.*

Advantages
– Image on real-time
– Many sections
– Vaginal inspection through display
– Easy practice
– Low operative cost
– Endo-abdominal profile of the vaginal cupola
– Small ascitic bed
– Lymph Nodes
Disadvantages
– Mesentery
– Retroperitoneum
– Gas bowel
– Anus praeter
– Retrocavity of epiploon
– Spreading of minimal cancer
– Obesity

Table 7. — *Correlations among the true negatives (specificity), the true positives (sensitivity), the predictive value and accuracy studied with ultrasound and laparotomy second-look.*

Ultrasound	Laparotomy Second-look				
	Nodes	Omentum	Ascites	Bowel-peritoneum	Overall
	%	%	%	%	%
Specificity	88	91	74	83	64
Sensitivity	29	19	100	16	53
Predictive value	82	89	100	100	78
Accuracy	74	73	100	40	72

the initial management, debulking and follow-up of ovarian cancer. Our aim was the standardization of some U.S. parameters useful to an unchanging evaluation of the abdomen, removing the subjectiveness characteristic of a real time examination.

This procedure allowed us to identify some technical advantages versus the C.A.T., Laparoscopy and Laparotomy (tab. 6) and everything the U.S. cannot give us.

As regard to our experience C.A.T. Surgery ([6]), the U.S. sensitivity (that is, the ability to recognize the true positives) was higher (53%); vice versa the U.S. specificity (that is, the ability to recognize the true negatives-free-disease cases) was lower (68%). Finally, in our opinion, the upper U.S. predictive value (78%) is a sufficient warranty for screening the patients at C.A.T. before a new surgery.

We have sufficient data at present, to support the use of U.S. as a screening test for early detection of ovarian cancer; in fact by monitoring endocrinological morphology of the ovary in young women it is possible to detect morphological abnormalities (irregular out-lines, cystic ovary etc.) till to malignant changes like the presence of more complex lesions as thick septa and solid areas.

In the initial or preoperative management, the U.S. informs the surgeon about the primary sites of the disease and their extension into the pelvic and abdominal regions. Once initial surgery has been performed, ultrasound has a value in monitoring response to therapy and in detecting tumor recurrence.

This monitoring must be done with a particularly criteria to guide the second-look laparotomy to assessment, debulking or removal of residual disease in patients who were apparently responding to chemotherapy.

Finally, we must remember the high values of accuracy (tab. 7) obtained from the pelvis, liver and ascites; but U.S. was insensitive to peritoneal disease.

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EFFECTS OF ESTRIOL ADMINISTRATION ON HUMAN POSTMENOPAUSAL ENDOMETRIUM

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Summary: Forty eight women with atrophic endometrium were treated with estriol, 1 mg twice daily, by mouth for a minimum of 10 days and a maximum of 25 days. Vaginal hysterectomy was then performed and specimens were examined histologically. Results showed that estriol produces endometrial hyperplasia in 70.8% of the examined women; only 29.2% of the patients retained atrophic endometrium after treatment.

Key words: estrogen replacement, endometrial hyperplasia, menopause, endometrium.

INTRODUCTION

Estriol has been considered a "weak estrogen" or an "impeded estrogen" for many years ([1, 2]).

Much evidence, concerning the biological effect of estrogens, suggests that uterine responses are correlated to the activity time of the receptor-estrogen complex in the nucleus.

Some experiments support the hypothesis that estriol is unable to promote a sufficient proliferative effect because its intranuclear activity is very short ([3]). Therefore, estriol was classified as "short acting estrogen ([4]).

In many gynecological departments postmenopausal women have been treated with estriol. Dosages varied from 1 mg/day up to 8 mg/day. When estriol was given once a day or in small doses no or minimal effect on the endometrium was found, but trophic activity on the cervix, vagina, urethra, bladder and skin was observed ([4, 5, 6]).

These results were obtained regarding withdrawal bleeding or spotting as the only standard for evaluation of the effect on the endometrial proliferation.

When dilatation and curettage were performed, histological examination showed an atrophic endometrium in most cases. Therefore, withdrawal bleeding or spotting can not be regarded as reliable indices for endometrial proliferation because every kind of endometrium is liable to bleed ([5, 7, 8, 9, 10]).

Clin. Exp. Obst. Gyn. - ISSN: 0390-6663
XIV, n. 3, 1987