Ultrasound as a possible screening method in ovarian cancer

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Summary

Ultrasound is a diagnostic method suitable for first level screening of ovarian cancer.

The results in 4350 patients confirmed that ultrasound examination, both transabdominal and transvaginal, can be considered quite satisfactory because the sensibility was 100%.

Key words: ultrasound; ovarian cancer screening.

Introduction

It is well known that the very poor prognosis of advanced ovarian cancer is due to late and atypical symptoms and to the fast spread and aggressiveness of the neoplasm.

The natural history is unknown and this is a great handicap for prophylaxis, prevention, and early diagnosis of ovarian cancer. Moreover we do not have, up to today, a valid method for screening of ovarian cancer [1, 2].

– Gynecological examination is not efficient: 43% of small ovarian masses and 19% of large masses are not diagnosed [3].

– CA-125: this test is not trustworthy for screening because of its low specificity – other diseases may increase its level [4, 5] – and for its low sensibility as Jacobs [6] demonstrated performing CA-125 assay in 22,000 asymptomatic women; only 11 out of 41 patients with positive CA-125 assay were affected by ovarian neoplasms, but among all the negative patients eight later developed ovarian cancer.

– The ultrasonography test, both transabdominal and transvaginal, is the best method: it is not invasive, it can be repeated, it gives us the information about mass pelvic origin, size, volume, mono or bilaterality, structure and presence of ascites [7].

Moreover it is possible to distinguish malignant and benign masses by studing the morphologic characteristics of the lesions [8-12, 13-25].

Some authors [5, 12, 18] introduced a scoring system to define the characteristics of ovarian cancer masses.

Merz [18] codified ten parameters for the scoring system: structure, borders, thickness, echoes of cystic component, septa, characteristics of solid component, echoes of solid mass, acoustic shadow, ascites, metastasis.

The sensibility of this method is high, while the specificity is not, up to now, satisfactory.

Materials and Methods

The aim of our study was to verify if ultrasound as a first level test can be trusted as a screening test for ovarian cancer.

From September 1st 1996 to September 30th 2001 we evaluated by ultrasound 4,350 patients for periodic check-ups. The average age was 49 years [21-23]. Both transabdominal and transvaginal probes were employed. Anamnestic obstetric data, eventual risk factors for ovarian neoplasm, previous ovarian disease and follow-up were evaluated when some abnormalities were found by ultrasound.

We studied the possible correlations among age, parity, ovulation, and the ovarian abnormalities found; moreover the correlation between size of the ovarian lesion and symptomatology was evaluated.

If patients underwent surgical therapy, the histopathological findings and ultrasound images were compared.

Periodical follow-up was performed both for the patients treated to control the efficacy of therapy, and for the non treated patients to control the evolution of ovarian disease.

The Fisher test and χ^2 test were employed for statistical qualitative analysis; specificity, sensibility, positive or negative predictive value of the ultrasound test were calculated.

Results

One hundred and seventy-six patients tested positive for ovarian cancer by ultrasound examination (Table 1).

Among nulliparous patients, 59 out of 1,337 (4.41%) had ultrasound findings of lesions; 117 out of 3,013 pluriparous patients (3.88%) were positive while only

Table 1 — *Results of ultrasound for all patients.*

Negative		Positive		Total
n.	%	n.	%	
4174	95.95	176	4.05	4350

Table 2 — *Presence of symptomatology in all patients.*

Asymptomatic		Symptomatic		Total
n.	%	n.	%	
3832	88.09	518	11.9	4350

Table 3 — *Correlations between results of ultrasound and symptomatology.*

	Positive		Negative		Total
	n.	%	n.	%	
Asymptomatic	132	3.44	3700	96.56	3832
Symptomatic	44	8.49	474	91.51	518
Total	176	4.05	4174	95.95	4350

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Table 4 — *Correlations between symptoms and ultrasound.*

	Total		Positive		Negative	
	n.	%	n.	%	n.	%
Pelvic and abdominal pain	162	31.2	6	3.7	156	96.3
Metrorrhagia and atypical bleeding	81	15.64	7	8.64	74	91.36
Menstrual irregularity	188	36.29	28	14.89	160	85.11
Urinary disturbances	87	16.8	3	3.45	84	96.55
Total	518	100	44	8.49	474	91.51

Table 5 — *Correlations between symptoms and size of ovarian lesions.*

	Symptomatic		Asymptomatic		Total	
	n.	%	n.	%	n.	%
0-2 cm	9	24.32	28	75.68	37	21.02
3-5 cm	30	26.55	83	73.45	113	64.21
6-8 cm	3	18.75	13	81.25	16	9.09
> 8 cm	2	20	8	80	10	5.68
Total	44	25	132	75	176	100

Table 6 — *Ultrasound findings indicative of benign or malignant lesions.*

BENIGN	n.	%
Functional cysts	24	16.33
Simple cysts	78	53.06
Endometriotic cysts	31	21.09
Dermoid cysts	9	6.12
Serous and endometriotic cysts	3	2.04
Hydatiform cysts	1	0.68
Ovarian cystoma	1	0.68
Total	147	100
MALIGNANT		
Possible		
Septum cysts	1	3.45
Plurilobular cysts	6	20.68
Granular cysts	4	13.79
Solid and liquid cysts	7	24.15
Probable		
Fibrinoid cysts	5	17.25
Solid mass	4	13.79
Cysts with endoluminal vegetation	2	6.89
Total	29	100

Table 7 — *Correlations between site and lesion.*

	Monolateral		Bilateral		Total
	n.	%	n.	%	
Benign					
Functional cysts	18	75	6	25	24
Simple cysts	72	92.31	6	7.69	78
Endometriotic cysts	27	87.1	4	12.9	31
Dermoid cysts	9	100	0	0	9
Ovarian cystoma	1	100	0	0	1
Serous and endometriotic cysts	2	66.67	1	33.33	3
Hydatiform cysts	1	100	0	0	1
Total	130	88.43	17	11.57	147
Malignant					
Septum cysts	1	100	0	0	1
Plurilobular cysts	5	83.33	1	16.67	6
Granular cysts	4	100	0	0	4
Solid and liquid cysts	7	100	0	0	7
Fibrinoid cysts	5	100	0	0	5
Solid mass	3	75	1	25	4
Cysts with endoluminal vegetation	2	100	0	0	2
Total	27	93.1	2	6.9	29

Table 8 — *Ultrasound diagnosis and therapy.*

		Therapy					
	Ultrasound diagnosis	Surgical		Medical		None	
	n. %	n.	%	n	%	n	%
Functional cysts	24 13.64	1	4.17	11	45.83	12	50
Simple cysts	78 44.32	14	17.95	16	20.51	48	61.54
Endometriotic cysts	31 17.62	15	48.39	7	22.58	9	29.03
Dermoid cysts	9 5.11	2	22.22	1	11.11	6	66.67
Serous and endometriotic cysts	3 1.7	2	66.67	0	0	1	33.33
Hydatiform cysts	1 0.57	0	0	0	0	1	100
Ovarian cystoma	1 0.57	1	100	0	0	0	0
Septum cysts	1 0.57	1	100	0	0	0	0
Plurilobular cysts	6 3.41	4	66.67	0	0	2	33.33
Granular cysts	4 2.27	0	0	1	25	3	75
Solid and liquid cysts	7 3.98	0	0	1	14.29	6	85.71
Fibrinoid cysts	5 2.84	1	20	3	60	1	20
Solid mass	4 2.27	3	75	0	0	1	25
Cysts with endoluminal vegetation	2 1.14	1	50	0	0	1	50
Total	176 100	45	25.57	40	22.73	91	51.7

11.91% of patients with symptoms were submitted to ultrasound examination and 8.49% were positive (Tables 2 and 3).

Patients' symptoms are reported in Table 4; the most frequent symptom was menstrual disorders - present in 63.63% of positive symptomatic patients (Tables 3 and 4).

No correlations were found between size of the lesion and symptoms (Table 5).

Twenty-nine patients (16.48%) had ultrasound findings indicative of malignant lesions and 147 (83.52%) findings of benign lesions (Table 6).

Mono- or bilateral lesions showed no statistically significant differences and correlated with abnormal ultrasound findings (Table 7).

In Table 8 we can see that 45 patients underwent surgical therapy, 40 medical therapy and 91 had no therapy.

In Tables 9, 10 and 11 the histopathological findings and the correlation with lesions found by ultrasound are reported. One borderline tumor was correctly diagnosed as a possible malignant lesion (pleurilobular cyst) and one Krukenberg tumor was also correctly diagnosed as a possible malignant tumor (solid mass). Endometriotic cysts were also confirmed in 15 cases out of 17 (88.2%). Patients with endometriotic cysts were followed-up with ultrasound; only 19 patients in the group (45 cases) were treated by surgery.

Only two lesions were found: one simple cyst of three treated and one simple cyst in the patient treated for a

borderline-tumor. This patient is being followed closely and is undergoing estrogen-progestin therapy (Table 12).

The 26 patients who did not have check-ups in our Center were interviewed by phone and they confirmed that they had not had any control in any other center but they had no symptoms.

In the group of patients treated by medical therapy (40 cases), 24 had no ultrasound control and by phone they confirmed that they had not had a control in any other center because they were asymptomatic.

Among the 16 patients checked, 11 have been cured and five have persistence of disease and are programed to undergo surgery (Table 13).

In the third group of 91 untreated patients only 26 were checked by ultrasound: 13 (50%) resulted negative and 13 (50%) had persistence of the lesions. These patients are scheduled for surgery or medical therapy.

Forty-two patients who were phoned confirmed that they had had no control but that they were asymptomatic; 23 patients in this group were lost at follow-up (Table 14).

Table 9 — *Histopathological findings.*

	n.	%
Functional cysts	3	6.66
Simple cysts	11	24.45
Endometriotic cysts	17	37.78
Dermoid cysts	3	6.66
Multilocular cysts	1	2.22
Ovarian cystoma	5	11.12
Cystoadenofibroma	2	4.45
Ovarian fibroma	1	2.22
Borderline mucinous cystoadenoma	1	2.22
Krukenberg tumor	1	2.22
Total	45	100

Table 10 — *Correlations between histopathological findings and ultrasound lesions in operated patients.*

Histopathological findings		Ultrasound lesions
Functional cysts	3	2 Simple cysts
		1 Serous and endometriod cyst
Simple cysts	11	10 Simple cysts
		1 Cyst with endoluminal vegetation
Endometriotic cysts	17	15 Endometriotic cysts
		1 Fibrinoid cyst
		1 Serous and endometriotic cyst
Dermoid cysts	3	2 Dermoid cysts
		1 Solid mass
Multilocular cysts	1	1 Plurilobular cyst
Ovarian cystoma	5	1 Simple cyst
		1 Septum cyst
		1 Ovarian cystoma
		2 Plurilobular cysts
Cystoadenofibroma	2	2 Simple cysts
Ovarian fibroma	1	1 Solid mass
Borderline mucinous cystoadenoma	1	1 Plurilobular cyst
Krukenberg tumor	1	1 Solid mass

Table 11 — *Correlations between possible and probable malignant ultrasound lesions and histopathological findings in operated patients.*

Possible and Probable Malignant ultrasound lesions		Histopathological findings
Septum cyst	1	1 Ovarian cystoma
Plurilobular cysts	4	1 Borderline mucinous cystoadenoma
		1 Multilocular cyst
		2 Ovarian cystomas
Fibrinoid cyst	1	1 Endometriotic cyst
Solid mass	3	1 Krukenberg tumor
		1 Ovarian fibroma
		1 Dermoid cyst
Cysts with endoluminal vegetation	1	1 Simple cyst

Table 12 — *Follow-up of patients treated by surgery*

	Control						
	No Control		Negative		Positive		Total
	n.	%	n.	%	n	%	
Functional cysts	2	7.69	1	5.26	0	0	1
Simple cysts	7	26.92	3	15.8	1	5.26	4
Endometriotic cysts	12	46.15	5	26.32	0	0	5
Dermoid cysts	2	7.69	1	5.26	0	0	1
Multilocular cysts	0	0	1	5.26	0	0	1
Ovarian cystoma	2	7.69	3	15.8	0	0	3
Cystoadenofibroma	1	3.48	1	5.26	0	0	1
Borderline mucinous cystoadenoma	0	0	0	0	1	5.26	1
Krukenberg tumor	0	0	1	5.26	0	0	1
Total	26	100	17	89.48	2	10.52	19

Table 13 — *Follow-up of patients treated by medical therapy*

	Control						
	No Control		Negative		Positive		Total
	n.	%	n.	%	n	%	
Functional cysts	9	37.5	1	6.25	1	6.25	2
Simple cysts	7	29.17	6	37.5	3	18.75	9
Endometriotic cysts	4	16.67	3	18.75	0	0	3
Dermoid cysts	1	4.16	0	0	0	0	0
Granular cysts	1	4.16	0	0	0	0	0
Fibrinoid cysts	2	8.34	1	6.25	0	0	1
Solid and liquid cysts	0	0	0	0	1	6.25	1
Total	24	100	11	68.75	5	31.25	16

Table 14 — *Follow-up of untreated patients*

	Control						
	No Control		Negative		Positive		Total
	n.	%	n.	%	n	%	
Functional cysts	13	30.96	5	19.23	3	11.54	8
Simple cysts	10	23.81	5	19.23	7	26.92	12
Endometriotic cysts	8	19.05	0	0	1	3.84	1
Dermoid cysts	3	7.14	0	0	0	0	0
Serous and endometriotic cysts	0	0	0	0	0	0	0
Hydatiform cysts	0	0	1	3.84	0	0	1
Plurilobular cysts	1	2.38	0	0	1	3.84	1
Granular cysts	1	2.38	1	3.84	1	3.84	2
Solid and liquid cysts	3	7.14	1	3.84	0	0	1
Fibrinoid cysts	1	2.38	0	0	0	0	0
Solid mass	1	2.38	0	0	0	0	0
Cysts with endoluminal vegetation	1	2.38	0	0	0	0	0
Total	42	100	13	50	13	50	26

Discussion and Conclusions

Our results confirm that the ultrasound test is simple, repeatable, not dangerous for the patient, and above all valid. Employing the scoring system, the examination leads us to an early diagnosis of probable malignancy [26].

In our case series 29 patients out of 176 were identified and the lesions were characterized as probable malignant or malignant according the scoring system.

It is very important that the two women with malignant lesions were identified by ultrasound; the sensibility of this method was confirmed (100%), also by the lack in number of negative lesions.

The specificity of the test has been discussed by different authors: for some [4, 19], specificity is not satisfactory, while for others [5, 13, 22, 27] specificity is high.

In our study we agree with the latter group of authors: in fact the possibility to pick out the patients who are truely negative for ovarian tumors is 99.81%.

The non-worked out problem of ultrasound diagnosis is the high number of false positive patients and so the predictive positive value is very low [20, 22, 23, 27]. These results were confirmed also in our patients: two out of ten patients treated by surgery for posible malignant lesions were truely positive at pathologic examination; the positive predictive value of our case series was 20%. In conclusion the ultrasound test can be considered a satisfactory screening test. It is not expensive, not dangerous for patients and simple. Moreover it is capable of picking out possible or malignant ovarian lesions. It is feasible in the near future that the ultrasound examination will allow us to achieve prevention of ovarian cancer, by the diagnosis of benign lesions with a possible evolution, and by an early diagnosis when malignant evolution has initiated.

The natural history of this neoplasm could be ascertained if all ovarian lesions could be checked during their evolution.

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