The role of three-dimensional (3D) sonography and 3D power Doppler in the preoperative assessment of borderline ovarian tumors

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Summary

Purpose of investigation: To determine the value of three-dimensional (3D) sonography and 3D power Doppler in distinguishing borderline ovarian tumors from benign cysts and malignant tumors. *Methods*: One hundred and seventy-two women with a mean age of 37 years (range 28-45) and diagnosis of a confirmed pelvic mass were referred for preoperative evaluation with 3D sonography and 3D power Doppler. Sonographic criteria used for the diagnosis of borderline tumors were based on a system that included morphological characteristics, histological evaluation and power Doppler imaging. *Results*: Ten lesions were histopathologically diagnosed as borderline ovarian tumors, 42 as malignant and 120 as benign. Three-dimensional sonography revealed 120 ovarian tumors which scored below 7 (benign), according to Kurjak's scale, 12 tumors which scored between 7-8 and 40 tumors between 9-13 (malignant). *Conclusions*: Preoperative assessment of borderline tumors by 3D imaging may promote improved patient care and introduce laparoscopic management as an alternative surgical approach.

Key words: Three-dimensional; Power Doppler; Borderline tumors; Ovarian cyst; Ovarian cancer.

Introduction

In 1929 Taylor [1] described a special group of epithelial ovarian tumors with intermediate histopathologic features and biologic behavior between clearly benign tumors and frankly malignant tumors. These tumors were called "semi- malignant" or "carcinoma of low malignant potential". The histological diagnosis of borderline tumors is based on the following criteria as established by Hart and Norris [2] and detailed by Scully [3]: epithelial cellular proliferation (stratification of the epithelial lining of the papillae, multi-layering of the epithelium, mitotic activity, and nuclear atypia) without stroma invasion.

Recorded information relating to the risk factors leading to a borderline tumor is limited. As yet, it is unknown whether some women have a genetic predisposition to the disease. Women with ovarian borderline tumors are younger than the women with invasive carcinoma [4]. The mean age is about 45 years compared to about 60 years for the latter. Women with a history of infertility and who are nulliparous have an increased risk of developing a borderline tumor whereas pregnancy, breast feeding and use of oral contraceptives appear to provide protection. Hypotheses concerning incessant ovulation and ovulatory age have been proposed [5, 6]. In addition, an endocrine disorder may also be a basic cause of borderline tumors [6].

Borderline ovarian tumors comprise 15-20% of all ovarian malignancies [7]. Compared with frankly invasive tumors they behave more indolently and are characterized by an earlier stage at presentation, longer survival and late recurrences [8]. Common signs and symptoms include abdominal-pelvic pain and a palpable adnexal mass. Although standard treatment for all patients includes at least bilateral salpingo-oophorectomy, many young patients who have not completed childbearing can be safely treated with unilateral salpingo-oophorectomy after comprehensive surgical staging, thereby preserving fertility. Recent studies from the Norwegian Radium Hospital and the Gynecologic Oncology Group (GOG) have shown that the preservation of reproductive organs is feasible [9, 10].

Several attempts have been made to accurately distinguish early-stage ovarian malignancy from questionable ovarian lesions on the basis of gray scale ultrasound and color Doppler features [11, 12]. It has been reported that the presence of intratumoral papillae, solid parts and thick septa suggest ovarian malignancy [13]. The detectability of these morphological findings varies and their diagnostic value has not yet been established.

Although previous studies reported that color Doppler ultrasound could provide clinically useful information regarding ovarian tumor vascularity [14, 15], the accurate distinction of ovarian tumors is debatable in the presence of an overlap of blood flow parameters [16]. However, the recent development of 3D sonography and 3D power Doppler may have clinical utility in the early identification of abnormal ovarian vascularity and morphology, and speed up the entire management process [17, 18]. The goal of this preliminary, non randomized study was to estimate the diagnostic value of the combined use of 3D sonography and 3D power Doppler in distinguishing borderline ovarian tumors from carcinomas and benign cysts.

Revised manuscript accepted for publication November 27, 2007

Material and Methods

A group of 172 women with adnexal masses of uncertain histology were evaluated with 3D and 3D power Doppler from January 2003 to February 2005. Sonography was performed by a Voluson 730 with a mechanized transvaginal 5 to 7.5 MHz probe. Once the region of interest had been identified the volume box was superimposed and the 3D ultrasound volume was generated by the automatic rotation of the mechanical transducer through 360°. Three perpendicular planes were displayed simultaneously thus enabling better understanding of the morphology of the ovarian lesions. Data from ultrasound findings, surgical procedures and histological type (serous, mucinous, non serous-mucinous) helped to evaluate the potential malignancy of the tumor. The 3D technique analyzed eight morphological criteria: wall structure (smooth or papillomatous >3 mm), shadowing, septa (thin ≤ 3 mm or thick >3 mm), solid components, echogenicity (low or mixed/high), peritoneal fluid, surface of the capsule and the relations with surrounding structures. The Doppler variable used for the diagnosis of ovarian malignancy was the resistance index (RI).

All the patients underwent 3D power Doppler examination which allowed detailed analysis of the tumor vascular architecture. Irregular and randomly dispersed vessels with complex branching which do not follow the geometry of the normal pre-existing vasculature with ever-smaller branches and diameters were associated with ovarian malignancy.

The scoring system for the evaluation of borderline ovarian tumors was based on ultrasonographic criteria, described by Kurjak *et al.* [19]. The presence of papillary projections greater than 3 mm, visualization of solid parts, high or mixed echogenicity of the tumor contents, irregular surface of the capsule, disturbed relationship with surrounding structures, complex vessel architecture and RI value lower than 0.42 received a score of two, whereas in cases with thick septa greater than 3 mm, shadowing, and peritoneal fluid we added one point. An increased score is associated with higher risk of ovarian malignancy.

All the women were in reproductive age (37; range 28-45) and operated on via laparotomy. Malignant tumors were classified according to the International Federation of Gynecology and Obstetrics (FIGO) system and the histopathological diagnosis was grouped into three categories: borderline ovarian tumor (BOTs), benign (BTs), and malignant (MTs). The study protocol was approved by the hospital ethical committee and all the patients consented to participate in the study.

Results

Ten lesions were histopathologically diagnosed as BOTs, 42 as MTs and 120 as BTs. The combined use of 3D and 3D power Doppler diagnosed 120 ovarian masses with scores lower than 7 (benign), 12 ovarian tumors with a score 7-8 (borderline) and 40 tumors with a score 9-17. By 3D sonography two BTs and one MT had scores of 7-8 and were misdiagnosed as BOTs. Comparison between histopathological results and 3D sonography findings was assessed by the Wilcoxon signed-rank test in which no significant difference was observed (p = 0.480) (Table 1).

Three-D and 3D power Doppler sonographic features of all the ovarian tumors are summarized in Table 2. Eight criteria out of ten have shown a statistically significant difference between BOTs, MTs and BTs. Distributional properties of 3D and 3D power Doppler outcome with respect to the ten criteria were investigated by chi-square statistics (x^2-test).

Table 1. — *Association between histopathological results and 3D imaging findings (p = 0.480).*

	HISTOPATHOLOGY			
Score by 3D	BTs	BOTs	MTs	Total
< 7	118	1	1	120
7-8	2	9	1	12
9-17	0	0	40	40
Total	120	10	42	172

Table 2. — *3D ultrasound findings in 172 ovarian tumors.*

Sonographic criteria		Malignant		Borderline		Benign		p-value
		N	%	N	%	N	%	
Septa	Yes	25	60%	5	50%	72	60%	0.825
	No	17	40%	5	50%	48	40%	
Papillary projections	Yes	22	52%	3	30%	4	3%	< 0.001
	No	20	48%	7	70%	116	97%	
Solid part	Yes	31	74%	7	70%	4	3%	< 0.001
	No	11	26%	3	30%	116	97%	
Echogenicity	Yes	39	93%	10	100%	65	54%	< 0.001
	No	3	7%	0	0%	55	46%	
Abnormal relationship	Yes	38	90%	8	80%	12	10%	< 0.001
	No	4	10%	2	20%	108	90%	
Peritoneal fluid	Yes	36	86%	2	20%	6	5%	< 0.001
	No	6	14%	8	80%	114	95%	
Surface	Yes	25	60%	6	60%	85	71%	< 0.353
	No	17	40%	4	40%	35	29%	
Abnormal shadowing	Yes	33	79%	7	70%	36	30%	< 0.001
	No	9	21%	3	30%	84	70%	
Vessel architecture	Yes	38	90%	2	20%	12	10%	< 0.001
	No	4	10%	8	80%	108	90%	
RI < 0.42	Yes	20	48%	3	30%	8	7%	< 0.001
	No	22	52%	7	70%	112	93%	

Three cases with papillary projections were detected in BOTs (30%) (Figure 1), five cases of septations (50%) (Figure 2), seven cases of solid parts (70%) and absence of shadowing in seven cases (70%). Mixed or high echogenicity was found in all cases of BOTs (Figure 3).

Papillary projections, in MTs were found in 22 cases (52%), septations in 25 cases (60%), solid parts in 31 cases (74%) and absence of shadowing in 33 cases (79%).

Papillary projections in BTs were diagnosed in four cases (3%), septations in 72 cases (60%), solid parts in four cases (3%) and absence of shadowing in 36 cases (30%). Mixed or high echogenic patterns were found in 39 cases of MTs (93%) and in 65 cases of BTs (54%).

A disturbed relationship with surrounding structures was found in eight cases of BOTs (80%), in 38 cases of MTs (90%) and in 12 cases of BTs (10%). Two cases of peritoneal fluid were found in BOTs (20%), 36 cases in

ig. 1

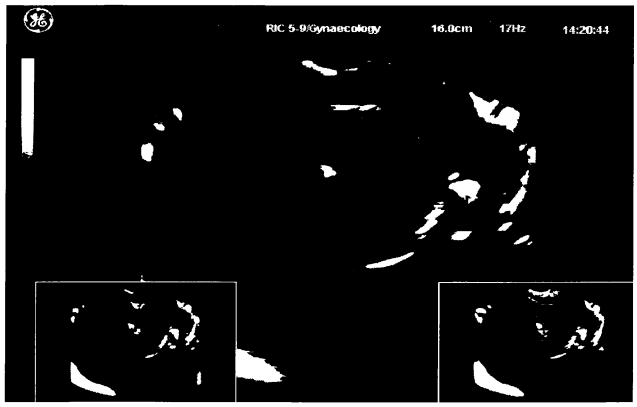
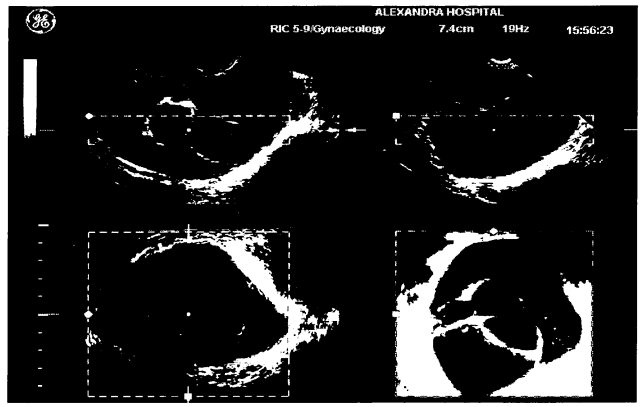


Fig. 2



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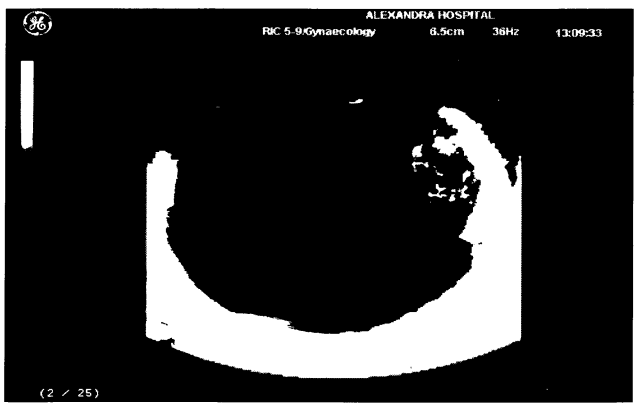

Fig. 4

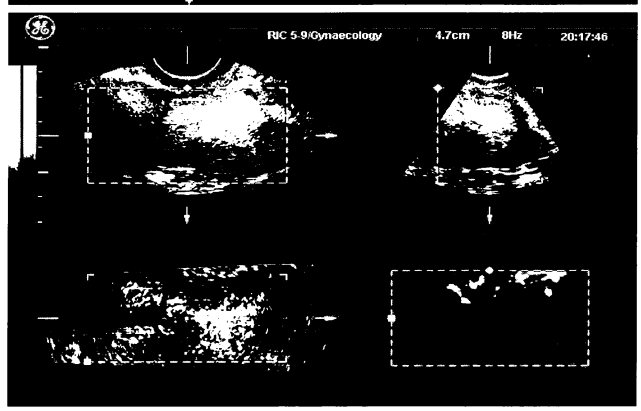

Figure 1. – 3D imaging: Ovarian tumor with mixed echogenicity, abnormal surface with papillary projections. A borderline ovarian tumor was confirmed by histopathology.
Figure 2. – 3D scan of a borderline ovarian tumor with septations and absence of echogenic reflection pattern.
Figure 3. – 3D surface view of an irregular wall with mixed echogenicity and no vascularization. Histopathology revealed a borderline ovarian tumor.
Figure 4. – 3D power Doppler in a borderline ovarian tumor with complex branching pattern and disturbed vessel architecture.

MTs (86%) and six cases in BTs (5%). The surface was irregular in six cases of BOTs (60%), in 25 cases of MTs (60%) and in 85 cases of BTs (71%).

Three-D power Doppler showed chaotic vessel architecture with complex branching pattern in only two cases of BOTs (20%), 12 cases of BTs (10%), and 38 cases of MTs (90%), (Figure 4). The RI value was lower than 0.42 in three cases of BOTs (30%), in 20 cases of MTs and in eight cases of BTs (7%).

Discussion

Borderline ovarian tumors were first recognized as a separate pathologic and clinical entity by the International Federation of Gynecology and Obstetrics (FIGO) in 1971 [20]. This was followed by World Health Organization acceptance in 1973 [21]. Approximately 3,000 cases are diagnosed each year [22].

The ovarian malignancy index is important in making treatment decisions and in providing prognostic information, particularly for patients in reproductive age. Transvaginal ultrasound with Doppler facilities is a non invasive technique capable of differentiating cystic from solid masses. A statistical correlation is found between ovarian malignancy and the presence of sonographic ovarian lesions such as papillae, solid components and thick septa.

Lim *et al.*, reported that the ultrasound scan in the preoperative assessment of the malignant potential of ovarian tumors had a high false-positive and a significant false-negative role. The sensitivity and specificity in the diagnosis of malignant BOTs is 82% and 86%, respectively [23]. Exacustos *et al.*, in a retrospective review using a transvaginal sonogram to distinguish BOTs from BTs and invasive malignant tumors, concluded that although close attention was paid to the cystic wall in ultrasound examination, they could not observe the very small papillae, which were found in histological analysis [24].

The addition of 3D ultrasound allowed better visualization of the inner wall irregularities, the wall thickness, the presence of thick septations or solid areas, evaluation of the echogenicity of the lesion and analysis of the distal shadowing. With this technique, identification of the ovarian malignancy became more accurate [17, 25, 26].

In our study, ovarian tumors detected by 3D and 3D power Doppler with an intermediate score of 7-8 were histopathologically diagnosed as BOTs and had solid

parts, a high echogenic pattern, abnormal relationship with surrounding structures, absence of shadowing but also poor vascular network. These 3D ultrasonographic findings may help differentiate BOTs from BTs and MTs.

Although some articles describe the sonographic appearance of BOTs [24-29], it is our belief that 3D techniques might offer a recognizable sonographic profile, differentiating BOTs from MTs allowing a further conservative operation via laparoscopy, especially in women of reproductive age [30, 31].

The prognostic value of the serum level of CA125 in the early detection of BOTs remains controversial. This marker does not seem to play a significant role in the detection of BOTs [22, 28, 31, 32]. In fact, it has been reported that approximately 85% of patients younger than 50 years with positive CA125 have a normal or benign condition, including pelvic inflammatory disease, endometriosis, early pregnancy and fibroids. In our study, this data was confirmed as we did not have any patient in the group of BOTs with elevated serum CA125.

Patients with BOTs present with early-stage disease (Stage I: 70%, Stage II: 10%, Stage III: 19% and Stage IV: 1%), whereas the majority of epithelial invasive ovarian cancer cases present with advanced disease stage [22]. In contrast to typical aggressive surgical treatment of invasive ovarian malignancy with total abdominal hysterectomy and bilateral salpingo-oophorectomy, BOTs may be treated effectively with unilateral oophorectomy or even with ovarian cystectomy via laparoscopy after proper surgical staging, thereby preserving the patient's fertility.

These preliminary findings suggest that a more accurate ultrasound technique would allow early recognition of these tumors and laparoscopic management.

Conclusion

The ability to identify BOTs non-invasively is important in deciding on the type of surgery required. Young patients in reproductive age who have not completed the family structure could be offered conservative surgical treatment through laparoscopy, avoiding post-surgical adhesions that could potentially influence fertility. We strongly believe that the knowledge acquired through this preliminary report has better equipped us to detect patients with such tumors for earlier diagnosis and appropriate surgical treatment. Further studies are needed to establish the role of 3D ultrasound in order to predict tumor prognosis and determine treatment options.

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