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Preoperative sonographic features of borderline ovarian tumors

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KEYWORDS: borderline ovarian tumors; low malignant potential ovarian tumors; power Doppler; transvaginal sonography

ABSTRACT

Objective *To determine the sonographic findings that distinguish borderline ovarian tumors (BOT) from both benign and invasive malignant tumors, thus allowing conservative treatment and laparoscopic management of these tumors.*

Methods *We reviewed retrospectively transvaginal sonograms of 33 women who, when evaluated further by surgery and histology, were found to have BOT. Twenty-three were premenopausal and 10 were postmenopausal (mean age ± SD, 45.8 ± 15.7 years). For each mass, size and morphological features and power Doppler characteristics were evaluated. We compared these findings with those of 337 patients with benign ovarian tumors and those of 82 patients with invasive malignant ovarian tumors. Patients with dermoid cysts were not included in the study.*

Results *Of the 33 BOT, 15 were mucinous and 18 were serous cystadenomas. The presence of papillae, defined as a small number of solid tissue projections, 1–15 mm in height and 1–10 mm in width (base) and length (base), into the cyst cavity from the cyst wall, was significantly more frequent in BOT (48%) than it was in benign (4%) and invasive (4%) malignant tumors. Intracystic solid tissue (> 15 mm in height or > 10 mm in width or length) was observed in 48% of invasive malignant masses but in only 18% of BOT and in 7% of benign tumors (P < 0.001). No sonographically unilocular, hypoechoic, smooth-walled adnexal cysts were invasively malignant but three unilocular cysts with a diameter of > 6 cm were serous BOT. Although close attention was paid to the cyst wall at ultrasound examination we did not observe in these three cysts the very small papillae which were found at histological analysis.*

Conclusions *The most frequent diagnostic feature on imaging BOT is the presence of papillae within the cyst. However, neither papillae nor other sonographic features constituted highly sensitive sonographic markers of BOT.*

INTRODUCTION

Borderline ovarian tumors (BOT) or tumors of low malignant potential are epithelial tumors with a slow growth rate and low invasive potential. These tumors tend to occur in younger women and are often diagnosed at an earlier stage of disease than are invasive carcinomas[1]. Patients with early-stage lesions have an excellent prognosis, while Stage III lesions with peritoneal implants, which are uncommon, are associated with a poor prognosis. Because of the generally good prognosis associated with BOT and the fact that they tend to occur in younger women, fertility-sparing conservative treatments have been proposed. Some authors[1–4] have proposed an endoscopic approach, after accurate surgical staging, for conservative treatment of BOT.

The identification of patients with ovarian lesions suspected of being BOT may be helpful in their management. Whereas transvaginal sonography has been established as a reliable method of differentiating benign from malignant adnexal masses, little is known about sonographic features in the diagnosis of BOT[5–9]. The aim of this study was to determine the sonographic findings that distinguish BOT from both benign and invasive malignant tumors, thus making it possible to treat them in a more conservative way.

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METHODS

We reviewed retrospectively transvaginal sonograms of women with adnexal tumors who were evaluated further by surgery and histology. Between January 1997 and April 2003, 33 patients with BOT underwent transvaginal sonography and were treated at our institution. This study group was compared with 403 patients with benign ovarian tumors and 82 patients with invasive malignant tumors managed at our institution in the same period. All patients underwent gray-scale sonographic and power Doppler examination of the pelvis within 1 month prior to surgery.

In all patients serum levels of CA 125 were preoperatively determined and in the case of suspected malignancy presurgical and surgical staging was performed according to FIGO criteria[10]. The CA 125 assays were performed with an immunoassay method using two monoclonal antibodies (CA 125 II Elecsys Sistemas 1010/2010, Centocor, Malvern, PA, USA) with a limit of detection of 0.6 U/mL. Histological classification was performed in accordance with the WHO classification[11,12].

A transvaginal sonographic examination, accompanied if necessary by a transabdominal examination, was performed on all patients using an Esaote Technos (Esaote, Genova, Italy) ultrasound machine with color and power Doppler capability, equipped with a 2.5–5.5-MHz convex transabdominal transducer and a 5.5–8.5-MHz transvaginal probe. Size and echostructure of the uterus, endometrial thickness and any irregular findings and intraperitoneal free fluid (pouch of Douglas or ascites) were recorded. Ovarian shape and size were examined transvaginally.

For each adnexal mass, longitudinal (LD), transverse (TD) and anteroposterior (APD) diameters were measured and adnexal volumes were calculated by means of a prolate ellipsoid formula: volume = $0.5233 \times LD \times TD \times APD$ in cm.

The morphology of each adnexal mass was described according to the following different types of sonographic morphological tumor characteristic:

1. Unilocular cyst: smooth-walled unilocular cyst with clear fluid or dense (echogenic) fluid content.
2. Cyst with septa: smooth-walled cyst with clear fluid or dense (echogenic) fluid content and only septa inside the cyst, not papillary projections or solid tissue. Septa were further classified as:
   a) thin septa (≤ 3 mm);
   b) thick septa (> 3 mm);
   c) no more than three septa (cyst with 1–3 septa);
   d) more than three septa (multilocular cyst).
3. Cyst with papillae: cyst with clear fluid or dense (echogenic) fluid content and papillae, defined as a small number of solid tissue projections, 1–15 mm in height and 1–10 mm in width (base) and length (base), into the cyst cavity from the cyst wall. Papillae were described further and classified as:
   a) small papilla (≤ 3 mm in height, length and width);
   b) large papilla (> 3 mm in height, length and width);
   c) only one papilla;
   d) more than three papillae (cyst with > 3 papillae).
4. Tumors with fluid/solid content: cyst with clear fluid or dense (echogenic) fluid and solid content defined as a solid part > 15 mm in height and > 10 mm in width and length.
5. Pure solid tumors: tumors composed of only solid tissue.

Each adnexal tumor was classified on the basis of the worst sonographic pattern, according to various published scoring systems[13–15]; in the presence of septa and papillae the cyst was classified as having papillae, and in the presence of solid tissue and septa or papillae the solid tissue was considered predominant and the cyst was classified as tumor with fluid/solid content. In the case of multiple papillae the largest was considered, and in the case of multiple septa the thickest was considered.

The entire adnexal mass was surveyed by power Doppler imaging. This was performed with gain adjusted to avoid color noise, thus allowing detection of the vessels inside and just outside the tumor. The power gain setting was set to maximize visualization of the vessels while minimizing artifacts. A subjective semiquantitative assessment of the amount of blood flow (area and color scale) at the level of the tumor capsule and inside the tumor was made[16–20]. Vascularization was described as being present or absent and, if present, as being central (intratumoral, i.e. in solid tissue, septa or papillae) or peripheral (capsule, pericystic).

When color signals were observed inside the tumor, blood flow velocity waveforms were recorded by placing the sample volume over the colored area and initiating the pulsed Doppler mode. At least three consecutive correctly imaged blood flow velocity waveforms were analyzed and the pulsatility index (PI = maximum systolic velocity − least diastolic velocity/mean velocity) and the resistance index (RI = maximum systolic velocity − least diastolic velocity/maximum systolic velocity) were calculated. If more color signals were detectable peripherally or centrally in the tumor, at least three different arteries were analyzed, and the lowest PI and RI values were used for further analysis. If only peripheral flow was observed and no color signal was detectable centrally, the peripheral waveforms were considered for analysis. Otherwise, the PI and RI values of the waveform obtained from the structures inside the tumors (septa, papillae or solid tissue) were considered for data analysis.

We excluded patients with histologically confirmed dermoid cysts from the analysis. These cysts have characteristics similar to those of malignant complex tumors but their sonographic appearance is pathognomonic and easily identified[21,22]. Subtracting the 66 mature teratomas from the 403 benign ovarian tumors observed, we considered 337 benign masses in the final analysis (Table 1). If the adnexal masses were bilateral, the more morphologically complex tumor was considered, and if both masses were morphologically similar, the largest one was considered in the final statistical analysis. Histological

Table 1 Histological types of benign, borderline and malignant ovarian tumors observed in pre- and postmenopausal women

Histology of ovarian tumor	*Premenopausal* (n *(%))*	*Postmenopausal* (n *(%))*	*Total* (n *(%))*
Benign	$n = 306$	$n = 97$	$n = 403$
Simple cyst	25 (8.2)	28 (28.9)	53 (13.2)
Serous cystadenoma	11 (3.6)	12 (12.4)	23 (5.8)
Mucinous cystadenoma	15 (4.9)	12 (12.4)	27 (6.7)
Endometriosis	116 (37.9)	8 (8.3)	124 (30.8)
Mature teratoma	63 (20.6)	3 (3.1)	66 (16.4)
Functional cyst	20 (6.5)	3 (3.1)	23 (5.7)
Cystadenofibroma	15 (4.9)	4 (4.1)	19 (4.7)
Salpingo-ovarian pathology	7 (2.3)	2 (2)	9 (2.2)
Paraovarian cyst	21 (6.9)	9 (9.3)	30 (7.4)
Ovarian fibroma	2 (0.6)	9 (9.3)	11 (2.7)
Ovarian thecoma	4 (1.3)	2 (2)	6 (1.5)
Other	7 (2.3)	5 (5.1)	12 (2.9)
Borderline	$n = 23$	$n = 10$	$n = 33$
Serous cystadenoma	12 (64.3)*	6 (60)	18 (55)
Mucinous cystadenoma	11 (35.7)*	4 (40)*	15 (45)
Malignant	$n = 22$	$n = 60$	$n = 82$
Serous adenocarcinoma	5 (23)	26 (43)	31 (38)
Mucinous adenocarcinoma	2 (9)	5 (8)	7 (9)
Endometrioid adenocarcinoma	8 (36)	12 (20)	20 (24)
Undifferentiated carcinoma	1 (5)	5 (8)	6 (7)
Immature teratoma	1 (5)	0	1 (1)
Granulosa cells	2 (9)	2 (3)	4 (5)
Germ cells	1 (5)	0	1 (1)
Brenner's tumor	1 (5)	2 (3)	3 (4)
Metastatic tumor	1 (5)	8 (13)	9 (11)

*$P < 0.001$ borderline vs. malignant ovarian tumors.

findings were compared with sonographic appearance of the adnexal masses.

To evaluate the accuracy of ultrasound in identifying BOT, sensitivity, specificity, positive and negative predictive values and likelihood ratios were calculated.

The 95% CIs for prevalence of the presence of power Doppler signals in the papillae in the different types of ovarian tumor were calculated according to the recommended method of Wilson[23,24]. This method has better statistical properties than does the traditional method, having the advantage that it can be used for any data[24].

Statistical analysis was performed using the chi-square test and the unpaired Student's *t*-test. A *P*-value of < 0.05 was considered significant.

RESULTS

The type and stage of BOT and invasive malignant tumor are reported in Tables 1 and 2. A significantly higher percentage of Stage Ia was observed in patients with BOT (64%) compared with those with invasive malignant masses (24%).

The mean ± SD age of patients was 45.8 ± 15.7 years for those with BOT, which was significantly lower than the age of those with invasive malignant tumors and similar to the age of those with benign tumors (Table 3). The percentage of BOT patients aged less than 35 years was also similar to that for benign tumors.

The maximum diameter of BOT was similar to that of invasive malignant tumors but significantly greater than that of benign tumors. However, the percentage of cysts ≤ 5 cm was similar to that of benign and significantly higher than that of invasive malignant tumors (Table 3).

The analysis of the different morphological echopatterns of the adnexal masses is reported in Table 4. The distribution of small and large papillae was not significantly different in BOT and benign and malignant tumors; therefore, we considered only the presence and the number of papillae. No difference was observed in the distribution of thick or thin septa in BOT and benign and invasive malignant tumors, but the number of septa did vary in the different types of mass and multilocular cysts were considered separately.

We observed numerous unilocular smooth-walled cysts in patients with benign tumors and no unilocular cysts in patients with invasive malignant tumors. Moreover, we found three (9%) unilocular smooth-walled cysts in patients with BOT. These three patients were over 35 years old and the cyst diameters were > 6 cm (6.5 cm, 10 cm and 12 cm). The three cysts were serous BOT, and very small papillae on the cyst wall were observed on histological analysis.

Sixteen (48%) BOT showed papillae, and eight (24%) showed septa, of which six (18%) were multilocular. The percentage of pure solid and fluid/solid tumors was significantly higher in patients with invasive malignant tumors compared with those with BOT (Table 4).

Table 2 Stages of the borderline and malignant ovarian tumors

Ovarian tumor	*Total Cases* (n)	*Stage Ia* (n (%))	*Stage Ib* (n (%))	*Stage Ic* (n (%))	*Stage II* (n (%))	*Stage III* (n (%))	*Stage IV* (n (%))
Borderline	33	21 (64)*	4 (12)	5 (15)	1 (3)	2 (6)*	0
Malignant†	82	20 (24)	1 (1)	11 (13)	7 (9)	30 (37)	4 (5)

*$P < 0.001$ borderline vs. malignant ovarian tumors; †Nine cases were metastatic.

Table 3 Comparison between patient age, menopausal status and maximum diameter of benign, malignant and borderline ovarian tumors

	Type of ovarian tumor (No. of cases)		
	Benign (n = 337)	*Borderline* (n = 33)	*Malignant* (n = 82)
Age			
Range (years)	12–82	24–74	28–82
Mean age ± SD (years)	40.5 ± 14.9§	45.8 ± 15.7†	57.9 ± 12.9
Patients < 35 years (*n* (%))	146 (43)§	12 (36)†	4 (5)
Menopausal status: premenopausal (*n* (%))	243 (72)§	23 (70)†	22 (27)
Tumor maximum diameter			
Mean ± SD (cm)	6.3 ± 3.7§	9.3 ± 7.2‡	11.0 ± 6.3
≤ 5 cm (*n* (%))	154 (46)§	13 (39)*	13 (16)
≤ 8 cm (*n* (%))	267 (79)§	19 (58)	34 (42)

*$P < 0.05$ borderline vs. malignant ovarian tumors. †$P < 0.01$ borderline vs. malignant ovarian tumors. ‡$P < 0.01$ borderline vs. benign ovarian tumors. §$P < 0.01$ benign vs. malignant ovarian tumors.

Table 4 Main morphological characteristics of adnexal tumors correlated with histological type of benign, malignant and borderline ovarian tumors

Morphological characteristic	*Benign* (n = 337) (n (%))	*Borderline* (n = 33) (n (%))	*Malignant* (n = 82) (n (%))
Unilocular cyst	224 (67)	3 (9)*	0 (0)§
Cyst with septa	54 (16)	8 (24)†	4 (5)§
Cyst with ≤ 3 septa	45 (13)	2 (6)	1 (1)§
Multilocular cyst	9 (3)	6 (18)*‡	3 (4)
Cyst with papillae	14 (4)	16 (48)*†	3 (4)
Cyst with 1 papilla	9 (3)	3 (9)	0 (0)
Cyst with > 3 papillae	0 (0)	9 (27)*†	3 (4)
Fluid/solid tumor	25 (7)	6 (18)†	39 (48)§
Pure solid tumor	20 (6)	0 (0)†	36 (44)§

*$P < 0.01$ borderline vs. benign ovarian tumors. †$P < 0.01$ borderline vs. malignant ovarian tumors. ‡$P < 0.05$ borderline vs. malignant ovarian tumors. §$P < 0.01$ malignant vs. benign ovarian tumors.

The diagnostic image that appeared to be best correlated with BOT was that of a cyst with papillae ($P < 0.01$ vs. invasive malignant and benign tumors) (Figure 1). In addition, the multilocular echopattern seemed to be frequent in BOT ($P < 0.05$ vs. malignant, $P < 0.01$ vs. benign) (Table 4). Considering the invasive malignant tumors with only papillae, there were two serous adenocarcinomas (Stages Ic and III) and one endometrioid cystadenocarcinoma (Stage III), all well differentiated (one of the serous tumors was considered BOT at frozen section but the final pathological diagnosis was cancer Grade 1). Analyzing benign tumors with papillae we observed eight serous tumors (three cystadenofibromas and five serous cystadenomas), one mucinous cystadenoma and five endometriomas (Figure 2).

Table 5 shows our morphological analysis of serous and mucinous tumors only, in order to clarify whether there was a difference between BOT, benign and invasive malignant tumors. Again, the presence of internal papillae and of multiple septa was the most significant sonographic pattern associated with BOT. Moreover, the sonographic morphology of mucinous and serous BOT was similar, but seemed to differ between mucinous and serous benign tumors.

Table 6 shows the percentages of tumors with positive findings on power Doppler imaging and the location of detectable blood flow (peripheral or intratumoral). The percentage of intratumoral vascularization is reported when present, otherwise the peripheral vascularization is given. Qualitative analysis revealed statistically significant differences: peripheral vascularization between invasive malignant tumors and the other adnexal masses differed ($P < 0.01$ vs. BOT and vs. benign tumors), while there was no difference between BOT and benign tumors. Intratumoral presence of power Doppler signals, in particular intrapapillae power Doppler signals, was more frequent in borderline (56.3%; 95% CI, 33.2–76.9%) and in invasive malignant tumors (66.7%; 95% CI, 20.0–93.6%) than it was in benign tumors (0%; 95% CI, 0–21.5%). Moreover, statistically significant differences were observed in the lowest PI and RI values of benign compared with borderline and invasive malignant ovarian tumors. No statistically significant differences in lowest PI

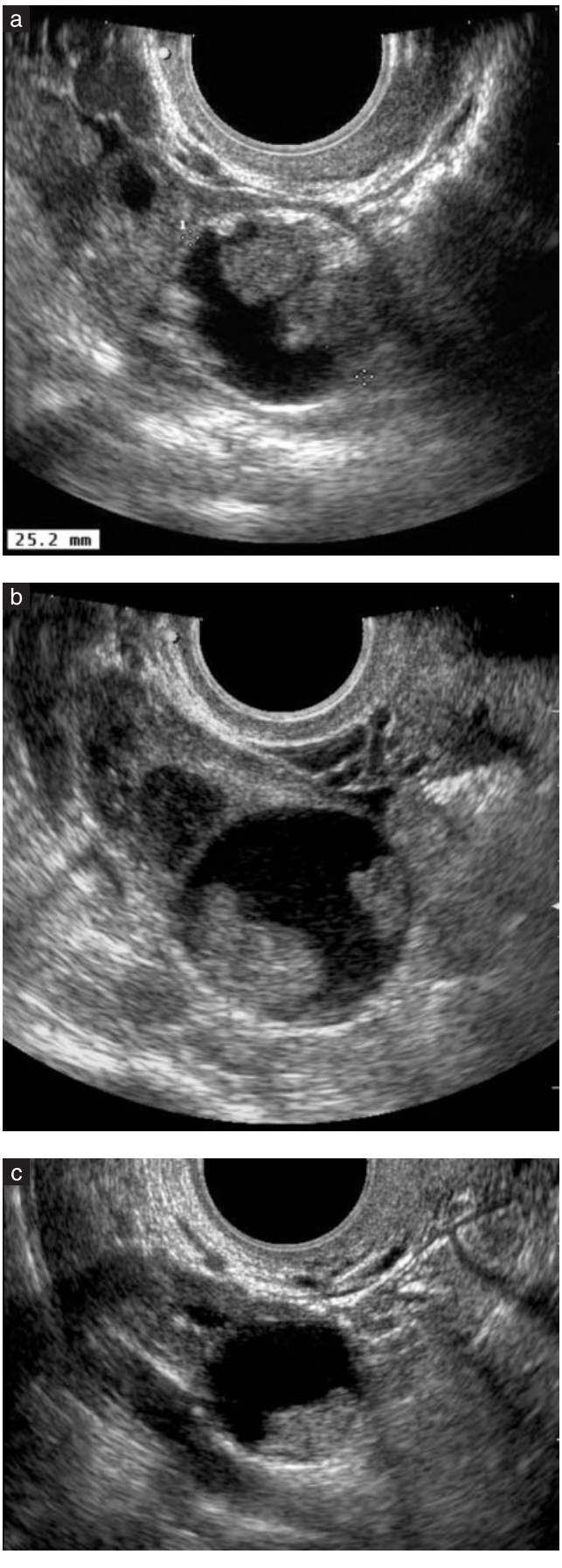

Figure 1 Ultrasound images of three different cases of serous borderline ovarian tumor in premenopausal patients, all with a small ovarian cyst with internal papillae.

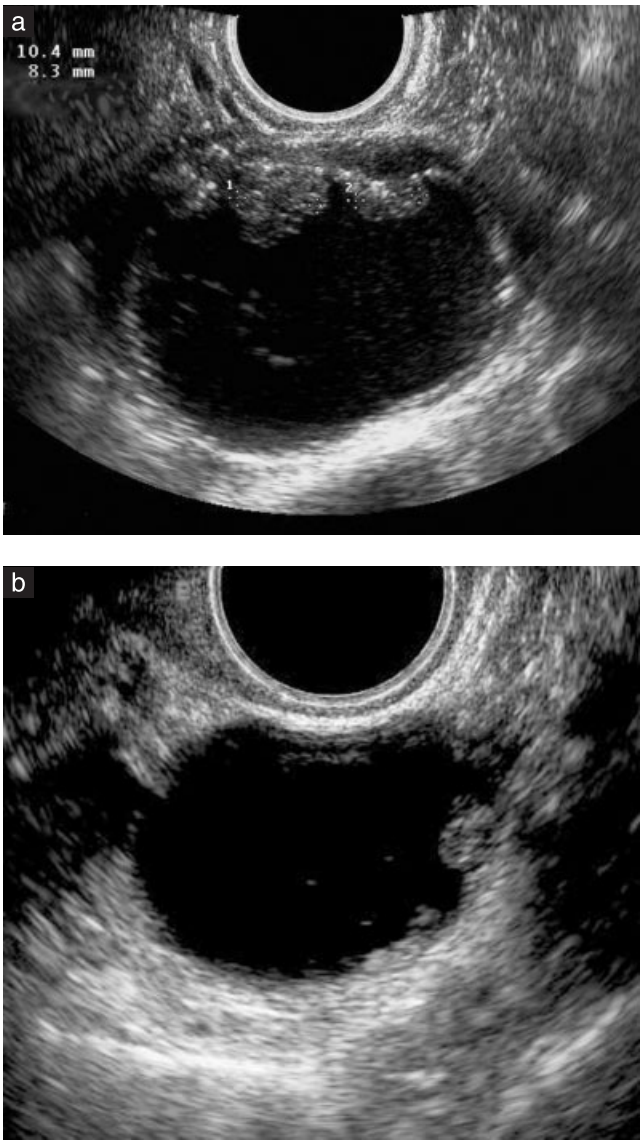

Figure 2 Ultrasound images comparing a serous papillary borderline ovarian tumor in a 48-year-old patient (a) with a benign serous papillary cystadenoma in a 52-year-old patient (b) showing the similar sonographic features: cyst with small papillae.

and RI values were observed between invasive malignant tumors and BOT.

Analyzing diagnostic accuracy in differentiating BOT from other adnexal tumors we considered at first only the two typical morphological patterns of BOT (papillae and multiple septa), obtaining a poor positive predictive value and poor sensitivity, even though the specificity and negative predictive value were high (Table 7). When the sonographic appearance of papillae was combined with the presence of internal vascularization, we obtained a specificity of 100% but the sensitivity decreased to 27% (Table 7; Figures 3–5).

We found that CA 125 levels did not improve the recognition of BOT and in our population these were very similar to those of benign cysts (< 35 U/mL in 82% of BOT, 78% of benign and 29% of invasive malignant tumors).

Table 5 Morphological characteristics of benign, borderline and malignant ovarian tumors of serous and mucinous histological type

	Benign (n = *123)*		*Borderline* (n = *33)*		*Malignant* (n = *38)*	
Morphological characteristic	*Mucinous* (n = *27)* (n *(%))*	*Serous* (n = *96)* (n *(%))*	*Mucinous* (n = *15)* (n *(%))*	*Serous* (n = *18)* (n *(%))*	*Mucinous* (n = *7)* (n *(%))*	*Serous* (n = *31)* (n *(%))*
Unilocular	17 (63.0)	68 (70.8)	0	3 (16.7)	0	0
Cyst with septa	8 (29.6)	13 (13.5)	4 (26.7)	4 (22.2)	1 (14.3)	1 (3.2)
Cyst with ≤ 3 septa	3 (11.1)	12 (12.5)	1 (6.7)	1 (5.6)	0	1 (3.2%)
Multilocular cyst	5 (18.5)	1 (1.0)‡	3 (20.0)	3 (16.7)*	1 (14.3)	0
Cyst with papillae	1 (3.7)	8 (8.3)	8 (53.3)*†	8 (44.4)*†	0	2 (6.5)
Cyst with 1 papilla	1 (3.7)	6 (6.3)	0	3 (16.7)	0	0
Cyst with > 3 papillae	0	0	5 (33.3)*†	4 (22.2)*	0	2 (6.5%)
Fluid/solid content	1 (3.7)	7 (7.3)	3 (20.0)	3 (16.7)	5 (71.4)	14 (45.2)
Pure solid content	0	0	0	0	1 (14.3)	14 (45.2)

*$P < 0.05$ borderline vs. benign ovarian tumors. †$P < 0.05$ borderline vs. malignant ovarian tumors. ‡$P < 0.01$ mucinous vs. serous.

Table 6 Power Doppler imaging (PDI) characteristics of ovarian tumors correlated with histological type

PDI characteristic	*Benign* (n = *337)*	*Borderline* (n = *33)*	*Malignant* (n = *82)*
Flow present (% (No. of cases))	82 (276/337)	97 (32/33)	100 (82/82)
Peripheral (tumors with positive findings on PDI, % (No. of cases))	71 (195/276)‡	34 (11/32)†	4 (3/82)
Intratumoral (tumors with positive findings on PDI, % (No. of cases))	29 (81/276)‡	66 (21/32)*	96 (79/82)
Intrapapillae ('cyst with papillae', % (No. of cases))	0 (0/14)‡	56 (9/16)*	67 (2/3)
Lowest PI (mean ± SD)	2.29 ± 0.86‡	0.91 ± 0.50*	0.75 ± 0.25
Lowest RI (mean ± SD)	0.83 ± 0.14‡	0.45 ± 0.08*	0.50 ± 0.11

*$P < 0.01$ borderline vs. benign ovarian tumors. †$P < 0.01$ borderline vs. malignant ovarian tumors. ‡$P < 0.01$ benign vs. malignant tumors.

Table 7 Comparison of different sonographic criteria and their diagnostic accuracy in differentiating borderline from benign and malignant ovarian tumors

	Ovarian cyst with		
	Papillae	*Papillae or multiple septa*	*Papillae and intrapapillae flow**
True positive (*n*)	16	22	9
False positive (*n*)	17	29	2
True negative (*n*)	402	390	417
False negative (*n*)	17	11	24
Sensitivity (%)	48	68	27
Specificity (%)	96	93	100
PPV (%)	48	43	82
NPV (%)	96	97	95
Positive likelihood ratio	12	10	27
Negative likelihood ratio	0.54	0.34	0.73

Prevalence of borderline tumors = 7%. *Papilla with internal vessels seen with power Doppler imaging. PPV, positive predictive value; NPV, negative predictive value.

DISCUSSION

Approximately 15% of epithelial ovarian malignancies are BOT[1]. It has been clearly established in several series that these tumors occur in patients who are younger compared with those who develop invasive carcinomas and they have been reported to exhibit a relatively benign clinical course. Therefore, the preoperative evaluation of BOT is becoming increasingly important in premenopausal women when the clinician is faced with the dilemma of avoiding unnecessary surgery while identifying possible ovarian cancer in good time. Because of the desirability of preserving ovarian function, particularly if retention of childbearing capacity is an issue, several authors have recommended less radical surgery (unilateral oophorectomy or cystectomy) for the group of young patients with unilateral BOT[1–4,25–27].

It is well known that ultrasound is effective in differentiating benign from malignant ovarian tumors and is actually one of the most important presurgical diagnostic tests in the management of adnexal lesions. However, in most studies reporting sonographic features of ovarian tumors, BOT have been considered together with invasive malignant tumors. Only a few studies[1,5–9], most of which involved a small number of cases, have focused on the sonographic appearance of BOT. Darai *et al.*[1] reported that the majority (67.7%) of BOT at sonographic examination are multilocular, have thick septa and are sonolucent or of mixed echogenicity.

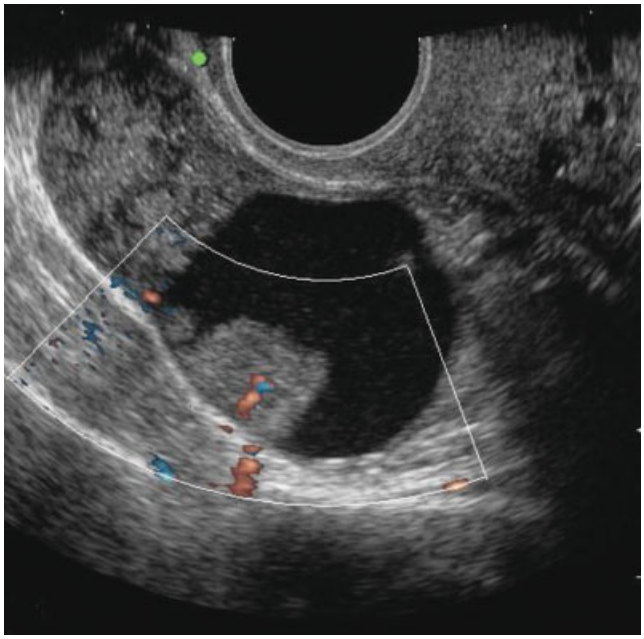

Figure 3 Power Doppler ultrasound image showing cyst with vascularized papilla: serous borderline ovarian tumor.

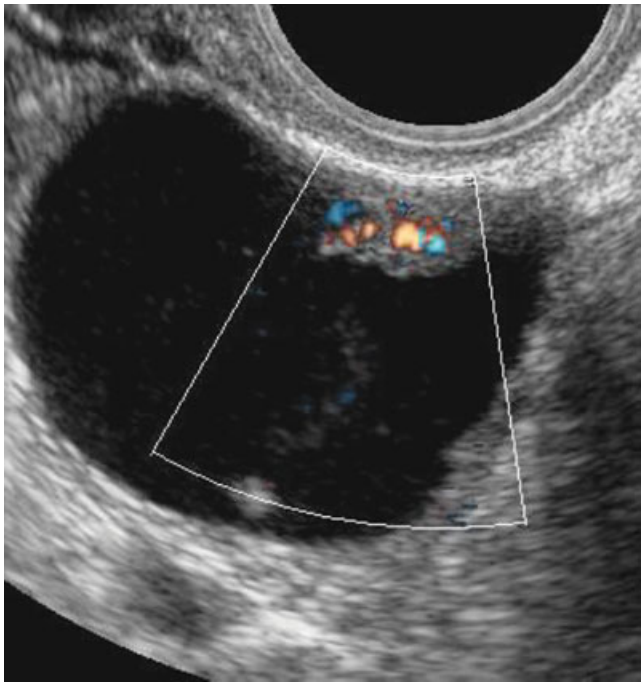

Figure 4 Power Doppler ultrasound image showing cyst with vascularized papilla: well-differentiated serous cystadencarcinoma Stage 1c.

Mucinous tumors tend to be larger at presentation but some authors observed no significant difference in diameter between invasive malignant tumors and BOT[6]. In our study the maximum diameter of BOT was similar to that of invasive malignant tumors; however, the percentage of cysts ≤ 5 cm was similar to that of benign ones (Table 3).

Furthermore, other studies[1,7,8,28,29] have reported that BOT can exhibit sonographic features such as unilocular smooth anechoic cysts without endophytic papillary growth. Gotlieb *et al.*[8] reported 13% and Emoto *et al.*[7] reported 17% of BOT with a sonographic appearance of unilocular cysts, while in a prospective study of 1072 premenopausal ovarian tumors, Osmers *et al.*[28] demonstrated that malignancy occurred in 0.8% of unilocular smooth-walled cysts, and that 0.5% of unilocular smooth-walled cysts were BOT. Nevertheless, they found no ovarian cancer in women < 20 years old and none in those with simple ovarian cysts of a mean size < 40 mm, which allowed them to conclude that the risk of finding a malignant growth in a simple ovarian cyst decreases along with decreasing tumor size and decreasing age[28].

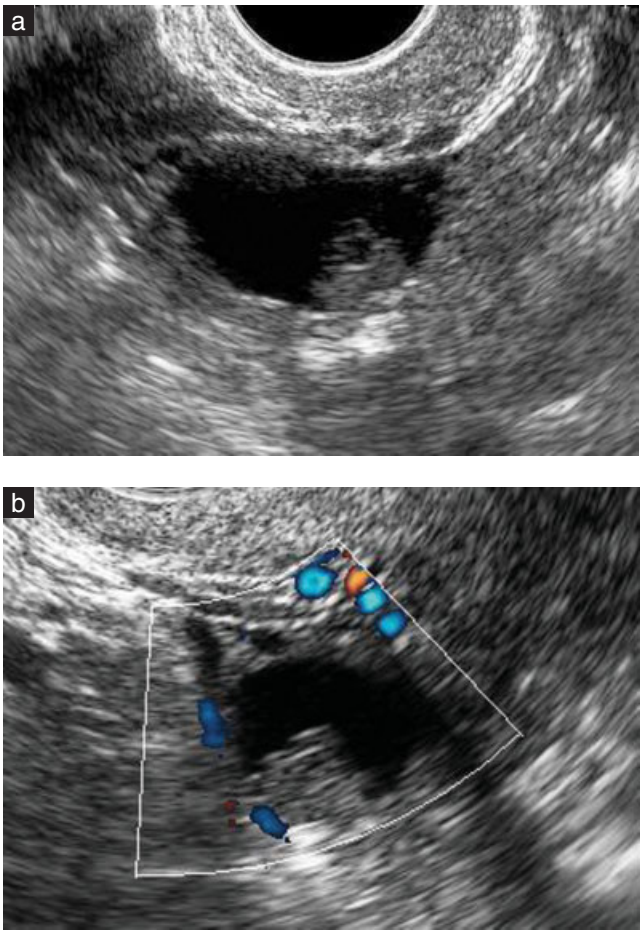

Figure 5 Ultrasound images showing benign serous cystadenoma: (a) gray-scale image showing small cyst with internal papilla; (b) power Doppler imaging did not show internal vascularization of the papilla.

We found no invasive malignancies in simple ovarian cysts in our population but we observed unilocular smooth-walled cysts in three cases (9%) of BOT. All three cysts were detected in premenopausal women and had a diameter > 6 cm. Although our ultrasound examination of the cyst wall was very careful, we did not observe in these three cysts the very small papillae which were described among the histological features. This could be due to the fact that the transvaginal sonographic examination of large cysts may have been less accurate because the distal cyst wall was too far away to be clearly visible on the screen. On the other hand the sonographic

transabdominal evaluation of large cysts is unable to identify small papillae because of technical features (such as the need to use a lower frequency probe because of a thick abdominal wall). New machines and transvaginal sonographic probes with different characteristics (larger vision angle, possibility of changing frequency, harmonic imaging, three-dimensional imaging) could probably eliminate these problems; however, large unilocular cysts should be managed with more caution than are smaller ones (≤ 5 cm).

In 85% of BOT we detected sonographic features with some degree of complexity. The diagnostic image that seemed to best correlate with BOT was that of a cyst with papillae (48%) or one with multiple septa (18%). These findings were similar to those of other recent studies[8,9], which reported the presence of papillae in 63–65% of BOT.

Analyzing benign tumors with papillae we observed eight serous tumors, one mucinous cystadenoma and five endometriomas. Benign tumors such as endometriomas often present a typical echostructure that permits the identification of the type of tumor (i.e. 'ground glass' appearance). An experienced sonographer is often able to identify the type of tumor (endometrioma, sactosalpinx, paraovarian cyst, ovarian fibroid)[30–32] and this subjective pattern recognition has been reported by many authors to be very accurate, especially for endometriosis[30,31,33,34]. We therefore focused our morphological analysis only on serous and mucinous tumors (Table 5), and the presence of internal papillae and of multiple septa was again the most significant sonographic pattern associated with BOT. No difference in sonographic features was observed between mucinous and serous BOT. This can be explained by the fact that both types of tumor can present a different appearance on analysis of gross histological section[35,36]. The mucinous tumors were mostly multicystic and filled with mucinous material (Figure 6), but could also contain solid tissue and endophytic papillae[37,38]. Papillary projections seemed to be more typical in serous tumors; however, unilocular and septate cysts were also observed[35,36,39].

Our power Doppler examination of BOT revealed PI and RI values similar to those of invasive malignant tumors and a vascular distribution (central vs. peripheral vascularization) between those of benign and invasive malignant tumors. According also to other studies[6,8,9], no specific Doppler velocimetry flow evaluation is currently available to diagnose BOT. Despite this, Zanetta *et al.*[6] proposed a model for differentiating BOT from invasive malignant and benign tumors that involved Doppler flow parameters. This model was based on the presence of intracystic complexity (either septa or papillae), a PI < 1.0, absence of intratumoral confluence of vessels and CA 125 levels < 150 U/L in women under the age of 60 years, and it yielded an accuracy of 91%. However, the same authors recognized the limited value of this model clinically, considering that the fit of such a model is always greater when derived retrospectively than when applied prospectively.

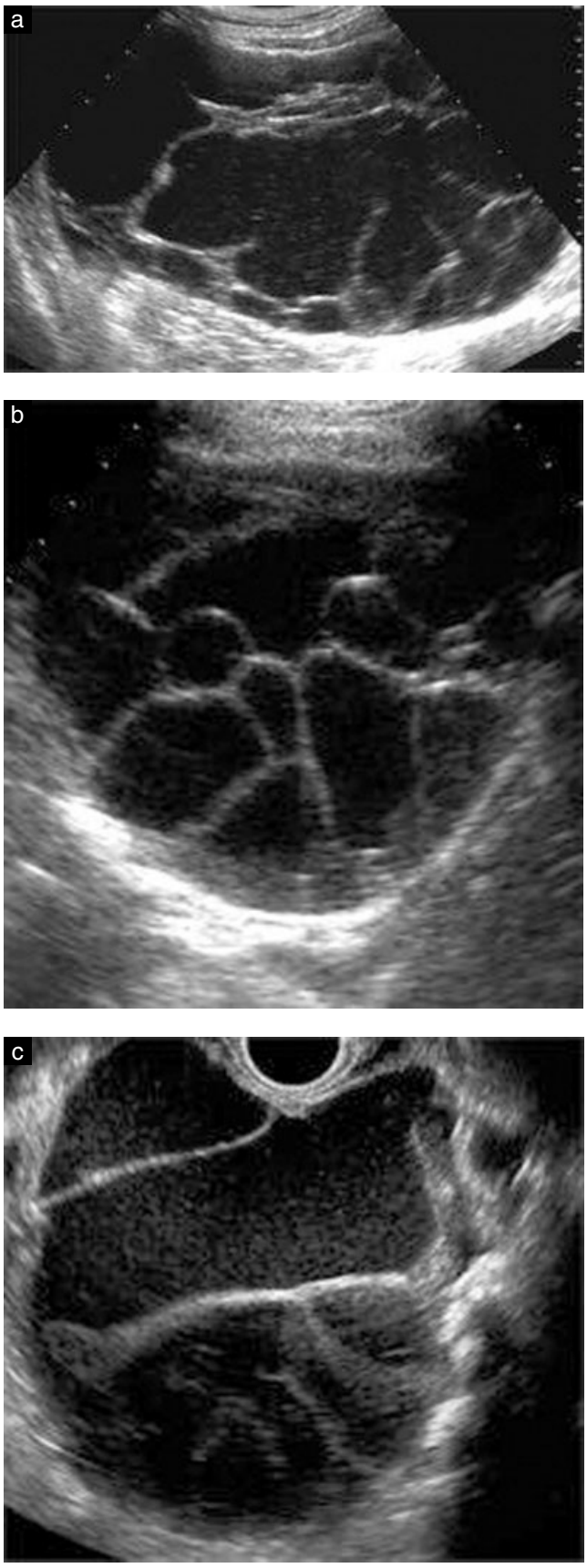

Figure 6 Ultrasound images showing multiseptate cysts: (a) large benign mucinous cystadenomas; (b) transabdominal and (c) transvaginal views of a mucinous borderline ovarian tumor.

The problem that arises from all the sonographic studies on BOT and from our results is not only the inability to differentiate benign tumors from BOT but especially the inaccuracy in distinguishing BOT from malignancy. It seems that BOT also have a borderline sonographic appearance and do not have a pathognomonic or typical sonographic pattern. In fact, the presence of papillae can also be found in benign serous tumors[40] (Figures 2 and 5) and if internal vascularization of the papillae is considered, it is very difficult to distinguish BOT from invasive malignant tumors (Figures 3 and 4). Histopathological analysis can help, and gross section and angiogenesis in particular could be helpful in interpreting these findings. In histopathological specimens it has been shown recently that microvessel count is more intense in invasive ovarian carcinomas than it is in BOT[41]. It has also been noted[42] that there is little difference between BOT and well-differentiated invasive malignant tumors. Tumors that are of higher grading or are undifferentiated are associated with a greater amount of solid tissue with marked and irregular vascularization[42,43], whereas low-grade malignant tumors preserve the structural characteristics of the original histological type. Therefore differentiation between BOT and invasive malignant tumors seems not to be stage-dependent, but is probably grade-dependent. In other words, it seems to be very difficult to distinguish a well-differentiated serous ovarian carcinoma from a serous BOT, since both can appear at ultrasound as a cyst with vascularized papillae (Figures 3 and 4). A Grade 3 serous carcinoma, however, generally presents a sonographically more complex structure with a large amount of solid tissue. On the other hand, papillae can also be observed in benign cystadenomas or cystadenofibromas and in these cases perhaps the vascularization inside the papilla could suggest BOT or malignancy, even though avascular papilla is not always associated with benign tumors and vice versa (95% CI, 0–22%).

Finally, our results show that accurate sonographic examination can suggest BOT on the basis of the presence of papillae or multiple septa. However, neither papillae nor septa constitute highly sensitive sonographic markers. The main concern for BOT remains that they must not be managed with overly aggressive therapy, and therefore a very accurate presurgical diagnosis is desirable. This means that conservative surgery for a suspected BOT, the actual sonographic diagnosis not being able to exclude totally invasive malignancy, has to be associated with frozen section, and greater care than normal should be taken not to rupture the cyst capsule. However, the precision of frozen-section diagnosis of BOT has been questioned[44,45] and the risk of spread of BOT and invasive malignant tumors treated conservatively has yet to be established.

It is to be hoped that further advances in the application of three-dimensional and power Doppler imaging and sonographic contrast media for the detection of microvessels may be able to identify more accurately BOT and prevent the overtreatment of these lesions.

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