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Ultrasound features of different histopathological subtypes of borderline ovarian tumors

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KEYWORDS: borderline ovarian tumors; color Doppler imaging; gynecology; pathology; sonography

ABSTRACT

Objective *To describe the gray-scale sonographic and color Doppler imaging features of the most common histopathological subtypes of borderline ovarian tumors.*

Methods *We analyzed retrospectively the preoperative transvaginal sonographic reports of patients with a histological diagnosis of borderline ovarian tumor. All patients were scanned consecutively by two of the investigators using transabdominal and transvaginal gray-scale imaging to assess the morphology and color Doppler to obtain indices of the blood flow. Sonographic findings were compared to histopathological data.*

Results *A total of 113 consecutive cases were reviewed from two referral centers for gynecological oncology. At histological examination 50 tumors (44%) were classified as being serous borderline ovarian tumors (SBOT), 61 (54%) were mucinous borderline ovarian tumors (MBOT) (42 intestinal type and 19 endocervical type), and two patients (2%) presented with borderline endometrioid tumors. SBOTs and endocervical-type MBOTs had very similar sonographic features and a smaller diameter, fewer locules (usually unilocular-solid lesions) and a higher color score than intestinal-type MBOTs. Intestinal-type MBOTs were characterized by a significantly higher percentage of lesions with >10 locules when compared with the endocervical-type MBOTs.*

Conclusion *Intestinal-type MBOTs have different sonographic features from other common borderline ovarian tumors. Copyright © 2005 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Borderline ovarian tumors (BOTs) constitute only 10–15% of all malignant ovarian tumors, but they are enigmatic neoplasms that have caused confusion and apprehension disproportionate to their incidence. The favorable prognosis of BOTs, which occur mostly in young women of reproductive age, supports the adoption of conservative surgical treatment. Therefore, accurate diagnosis is essential for planning appropriate patient management[1].

Ultrasound is a well-established imaging modality for the assessment of pelvic masses and an expert sonologist's subjective evaluation of the gray-scale ultrasound image can achieve an accuracy of more than 90% in discriminating between benign and malignant adnexal masses[2,3], while a correct specific diagnosis on the basis of pattern recognition of the gray-scale ultrasound image has an accuracy of 42%[4]. BOT is one of the groups of ovarian tumors that are difficult to classify correctly[5–9]. Color and power Doppler ultrasound provide information about the vascularization pattern of gynecological pathology[10], although it has been observed that Doppler examination increases the percentage of correct specific diagnoses in only 5% of cases[4].

In the last 10 years several studies have been conducted to identify the gray-scale and color Doppler ultrasound characteristics that could help to distinguish BOTs from primary invasive ovarian cancers. Pascual *et al.*[5] studied retrospectively 383 ovarian lesions and noted that BOTs (27 cases) showed a greater similarity to malignant lesions (absence of anechoic pattern, presence of diffuse internal echoes and intracystic papillae) than to benign tumors (absence of septa, absence of solid or heterogeneous

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pattern). However, multivariate analysis of the gray-scale features revealed that the presence of intracystic papillae was the only independent variable distinguishing borderline cystic tumors from other types of lesion, and this has been confirmed by other studies[6].

Using color Doppler ultrasound, Wu *et al.*[11] reported a significant gradual decrease in the mean value of the resistance index (RI) from benign tumors (0.695), to borderline malignancy (0.535) and early stage ovarian carcinoma (0.485), to advanced stage ovarian malignancies (0.398), as also reported by Emoto *et al.*[7]. Yet the diagnostic role of vessel distribution inside the tumor remains controversial: some authors reported similar intratumoral blood flow characteristics at color Doppler ultrasound in borderline and malignant ovarian tumors[5,7], while others found no significant difference between benign and borderline lesions[8,12].

To our knowledge, only two studies[6,13] have examined the sonographic characteristics of different histological types of BOT, but without distinguishing endocervical-type and intestinal-type mucinous BOTs (MBOTs). The aim of our study was to describe the sonographic features of the different histopathological subtypes of BOT.

METHODS

We analyzed retrospectively the preoperative transvaginal sonographic reports of patients with a histological diagnosis of BOT. The study was conducted in two referral centers for gynecological oncology: the Gynecology Oncology Unit, University of Sacred Heart, Rome (Italy) and the Department of Obstetrics and Gynecology, Katholieke Universiteit Leuven (Belgium). Those eligible were consecutive patients with BOT at histopathology, who had been scanned between 1994 and 2004 by one of two investigators (A.C.T. in Rome and D.T. in Leuven), using transabdominal and transvaginal gray-scale imaging in order to assess the morphology, and color Doppler imaging to obtain indices of blood flow.

Sonography

The methodology used for sonography was standardized; details have been published previously[14]. All ultrasound scans were performed using either the ESAOTE AU5 and ESAOTE Technos (Esaote, Genova, Italy) or an Acuson Sequoia (Siemens-Acuson Inc., Mountain View, CA, USA) ultrasound system. A transvaginal scan of the pelvic organs was performed using a multifrequency endovaginal probe (ESAOTE: EC 123; range, 9.0–5.0 MHz and Siemens-Acuson: range, 8.0–5.0 MHz) and was followed by a transabdominal scan, with a 3- or 3.5–5.0-MHz convex transducer. In the color, spectral and power modes, the Doppler ultrasound had a frequency of 5 MHz. The wall filter was set at 50 or 100 Hz. Ovarian lesions were classified as unilocular, unilocular solid, multilocular, multilocular solid or solid, according to the classification reported for adnexal masses[14]. In particular, in the presence of intralesional solid tissue, the ovarian mass was described as unilocular-solid or multilocular-solid, depending whether a single cystic locule or multiple locules were found. If the percentage of the solid component was greater than 80%, the ovarian neoplasm was defined as solid. If the solid tissue appeared as an echogenic structure projecting within the cystic component, this was defined as 'papilla'. In the case of multiple masses only the most complex mass was examined; in the case of similar ultrasound morphology the largest mass or that most easily accessible for the examination was selected.

All color Doppler examinations began with the same settings of the ultrasound system: the highest sensitivity for detection of color Doppler signals was used allowing detection of blood flow velocities ≥ 3 cm/s, and the color gain was set just below the background noise level to increase, as far as possible, the Doppler sensitivity for low-velocity flow detection. A subjective semiquantitative assessment of the amount of blood flow within the examined tumor was made (color score): a score of 1 was given when no color could be found in the lesion, a score of 2 was given when only minimal color could be detected, a score of 3 was given when a moderate amount of color was present, and a score of 4 was given when the tumor appeared highly vascular, showing a large area of color signals[14,15].

When flow signals were detected, the examiner tried to identify the tumor artery with the highest blood flow velocity. For this purpose the color Doppler sensitivity was reduced by increasing the pulse repetition frequency until only one vessel was detectable. Pulsed Doppler examination of this vessel enabled spectral analysis of the blood flow. The pulsatility index (PI), the RI, the peak systolic velocity and the time averaged maximum velocity were recorded. Photographic images were printed and ultrasound digital images were stored on a hard disk for subsequent review and analysis.

Tumor markers

The serum levels of CA 125 were measured using the CA 125 II immunoradiometric assay (Centocor, Malvern, PA, USA or Abbott Axsym system, REF 3B41-22, Abbott Laboratories Diagnostic Division, IL, USA), and the results expressed in U/mL.

Study outcome

The final outcome of the study was based on the histological diagnosis and the surgical stage of the tumors. Surgery was performed either laparoscopically or via laparotomy depending on the surgeon's clinical judgement. All surgically removed tissues were sampled extensively for histological examination. Tumors were classified according to the criteria recommended by the International Federation of Gynecology and Obstetrics (FIGO)[16]. In particular, MBOTs were subclassified as endocervical or intestinal-type according to the criteria described by Scully *et al.*[17]. MBOTs of mixed endocervical-type and intestinal-type were classified as

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intestinal-type tumors in agreement with the WHO's histological classification of tumors of the ovary[18].

Statistical analysis

Univariate analysis was performed using Fisher's exact test for categorical data and the Kruskal–Wallis test (comparison of three groups) or Wilcoxon's rank-sum test (comparison of two groups) for numerical data. Where appropriate, two-sided tests were used and 5% was used as the general level of significance (α-level = 0.05). Statistical analysis was performed using the SAS software package (Release 8.01; SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 113 women were recruited for the study; their clinical characteristics are shown in Table 1.

At histological examination 50 tumors (44%) were classified as serous BOT (SBOT), 61 (54%) as MBOT (42 intestinal-type and 19 endocervical-type), and two patients (2%) presented with borderline endometrioid tumor. There were six cases with MBOT who had mixed endocervical-type and intestinal-type pathology and these were classified as intestinal-type tumors[18]. Twenty-six tumors (59%) in the SBOT group presented an elevated CA 125 serum level (above 35 U/mL), whereas only four (21%) tumors in the MBOT endocervical-type group and thirteen (34%) tumors in the MBOT intestinal-type group had an elevated CA 125 value.

Sonographic characteristics of the study population are shown in Tables 2 and 3. The median maximum tumor diameter was significantly greater in the intestinal-type MBOTs compared with the endocervical-type MBOTs and the SBOTs. With respect to morphology, unilocular lesions were rare in the three groups. We found only four unilocular cysts: one intestinal-type MBOT of 160 mm, one endocervical-type MBOT of 58 mm and two SBOTs of 35 mm and 77 mm. Both SBOTs and endocervical-type MBOTs were characterized by a statistically significantly different morphology when compared with intestinal-type MBOTs. SBOTs and endocervical-type MBOTs were characterized by a higher rate of unilocular-solid lesions (Figures 1 and 2), a higher number of papillary excrescences, a lower percentage of multilocular lesions and a lower number of locules when compared with the intestinal-type MBOTs (Figure 3). Solid tumors were found only in the SBOT category.

At color Doppler analysis the number of papillary excrescences with vessel signals was significantly lower in intestinal-type MBOTs when compared with the endocervical-type MBOTs and the SBOTs. No statistically significant differences were found between the endocervical-type MBOT and the SBOT groups.

The two patients with borderline endometrioid tumors were > 50 years in age. They presented multilocular-solid lesions which were vascularized at color Doppler, measuring 99 mm and 133 mm in maximum diameter. The CA 125 serum levels were high in both cases (651 and 754 U/mL, respectively).

DISCUSSION

To our knowledge, this is the first study to describe the gray-scale and color Doppler imaging features of a large series of BOTs according to the most common histopathological subtypes: SBOT and MBOT.

The preoperative differentiation of these masses could play a role in the management, prognosis and surgical treatment of the disease. In fact, while SBOTs present at stage I in approximately 65–70% of cases[19] with a 5-year survival rate of 95% in patients with non-invasive implants and 66% in patients with invasive implants[20], the vast majority of MBOTs are stage I with an overwhelmingly benign behavior[21,22]. The less common endocervical type of MBOT has a worse prognosis, presenting with implants (> stage I) in a higher number of cases, and recurring more frequently than does the intestinal type[23,24]. In this context, our observation that endocervical-type MBOTs are more similar to SBOTs than they are to intestinal-type MBOTs could be clinically relevant.

Table 1 Clinical characteristics of the study population according to the histopathological classification of the tumors

Histotype	*Endocervical-type MBOT*	*Intestinal-type MBOT*	*SBOT*	*Intestinal-type MBOT vs. endocervical-type MBOT*	*Intestinal-type MBOT vs. SBOT*	*Endocervical-type MBOT vs. SBOT*	*Difference among all three groups (Kruskal–Wallis test or Fisher's exact test)*
Patients (*n*)	19	42	50				
Age (*n* (%))							
< 40 years	6 (32)	12 (29)	20 (40)	NS	NS	NS	NS
≥ 40 years	13 (68)	30 (71)	30 (60)				
CA 125 median (U/mL, range)	20.1 (4–726)	24 (1–298)	57 (5–2779)	NS	$P = 0.0013$	$P = 0.0041$	$P < 0.001$
Bilaterality (*n* (%))	1 (5)	1 (2)	12 (24)	NS	$P = 0.0027$	NS	$P = 0.0045$
Ascites (*n* (%))	4 (21)	14 (33)	18 (36)	NS	NS	NS	NS
Stage I (*n* (%))	19 (100)	42 (100)	39 (78)	—	—	—	—
Stage II–III (*n* (%))	—	—	11 (22)	—	—	—	—

The two patients with borderline endometrioid tumor are not included in the table. MBOT, mucinous borderline ovarian tumor; NS, not significant; SBOT, serous borderline ovarian tumor.

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Table 2 Gray-scale sonographic characteristics of the study population according to the histopathological classification of the tumors

Histotype	*Endocervical-type MBOT*	*Intestinal-type MBOT*	*SBOT*	*Intestinal-type MBOT vs. endocervical-type MBOT*	*Intestinal-type MBOT vs. SBOT*	*Endocervical-type MBOT vs. SBOT*	*Difference among all three groups (Kruskal–Wallis test or Fisher's exact test)*
Patients (*n*)	19	42	50				
Morphology (*n* (%))							
Unilocular	1 (5)	1 (2)	2 (4)	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$
Unilocular-solid	9 (48)	—	21 (42)				
Multilocular	4 (21)	23 (55)	3 (6)				
Multilocular-solid	5 (26)	18 (43)	19 (38)				
Solid	—	—	5 (10)				
Median maximum diameter (mm, range)	106 (16–340)	186 (63–356)	78 (18–300)	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$
Presence of papilla (*n* (%))	14 (74)	15 (36)	41 (82)	$P = 0.0117$	$P < 0.001$	NS	$P < 0.001$
Median number of locules	1	10	1	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$
Cysts with > 10 locules (*n* (%))	4 (21)	33 (79)	2 (4)	$P < 0.001$	$P < 0.001$	$P = 0.0447$	$P < 0.001$

The two patients with borderline endometrioid tumor are not included in the table. MBOT, mucinous borderline ovarian tumor; NS, not significant; SBOT, serous borderline ovarian tumor.

Table 3 Color Doppler sonographic characteristics of the study population according to the histopathological classification of the tumors

Histotype	*Endocervical-type MBOT*	*Intestinal-type MBOT*	*SBOT*	*Intestinal-type MBOT vs. endocervical-type MBOT*	*Intestinal-type MBOT vs. SBOT*	*Endocervical-type MBOT vs. SBOT*	*Difference among all three groups (Kruskal–Wallis test or Fisher's exact test)*
Patients (*n*)	19	42	50				
Flow in papilla (*n* (%))	11 (79)	8 (53)	33 (80)	$P = 0.0061$	$P < 0.001$	NS	$P < 0.001$
Color score							
Mean	2.3	2.4	2.3	NS	NS	NS	NS
1 (*n* (%))	3 (16)	6 (14)	7 (14)				
2 (*n* (%))	9 (48)	17 (40)	26 (52)				
3 (*n* (%))	5 (26)	15 (36)	12 (24)				
4 (*n* (%))	2 (10)	4 (10)	5 (10)				
PI (median (range))	0.61 (0.35–1.45)	0.73 (0.44–1.66)	0.64 (0.33–1.92)	NS	NS	NS	NS
RI (median (range))	0.47 (0.28–0.76)	0.44 (0.29–0.79)	0.45 (0.27–0.83)	NS	NS	NS	NS
PSV (cm/s, median (range))	16.8 (5–59)	20.3 (2.1–61)	19.95 (6.8–75)	NS	NS	NS	NS
TAMXV (cm/s, median (range))	12.4 (3–44.3)	15 (1.6–51)	13.25 (5–50.9)	NS	NS	NS	NS

The two patients with borderline endometrioid tumor are not included in the table. MBOT, mucinous borderline ovarian tumor; NS, not significant; PI, pulsatility index; PSV, peak systolic velocity; RI, resistance index; SBOT, serous borderline ovarian tumor; TAMXV, time-averaged maximum velocity.

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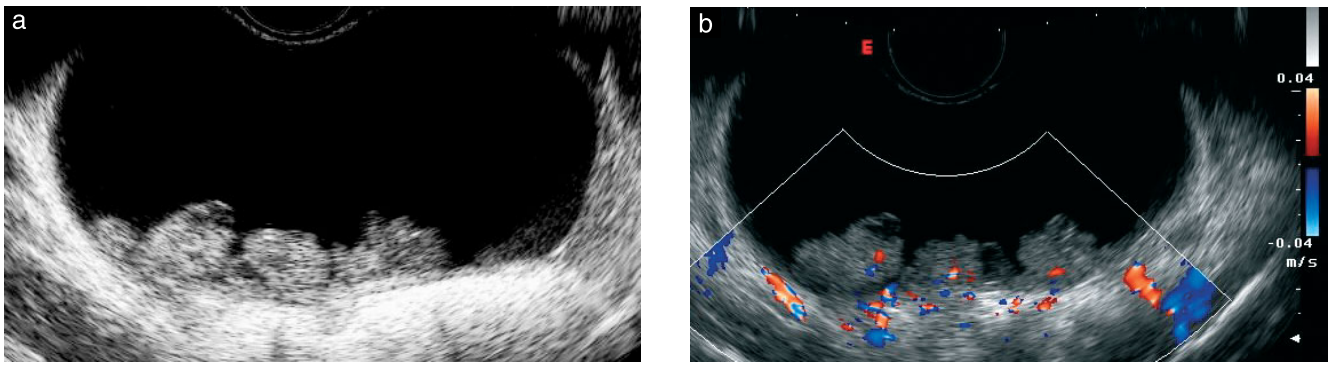


Figure 1 Gray-scale (a) and color Doppler (b) ultrasound features of a serous borderline ovarian tumor (SBOT).

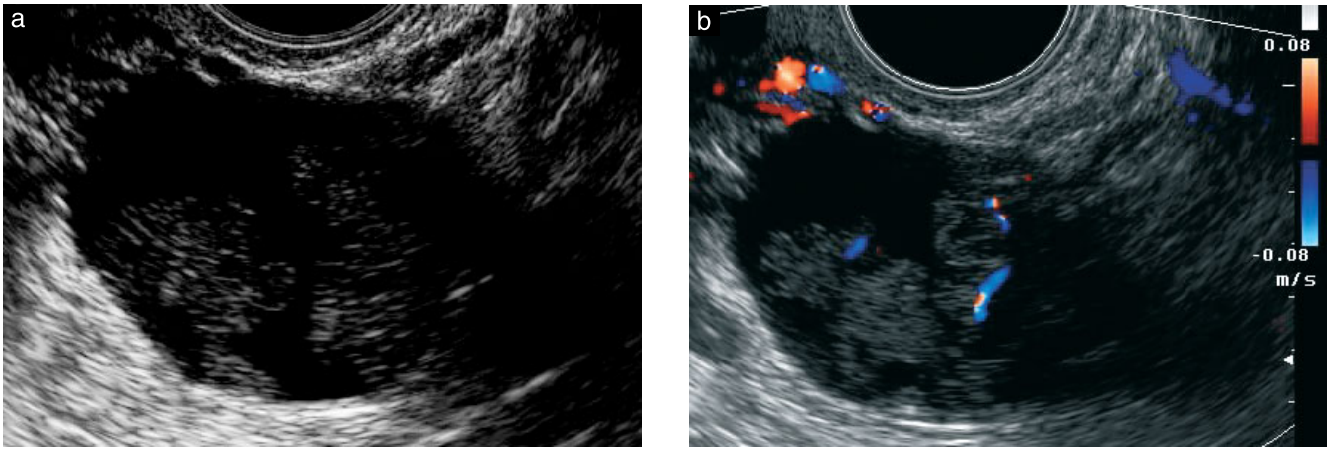


Figure 2 Gray-scale (a) and color Doppler (b) ultrasound features of an endocervical-type mucinous borderline ovarian tumor (MBOT).

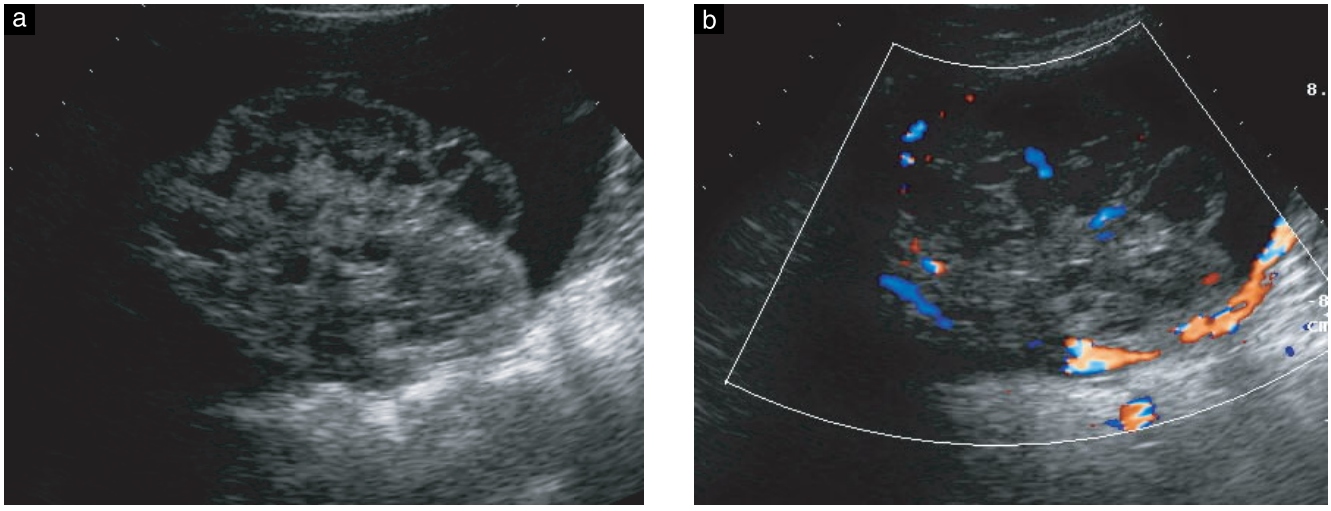


Figure 3 Gray-scale (a) and color Doppler (b) ultrasound features of an intestinal-type mucinous borderline ovarian tumor (MBOT).

The issue of discrimination between ovarian neoplasms with different degrees of malignancy has already been addressed: Gotlieb *et al.*[13] analyzed retrospectively 91 cases of BOT and described the different gray-scale and color Doppler ultrasound characteristics of MBOTs and SBOTs. SBOTs were found to be significantly smaller than MBOTs, were multilocular in 30% of cases and presented with solid parts or papillary pattern in the majority of cases (78%), while MBOTs were multilocular in 50% of cases and presented with solid parts or papillary pattern in only 40% of cases. Moreover, the RI at color Doppler examination was < 0.4 in 30% of mucinous and 50% of serous borderline neoplasms. Exacoustos *et al.*[6] recently compared SBOTs and MBOTs and found no significantly different sonographic parameters. It must be noted that in both studies MBOTs were

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considered all together without distinguishing endocervical and intestinal types. This could explain the lack of significant sonographic differences.

Our current study found SBOTs and endocervical-type MBOTs to have similar sonographic features. Compared with the intestinal-type MBOTs, these tumors were characterized by a smaller maximum diameter, fewer locules (they were usually unilocular-solid lesions), a higher number of papillary excrescences within the lesions and a higher rate of vessels inside the papillations. This is in agreement with data from the pathology literature that report that endocervical-type MBOTs resemble SBOTs architecturally[22].

The sonographic characteristics of intestinal-type MBOTs in our series were in agreement with the pathological descriptions of these tumors reported by Ronnett *et al.*[25]: unilateral, large, multicystic tumor with a smooth capsule. In comparison with other BOTs, intestinal-type MBOTs were characterized by a larger diameter and a multilocular aspect, with hyperechoic tissue connecting the multiple locules and no clear definition of solid tissue or papillary projection.

This preoperative information is important, since neither serum tumor marker nor frozen section are particularly accurate in the diagnosis of borderline tumors. According to the data of Milojkovic *et al.*[26] we observed that the serum CA 125 level was elevated (> 35 U/mL) in only 43% of the patients with BOT (59% in the SBOT group, 21% in the MBOT endocervical-type group and 34% in the MBOT intestinal-type group).

This study did not compare benign vs. borderline and vs. malignant ovarian tumors; the clinical importance of the description of the different subtypes of BOT could be questionable. However, it must be underlined that intestinal-type tumors are characterized by specific pathological findings and a very good prognosis[25].

In conclusion, this is the first study to describe sonographic characteristics that discriminate between SBOTs and endocervical- and intestinal-type MBOTs. In particular, we report that endocervical MBOT more closely resembles SBOT than it does intestinal MBOT, which is a commonly accepted finding in human pathology. Whether this observation could have clinical implications for preoperative management deserves further attention.

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