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Imaging in gynecological disease (11): clinical and ultrasound features of mucinous ovarian tumors

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KEYWORDS: histology; mucinous; multilocular cyst; ovarian tumor; ultrasound

ABSTRACT

Objective *To describe the clinical and ultrasound findings in patients with mucinous ovarian tumors.*

Methods *In this retrospective study, women with a histological diagnosis of mucinous ovarian tumor who had undergone preoperative ultrasound examination were identified from the database of a single ultrasound center. The histological examination was performed by the same pathologist in all cases, and the ultrasound appearance of the tumors was described using the terms and definitions of the International Ovarian Tumor Analysis group.*

Results *We identified 123 women with a histological diagnosis of mucinous ovarian tumor, of whom 57 (46%) had benign cystadenoma, 34 (28%) had gastrointestinal (GI)-type borderline tumor, 10 (8%) had endocervical-type borderline tumor and 22 (18%) had GI-type invasive carcinoma. On ultrasound examination, 65% (37/57) of cystadenomas were multilocular, of which 59% had ≤ 10 locules, and 79% (27/34) of GI-type borderline tumors were multilocular, of which 89% had > 10 locules. Conversely, 60% (6/10) of endocervical-type borderline tumors had papillations. Eighty-two percent (18/22) of invasive masses contained solid components and 55% (12/22) were multilocular-solid cysts. Bilateral mucinous cystadenomas were found in two women (4% of women with benign tumors) and bilateral borderline tumors of endocervical type in two women (20% of women with borderline tumors of endocervical type). No woman had a bilateral GI-type borderline tumor or a bilateral invasive tumor.*

Conclusions *A multilocular cyst with 2–10 locules is representative of a benign cystadenoma, whereas a multilocular cyst with > 10 locules is indicative of a GI-type borderline tumor. Most invasive tumors of mucinous GI-type contain solid components, the most typical ultrasound appearance being that of a multilocular-solid tumor. Papillary projections are typical features of endocervical-type borderline tumors.* *Copyright © 2016 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Aim

The aim of this study was to provide a systematic overview of the sonographic characteristics of the different types of mucinous ovarian tumors.

Background

Epidemiology

Mucinous ovarian tumors denote a spectrum of neoplastic disorders, including benign mucinous cystadenoma (MC), mucinous borderline ovarian tumor (MBOT) and invasive mucinous epithelial ovarian carcinoma (MEOC). These tumors are distinct from other histological subtypes of epithelial ovarian neoplasms from a clinical, histological and molecular standpoint[1]. MCs account for approximately 10–15% of benign ovarian neoplasms and 80% of all primary mucinous ovarian tumors[2,3]. MBOTs comprise 30–50% of borderline tumors and are more common than their invasive counterparts[4]. MEOCs are less frequent, comprising 3% of all malignant epithelial tumors[5].

Microscopy

Mucinous tumors can be composed of gastrointestinal (GI)- or endocervical-type mucinous epithelium. MCs

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are a collection of glands and cysts, lined by epithelium resembling gastric foveolar-type or intestinal epithelium containing goblet cells (GI-type)[6] or by a single layer of cylindrical epithelium (endocervical-type)[7], and atypia is absent. The histological features that distinguish borderline ovarian tumors from their benign counterparts are those of epithelial proliferation and the varying degree of nuclear atypia[8]. Except for the microinvasive variety, these tumors do not exhibit stromal invasion, and a cystadenoma can be defined as borderline when the proportion of abnormal proliferative foci constitutes at least 10% of the tumor, otherwise it is called MC with focal atypia[8] (focal atypia is of no clinical relevance). The architecture of endocervical-type MBOTs is characterized by both large, bulbous papillae and smaller papillae with prominent cellular budding. The papillae are lined with slightly or moderately atypical cells. The criteria for the diagnosis of GI-type MBOTs include the following elements: tumors contain cystic spaces lined by GI-type mucinous epithelium with stratification and may form filiform papillae with stromal support; nuclei are slightly larger than those seen in cystadenomas; mitotic activity is present; goblet cells and sometimes Paneth cells are present; and stromal invasion is absent[9]. The diagnosis of invasive MEOCs requires stromal invasion measuring $>10\,mm^2$ in area and at least 3 mm in depth[10]. The vast majority of MEOCs are GI-type. Two different patterns of stromal invasion can be recognized in GI-type adenocarcinoma, according to the classification of Lee and Scully[10]: (1) confluent or expansile pattern, exhibiting confluent or complex malignant glands, with or without minimal intervening stroma and exceeding $10\,mm^2$ in area; (2) infiltrative or destructive pattern, which is characterized by obvious stromal invasion in the form of glands, cell clusters or individual cells, infiltrating the stroma in a disorderly manner and frequently associated with a desmoplastic stromal reaction[11]. The endocervical-type carcinomas are generally papillary and display epithelial stratification closely resembling serous tumors. The most common pattern of invasion is cribriform and confluent[12].

Macroscopy

GI-type MCs are unilocular or multilocular tumors of variable size, ranging from a few to over 30 cm[13]. They are often unilateral, the capsula is thick and white with a smooth outer surface and the mucinous cyst contains gelatinous material. Endocervical-type MCs typically present as a unilocular cyst with a smooth surface and inner lining. They occasionally have a solid component with a white homogeneous cut surface[7]. GI-type MBOTs present as large and multicystic masses. Typically, they have thin walls and contain thick to watery mucinous fluid. In contrast to GI-type MBOTs, endocervical-type MBOTs are smaller and contain fewer locules. They often contain papillae or solid areas which may be soft and mucoid[14]. GI-type MEOCs form large, typically unilateral, complex, solid and cystic masses. In one series, endocervical-type MEOCs were described as unilocular or multilocular with solid areas[12]. Papillary excrescences were present on the inner lining of the cysts and on the surface. The mean tumor size was 12 cm, and over half of the tumors were bilateral.

Clinical features and prognosis

MCs occur most commonly in women aged 20–40 years, but occurrence in adolescent and even in premenarchal girls, as well as in postmenopausal patients, has been documented[1]. They are unilateral in 95% of cases[6]. Although benign, recurrence may be seen in cases treated with cystectomy[15]. GI-type MBOTs occur across a wide age range, from 18–88 years, with a mean age of 40–49 years[4,6,10,16]. Patients most often present with an abdominal mass that is nearly always unilateral and confined to the ovary, although some bilateral cases have been reported[6]. The prognosis is excellent and only a few cases of progression to carcinoma have been described[6]. There have been no well-documented cases of GI-type MBOTs associated with peritoneal implants[6]. The average age of patients with an endocervical-type MBOT is 33–34 years[7]. Typically, women with an endocervical-type MBOT present with non-specific signs and symptoms related to an adnexal mass. Most patients are in an early stage, but a minority of cases are in an advanced stage of disease in the form of implants and/or lymph-node involvement. These tumors are associated with a good outcome even in the presence of peritoneal implants[7]. The mean age at presentation of both GI-type and endocervical-type MEOCs is 45 years, and patients typically present with abdominal swelling or pain[7]. The majority of GI-type MEOCs present as an expansile pattern, while the infiltrative pattern is rarer. Those of the expansile type are confined mainly to one ovary (Stage I) at presentation and patients have an excellent prognosis[1,17,18]. Infiltrative MEOC is frequently associated with lymph-node metastasis and has a worse prognosis[19]. Endocervical-type MEOCs are quite uncommon, therefore few data on their prognosis are available. The outcome appears to be favorable for women with Stage-I disease, and only half of the patients with advanced disease have a poor prognosis[12].

METHODS

This was a retrospective study designed at the Department of Gynecological Oncology, Policlinico Gemelli, Rome, Italy. From the ultrasound database, 123 consecutive women with a histological diagnosis of mucinous ovarian tumor who had undergone preoperative ultrasound examination between February 2010 and January 2016 were identified. The histological examination was performed by the same pathologist in all cases. All ultrasound examiners had more than 10 years' experience in gynecological ultrasound. Sixty-four (52%) of these women

had been included in the International Ovarian Tumor Analysis (IOTA) studies[20,21] and so had been examined using a standardized technique[22] and following a strict research protocol with predefined clinical and ultrasound information collected prospectively. The remaining 59 (48%) women had undergone ultrasound examination in a standardized manner, and the IOTA terminology was used to describe the ultrasound images of the adnexal masses. For women who had been examined outside the IOTA protocol and for women with missing ultrasound information in the IOTA database (i.e. honeycomb nodule)[23], one author (F.M.), blinded to the histological findings and with more than 10 years' experience in gynecological ultrasound, retrospectively reviewed stored ultrasound images and reports, and described the adnexal masses on the basis of this information using the IOTA terminology[22]. Clinical parameters, including age, body mass index (BMI), parity, postmenopausal status, current hormonal therapy, family and personal history of breast or ovarian cancer, CA 125 and CA 19.9 data, were collected retrospectively from patient records for women not included in the IOTA studies. For women who had been included in the IOTA studies, clinical parameters, including age, postmenopausal status, current hormonal therapy, family and personal history of ovarian cancer and CA 125 data, were collected prospectively, whereas personal and family history of breast cancer, parity, BMI and CA 19.9 data were collected retrospectively from patient records.

All women were examined with transvaginal and transabdominal ultrasound to ensure complete examination of the entire abdominal cavity. All ultrasound examinations were carried out using high-end ultrasound equipment, the frequency of the vaginal probes varying between 5.0 and 9.0 MHz and that of the abdominal probes between 3.5 and 5.0 MHz.

In the case of bilateral masses, if the tumor was mucinous on one side and non-mucinous on the other, the mucinous tumor was included in the analysis, and if the tumor was benign mucinous on one side and MBOT (or invasive) on the other, the MBOT (or invasive tumor) was included in the analysis. Moreover, if both masses presented the same histology (both were benign, borderline or malignant), data from the mass with the more complex ultrasound morphology or, in the case of similar morphology, from the larger mass, were used for analysis.

The masses were described using the terms and definitions of the IOTA group[22], including size and characteristics of the lesions. The presence of ascites and fluid in the pouch of Douglas was also reported. Solid papillary projections were defined as any solid projection into the cystic cavity of the mass arising from the cyst wall or septum with a height ≥ 3 mm. The largest solid component other than a papillary projection was also measured. In some cases, a solid papillary projection was the largest solid component. If this was the case, the papillary projection was recorded and measured both as a papillary projection and as the largest solid component of the mass. The presence of a multilocular nodule (honeycomb nodule) was also reported, as described previously[23]. The ovarian crescent sign was defined as visible hypoechoic tissue, with or without ovarian follicle, located adjacent to the cyst wall[24].

Ovarian masses were also assessed by color Doppler examination, with results reported in terms of a color score. A color score of 1 means that no color or power Doppler signals are detected in the tumor, a score of 2 that a minimal amount of color Doppler signals is detected, a score of 3 that a moderate amount is detected and a score of 4 that abundant color is detected.

In addition to presenting the results using IOTA terminology, the tumor pattern recognition method was used prospectively to differentiate between benign, borderline and invasive ovarian tumors. The specific diagnosis suggested by the original ultrasound examiner (i.e. benign MC, GI-type MBOT, endocervical-type MBOT, GI-type invasive MEOC) was also recorded. Ovarian malignancies were staged according to the International Federation of Gynecology and Obstetrics (FIGO) classification[25,26]. All clinical and ultrasound information was entered into a dedicated Excel spreadsheet for statistical analysis (Microsoft Office Excel 2007, Redmond, WA, USA).

RESULTS

One hundred and twenty-three women had a final diagnosis of mucinous ovarian tumor on histological examination. A benign MC was diagnosed in 57 (46%) women, endocervical-type MBOT in 10 (8%), GI-type MBOT in 34 (28%) and invasive MEOC in 22 (18%). All cases of invasive MEOC were of GI-type with an expansile pattern. Median age of the 123 women was 50 (range, 19–82) years and 61 (50%) women were premenopausal. Demographic data of the patients, clinical parameters, FIGO staging and surgery procedures are shown in Table 1.

Results of serum CA 125 measurements at diagnosis were available for 101 patients, of whom 64 (63%) had values < 35 U/mL: 39/44 (89%) benign cases, 13/28 (46%) GI-type MBOTs, 5/10 (50%) endocervical-type MBOTs and 7/19 (37%) malignant cases. Results of serum CA 19.9 measurements at diagnosis were available for 77 patients, of whom 52 (68%) had values < 37 U/mL: 28/33 (85%) benign cases, 8/18 (44%) GI-type MBOTs, 6/8 (75%) endocervical-type MBOTs and 10/18 (56%) malignant cases. All borderline cases that were staged according to FIGO were Stage I. Similarly, all, except one, invasive tumors were Stage I (Table 1).

Conservative surgery was performed in 25/28 (89%) premenopausal patients with a benign mass, 13/16 (81%) premenopausal patients with a GI-type MBOT, 7/8 (88%) premenopausal women with an endocervical-type MBOT and 4/9 (44%) premenopausal patients with invasive ovarian cancer (Table 1).

The sonographic characteristics of the mucinous ovarian tumors according to histological type and

Table 1 Clinical characteristics of 123 women with histological diagnosis of mucinous ovarian tumor

	Type of tumor				
Characteristic	*Benign (n = 57)*	*Endocervical borderline (n = 10)*	*Gastrointestinal borderline (n = 34)*	*Malignant (n = 22)*	*All (n = 123)*
Age at diagnosis (years)	50 (19–81)	39 (30–77)	50 (22–82)	53 (24–79)	50 (19–82)
BMI (kg/m^2)*	24.5 (19–43)	24.5 (16–30)	24 (18–46)	24.5 (17–46)	24 (16–46)
Nulliparous	15 (26)	2 (20)	13 (38)	7 (32)	37 (30)
Current hormonal therapy†	2 (4)	0 (0)	0 (0)	1 (5)	3 (2)
At least one first-degree relative with ovarian cancer	0 (0)	1 (10)	0 (0)	1 (5)	2 (2)
At least one first-degree relative with breast cancer	4 (7)	0 (0)	2 (6)	2 (9)	8 (7)
Personal history of ovarian cancer	0 (0)	0 (0)	1 (3)	0 (0)	1 (1)
Personal history of breast cancer	4 (7)	2 (20)	2 (6)	1 (5)	9 (7)
CA 125 at diagnosis (U/mL)‡	15.5 (3–125)	21.8 (10–189)	39.5 (4.4–476)	42 (4–664)	19 (3–664)
CA 19.9 at diagnosis (U/mL)§	9 (0.4–359.2)	10 (0.8–37.2)	35.7 (2.5–843)	16.7 (1.3–700 000)	10.9 (0.4–700 000)
Surgical treatment					
Conservative					
Unilateral cystectomy	7 (12)	2 (20)	3 (9)	0 (0)	12 (10)
Bilateral cystectomy	0 (0)	1 (10)	0 (0)	0 (0)	1 (1)
Unilateral oophorectomy	16 (28)	4 (40)	10 (29)	4 (18)¶	34 (28)
Unilateral oophorectomy and contralateral cystectomy	2 (4)	0 (0)	0 (0)	0 (0)	2 (2)
Non-conservative					
Bilateral oophorectomy	21 (37)	0 (0)	2 (6)	0 (0)	23 (19)
Bilateral oophorectomy and hysterectomy	11 (19)	3 (30)	19 (56)	18 (82)	51 (41)
FIGO stage					
I	0 (0)	10 (100)	33 (97)	21 (95)	64 (52)
II	0 (0)	0 (0)	0 (0)	1 (5)	1 (1)
Not described	57 (100)	0 (0)	1 (3)	0 (0)	58 (47)

Data are given as median (range) or *n* (%). Data available for: *88 cases; †117 cases; ‡101 cases; §77 cases. ¶Underwent unilateral salpingo-oophorectomy with conservation of uterus and contralateral ovary. Surgery also included appendicectomy, omentectomy and peritoneal biopsy. BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics[25,26].

the diagnosis suggested by the original ultrasound examiner and the presumed histological diagnosis are summarized in Table 2. The median maximum diameter of all tumors was 144 (range, 20–387) mm. Most benign MCs were multilocular with 2–10 locules (Figure 1). Most GI-type MBOTs were multilocular with > 10 locules (Figure 2). Most endocervical-type MBOTs were multilocular-solid or unilocular solid cysts with papillary projections (Figure 3). Most invasive MEOCs contained solid components, the most common ultrasound appearance being that of a multilocular-solid tumor (Figure 4 and Videoclip S1). Most mucinous tumors were vascularized on color Doppler examination: 52% of benign lesions, 82% of GI-type MBOTs, 100% of endocervical-type MBOTs and 95% of invasive carcinomas.

On ultrasound examination, bilateral masses were described for two (4%) benign tumors, two (20%) endocervical-type MBOTs and two (9%) invasive malignant tumors. Both cases of bilateral benign tumor had a histological diagnosis of bilateral MC, and both cases of bilateral MBOT had a histological diagnosis of bilateral endocervical-type MBOT. Conversely, both cases of invasive malignant tumor suspected of being bilateral tumors on ultrasound examination had a histological diagnosis of unilateral carcinoma, and histology of the contralateral mass was a benign cystadenoma in one case and functional cyst in the other.

Using pattern recognition, the ultrasound examiner classified correctly 39 (68%) cystadenomas as benign lesions, seven (70%) of the endocervical-type MBOTs and 12 (35%) GI-type MBOTs as borderline lesions and 16 (73%) carcinomas as malignant tumors.

DISCUSSION

Our study describes the ultrasound features of different types of ovarian mucinous tumors. A multilocular cyst with 2–10 locules is a typical characteristic of a MC, whereas a multilocular cyst with > 10 locules and a honeycomb nodule is suggestive of a GI-type MBOT. A multilocular-solid cyst is a typical feature of an invasive MEOC, while papillary projection is a typical ultrasound feature of endocervical-type MBOTs.

The strength of our study is the large series examined in a single center in which the histological

Table 2 Sonographic characteristics as described using International Ovarian Tumor Analysis group terminology in 123 women with histological diagnosis of mucinous ovarian tumor and diagnosis suggested by original ultrasound examiner

	Type of tumor				
Parameter	*Benign* (n = *57*)	*Endocervical borderline* (n = *10*)	*Gastrointestinal borderline* (n = *34*)	*Malignant* (n = *22*)	*All* (n = *123*)
Maximum diameter of lesion (mm)	112.5 (31–301)	37 (20–154)	195 (32–387)	197 (49–300)	144 (20–387)
Type of tumor					
Unilocular	10 (18)	1 (10)	5 (15)	0 (0)	16 (13)
Unilocular-solid	1 (2)	4 (40)	0 (0)	2 (9)	7 (6)
Multilocular	37 (65)	0 (0)	27 (79)	4 (18)	68 (55)
Multilocular-solid	9 (16)	5 (50)	2 (6)	12 (55)	28 (23)
Solid	0 (0)	0 (0)	0 (0)	4 (18)	4 (3)
Number of locules in multilocular mass					
2–10	22/37 (59)	0 (0)	3/27 (11)	0/4 (0)	25/68 (37)
> 10	15/37 (41)	0 (0)	24/27 (89)	4/4 (100)	43/68 (63)
Number of locules in multilocular-solid mass					
2–10	4/9 (44)	5/5 (100)	1/2 (50)	4/12 (33)	14/28 (50)
> 10	5/9 (56)	0/5 (0)	1/2 (50)	8/12 (67)	14/28 (50)
Echogenicity of cyst fluid					
Anechoic	11 (19)	0 (0)	3 (9)	1 (5)	15 (12)
Low-level	41 (72)	4 (40)	30 (88)	16 (73)	91 (74)
Ground-glass	3 (5)	5 (50)	0 (0)	1 (5)	9 (7)
Mixed	2 (4)	1 (10)	1 (3)	3 (14)	7 (6)
No cyst fluid	0 (0)	0 (0)	0 (0)	1 (5)	1 (1)
Presence of honeycomb nodule	4 (7)	0 (0)	9 (26)	0 (0)	13 (11)
Presence of solid component	10 (18)	9 (90)	2 (6)	18 (82)	39 (32)
Largest solid component (mm)	17.5 (6–176)	26 (7–116)	64.5 (46–83)	72 (16–250)	46 (6–250)
Presence of papillary projection	1 (2)	6 (60)	0 (0)	1 (5)	8 (7)
Irregular papillary projection	1/1 (100)	6/6 (100)	0 (0)	1/1 (100)	8/8 (100)
Number of papillary projections					
1	1/1 (100)	4/6 (67)	0 (0)	0/1 (0)	5/8 (63)
2	0/1 (0)	0/6 (0)	0 (0)	0/1 (0)	0/8 (0)
≥ 3	0/1 (0)	2/6 (33)	0 (0)	1/1 (100)	3/8 (38)
Height of largest papillary projection (mm)	7 (7–7)	21.5 (7–35)	0 (0)	12 (12–12)	14.5 (7–35)
Irregular internal cyst wall	12 (21)	9 (90)	12 (35)	17 (77)	50 (41)
Ovarian crescent sign present	12 (21)	5 (50)	2 (6)	1 (5)	20 (16)
Fluid in pouch of Douglas	7 (12)	5 (50)	10 (29)	7 (32)	29 (24)
Ascites	1 (2)	0 (0)	6 (18)	3 (14)	10 (8)
Color score					
1	27 (47)	0 (0)	6 (18)	1 (5)	34 (28)
2	23 (40)	6 (60)	22 (65)	6 (27)	57 (46)
3	7 (12)	4 (40)	5 (15)	13 (59)	29 (24)
4	0 (0)	0 (0)	1 (3)	2 (9)	3 (2)
Diagnosis on basis of subjective assessment					
Benign	39 (68)	0 (0)	8 (24)	1 (5)	48 (39)
Borderline	12 (21)	7 (70)	12 (35)	5 (23)	36 (29)
Invasive malignant	3 (5)	2 (20)	10 (29)	16 (73)	31 (25)
Uncertain	1 (2)	1 (10)	3 (9)	0 (0)	5 (4)
Not described	2 (4)	0 (0)	1 (3)	0 (0)	3 (2)
Presumed histological diagnosis					
Cystadenoma	22 (39)	0 (0)	7 (21)	1 (5)	30 (24)
Dermoid	1 (2)	0 (0)	0 (0)	0 (0)	1 (1)
Endometrioma	1 (2)	1 (10)	0 (0)	0 (0)	2 (2)
Simple cyst	1 (2)	0 (0)	1 (3)	0 (0)	2 (2)
Teratoma	1 (2)	0 (0)	0 (0)	0 (0)	1 (1)
Borderline malignant tumor	9 (16)	6 (60)	4 (12)	3 (14)	22 (18)
Gastrointestinal mucinous borderline tumor	3 (5)	0 (0)	8 (24)	2 (9)	13 (11)
Primary mucinous ovarian cancer	0 (0)	0 (0)	0 (0)	1 (5)	1 (1)
Primary ovarian cancer	3 (5)	2 (20)	4 (12)	7 (32)	16 (13)
Uncertain	0 (0)	1 (10)	0 (0)	0 (0)	1 (1)
Not described	16 (28)	0 (0)	10 (29)	8 (36)	34 (28)

Data are given as median (range), *n* (%) or *n*/*N* (%).

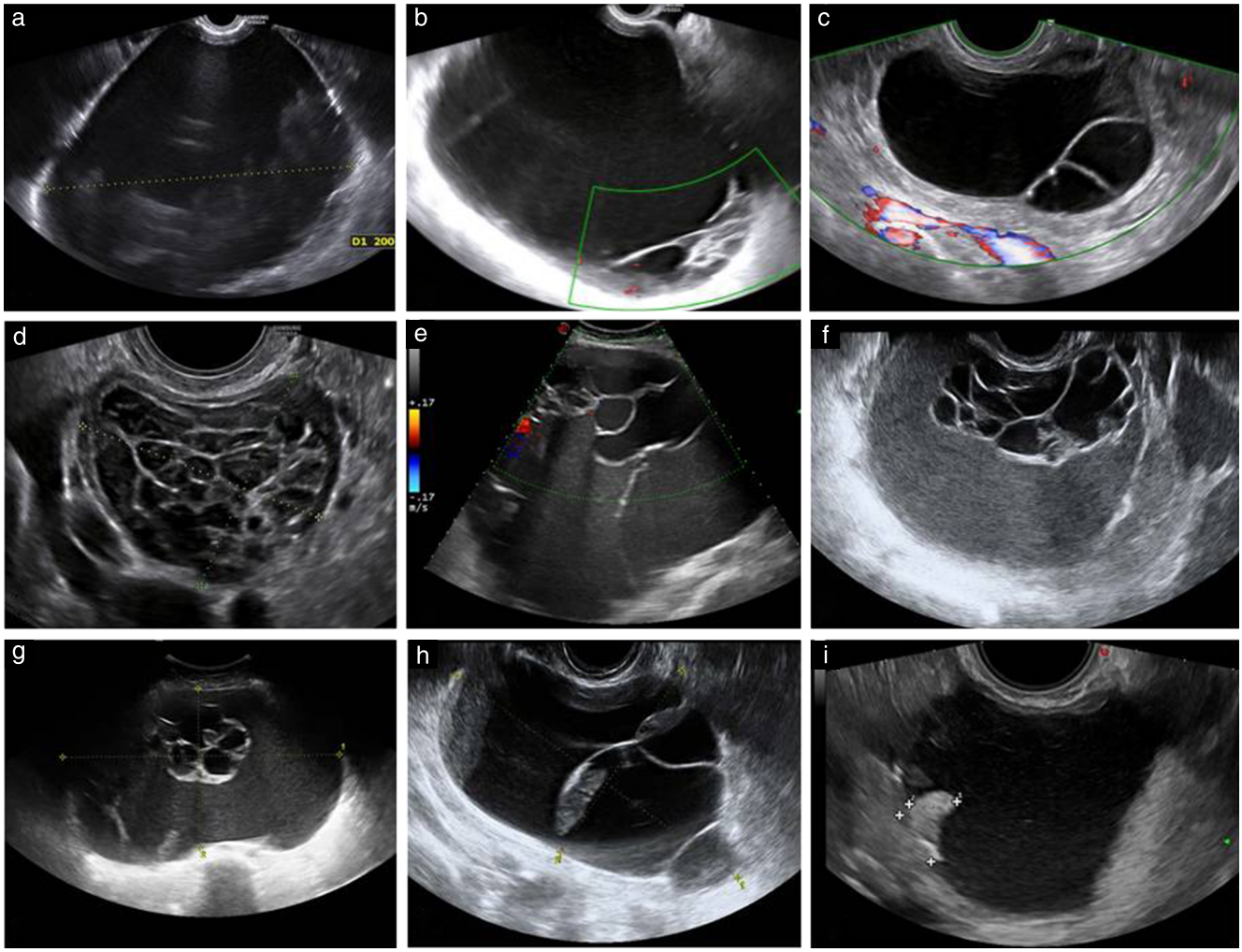

Figure 1 Ultrasound images of benign mucinous cystadenomas, presenting as unilocular (a), multilocular (b–g), multilocular-solid (h) or unilocular-solid (i) cysts, the majority being multilocular with 2–10 locules (b,c) or > 10 locules (d–g). Honeycomb nodule can sometimes be visualized (g). Lesions in (a–e) were diagnosed correctly by ultrasound examiner as benign, mass in (f) was misdiagnosed as borderline, masses in (g,h) were misdiagnosed as invasive and mass in (i) had uncertain diagnosis.

examination was performed by the same pathologist; a multicenter study could be biased, as pathological criteria may differ between centers[1,9,17]. Over the past few years, pathological classification of mucinous tumors has been an area of considerable debate among surgical pathologists[3,9]. The histological diagnosis *per se* represents a real challenge, as mucinous tumors are very large lesions and a mixture of benign, borderline and malignant elements is often found within an individual neoplasm. Consequently, a mucinous tumor requires careful gross examination with extensive sampling of the mass; one block per cm should be taken from tumors measuring ≤ 10 cm and two blocks per cm for larger neoplasms[3,27]. Another unresolved issue involves determination of the minimal criteria for distinction between a MBOT and an invasive MEOC[17].

The choice not to enroll in the study women with mucinous tumors from different institutions represents, at the same time, a limitation of the study, as it prevented us from accumulating data on a larger number of invasive carcinomas including, perhaps, cases of carcinomas with an infiltrative pattern. Another limitation is that some information had to be retrieved retrospectively from ultrasound images and patient records, and information collected retrospectively tends to be less reliable than information collected prospectively.

Ultrasound morphology of the MBOTs in our study is consistent with the results of our previous study[28]: unilocular-solid cyst with papillations is characteristic of endocervical-type MBOT and multilocular cyst without papillations is characteristic of GI-type MBOT. In a prospective study, Yazbek *et al.*[23] first described the honeycomb nodule as an ultrasound feature of GI-type MBOTs. In comparison with their data, the prevalence of a honeycomb nodule in GI-type MBOTs in our series was lower (26% *vs* 53.3%) and in benign MCs it was higher (7% *vs* 2.8%). These discrepancies could be related to the different pathological criteria used at the two institutions and also to the subjectivity of assessing whether or not there was a honeycomb nodule. In a retrospective study describing ultrasound features of ovarian masses, Exacoustos *et al.*[29] included 49 cases of mucinous tumor

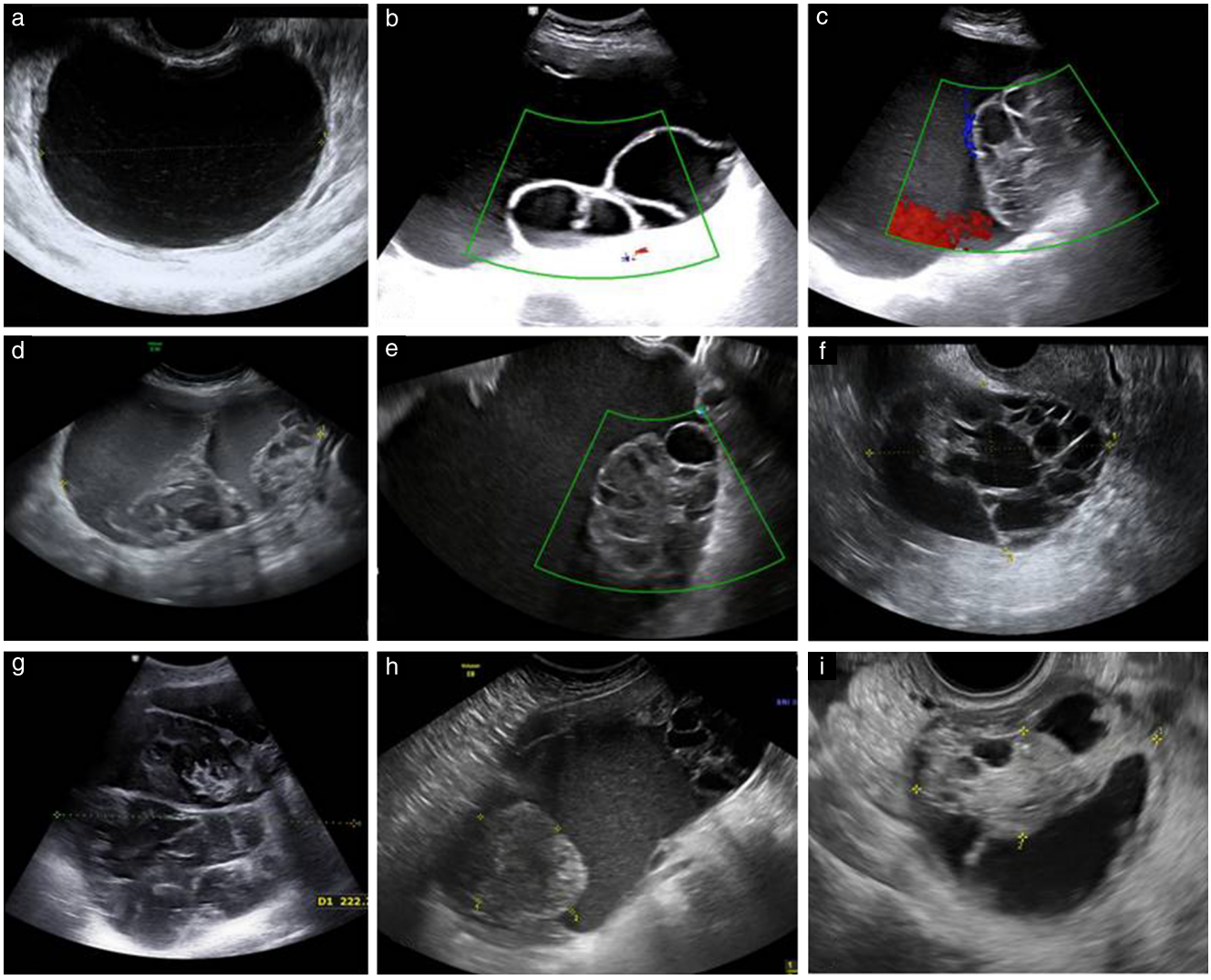

Figure 2 Ultrasound images of gastrointestinal-type borderline ovarian tumors, presenting as unilocular (a), multilocular (b–g) or multilocular-solid (h,i) cysts, the majority being multilocular cysts with > 10 locules (c–g), rather than 2–10 locules (b). Honeycomb nodule can often be visualized (c–e). Lesions in (c–e) were diagnosed correctly by ultrasound examiner as borderline, masses in (a,b) were misdiagnosed as benign and masses in (f–i) were misdiagnosed as invasive.

(27 benign, 15 borderline and seven invasive). In contrast to our results, they reported a higher prevalence of unilocular cysts (63%) in benign MCs and a lower prevalence of multilocular cysts (20%) in MBOTs. Of note, they reported a high prevalence (53.3%) of cysts with papillae among the MBOTs. A possible explanation for these differences in ultrasound appearance between the two studies could be the different indications for surgery in the two clinics (perhaps a higher proportion of unilocular cysts were surgically removed in the study of Exacoustos *et al.* than in ours). The lower prevalence of multilocular cysts among MBOTs observed by Exacoustos *et al.* is also probably due to the fact that they did not report results separately for endocervical- and GI-type MBOTs. To the best of our knowledge, the largest series of mucinous ovarian tumors was reported by Alcázar *et al.*[30] in a multicenter retrospective study. Similarly to our findings, they described most benign cases as multilocular cysts and most invasive carcinomas as multilocular-solid lesions. However, they reported a lower prevalence of multilocular cysts (39.4%) in MBOTs than that reported in our series. This discrepancy could be explained by a different distribution of GI and endocervical subtypes in the two series.

The ultrasound characteristics of mucinous tumors described in our study are in line with the macroscopic features reported in textbooks of pathology[6,7]; benign and GI-type MBOTs present as large multicystic masses, whereas endocervical-type MBOTs are smaller and contain fewer locules with papillae areas, and GI-type MEOCs are complex masses with cystic and solid components.

The opportunity to compare the ultrasound features of benign, borderline and malignant mucinous tumors has thus permitted us to explore the possible preoperative ultrasound differences of these three categories of tumor. Although a large number of benign, GI-type borderline and malignant tumors present with similar ultrasound

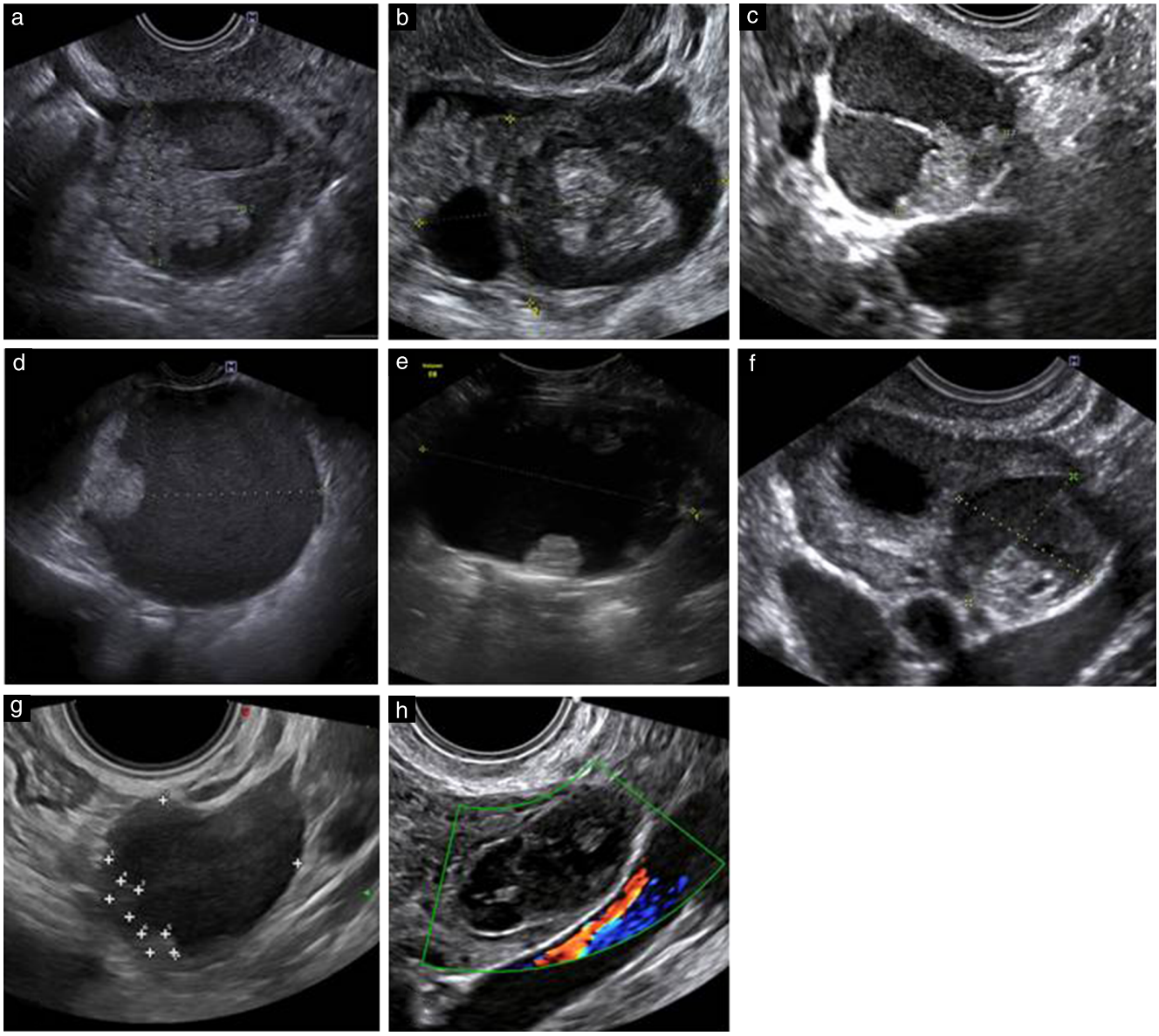

Figure 3 Ultrasound images of endocervical-type borderline ovarian tumors, presenting as multilocular-solid (a–d), unilocular-solid (e–g) or unilocular (h) cysts, the majority being multilocular-solid. Papillary projections are commonly noted (a,c–g). Lesions in (b–g) were diagnosed correctly by ultrasound examiner as borderline, mass in (a) was misdiagnosed as invasive and mass in (h) had uncertain diagnosis.

features, our results have highlighted some typical features that could be used for recognizing these tumors. The opportunity to distinguish preoperatively a GI-type MBOT from a GI-type MEOC on ultrasound examination is clinically important. For patients who wish to preserve their fertility, it is important to know not only if an ovarian lesion is benign or malignant, but also if it is borderline or invasive, as a borderline malignancy can be treated with conservative surgery in a gynecological cancer center[31]. The ability to recognize preoperatively an endocervical-type MBOT could also have clinical advantages. In fact, although the vast majority of GI-type MBOTs are Stage I with an overwhelmingly benign behavior[32], the less common endocervical-type present with implants (> Stage I) in a higher number of cases and recur more frequently than do the GI-type[12]. Endocervical-type MBOTs have morphological features and prognosis similar to those of serous borderline tumors[7].

In conclusion, our study suggests that preoperative ultrasound can be helpful in recognizing mucinous ovarian tumors; however, the overlapping ultrasound features among some benign, GI-type borderline and invasive masses often make the diagnosis of these three categories difficult. It would be desirable to perform a multicenter prospective study to gather data on a large number of invasive MEOCs, including endocervical- and GI-type carcinomas with an infiltrative pattern, after pathologists at the different centers involved have agreed on a common way to categorize these tumors. In particular, based on available evidence, it can be estimated that about 75 patients with a primary invasive MEOC should be included to have at least 10 patients with an endocervical-type pattern, which is known to be the least frequent form[19].

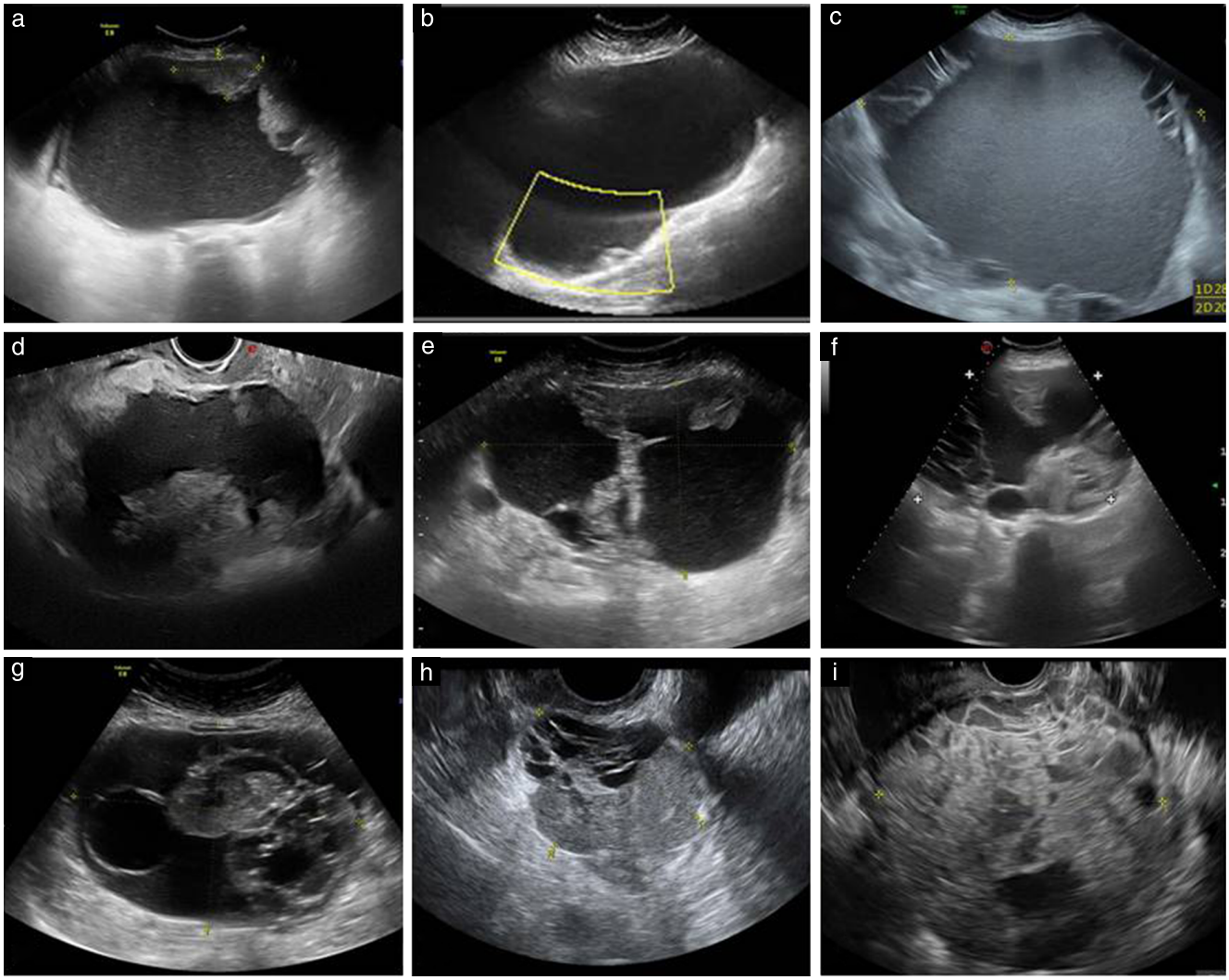

Figure 4 Ultrasound images of gastrointestinal-type invasive mucinous carcinomas, presenting as unilocular-solid (a,b), multilocular (c), multilocular-solid (d–g) or solid (h,i) cysts, the majority being multilocular-solid cysts with > 10 locules (f,g), rather than 2–10 locules (d,e). Lesions in (a,c–e,g–i) were diagnosed correctly by ultrasound examiner as invasive, mass in (f) was misdiagnosed as borderline and mass in (b) was misdiagnosed as benign.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Videoclip S1 Ultrasound assessment of 130-mm multilocular-solid ovarian tumor with more than 10 locules in 24-year-old patient. Final histological diagnosis was invasive mucinous tumor FIGO Stage I.