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Synchronous primary cancers of endometrium and ovary *vs* endometrial cancer with ovarian metastasis: an observational study

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KEYWORDS: endometrial neoplasm; ovarian neoplasms; primary neoplasm; ultrasonography

ABSTRACT

Objective *To compare the ultrasound characteristics of patients with synchronous primary cancers of the endometrium and ovary* vs *those of patients with endometrial cancer with ovarian metastasis.*

Methods *This was a single-institution retrospective observational study of patients with a histological diagnosis of endometrial cancer and an ovarian malignant mass, who had undergone preoperative ultrasound examination at our unit. Based on the histological diagnosis, patients were classified into two groups: those with synchronous primary cancers of the endometrium and ovary (synchronous group) and patients with endometrial cancer with ovarian metastasis (metastasis group). We compared the ultrasound features of ovarian malignant masses and of endometrial cancers between the two groups. Student's* t*-test, Mann–Whitney* U*-test,* χ^2 *test or Fisher's exact test were used for comparisons of variables between the two histological groups, as appropriate.*

Results *We identified 131 patients, of whom 51 had synchronous primary cancers of the endometrium and ovary (synchronous group) and 80 had endometrial cancer with ovarian metastasis (metastasis group). On ultrasound examination, ovarian masses in the synchronous group were more often multilocular-solid and less often bilateral than those in the metastasis group. With respect to the ultrasound features of the endometrial lesions, the median largest diameter was 29 (range, 11–118) mm in the synchronous group in comparison with 51.5 (range, 6–150) mm in the metastasis group (*$P < 0.0001$*). Endometrial lesions in the synchronous group presented more often with no myometrial infiltration and less often with a multiple-vessel pattern on color Doppler compared with the endometrial lesions in the metastasis group.*

Conclusions *Synchronous primary cancers of the endometrium and ovary have significantly different sonomorphological patterns compared with endometrial cancer with ovarian metastasis. Ovarian masses in women with synchronous primary cancers of the endometrium and ovary appeared as unilateral multilocular-solid or solid masses, whereas ovarian masses in women with endometrial cancer with ovarian metastasis were mostly bilateral solid masses. The different sonomorphology of these two cancers may facilitate their preoperative identification, helping the surgeon to determine optimum management for the patient. Copyright © 2019 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Endometrial cancer is the most common female pelvic malignancy in developed countries[1] and is usually diagnosed at an early stage (80% diagnosed at Stage I, with a 5-year survival rate > 95%)[1]. A concomitant diagnosis of an ovarian malignant mass is not a rare finding in patients with endometrial cancer, reported in 2–11% of these women[2,3]. Ovarian involvement may be interpreted as metastatic disease or as synchronous primary ovarian cancer, and the differential diagnosis often represents a clinical and histological challenge[4–6].

The differential diagnosis between synchronous endometrial and ovarian cancers and endometrial cancer with ovarian metastasis has prognostic and therapeutic implications. For example, Oranratanaphan *et al.* reported a 5-year overall survival rate of 92% in women

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with synchronous cancers of the endometrium and ovary *vs* 48% in those with endometrial cancer with ovarian metastasis[6]. In addition, patients with endometrial cancer with ovarian metastasis are eligible for a multimodality therapy, starting with radical surgery and followed by adjuvant platinum-based chemotherapy with radiotherapy[7,8]. On the other hand, most patients with synchronous primary cancers of the endometrium and ovary are at an early stage, requiring only surgical treatment[9].

To date, discrimination between these pathologies is possible only after surgery, by histopathological examination[10], using pathological criteria set by Ulbright and Roth[11] and later modified by Scully *et al.*[12].

Currently, transvaginal ultrasound is considered an excellent method to diagnose endometrial tumors and ovarian masses[13–16]. Although ultrasound features of ovarian metastasis from the gastrointestinal tract or breasts have been widely documented[17–20], the features of ovarian metastases from endometrial cancer have been poorly reported and very few data are available on ultrasound characteristics of ovarian malignant masses of synchronous primary cancers of the endometrium and ovary[21,22]. The ability to discriminate preoperatively between synchronous primary endometrial and ovarian cancers and endometrial cancer with ovarian metastasis might help the surgeon to counsel the patient and plan the best surgical treatment.

The aim of this study was to compare the ultrasound features of ovarian malignant masses between patients with synchronous primary cancers of the endometrium and ovary *vs* patients with endometrial cancer with ovarian metastasis. The ultrasound features of the endometrial tumors between the two groups of patients were also evaluated.

METHODS

This was a single-institution retrospective observational study performed at the tertiary referral center of gynecological oncology at Fondazione Policlinico Universitario A. Gemelli in Rome, Italy. From histological reports, we selected consecutive patients with endometrial cancer and a malignant ovarian mass, operated on between 2010 and 2018. We included only patients who had undergone a preoperative ultrasound examination at our unit. Patients who participated in the International Ovarian Tumor Analysis studies (IOTA Phase 1, 1b, 2, 3)[23–26] and/or in the International Endometrial Tumor Analysis (IETA) (Phase 4) protocol[16], as well as those investigated outside the IOTA and IETA studies, were included in the study. The study protocol was approved by the Institutional Board.

All patients had been examined preoperatively using transvaginal ultrasound (supplemented with a transabdominal scan, if necessary) using a standardized examination technique[27]. All ultrasound examiners had more than 10 years' experience in gynecological ultrasound, and the ultrasound examinations were carried out using mainly high-end ultrasound equipment. The frequency of the vaginal probes varied between 5.0 and 9.0 MHz and that of the abdominal probes between 3.5 and 5.0 MHz.

Clinical and ultrasound data were obtained from the IOTA and IETA databases and, for information not included in the IOTA or IETA protocols, from clinical reports. For patients not included in the IOTA and/or IETA studies, clinical data were acquired from patient records and ultrasound parameters were acquired from the original reports, which routinely include parameters reported according to the IOTA and IETA terminology[27,28].

Demographic data (age at diagnosis, body mass index, parity and pre/postmenopausal status), related medical history (previous unilateral salpingo-oophorectomy and history of breast cancer or endometriosis) and symptoms such as abnormal vaginal bleeding, abdominal pain or swelling, constipation and CA 125 and CA 19-9 values were evaluated. Final histology, tumor grade and FIGO (International Federation of Gynecology and Obstetrics) stage[29,30] were also recorded.

On ultrasound examination, ovarian masses were classified as unilocular, unilocular-solid, multilocular, mutlilocular-solid or solid, according to the IOTA consensus[27]. Papillary projections were defined as projections of solid tissue into the cystic cavity, arising from the cyst wall or from a septum, with a height of ≥ 3 mm. The largest solid component other than a papillary projection (i.e. a solid component not protruding into the cystic cavity) was also measured. In accordance with the IOTA consensus statement, if a papillary projection was the largest solid component of a mass, the papillary projection was recorded and measured both as a papillary projection and as the largest solid component[27]. The vascularization of the tumors on color Doppler was described using the IOTA color score[27]: no detectable blood flow (color score = 1), minimal blood flow (color score = 2), moderate

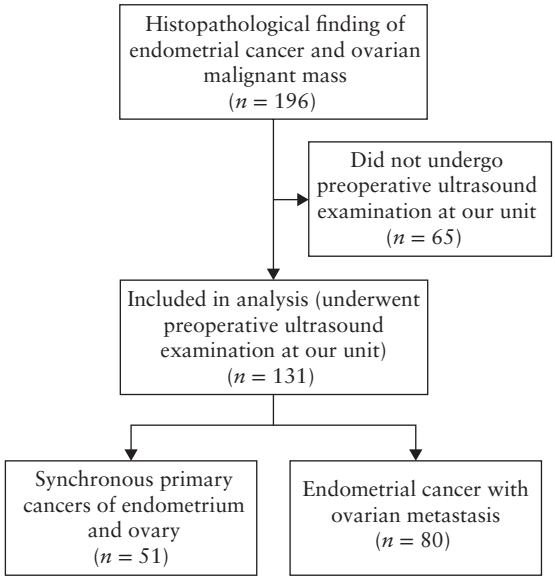

Figure 1 Flowchart of inclusion in study population of patients with endometrial cancer associated with ovarian malignant mass.

blood flow (color score = 3) or abundant blood flow (color score = 4). In case of bilateral adnexal masses, the mass with the most complex ultrasound morphology was used in the analysis. If both masses had similar ultrasound morphology, the largest mass or the one most easily accessible by ultrasound was included. The presence of ascites and fluid in the pouch of Douglas was noted. The specific diagnosis suggested by the original ultrasound examiner in the original ultrasound report was also recorded.

The endometrial lesion was described according to the IETA terminology[28]. The endometrial–myometrial junction was defined as either 'regular' or 'irregular'. The endometrial midline was defined as 'linear' if a straight hyperechogenic interface within the endometrium was visualized, as 'non-linear' if a wavy hyperechogenic interface was seen, and as 'not defined' in the absence of a distinct interface. Endometrial thickness was measured in the sagittal plane as the maximum anteroposterior diameter of the uterus and endometrium. When the intracavity lesion was visible, its three perpendicular diameters were measured in millimeters; however, only the largest diameter of the tumor was used in the analysis. The echogenicity of the endometrium was described as hyperechogenic, isoechogenic or hypoechogenic in comparison to the echogenicity of the myometrium. The echogenicity was defined as 'uniform' if the endometrium was homogeneous and as 'non-uniform' in cases in which the endometrium appeared heterogeneous, asymmetrical

Table 1 Clinical and tumor characteristics of 131 patients with endometrial cancer associated with ovarian malignant mass, overall and according to whether they were diagnosed with synchronous primary endometrial and ovarian cancers or endometrial cancer with ovarian metastasis

Characteristic	*All* (n = *131*)	*Synchronous endometrial and ovarian cancers* (n = *51*)	*Endometrial cancer metastatic to ovaries* (n = *80*)	P*
Age at diagnosis (years)	58.9 ± 11.7	57.7 ± 11.8	59.6 ± 11.7	0.35
BMI (kg/m^2)†	27.68 ± 6.97	26.78 ± 5.63	28.29 ± 7.72	0.38
Nulliparous	47/126 (37.3)	15/47 (31.9)	32/79 (40.5)	0.044
Premenopausal	41/131 (31.3)	18/51 (35.3)	23/80 (28.8)	0.43
History of breast cancer	5/129 (3.9)	0/49 (0)	5/80 (6.3)	0.074
History of endometriosis	15/130 (11.5)	11/50 (22.0)	4/80 (5.0)	0.0030
Unilateral oophorectomy	7/130 (5.4)	2/50 (4.0)	5/80 (6.3)	0.58
Asymptomatic	19/125 (15.2)	13/47 (27.7)	6/78 (7.7)	0.0030
Abnormal bleeding	74/125 (59.2)	20/47 (42.6)	54/78 (69.2)	0.0030
Abdominal pain	31/125 (24.8)	14/47 (29.8)	17/78 (21.8)	0.32
Constipation	6/125 (4.8)	2/47 (4.3)	4/78 (5.1)	0.83
Abdominal swelling	13/125 (10.4)	4/47 (8.5)	9/78 (11.5)	0.59
CA 125 serum level at diagnosis (U/mL)‡	524.4 ± 926.8	548.1 ± 868.0	504.9 ± 981.7	0.90
CA 19-9 serum level at diagnosis (U/mL)§	362.6 ± 1108.8	393.4 ± 769.0	340.0 ± 1315.2	0.46
FIGO stage of endometrial cancer				< 0.0001
I	43/129 (33.3)	43/51 (84.3)	0/78 (0)	
II	6/129 (4.7)	6/51 (11.8)	0/78 (0)	
III	52/129 (40.3)	2/51 (3.9)	50/78 (64.1)	
IV	28/129 (21.7)	0/51 (0)	28/78 (35.9)	
Histological type and grading of endometrial cancer				< 0.0001
Endometrioid Grade 1	15/131 (11.5)	13/51 (25.5)	2/80 (2.5)	
Endometrioid Grade 2	45/131 (34.4)	24/51 (47.1)	21/80 (26.3)	
Endometrioid Grade 3	30/131 (22.9)	6/51 (11.8)	24/80 (30.0)	
Non-endometrioid	41/131 (31.3)	8/51 (15.7)	33/80 (41.3)	
FIGO stage of ovarian cancer				—
I	29/51 (56.9)	29/51 (56.9)	—	
II	8/51 (15.7)	8/51 (15.7)	—	
III	14/51 (27.5)	14/51 (27.5)	—	
Histological type and grading of ovarian cancer				—
Endometrioid Grade 1	2/51 (3.9)	2/51 (3.9)	—	
Endometrioid Grade 2	23/51 (45.1)	23/51 (45.1)	—	
Endometrioid Grade 3	5/51 (9.8)	5/51 (9.8)	—	
High-grade serous carcinoma	10/51 (19.6)	10/51 (19.6)	—	
Clear-cell carcinoma	3/51 (5.9)	3/51 (5.9)	—	
Mixed	3/51 (5.9)	3/51 (5.9)	—	
Tubal cancer	2/51 (3.9)	2/51 (3.9)	—	
Other	3/51 (5.9)	3/51 (5.9)	—	

Data are presented as mean ± SD or *n*/*N* (%). Denominators indicate number of patients for whom data were available. *Comparison between patients with synchronous primary endometrial and ovarian cancers and those with endometrial cancer with ovarian metastasis. †Data available for 121 patients; normal distribution resulted from inverse transformation. ‡Data available for 82 patients; normal distribution resulted from log10 transformation. §Data available for 59 patients; normal distribution resulted from log10 transformation. BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics.

or cystic. The 'bright edge' was defined as the echo formed by the interface between an intracavitary lesion and the endometrium[31].

Assessment of myometrial infiltration was based on the examiner's subjective impression[32,33] and was classified as no infiltration or superficial (< 50%) or deep (≥ 50%) infiltration[34]. The color content of the endometrium was scored using the IOTA color score[27]. The vascular pattern was reported with respect to the presence of 'no flow', 'single vessel', 'multiple vessels' or 'scattered vessels'.

All pathological examinations were performed by the same pathologist (G.F.Z.) with more than 10 years of

Table 2 Ultrasound characteristics of ovarian masses of 131 patients with endometrial cancer associated with ovarian malignant mass, overall and according to whether they were diagnosed with synchronous primary endometrial and ovarian cancers or endometrial cancer with ovarian metastasis

Characteristic	*All* (n = *131*)	*Synchronous endometrial and ovarian cancers* (n = *51*)	*Endometrial cancer metastatic to ovaries* (n = *80*)	P*
Bilateral tumor	41/110 (37.3)	13/50 (26.0)	28/60 (46.7)	0.026
Ascites	21/131 (16.0)	10/51 (19.6)	11/80 (13.8)	0.37
Free fluid in pouch of Douglas	34/131 (26.0)	17/51 (33.3)	17/80 (21.3)	0.12
Metastases	17/131 (13.0)	1/51 (2.0)	16/80 (20.0)	0.003
Ovarian mass				0.002
Visible	110/131 (84.0)	50/51 (98.0)	60/80 (75.0)	
Not visible and ovaries normal on ultrasound	8/131 (6.1)	1/51 (2.0)	7/80 (8.8)	
Not visible and ovaries not assessable	13/131 (9.9)	0/51 (0)	13/80 (16.3)	
Largest diameter of mass (mm)†	81.5 (7–358)	89.5 (30–300)	66.5 (7–358)	0.13
Type of tumor				0.007
Unilocular	3/110 (2.7)	0/50 (0)	3/60 (5.0)	
Multilocular	1/110 (0.9)	1/50 (2.0)	0/60 (0)	
Unilocular-solid	8/110 (7.3)	3/50 (6.0)	5/60 (8.3)	
Multilocular-solid	37/110 (33.6)	25/50 (50.0)	12/60 (20.0)	
Solid	61/110 (55.5)	21/50 (42.0)	40/60 (66.7)	
Number of locules in multilocular and multilocular-solid masses				0.56
≤ 10	9/24 (37.5)	7/17 (41.2)	2/7 (28.6)	
> 10	15/24 (62.5)	10/17 (58.8)	5/7 (71.4)	
Echogenicity of cystic fluid in tumors not classified as solid				0.19
Anechoic	11/36 (30.6)	5/22 (22.7)	6/14 (42.9)	
Low level	22/36 (61.1)	16/22 (72.7)	6/14 (42.9)	
Ground glass	1/36 (2.8)	1/22 (4.5)	0/14 (0)	
Hemorrhagic	1/36 (2.8)	0/22 (0)	1/14 (7.1)	
Mixed	1/36 (2.8)	0/22 (0)	1/14 (7.1)	
Largest solid component (mm)‡	62 (5–358)	64 (13–242)	62 (5–358)	0.9
Presence of papillary projection(s)	10/110 (9.1)	6/50 (12.0)	4/60 (6.7)	0.33
Number of papillary projections, if present				0.20
1	1/8 (12.5)	0/4 (0)	1/4 (25.0)	
2	0/8 (0)	0/4 (0)	0/4 (0)	
3	2/8 (25.0)	2/4 (50.0)	0/4 (0)	
> 3	5/8 (62.5)	2/4 (50.0)	3/4 (75.0)	
Height of largest papillary projection (mm)§	17.5 (3–60)	9.5 (6–23)	35 (3–60)	0.25
Papillation flow if papillations present	7/9 (77.8)	5/5 (100)	2/4 (50.0)	0.073
Incomplete septa	1/110 (0.9)	1/50 (2.0)	0/60 (0)	0.27
Shadowing	1/110 (0.9)	1/50 (2.0)	0/60 (0)	0.27
Color score				0.39
1	10/105 (9.5)	2/47 (4.3)	8/58 (13.8)	
2	24/105 (22.9)	11/47 (23.4)	13/58 (22.4)	
3	48/105 (45.7)	22/47 (46.8)	26/58 (44.8)	
4	23/105 (21.9)	12/47 (25.5)	11/58 (19.0)	
Diagnosis based on subjective assessment				0.64
Benign	3/107 (2.8)	1/50 (2.0)	2/57 (3.5)	
Malignant	104/107 (97.2)	49/50 (98.0)	55/57 (96.5)	
Diagnosis suggested by original ultrasound examiner				< 0.0001
Abscess/pelvic inflammatory disease	1/110 (0.9)	1/50 (2.0)	0/60 (0)	
Borderline malignant tumor	1/110 (0.9)	1/50 (2.0)	0/60 (0)	
Primary ovarian cancer	50/110 (45.5)	36/50 (72.0)	14/60 (23.3)	
Metastatic ovarian cancer	23/110 (20.9)	3/50 (6.0)	20/60 (33.3)	
Not assessed	35/110 (31.8)	9/50 (18.0)	26/60 (43.3)	

Data are presented as *n*/*N* (%) or median (range). Denominators indicate number of patients for whom data were available. *Comparison between patients with synchronous primary endometrial and ovarian cancers and those with endometrial cancer with ovarian metastasis. †Data available for 110 patients. ‡Data available for 36 patients. §Data available for 8/10 patients.

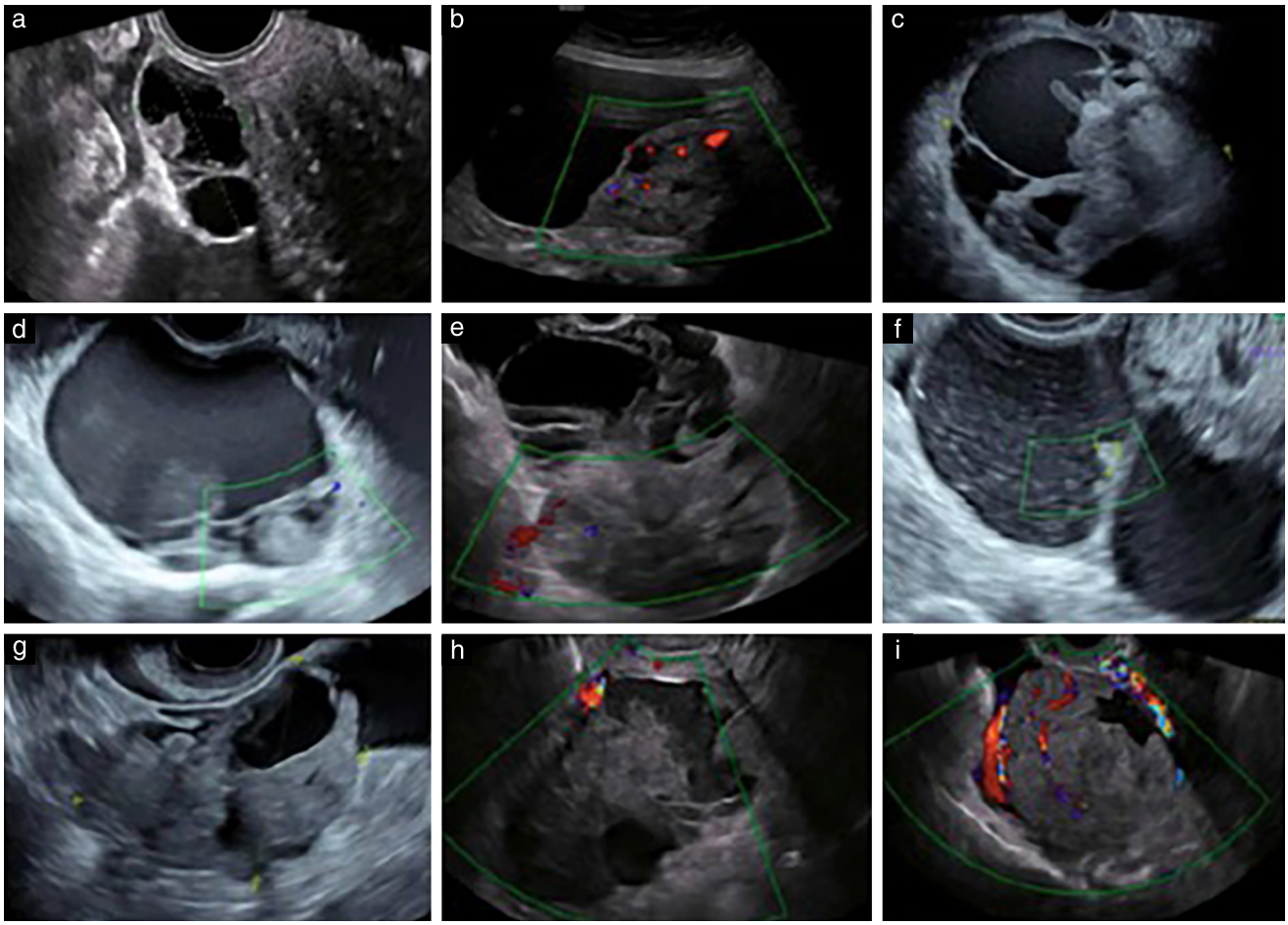

Figure 2 Ultrasound images of ovarian mass in patients with synchronous primary endometrial and ovarian cancers described as multilocular-solid (a–f) or solid (g–i) mass.

experience in gynecological pathology. The pathologist classified synchronous and metastatic disease according to the pathological criteria described in a pathology textbook[35]. Ten of the synchronous endometrial and ovarian cancers included in this study have already been described in a previous report[22].

According to the histological findings, the recruited patients were grouped into two cohorts for comparison: those with synchronous primary cancers of the endometrium and ovary (synchronous group) and those with endometrial cancer with ovarian metastasis (metastasis group). The primary endpoint of the study was to compare the ultrasound features of ovarian malignant masses between the synchronous and the metastatic groups. The secondary endpoint was to compare the ultrasound features of endometrial cancers between the two study groups.

All clinical and ultrasound data were entered into a dedicated Excel file (Microsoft Office Excel 2007, Redmond, WA, USA). Results are presented as absolute frequency (percentage) for nominal variables, as mean ± SD for normally distributed continuous variables or those that were normally distributed after transformation, and as median (range) for continuous variables that were not normally distributed. The Shapiro–Wilk test was used to assess the normality of the distribution of variables. Student's *t*-test and the Mann–Whitney *U*-test were used for comparisons between the two histological groups in the case of normally distributed (or normally distributed after transformation) and not normally distributed variables, respectively. The χ^2 or Fisher's exact test was used as appropriate for comparisons between the two groups in the case of nominal variables. All statistical analyses were performed using SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA). Two-sided tests were used and the significance level was set at $P < 0.05$.

RESULTS

We identified 196 patients with a histological diagnosis of endometrial cancer associated with an ovarian malignant mass, of whom 131 had been assessed preoperatively by ultrasound at our unit and were therefore considered for the analysis. These comprised 51 patients with synchronous primary cancers of the endometrium and ovary (synchronous group) and 80 with endometrial cancer with ovarian metastasis (metastasis group) (Figure 1).

Demographic background data and tumor characteristics of patients in the two groups are presented in Table 1. Mean age at diagnosis was 58.9 ± 11.7 years and

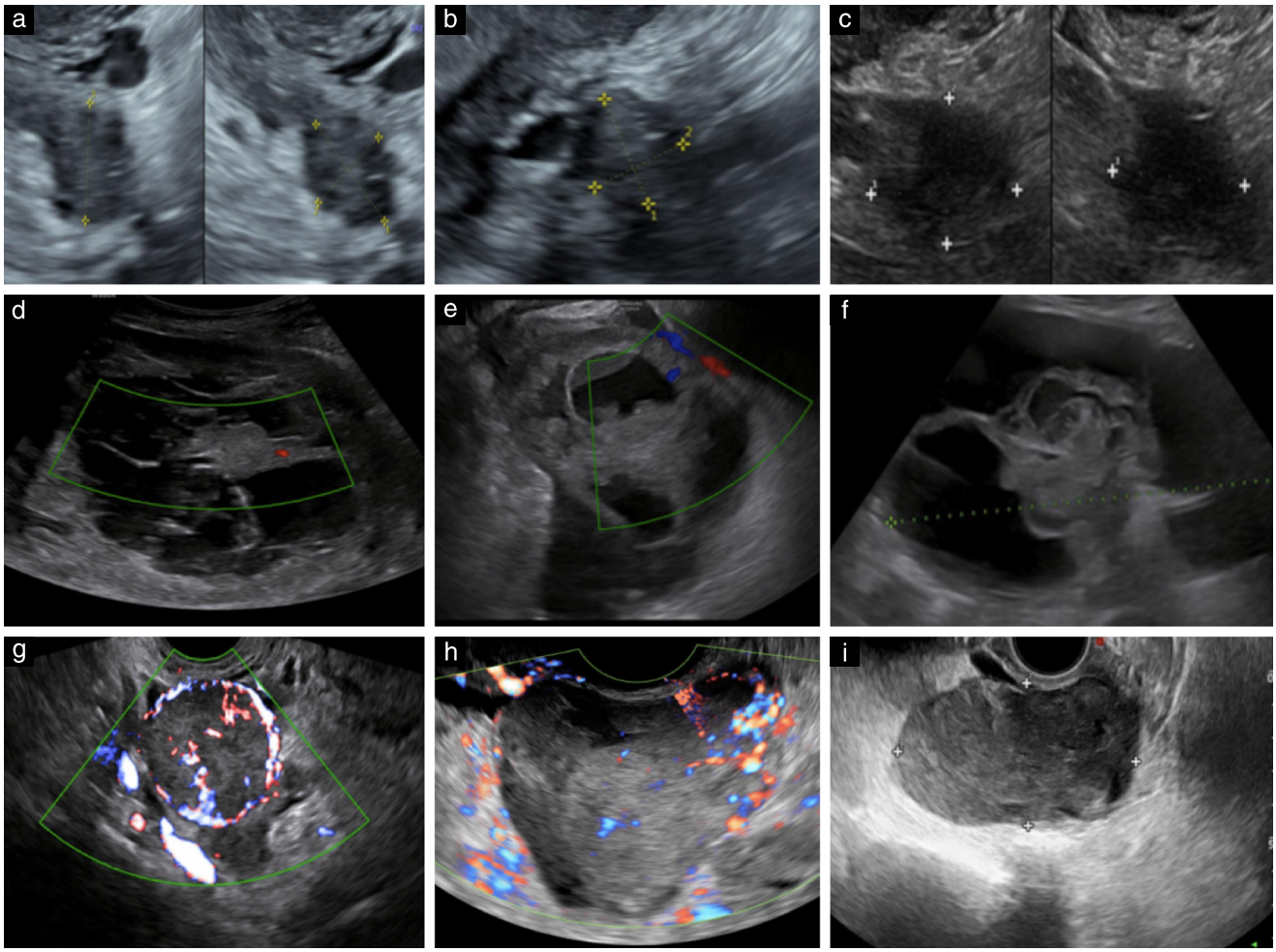

Figure 3 Ultrasound images of ovarian metastasis in patients with endometrial cancer metastatic to ovary. On ultrasound, ovaries appeared normal (a–c) or as having multilocular-solid (d–f) or solid (g–i) mass.

41 (31.3%) patients were premenopausal, with no difference in the proportion of premenopausal women between the two groups. Most patients (74/125; 59.2%) sought medical assistance due to symptoms related to the endometrial cancer (abnormal bleeding) or due to abdominal pain (31/125; 24.8%).

Ultrasound characteristics of the ovarian masses of patients in the synchronous group and those in the metastasis group are shown in Table 2 and in Figures 2 and 3. Ovarian masses in the synchronous group were less often bilateral than those in the metastatic group (13/50 (26.0%) *vs* 28/60 (46.7%); $P = 0.026$). Patients in the synchronous group presented more often with an ovarian mass detectable on ultrasound compared with the metastasis group (50/51 (98.0%) *vs* 60/80 (75.0%)). Ovarian masses in the synchronous group were more often described as multilocular-solid than were those in the metastasis group (25/50 (50.0%) *vs* 12/60 (20.0%)).

Ultrasound characteristics of endometrial lesions in the two groups are shown in Table 3 and in Figure 4. The median largest diameter of endometrial tumor was 29 (range, 11–118) mm in the synchronous group in comparison with 51.5 (range, 6–150) mm in the metastasis group ($P < 0.0001$). Endometrial lesions were described as hyperechoic more often in the synchronous group than in the metastasis group (29/40 (72.5%) *vs* 27/71 (38.0%)). Endometrial tumors of patients in the synchronous group presented more frequently with no myometrial infiltration than did endometrial tumors of patients in the metastasis group (23/35 (65.7%) *vs* 13/65 (20.0%)), whereas endometrial tumors of patients in the metastasis group presented more frequently with deep myometrial infiltration ($\geq 50\%$) than did those of patients in the metastasis group (45/65 (69.2%) *vs* (5/35 (14.3%)). Endometrial lesions in the synchronous group were more often not vascularized (color score 1) (12/40 (30.0%) *vs* 9/70 (12.9%)) and presented less often with multiple-vessel pattern (9/37 (24.3%) *vs* 36/56 (64.3%)) than those in the metastasis group.

DISCUSSION

In this study, we compared the ultrasound characteristics of ovarian malignant masses between patients with synchronous primary cancers of the endometrium and ovary and those with endometrial cancer with ovarian metastasis. Ovarian masses in the synchronous group appeared mainly as unilateral multilocular-solid or solid

Table 3 Ultrasound characteristics of endometrial lesions in 131 patients with endometrial cancer associated with ovarian malignant mass, overall and according to whether they were diagnosed with synchronous primary endometrial and ovarian cancers or endometrial cancer with ovarian metastasis

Characteristic	*All (n = 131)*	*Synchronous endometrial and ovarian cancers (n = 51)*	*Endometrial cancer metastatic to ovaries (n = 80)*	P*
Tumor defined	88/130 (67.7)	27/50 (54.0)	61/80 (76.3)	0.006
Endometrium visible	38/130 (29.2)	23/50 (46.0)	15/80 (18.8)	0.036
Myometrial abnormality				0.24
Fibroid	28/121 (23.1)	13/46 (28.3)	15/75 (20.0)	
Adenomyosis	1/121 (0.8)	1/46 (2.2)	0/75 (0)	
None	92/121 (76.0)	32/46 (69.6)	60/75 (80.0)	
Endometrial–myometrial junction				< 0.0001
Regular	29/105 (27.6)	19/35 (54.3)	10/70 (14.3)	
Irregular	76/105 (72.4)	16/35 (45.7)	60/70 (85.7)	
Endometrial midline				0.067
Seen	2/114 (1.8)	2/43 (4.7)	0/71 (0)	
Undefined/not seen	112/114 (98.2)	41/43 (95.3)	71/71 (100)	
Endometrial thickness (mm)†	8 (2–34)	8 (2–34)	8 (3–22)	
Largest diameter of tumor (mm)‡	44 (6–150)	29 (11–118)	51.5 (6–150)	< 0.0001
Echogenicity of tumor				0.0010
Uniform hyperechogenic	56/111 (50.5)	29/40 (72.5)	27/71 (38.0)	
Uniform hypoechogenic	20/111 (18.0)	7/40 (17.5)	13/71 (18.3)	
Uniform isoechogenic	17/111 (15.3)	1/40 (2.5)	16/71 (22.5)	
None	18/111 (16.2)	3/40 (7.5)	15/71 (21.1)	
Myometrial infiltration				< 0.0001
None	36/100 (36.0)	23/35 (65.7)	13/65 (20.0)	
< 50%	14/100 (14.0)	7/35 (20.0)	7/65 (10.8)	
≥ 50%	50/100 (50.0)	5/35 (14.3)	45/65 (69.2)	
Normal myometrium visible	96/114 (84.2)	43/43 (100)	53/71 (74.6)	< 0.0001
Bright edge present	2/115 (1.7)	2/43 (4.7)	0/72 (0)	0.065
Color score				< 0.0001
1	21/110 (19.1)	12/40 (30.0)	9/70 (12.9)	
2	21/110 (19.1)	14/40 (35.0)	7/70 (10.0)	
3	39/110 (35.5)	6/40 (15.0)	33/70 (47.1)	
4	29/110 (26.4)	8/40 (20.0)	21/70 (30.0)	
Vascular pattern				0.002
No flow	21/93 (22.6)	12/37 (32.4)	9/56 (16.1)	
Single vessel with or without branching	9/93 (9.7)	6/37 (16.2)	3/56 (5.4)	
Multiple vessels	45/93 (48.4)	9/37 (24.3)	36/56 (64.3)	
Scattered vessels	18/93 (19.4)	10/37 (27.0)	8/56 (14.3)	
Cervical infiltration	35/113 (31.0)	7/43 (16.3)	28/70 (40.0)	0.008

Data are presented as *n*/*N* (%) or median (range). Denominators indicate number of patients for whom data were available. *Comparison between patients with synchronous primary endometrial and ovarian cancers and those with endometrial cancer with ovarian metastasis. †Data available for 38 patients. ‡Data available for 87 patients.

masses, whereas those in the metastasis group were mostly bilateral solid masses.

We also compared ultrasound features of the endometrial lesions between the two groups. As expected, the synchronous group presented in most cases with a small hyperechoic endometrial lesion with no myometrial infiltration and with no or minimal vascularization, whereas patients in the metastasis group presented more often with a large endometrial lesion with deep myometrial infiltration, with moderate or rich vascularization and multiple-vessel pattern.

The main strength of this study is that it included a large series of patients with ovarian metastasis from endometrial cancer. Moreover, to the best of our knowledge, this is the first study comparing the ultrasound characteristics between patients with synchronous primary endometrial and ovarian cancers and those with endometrial cancer with ovarian metastasis. However, the study has some limitations. First, due to its retrospective nature, some clinical and ultrasound information was missing. Ultrasound images or videoclips were not available for all cases, and this may have limited our ability to detect typical ultrasound features. Moreover, the very high number of variables examined in a relatively small sample size could represent a weakness of the analysis, in terms of generating new hypotheses.

Our results are consistent with those of a recent study by Epstein *et al.*[16], describing the largest series of ultrasound features of endometrial cancers. The authors found that low-risk tumors (Stage IA of endometrioid-type Grade 1 or 2) are likely to be a small lesion, with hyperechoic echogenicity and a regular endometrial–myometrial junction. On the other hand, high-risk tumors (Stage IA of Grade 3 endometrioid-type

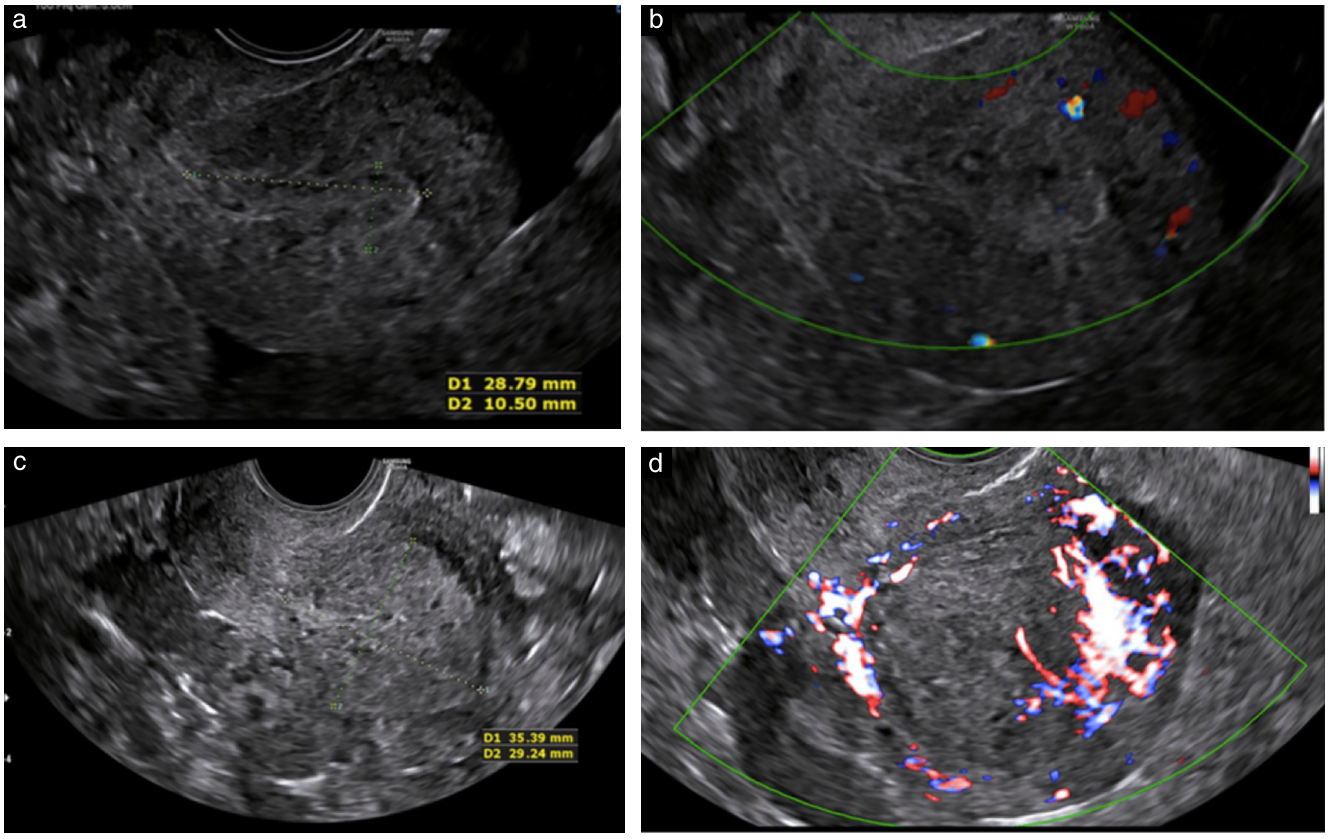

Figure 4 (a,b) Grayscale (a) and color Doppler (b) images of hyperechoic endometrial lesion measuring 28 × 10 mm, with no myometrial infiltration and no vascularization on color Doppler examination, in patient with synchronous endometrial and ovarian cancers; final histological diagnosis was endometrial cancer of FIGO (International Federation of Gynecology and Obstetrics) Stage IA and of endometrioid-type Grade 1. (c,d) Grayscale (c) and color Doppler (d) images of isoechoic endometrial lesion measuring 35 × 29 mm, with deep myometrial infiltration, rich vascularization and multiple-vessel pattern, in patient with endometrial cancer metastatic to ovary; final histological diagnosis was endometrial cancer of FIGO Stage IIIA and endometrioid-type Grade 3.

or non-endometrioid or ≥ Stage IB) were less likely to have a regular endometrial–myometrial junction, were larger and more frequently had non-uniform echogenicity, with multiple, multifocal-vessel pattern and moderate or high color score compared with low-risk tumors.

Our results are also in line with those previously reported on the ultrasound features of ovarian metastasis from endometrial cancer. Testa *et al.*[17] described 13 cases of ovarian metastasis from uterine disease and found that most of them (11/13) were solid and 2/13 were multilocular-solid masses. Guerriero *et al.*[18] described 17 cases of metastasis from endometrial cancer, reporting that 12/17 were solid and 5/17 were unilocular-solid or multilocular-solid. However, Guerriero *et al.* reported a lower number of cases with bilateral ovarian masses than was found in this study (21.4% *vs* 46.7%), probably due to the lower number of cases.

Regarding ovarian masses of synchronous cancers, in a recent study by our group on endometrioid ovarian tumors[22], we found that most endometrioid cancers are unilateral with multilocular-solid or solid morphology. In this series, including not only endometrioid histotypes, we found a lower number of ovarian masses with papillary projections.

Our clinical data are consistent with those reported by other authors, particularly with regard to the association between endometriosis and synchronous cancers: patients with synchronous primary cancers of the endometrium and ovary often have a history of endometriosis, whereas this is not reported for patients with endometrial cancer with ovarian metastasis[36].

Our findings could have some impact on clinical practice. The possibility to discriminate preoperatively between synchronous primary cancers of the endometrium and ovary and endometrial cancer with metastasis to the ovaries could be relevant for the surgeon to counsel the patient and plan the best surgical treatment. Indeed, in patients who wish to preserve fertility, preoperative suspicion of synchronous primary cancers of the endometrium and ovary at an early stage could support a strategy of a first-step fertility-sparing surgery[37].

In conclusion, synchronous primary cancers of the endometrium and ovary have significantly different sonomorphological patterns compared with endometrial cancer with ovarian metastasis. Ovarian masses in synchronous primary cancers of the endometrium and ovary appeared mostly as unilateral multilocular-solid or solid masses, whereas ovarian masses in endometrial cancers with ovarian metastasis were mostly bilateral

solid masses. The different sonomorphology of these two cancers may facilitate their preoperative discrimination, helping the surgeon to determine optimum management for the patient.

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