ORIGINAL RESEARCH

Ultrasound Features for Determining the Risk of Malignancy in Unilocular-Solid Adnexal Masses in Premenopausal Women without Ascites and/or Carcinomatosis

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ABSTRACT

Purpose: To assess what clinical and ultrasound features could be most helpful for discriminating benign from malignant unilocular cysts with solid components in premenopausal women with no signs of ascites or carcinomatosis.

Materials and methods: Retrospective study comprising 91 women with preoperative diagnosis of unilocular-solid cyst that underwent surgical removal. The following variables were assessed: age, complaints at presentation, bilaterality, mean size of the lesion, number of papillary projections, size of solid component, surface of solid component (smooth or irregular), amount of color within solid component (no flow, minimal flow, moderate flow, abundant flow). Definitive histopathological diagnosis was used as gold standard. Multivariate logistic regression analysis was performed to identify which variables were independent predictors of malignancy and their odds ratios (OR).

Results: Malignant lesions had significantly larger tumor size, more number of solid components, larger size of solid component, more frequency of irregular surface in the solid component and more frequent moderate or abundant vascularization within the solid component. Logistic regression analysis identified amount of color (OR: 48.7), solid component's surface (OR: 29.1) and mean size of the lesion (OR: 1.58) as independent predictors for malignancy.

Conclusion: Tumor size, irregular surface and the presence of moderate or abundant color score within the solid component are the features more frequently associated to malignancy in unilocular-solid adnexal cysts in premenopausal women.

Keywords: Malignancy, Premenopause, Ultrasound, Unilocular cyst.

How to cite this article: Juez L, Peces A, Corral TMA, Orozco R, Utrilla-Layna J, Caparros M, Alcazar JL. Ultrasound Features for Determining the Risk of Malignancy in Unilocular-Solid Adnexal Masses in Premenopausal Women without Ascites and/or Carcinomatosis. Donald School J Ultrasound Obstet Gynecol 2015;9(2):112-117.

INTRODUCTION

Transvaginal ultrasound has been shown as an excellent diagnostic tool for discriminating benign from malignant adnexal masses when performed by expert examiners.[1-3] Most ovarian cancers appear as solid or multilocular-solid masses, many times with signs of intra-abdominal spread, such as ascites or frank carcinomatosis.[4-6] On the contrary, unilocular cysts are rarely malignant lesions.[7]

The finding of solid tissue within an unilocular cyst rises the suspicion of a possible malignancy. However, many benign masses exhibit this ultrasound appearance.[8-10] For this reason, an unilocular cyst with solid components represents an actual diagnostic challenge. In fact, some studies conclude that this type of adnexal mass is the most difficult to categorize when no other signs of malignancy like ascites or carcinomatosis are present.[11,12]

When managing surgically ovarian lesions of uncertain nature, such as unilocular-solid cysts, the surgeon must choose between adnexectomy and cystectomy. This decision is important for fertility sparing surgery but bearing in mind that albeit ovarian cancer is not common in premenopausal women, but it does happen.[13]

Therefore, attempts for improving our diagnostic performance in this type of lesions in premenopausal women are advisable.

The aim of this study was to assess what clinical and ultrasound features could be most helpful for discriminating benign from malignant unilocular cysts with solid components in premenopausal women.

MATERIALS AND METHODS

This is a retrospective study performed at a single university tertiary care center. Institutional review board waived patient consent and gave approval.

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A search in our database for identifying women who underwent surgery for an adnexal masses at our center between January 1995 and December 2014 was performed.

Eligible patients were premenopausal women preoperatively diagnosed as having an adnexal mass categorized as 'unilocular-solid cyst' and evaluated by transvaginal sonography (TVS). We defined as 'unilocular-solid cyst' any cyst with a predominantly cystic component and solid excrescences with height of at least 3 mm but no upper limit of size protruding into the cyst cavity[14] (Fig. 1).

Clinical, ultrasound and histopathological records were reviewed by two of the authors (JLA, LJ). Stored video clips and/or 3D volumes from the masses were also retrieved for review.

We excluded women with incomplete data from clinical records, ultrasound report and histopathological report. We also excluded women if ultrasound report described the presence of ascites or carcinomatosis, were pregnant at diagnosis or no hard-print copies, video clips and/or 3D volumes were available for review. Finally, we excluded those cases that after reviewing hard-print copies, video clips and/or 3D volumes the mass did not fit the definition of 'unilocular-solid cyst'.

Ultrasound stored video clips and/or 3D volumes were reviewed by three sonologists who were blinded to histopathological results (AP, TMA, RO). All of them had with more than 2 years' experience in gynecological ultrasound and were trained in ultrasound assessment of adnexal masses by one of the authors (JLA).

The following variables were retrospectively assessed:
- Clinical records: age, complaints at presentation.
- *Histopathological report*: Definitive histological diagnosis. This data were used as gold standard. Malignancies were staged according to FIGO classification.[15] Borderline ovarian tumors (BOTs) were considered as malignant for analytical purposes.
- *Ultrasound features*:
  - Bilaterality.
  - Mean size of the lesion as determined by measuring tumor diameters in the three orthogonal planes.
  - Number of solid excrescences or papillary projections (Fig. 2).
  - Maximum size of solid excrescences or papillary projections as measured by two perpendicular planes (Fig. 3). In case of two or more solid excrescences or papillary projections we considered the largest one for analytical purposes.
  - Surface of solid excrescence or papillary projections, stated as smooth or irregular (Figs 4 and 5). In case of two or more solid excrescences or papillary projections with at least one exhibiting smooth and at least other with irregular surface
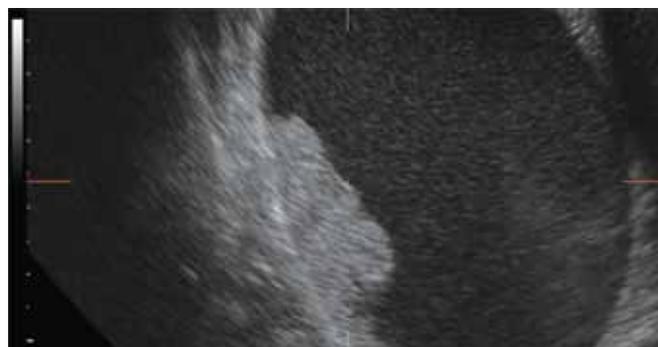
Fig. 1: Transvaginal ultrasound from a unilocular-solid cyst. A solid area is observed arising from internal cyst wall and protruding into the cyst's cavity

Fig. 2: Transvaginal ultrasound from a unilocular-solid cyst with two solid papillary projections of different size
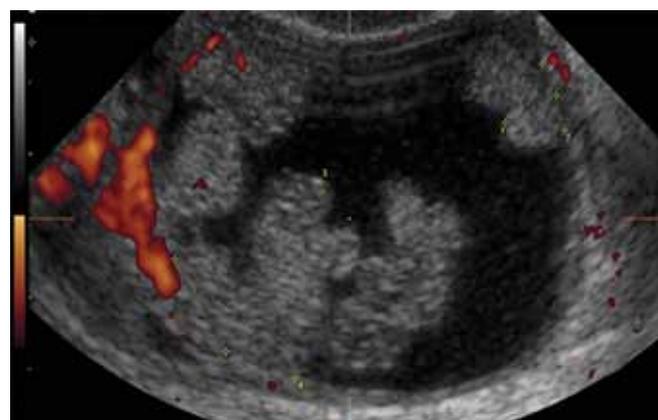
Fig. 3: Measurement of papillary projections in an unilocular-solid cyst. Height and perpendicularly the width
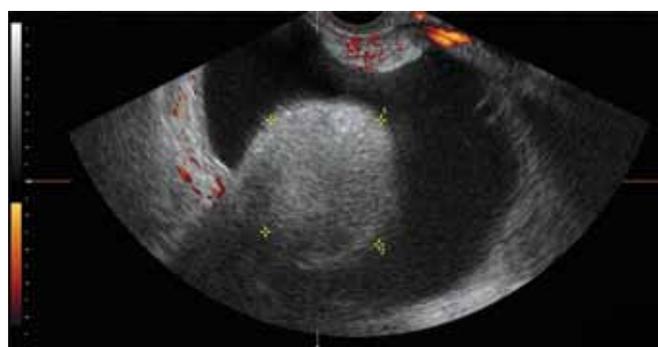
Fig. 4: Transvaginal ultrasound from a unilocular-solid cyst depicting a large solid area with smooth surface

Fig. 5: Unilocular-solid cyst exhibiting three papillary projections with irregular surface
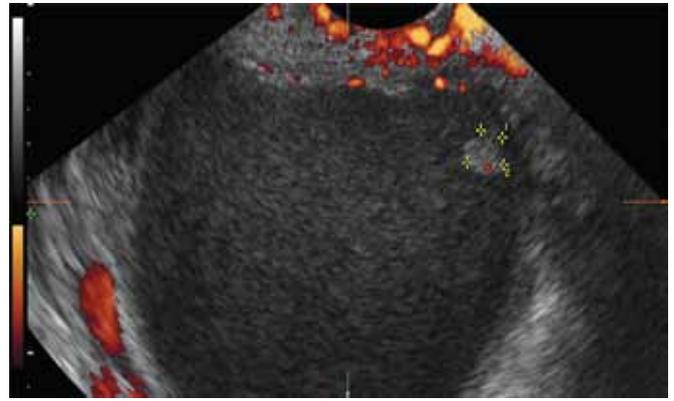
Fig. 6: Transvaginal ultrasound from a unilocular-solid cyst showing a small papillary projection with minimal color signals (color score 2)

we consider only the irregular one for analytical purposes.

– *Amount of color score within papillary projections as defined by IOTA*[14]: Color score (1) no flow, color score (2) minimal flow, color score (3) moderate flow and color score (4) abundant flow (Figs 6 and 7).

All ultrasound examinations had been performed or supervised by one examiner (JLA) according to a predefined scanning protocol described elsewhere.[16,17]

Kolmogorov-Smirnov test was used to assess normal distribution of continuous variables. Data are presented as mean with standard deviation (SD) or median with interquartile range (IQR).

Categorical variables were expressed as absolute number and percentage.

Univariate analysis was first performed to determine whether statistical differences between benign and malignant lesions exist for each individual variable. Continuous variables were compared using one-way ANOVA or Mann-Whitney U tests depending whether variables distributed normally or not. Categorical variables were compared using Chi-squared test. Those variables with statistical differences were then entered in a forward stepwise multivariate logistic regression analysis to identify which variables were independent predictors of malignancy and to determine their odds ratios with 95% confidence intervals (CIs).

A p-value less than 0.05 was considered as statistically significant for all analyses. Statistical package for social sciences (SPSS) version 22.0 was used for all statistical analyses.

RESULTS

From January 1995 to December 2014, 2135 women underwent surgery for an adnexal mass at our institution. After database search, we found out 91 women eligible for the study. Thirty-eight women were excluded (incomplete
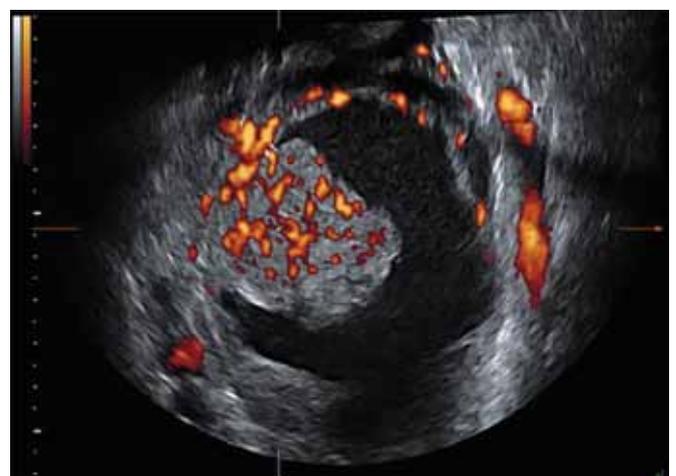
Fig. 7: Transvaginal ultrasound from a unilocular-solid cyst showing a large papillary projection with abundant color signals (color score 4)

data: n = 17; presence of ascites or carcinomatosis: n = 6; no video clips and/or 3D volumes available for review, n = 9; the mass did not fit definition of unilocular-solid cyst after hard-print copies, video clips and/or 3D volumes review, n = 4; and were pregnant at diagnosis, n = 2).

Ultimately, 53 women were included in this study. Patients' mean age was 38 years old (SD: 8.6), ranging from 17 to 52 years.

Complaints at presentation were as follows: asymptomatic, n = 38 (72.0%); pelvic/abdominal pain, n = 10 (18.9%); menstrual disorder, n = 3 (5.4%) and abdominal swelling, n = 2 (3.7%).

Five women had bilateral masses (9.4%). However, none of them had a bilateral unilocular-solid mass.

Mean diameter of the lesions was 67.5 mm (SD: 27.0), ranging from 17.0 mm to 139.5 mm. Median number of solid excrescences or papillary projections was 2 (IQR: 2), ranging from 1 to 8. Mean largest diameter of the solid component was 25.3 mm (SD: 21.1), ranging from 3.5 to 92.5 mm.

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Irregular surface of the solid component was present in 30 cases (56.6%) and it was smooth in 23 cases (43.3%).

Color score was absent in 14 cases (26.4%), minimal in 24 cases (45.3%), moderate in 8 cases (15.1%) and abundant in 7 cases (13.2%).

At histopathology analysis, 15 tumors (28.3%) were malignant and 38 (71.7%) were benign (Table 1). Tumor stage of malignant tumors were as follows: stage Ia, n = 6 (40.0%); stage Ib: n = 1 (6.7%); stage Ic, n = 3 (20%) and stage IIIc, n = 5 (33.3%).

Univariate analysis is shown in Table 2. We found that malignant lesions had significantly larger tumor size, more number of solid components, larger size of solid component, more frequency of irregular surface in the solid component and more frequent moderate or abundant vascularization within the solid component.

Table 1: Histopathological diagnosis of the lesions

Histology	N	Percent
Cystadenofibroma	11	20.8
Endometrioma	7	13.2
Teratoma	6	11.3
Serous cystadenoma	5	9.2
Mucinous cystadenoma	5	9.4
Hemorrhagic cyst	3	5.7
Peritoneal cyst	1	1.9
BOT lesion	4	7.5
Invasive carcinoma	11	20.8

BOT: Borderline ovarian tumor

Table 2: Results of univariate statistical analysis

Variable	Benign (n = 38)	Malignant (n = 15)	p-value
Age*	37.8 (9.1)	38.7 (7.4)	0.735
Complaints†			0.315
Asymptomatic	28 (73.7)	10 (66.7)	
Pelvic pain	6 (15.8)	3 (20.0)	
Menstrual disorder	3 (7.9)	0 (0)	
Abdominal swelling	1 (2.6)	2 (13.3)	
Bilaterality†	2 (5.3)	3 (20.0)	0.131
Tumor size (cm)*	5.9 (2.1)	8.9 (3.1)	0.001
Number solid components‡	1.0 (0.0)	2.0 (2.0)	0.001
Solid component size (mm)‡	14.3 (16.5)	30.0 (38.4)	0.002
Solid component surface†			0.001
Irregular	16 (42.1)	14 (93.3)	
Smooth	22 (57.9)	1 (6.7)	
Color score			0.001
Absent/scanty	34 (89.5)	4 (26.7)	
Moderate/abundant	4 (10.5)	11 (73.3)	

*Expressed as mean, standerd deviation in parentheses;
†Expressed as absolute number, percentage in parentheses;
‡Expressed as median, interquartile range in parentheses

Multivariate logistic regression analysis showed that only color score (odd ratio: 48.7, 95% CIs: 3.9-602.3; p = 0.002), irregular surface (odd ratio: 29.1, 95% CIs: 1.4-601.9; p = 0.029) and mean size of the lesion (odd ratio: 1.6, 95% CIs: 1.1-2.5; p = 0.039) were independent predictors for malignancy. The presence of one moderate/abundant color score or irregular surface of the solid component identified 100% of malignant lesions with a false-positive rate of 34%.

DISCUSSION

In the literature, there are many different prediction models for preoperative assessment of ovarian lesions. Some were using morphological, the others Doppler characterization, some were using both. Some even used 3D ultrasound.[18] However, it seems that subjective assessment by an expert using pattern recognition appears remains the best method of distinguishing between benign and malignant tumors.[1]

Some studies even used computational systems based on machine-learning techniques, such as artificial neural networks and support vector machines.[19] However, they did not confer additional discriminating power. Moreover, there is no evidence that any other imaging modality (such as CT, PET or PET CT) will perform any better than does ultrasound.[20]

In this study, we have assessed what clinical and ultrasound parameters could discriminate better between benign and malignant unilocular-solid adnexal cysts in premenopausal women without other obvious suspicious signs such as ascites and/or carcinomatosis. We have found that irregular surface of the solid component and the amount of color signals within the solid component are the best predictors for malignancy.

The main strength of this study is that we provide some new information that could be used by sonographers and sonologists. In fact, there is a significant paucity of data regarding this type of lesions in the literature. To the best of our knowledge, there is only a previous study that specifically addressed the ultrasound predictors for malignancy in unilocular-solid cysts in premenopausal women.

Fagotti et al evaluated 51 premenopausal women with unilocular-solid adnexal cysts to determine the diagnostic performance of different ultrasound parameters for discriminating benign from malignant lesions.[21] They found that a largest solid component > 14 mm and the presence of blood flow within the solid component, as detected by color Doppler, provided a 100% sensitivity and 80% specificity for distinguishing benign and BOT lesions from invasive carcinoma.

There are some similarities between Fagotti's and ours study. Both are retrospective analysis, both included a similar number of cases (51 and 53, respectively) and both had a similar prevalence of BOT and invasive carcinomas (30 and 28.3%, respectively).

However, there are some important differences. Probably, the main one is how both studies grouped the cases. Fagotti et al analyzed benign and BOT lesions *vs* invasive carcinomas. Whereas we analyzed benign tumors *vs* BOT and invasive carcinomas.

We consider this is an important difference from the clinical point of view. In premenopausal women benign adnexal lesions should be treated laparoscopically by the most conservative approach (cystectomy) whenever possible.[22] On the other hand, albeit fertility-sparing surgery may be considered, invasive cancer should be treated more radically by adnexectomy and complete surgical staging.[23] Borderline ovarian tumors may be treated by cystectomy, the when using this approach the risk of recurrence is significantly higher and the patient must be informed.[24] For this reason, we think that for diagnostic work-up and patient counseling BOT tumors should be considered as malignant. Even more when distinguishing preoperatively between invasive cancer and BOT is actually a difficult task.[25]

Like Fagotti et al[21] we found that the number of solid components or papillary projections and the largest diameter of the solid component were statistically significant larger in malignant tumors. However, in our study this statistical difference is lost in the multivariate logistic regression analysis.

Regarding color score we found that most BOT/Invasive cancers had moderate or abundant vascularization within the solid component. However, the presence of minimal and moderate color signals were observed in many benign lesions. Fagotti et al however, reported that just the presence/absence of color signals is a good discriminator. It could be argued that this controversial result could be explained by the subjective nature of color score assessment. However, at least two studies have shown that IOTA color score is reproducible among different examiners.[26,27]

Additionally, Fagotti et al did not find differences in surface of the solid component (irregular versus smooth). However, Hassen et al[28] and Valentin et al[29] also found that irregular surface of the solid component was predictive of malignancy (considering BOT and invasive carcinoma as malignant tumors in their respective statistical analysis). Notwithstanding, these two latter studies included pre- and postmenopausal women and did not reported specific data for premenopausal women.

In our opinion, these contradictory findings might be explained by the different criteria used for selecting and grouping cases.

Our study, obviously, had limitations. The main one is its retrospective design. This fact causes many exclusions and, therefore, a selection bias.

Second, the series is too small to allow us to draw definitive conclusions. For this reason, we did not estimate diagnostic performance and did not attempted to develop a predictive model.

According to this, we could conclude that irregular surface of the solid component and the presence of moderate or abundant color score within the solid component are those features more frequently associated to BOT or invasive carcinoma in unilocular-solid adnexal cysts in premenopausal women without ascites and/or carcinomatosis.

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