RESEARCH ARTICLE

Sonographic Pattern Recognition of Endometriomas Mimicking Ovarian Cancer

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Abstract

Background: To assess the accuracy of ultrasound in differentiating endometrioma from ovarian cancer and to describe pattern recognition for atypical endometriomas mimicking ovarian cancers. Materials and Methods: Patients scheduled for elective surgery for adnexal masses were sonographically evaluated for endometrioma within 24 hours of surgery. All examinations were performed by the same experienced sonographer, who had no any information of the patients, to differentiate between endometriomas and non-endometriomas using a simple rule (classic ground-glass appearance) and subjective impression (pattern recognition). The final diagnosis as a gold standard relied on either pathological or post-operative findings. Results: Of 638 patients available for analysis, 146 were proven to be endometriomas. Of them, the simple rule and subjective impression could sonographically detect endometriomas with sensitivities of 64.4% (94/146) and 89.7% (131/146), respectively. Of 52 endometriomas with false negative tests by the simple rule, 13 were predicted as benign masses and 39 were mistaken for malignancy. Solid masses and papillary projections were the most common forms mimicking ovarian cancer, consisting of 38.5% of the missed diagnoses. However, with pattern recognition (subjective impression), 32 from 39 cases mimicking ovarian cancer were correctly predicted for endometriomas. All endometriomas subjectively predicted for ovarian malignancy were associated with high vascularization in the solid masses. Conclusions: Pattern recognition of endometriomas by subjective assessment had a higher sensitivity than the simple rule in characterization of endometriomas. Most endometriomas mimicking ovarian malignancy could be correctly predicted by subjective impression based on familiarity of pattern recognition.

Keywords: Endometrioma - benign - malignancy - simple rule - pattern recognition - subjective impression

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Introduction

Differentiation of benign from malignant adnexal masses is of great value, since therapeutic approach is markedly different between the two entities. Benign ovarian masses, functional cysts or neoplasm, need more conservative approach, either closed follow-up or laparoscopic surgery, whereas malignant tumors require urgent laparotomy in most cases with planned systematic consultation of available oncologists, or referral to the tertiary center care. Thus, attempts should be made to distinguish benign from malignant tumors preoperatively. In general practice, management of adnexal masses directly depends on risk of malignancy index (RMI). Several guidelines, including Royal Thai College of Obstetricians and Gynecologists (RTCOG), suggest expertise consultation or oncologic referral in cases of high suspicion index for malignancy. RMI mainly depends on sonographic morphology which is highly suggestive of malignancy if it contains solid component, or nodular/papillary projections, or septations (>2-3 mm thickness), or strong vascularization. Endometrioma, a neoplasm-like condition, should be reliably discriminated from ovarian cancers. However, typical sonographic appearances of endometriomas, a unilocular cyst with homogeneous low-level echogenicity or ground glass pattern, are demonstrated in only 50-65% of cases (Guerriero et al., 1998; Bhatt et al., 2006; Van et al., 2010) and the remaining are atypical and often suspected of malignancy, resulting in over-preparation or unnecessary referrals. Therefore, reliability in sonographic diagnosis of atypical endometriomas is of concern and their characteristics need to be refined. Though songraphic features of endometriomas have been described several times (Guerriero et al., 1998; Patel et al., 1999; Jermy et al., 2001; Valentin, 2004; Kinkel et al., 2006; Van et al., 2010), the studies focusing on atypical forms, often confused with malignancy, are rare. The objectives of this study were to assess the accuracy of ultrasound in differentiating endometrioma from ovarian cancer and to describe pattern recognition for atypical endometriomas mimicking ovarian cancers.

Materials and Methods

A prospective study of diagnostic performance was conducted at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University with ethical approval of the

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Institute Review Boards. Between April 2006 and March 2012, women scheduled for elective pelvic surgery due to detection of an adnexal mass either by pelvic examination or previous pelvic ultrasound were recruited into the study with informed written consent.

Exclusion criteria consisted of: *i*) Patients with known diagnoses of ovarian cancer which was scheduled or referred for reoperation; *ii*) Patients with ovarian tumor diagnosed by previous CT or MRI before surgery; and *iii*) Women undergoing operation beyond 24 hours after ultrasound diagnosis.

All participants underwent ultrasound examination within 24 hours before surgery. All examinations were performed by the same experienced sonographer who had no any clinical information of the women using real-time 5-7.5MHz transvaginal or 3.5-5MHz transabdominal curvilinear transducer connected to and Aloka model SSD alpha-10 (Tokyo, Japan), both transabdominal and transvaginal approach. During the examination, assessments of sonographic morphology of the masses together with color Doppler study were also performed to categorize the masses to be endometrioma and non-endometrioma, using two methods including a sonographic simple rule and subjective assessment based on pattern recognition. The findings suggestive of endometrioma by sonographic simple rule included either a unilocular cyst, or cysts containing no more than 4 locules, with homogeneous low-level/ground glass echogenicity. Multiple areas of ground glass appearances or ground glass appearances with different echo-levels were also included in this category. Subjective sonographic impression of endometrioma, actually semi-objective and semi-subjective, was involved with pattern recognition by the expert sonographer, which was made and recorded during the examination. Though the prediction was subjective, its impression were mainly based on typical findings described above or atypical endometrioma (Figure 1), characterized as follows: *i*) Complex solid mass (with or without cystic areas) together with absence of internal vascularity (presence of pericystic flow at ovarian hilus); *ii*) A cyst with hyperechoic wall foci (irregular cyst wall or punctuate peripheral echogenic foci), usually different from wall nodularity; *iii*) Inside papillary projection with background of ground glass fluid and no vascularization or scanty flow; and *iv*) Calcium or hyperechoic deposits in the cyst, without other typical signs of cystic mature teratoma (Tongsong et al., 2008).

A sonographic diagnosis of endometrioma recorded at ultrasound examination was subsequently correlated with the final diagnosis made after surgery. The final diagnosis as a gold standard was based on either pathological examinations or intra-operative findings recorded by the surgeons in case of no pathological specimen. The pathological diagnoses were divided in to endometriomas and non-endometriomas and the latter were further sub-divided into benign and malignant tumors. The pathological diagnoses of borderline tumors were classified as malignancy.

Statistical analysis

The stored data were analyzed for the effectiveness of sonographic features based on the simple rule or subjective impression in predicting endometriomas, using the statistical package for the social sciences (SPSS) version 17.0 (Chicago, IL). The performance of sonographic diagnosis was assessed by sensitivity and specificity, negative and positive predictive value. The $p<0.05$ was considered statistically significant.

Results

During the study period, 721 women were initially diagnosed as ovarian tumors were recruited to undergo ultrasound examinations. Eighty-three women were

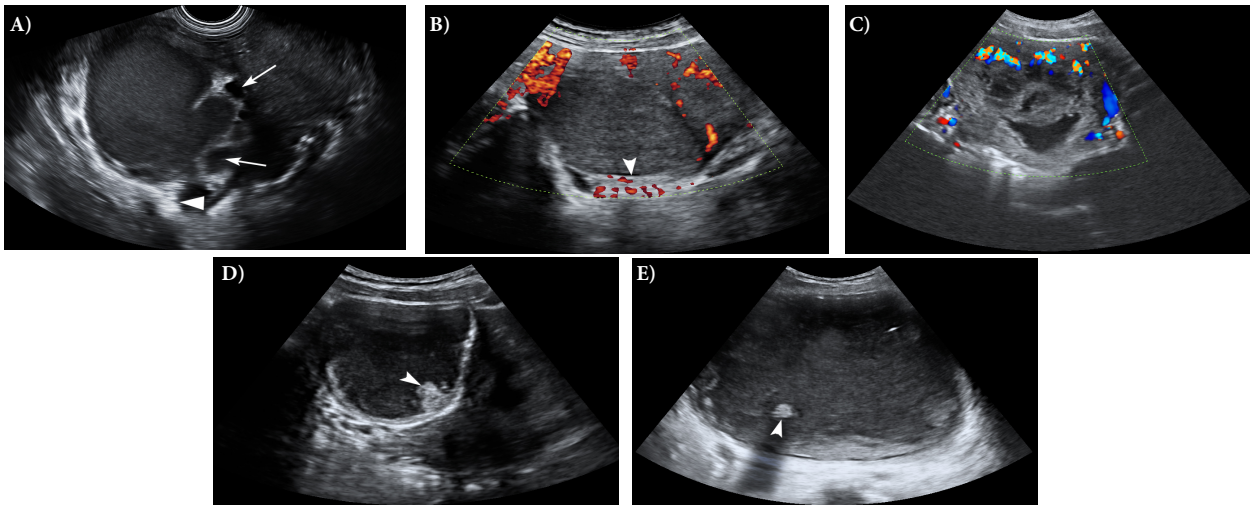

Figure 1. A) Classic Ground Glass Appearances of Endometrioma, but Atypical Cyst Wall. Irregular wall lined with multiple cystic structures (arrows) with hyperechoic walls (arrowhead); **B) Solid Appearances of Endometrioma.** Smooth wall (arrowhead) discriminated from the packed chocolate content, color flow mapping seen only in pericystic areas; **C) Complex Solid-Cystic Adnexal Mass with Heterogeneous Echogenicity.** Color Flow Mapping Seen Only in Pericystic Areas; **D) Unilocular Cyst with Inside Low-Level Echoes and a Papillary Projection (Arrowhead) From a Thick Cyst Wall Without Color Flow in The Projection (Not Shown); and E) Complex Adnexal Mass with Heterogeneous Ground-Glass Echogenicity and a Focal Calcification within the Endometrioma with Posterior Acoustic Shadowing (arrowhead)**

excluded because of pathological diagnoses of non-ovarian tumor including subserous myoma uteri, hydrosalpinx, etc. The remaining 638 were available for analysis. The mean (±SD) age of the patients was 43.5±14.1 years (range 12-81 years). Two hundred and thirty-three (36.5%) were nulliparous. Most women (442 cases, 69.3%) were in pre-menopausal age, 196 (30.7%) were post-menopausal period.

Of 638 cases, 146 were post-operatively diagnosed for endometriomas. Of them, the simple rule could sonographically detect endometriomas in 94 cases (64.4%) and predicted for non-endometriomas in 52 cases (false negative) (Table 1), whereas sonographic subjective impression by experienced sonographers could detect endometriomas in 131 cases (89.7%) and 15 cases for non-endometriomas (Table 2).

Focusing on the cases of endometriomas mistaken for malignant tumors, the false positive rate was 52 out of 146 cases for the sonographic simple rule but only 15 out of 146 cases for subjective impression by experienced sonographers. Of 52 cases of endmetriomas, 13 cases were predicted for benign (mature cystic teratoma, 2; tubo-ovarian abscess, 2; hemorrhagic cysts, 2; and mucinous/serous cystadenoma, 7). A total of 39 endometriomas were mistaken for malignancy as shown in Table 3. Note that solid mass and papillary projection were the most common forms mimicking ovarian cancer, consisting of 38.5% of the missed diagnoses. However, with pattern recognition (subjective impression), 32 from 39 cases mimicking ovarian cancer were correctly predicted for endometriomas. All endometriomas subjectively predicted for ovarian malignancy were associated with high vascularization in the solid masses.

Of note, false positive test (other lesions falsely predicted to be endometrioma) was found to be 3.5% (17/492) and 2.8% (14/492) for simple rule and subjective impression. Most of them were mature cystic teratoma, tubo-ovarian abscess, mucinous cystadenoma, and hemorrhagic cyst. Interestingly, only two cases of malignancy in both methods were mistaken to be endometriomas and both were mucinous cystadenocarcinoma in two postmenopausal women at age of 68 and 70 years. Both had a ground glass echogenicity with 2 and 4 locules without other features of malignancy.

Table 1. Diagnostic Indices of Simple Rules in Differentiating Endometrioma from Non-Endometrioma

Simple Rules	Pathologic Diagnoses		
	Endometrioma (Number)	Non-Endometrioma (Number)	Total
Positive	94	17	111
Negative	52	475	527
Total	146	492	638

*Sensitivity= 64.38% (94/146); 95%CI: 56.6%; 72.2%
Specificity= 96.54% (475/492); 95%CI: 94.9%; 98.2%
Positive predictive value= 84.70% (94/111); 95%CI: 78.0%; 91.4%
Negative predictive value= 90.10% (475/527); 95%CI: 84.6%; 95.7%

Table 2. Diagnostic Indices of Subjective Prediction Based on Pattern Recognition in Differentiating Endometrioma from Non-Endometrioma

Subjective Impression	Pathologic Diagnoses		
	Endometrioma (Number)	Non-Endometrioma (Number)	Total
Positive	131	14	145
Negative	15	478	493
Total	146	492	638

*Sensitivity= 89.73% (131/146); 95%CI: 84.8%; 94.7%
Specificity= 97.15% (478/492); 95%CI: 95.7%; 98.6%
Positive predictive value= 90.30% (131/145); 95%CI: 85.5%; 95.2%
Negative predictive value= 97.00% (478/493); 95%CI: 94.2%; 99.8%

Table 3. Distribution of Sonographic Appearances of Endometriomas Among False-Negative Tests According to Simple Rules and Subjective Prediction Based on Pattern Recognition

	Simple Rule		Subjective Impression	
	Frequency	%	Frequency	%
Benign prediction				
Simple cyst	7	13.5	5	33.3
Complex cyst	6	11.5	2	13.3
Malignant prediction				
Papillary projection	7	13.5	1	6.7
Hyperechoic / irregular wall	6	11.5	1	6.7
Predominantly solid mass	13	25	2	13.3
Calcified	4	7.7	1	6.7
Mixed	9	17.3	1	6.7
Total	52	100	15	100

Discussion

Both ultrasound and computed tomography have high accuracy in differentiating between malignant and benign ovarian masses (Tongsong et al., 2007; Khattak et al., 2013). Because of its non-invasiveness and high accuracy, ultrasound can be used as an initial modality of choice in the work up of every woman suspected of having an ovarian mass. It not only results in decreasing the mortality but also avoids unnecessary surgical interventions (Hafeez et al., 2013). Nevertheless, these modalities are not perfect, leading to false positive and negative tests in some patients. Endometriosis can also sometime be mistaken for malignancy. Our results suggest that pattern recognition of endometriomas may help sonographers improve accuracy in differentiating from malignancy.

Based on this study nearly two-third of endometriomas characterized by unilocular cyst (or containing few locules) with typical ground-glass (or homogeneous low-level) echogenicity. Approximately one-third of the cases showed atypical pattern of which unskilled examiners can commonly be mistaken for malignancy. These atypical endometriomas are associated with heterogeneity of the sonographic features which is impossible to develop a rule to discriminate endometriomas from other types of adnexal masses with confidence. However, these ultrasound appearances are associated some clues suggestive of endometriomas though clear-cut criteria could not been developed. As seen in subjective impression, familiarity with the ultrasound features is essential to develop the helpful skill. The pattern with which the examiners should be familiar include: *i*) Solid mass; *ii*) Cyst with hyperechoic/irregular wall foci; *iii*) papillary projection; and *iv*) endometrioma with calcium deposits. All of

these features are also commonly combined with areas of ground glass or homogeneous low-level echogenicity and poor vascularization. Note that subjective impression was relied on 2D grey-scale pattern recognition and color flow mapping. As reported in previous study (Haiyan and Min, 2011), experience of the operator was essential to differentiate the malignant solid portion in the mass from benign solid portion. Familiarity of these pattern mimicking malignant tumors can increase the sensitivity in diagnosis of endometriomas from about 65% to be nearly 90% with comparable specificity.

Our findings may probably encourage gynecologic sonographers to aware of false positive rate of atypical masses and try their best to characterize them with subjective impression based on pattern recognition. With this recognition, a large number of referrals for oncologic expertise could be obviated without compromise specificity and medical expenses could be substantially reduced. However, accuracy of the pattern recognition requires more practice and familiarity. It is not possible to develop the rules for differentiation of the solid masses secondary to various causes such as blood clot, impacted chocolate content, benign fibroma or active malignant masses but familiarity of these tumors can distinguish them in most cases.

Though several studies have been described about sonographic features of endometroma, they rarely focused on atypical findings. To the best of our knowledge, van Holsbeke C, et al reported a largest study of sonographic prediction of endometrioma (n=713 cases) using several rules of sonographic combination. However, several examiners and several machines were used for their study without statement of standardization. Additionally, they included the patients who had adnexal masses surgically removed within 120 days after the ultrasound examination, different from this study in which surgery was performed within 24 hours of ultrasound examination and all were performed by only one experienced examiner.

Based on this study as well as previous studies, endometrioma has its own sonographic characteristics, other than classic pattern, including ground glass/ homogeneous low-level echogenicity with 1-4 locules and no solid parts or papillary projections, atypical pattern mimicking ovarian cancer should be recognized are as follows: *i*) Multilocular cyst, though most endometriomas are unilocular, a significant number of them are multilocular but unlikely to be more than 4 locules; *ii*) solid mass, endometrioma can sonographically manifest as a complex solid adnexal mass, thereby raising the concern for malignancy, but they do not contain internal vascularity and often are similar homogeneous blood clot in the ground glass background. Color flow mapping showed only pericystic flow at the level of the ovarian hilus (Alcazar et al., 1997). The solid pattern like this has been found in 4.9% of endometriomas (Pascual et al., 2000). They may have some area of cystic space with low-level echogenicity in the solid areas; *iii*) endometrioma with hyperechoic wall foci (regular cyst wall or punctuate peripheral echogenic foci or cystic structures with hyperechoic margins lining the wall of the endometrioma: found in 5% among our cases of endometrioma different from that reported by Patel et al. (1999) who found in as high as 35% of the endometriomas, compared with 6% of the non-endometriomas. Combination of inside low-level internal echoes and hyperechoic wall foci, and no other neoplastic features is associated with 32 times more likely to be an endometrioma than another adnexal mass (Patel et al., 1999). This echogenic wall foci are thought to represent cholesterol deposits (Patel et al., 1999) or caused by hemosiderin or calcification (Brown et al., 2004); *iv*) Papillary projection from the cyst wall: inside papillary projection can be seen in endometriotic cyst, though it is usually regarded as malignancy. However, in endometrioma, the papillary projections are usually small and no strong vascularization, no flow or scanty flow (Guerriero et al., 1998); and *v*) endometrioma with calcium deposits: a finding typically associated with mature cystic teratoma (Bhatt et al., 2006). The absence of other typical ultrasound features of teratoma (fat or hair) is useful for the diagnosis of endometrioma. All of these atypical patterns are strongly suggestive of endometrioma if some areas of ground glass/low-level echogenictiy and poor vasucularity are demonstrated.

The strength of this study might include a large sample size, prospective nature of the study in which the ultrasound findings were recorded before surgery and pathological examination, no inter-observer variability since all examinations were performed by the same author who had no any clinical information of the patients. The weakness of this study may include some bias which might have been introduced by the fact that most acute hemorrhagic cysts, sonographically similar to endometriomas in some cases, were probably identified and received expectant management and not included in the study.

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