Exploring the value of the ovarian-adnexal reporting and data system combined with tumor markers in the differential diagnosis of benign and malignant ovarian-adnexal tumors

LIYAN ZHANG[1], LI XIAO[1,2], JIAXING WANG[1] and HAIYAN WANG[1]

[1]Functional Examination Department, Obstetrics and Gynecology Center, General Hospital of Ningxia Medical University, Yinchuan, Ningxia Hui Autonomous Region 750004, P.R. China; [2]First School of Clinical Medicine, Ningxia Medical University, Yinchuan, Ningxia Hui Autonomous Region 750004, P.R. China

Received September 17, 2025; Accepted January 23, 2026

DOI: 10.3892/mco.2026.2952

Abstract. To explore the value of the ovarian-adnexal reporting and data system (O-RADS) combined with tumor markers, risk of ovarian malignancy algorithm (ROMA) in the differential diagnosis of benign and malignant ovarian-adnexal tumors. A total of 426 patients with 524 cases of ovarian-adnexal tumors confirmed by surgery from January 2021 to January 2024 were included. Ultrasound O-RADS classification, ROMA and their combination were used for differential diagnosis. Taking pathological results as the gold standard, the sensitivity, specificity and the area under the receiver operating characteristic curves were calculated. Among the 524 tumors, there were 104 cases in category 2, 113 cases in category 3, 81 cases in category 4, 226 cases in category 5. The proportions of malignancy in O-RADS categories 2-5 were 0% (0/104), 4.42% (5/113), 53.09% (43/81) and 97.34% (220/226). Thus, it can be observed that the higher the ultrasound O-RADS classification, the higher the risk of malignancy. This was statistically significant. Taking O-RADS category 4 as the research objective, the patients were divided into two groups, pre-menopausal and post-menopausal for statistical analysis. Analysis revealed that the malignancy rate of postmenopausal O-RADS category 4 tumors was similar to that of O-RADS category 5. The risk of malignant tumors in postmenopausal women with O-RADS category 4 is significantly higher compared with that in premenopausal patients and the difference is statistically significant. The diagnostic efficacy of ROMA for benign and malignant tumors in postmenopausal patients was significantly greater when compared with premenopausal patients. When combined diagnosis is adopted, regardless of whether it is in the premenopausal or postmenopausal stage, the sensitivity and specificity of the diagnosis are significantly higher compared with those of a single diagnosis. Taking O-RADS category 4 as the research objective, the incidence of malignant tumors of O-RADS category 4 in postmenopausal women is similar to that of category 5. The diagnostic efficacy of ROMA for postmenopausal patients is greater when compared with that for premenopausal patients. The use of O-RADS classification combined with ROMA can improve the sensitivity and specificity for the differential diagnosis of benign and malignant ovarian-adnexal tumors.

Correspondence to: Dr Jiaxing Wang or Dr Haiyan Wang, Functional Examination Department, Obstetrics and Gynecology Center, General Hospital of Ningxia Medical University, 804 Shengli Street, Xingqing, Yinchuan, Ningxia Hui Autonomous Region 750004, P.R. China
E-mail: z15379982042@163.com
E-mail: 563545166@qq.com

Key words: ultrasonic, ovarian-adnexal reporting and data system, classification, risk of ovarian malignancy algorithm, combined diagnosis, ovarian-adnexal tumors

Introduction

Ovarian-adnexal tumors in women are common lesions of the reproductive system. The majority of patients have benign tumors; however, for patients with malignant tumors, early diagnosis is difficult with 75% of malignant tumors being diagnosed at an advanced stage (1). In previous years, the incidence and mortality rates of ovarian malignant tumors have been rising (2). Therefore, accurate differential diagnosis of benign and malignant ovarian-adnexal tumors is important for improving the survival rate of patients. The ultrasonic ovarian-adnexal reporting and data system (O-RADS) classification aims to differentiate and diagnose the benign and malignant nature of tumors through the image characteristics of ultrasound (3). Some studies have shown that the ultrasonic O-RADS classification has certain value in the differential diagnosis of benign and malignant ovarian-adnexal tumors (4-7).

The ultrasonic O-RADS classification provides a unified template for the expression of professional terms in ultrasound reports. This template improves the understanding of reports by doctors at different levels and plays an important role in effective clinical intervention and treatment (8). Serum tumor markers can provide laboratory evidence for differentiating the benign and malignant nature of ovarian-adnexal tumors. Currently, the most commonly used serum biomarker for the

early diagnosis of ovarian cancer is carbohydrate antigen 125 (CA125); however, CA125 has relatively low specificity (9).

Expression of CA125 may also increase in several benign gynecological diseases (such as endometriosis, pelvic inflammatory disease and ovarian cysts) as well as in some non-gynecological diseases (such as liver cirrhosis and tuberculous peritonitis). Therefore, relying solely on the elevation of CA125 to diagnose ovarian cancer can result in misdiagnosis (10,11).

Human epididymis protein 4 (HE4) shows favorable specificity in the diagnosis of ovarian cancer. Especially for the diagnosis of early-stage ovarian cancer, compared with some other markers. HE4 can more accurately distinguish ovarian cancer from benign gynecological diseases (12).

For example, in benign gynecological diseases such as endometriosis and pelvic inflammatory disease, expression levels of HE4 usually do not increase as markedly as they do in ovarian cancer (13,14). Research has shown that when HE4 and CA125 are used in combination, they play a complementary role (15).

The risk of ovarian malignancy algorithm (ROMA) utilizes serum biomarkers to improve the accuracy of diagnosing benign and malignant ovarian-adnexal tumors. This indicator combines HE4 and CA125. To some extent, ROMA avoids the shortcomings of using HE4 or CA125 alone. ROMA has been shown to complement imaging techniques and improve the diagnostic efficacy of tumors (16). The purpose of the present study is to evaluate the efficacy of the ultrasonic O-RADS classification combined with ROMA in the differential diagnosis of benign and malignant ovarian-adnexal tumors and seek indicators to improve the accurate diagnosis of benign and malignant ovarian-adnexal tumors and ultimately improve the prognosis of patients with ovarian-adnexal tumors through precise and timely intervention measures.

Materials and methods

Research subject. A retrospective analysis was conducted on a total of 524 cases of 426 patients who were initially diagnosed with ovarian-adnexal tumors and underwent surgery at the General Hospital of Ningxia Medical University, (Yinchuan, China) from January 2021 to January 2024. The average age of patients in the benign group was 42.3±13.5 years old, while that in the malignant group was 56.1±11.6 years old. Inclusion criteria were as follows: i) Patients were pathologically diagnosed with ovarian-adnexal tumors for the first time in the General Hospital of Ningxia Medical University (Yinchuan, China). ii) There were complete ultrasound examination images and serological examination data. iii) Patients and their family members signed the informed consent forms and agreed to participate in the present study.

Exclusion criteria: i) Patients with a history of radiotherapy or chemotherapy. ii) Patients who were pregnant. iii) Patients with tumors in other parts of the body. iv) Patients whose ss images are of poor quality and cannot be accurately classified.

The present study was approved by the Ethics Committee of the General Hospital of Ningxia Medical University (approval no. KYLL-2024-1182; Yinchuan, China). All patients provided written informed consent. The legal guardians/close relatives of the participants provided written informed consent for their participation in the present study.

Instruments. A Mindray Nuewa R9 Pro ultrasonic diagnostic apparatus equipped with an intracavitary probe, an abdominal probe and a rectal probe was used in the present study. The frequency of the endocavity probe was 3_10 MHz and that of the abdominal probe was 1-8 MHz. Under normal circumstances, transvaginal ultrasound examination was adopted for those with a history of sexual activity while transabdominal ultrasound examination was used for those without a history of sexual activity. Patients were asked to empty their bladders and assume the lithotomy position before using the intracavitary probe. For the abdominal probe, patients were required to fill their bladder. For low-quality abdominal images that may have affected the O-RADS classification, the transrectal ultrasound examination was adopted. This examination method is similar to that of the intracavitary probe. When the tumor was relatively large and could not be imaged by a single ultrasound examination method, a transvaginal ultrasound was combined with transabdominal ultrasound or transrectal ultrasound with transabdominal ultrasound for the examination.

Protocol. Examiners carefully scanned the ovarian-adnexal area and obtained images of the tumors, including the size, boundary, shape (regular or irregular), composition (cystic: Unilocular and multilocular; the proportion of solid and cystic-solid components), blood flow (no blood flow, a small amount of blood flow, a moderate amount of blood flow, abundant blood flow), the inner wall of the cyst (whether there were papillary protrusions as well as the size and number of papillary protrusions) and the presence or absence of ascites and peritoneal nodules. Two physicians who had been engaged in gynecological ultrasound for day ≥5 years classified the 524 tumors according to the O-RADS. The inclusion criteria were as follows: For patients with bilateral single lesions, all lesions were retained. For patients with unilateral multiple tumors, ultrasound assessment (including diameter, echogenicity, margin and presence of protrusions) was used to select the single most indicative lesion (such as the one with the highest suspected malignant risk) for inclusion. For patients with bilateral multiple tumors, the same criteria applied as for unilateral multiple cases. This strategy aimed to avoid over-replication of data from individual patients while preserving the most critical lesion information, thereby enhancing the validity of the analysis.

Before the operation, the detection of tumor markers CA125 and HE4 consists of four core procedures of patient preparation, specimen collection and processing, laboratory testing and result verification which are essential to ensuring the accuracy of test results and their clinical reference value. Specifically, for the detection of CA125 and HE4, 5 ml of fasting venous blood should be collected from patients before surgery. The blood samples are then centrifuged at 3,500 r/min (centrifugation force is ~1,644 x g). under low temperature conditions for 10 min to separate the serum. Serum levels of CA125 and HE4 must be measured within 2 h using the Roche cobas e602 electrochemiluminescence immunoassay analyzer, with the corresponding Roche CA125 Assay Kit and Roche HE4 Assay Kit serum. Samples were collected from the enrolled patients withing 24 h before surgery. Ultrasound examinations of ovarian tumors were

performed 3 days before surgery. Referring to the instructions of the reagent kit, for the single diagnostic criteria: A CA125 level ≥-35 U/ml was considered malignant and an HE4 level ≥-140 p mol/l was considered malignant. The ROMA value was calculated as follows (where PI, prediction index; LN, natural logarithm; e, the base of the natural logarithm) (16): For premenopausal women: PI=-12.0+2.38xLN[HE4] + 0.0626xLN[CA125]; for postmenopausal women: PI=-8.09+1.04xLN[HE4] + 0.732xLN[CA125]; ROMA value (%)=ePI/[1 + e PI] x100%. A ROMA value ≥-11.4% for premenopausal women and ≥29.9% for postmenopausal women were considered malignant.

Ultrasonic O-RADS classification. O-RADS classifies ovarian-adnexal tumors into categories 0_5 (17-19). i) Category 0: The tumor cannot be examined by ultrasound due to factors such as intestinal gas or a large tumor size. ii) Category 1: Normal ovaries, simple follicles and corpora lutea (≤-3.0 cm). iii) Category 2: Malignant risk <-1%. a. Simple cysts, unilocular cysts with a smooth inner margin (though not simple cysts), hemorrhagic cysts of typical benign lesions, dermoid cysts and endometriosis (the maximum diameter <-10 cm). b. Simple parovarian cysts of any size, peritoneal inclusion cysts and hydrosalpinx. iv) Category 3: Malignant risk ≥-1% and <-10%. a. Unilocular cysts, ovarian endometriotic cysts, hemorrhagic cysts (≥-10 cm). b. Unilocular cysts with an irregular inner wall and a thickness <-3 mm. c. Multilocular cysts with a maximum diameter <-10 cm, without solid components, a smooth inner wall and a blood flow score ≤-3. d. Solid or quasi-solid (solid component >-80%) lesions with a smooth outer margin and a blood flow score of 1. v) Category 4: Malignant risk ≥-10% and <-50%. a. Multilocular cysts without solid components and with a maximum diameter ≥-10 cm. b. Multilocular cysts with a blood flow score of 1-3 or a blood flow score of 4 regardless of size. c. Unilocular cystic-solid masses. d. Multilocular cystic-solid masses with a blood flow score of 2-3 and a smooth outer margin. e. Unilocular cysts with 0-3 solid components in the form of papillae. vi) Category 5: Malignant risk ≥-50%. a. Unilocular cysts with ≥-4 papillary protrusions, accompanied by ascites and/or peritoneal nodules. b. Irregular solid lesions. c. Multilocular cystic-solid masses with a blood flow score of 3-4, accompanied by ascites and/or peritoneal nodules.

Statistical methods. SPSS 27.0 statistical software (IBM Corp.) and MedCalc 19.0 (MedCalc Software Ltd.) were used to conduct statistical analysis on the collected data. Categorical variables were expressed as frequencies and percentages. The chi-square test was adopted for comparison between two groups. For continuous variables, normally distributed data were expressed as the mean ± standard deviation and compared using the unpaired Student's t-test. Agreement analysis was performed using the κ test. A κ value of ≥0.75 indicated good agreement, 0.4_0.75 indicated moderate agreement and <0.4 indicated poor agreement. P≤0.05 was considered to indicate a statistically significant difference. The independent variables that were statistically significant in the univariate analysis were screened and included in the binary Logistic regression analysis. The sensitivity, specificity and the area under the curve of ROMA, O-RADS and the combination of ROMA and O-RADS were calculated.

Results

General information. A total of 524 ovarian-adnexal tumors from 426 patients were included in the present study. Analysis revealed that there were 256 benign cases and 268 malignant cases. The results of the ultrasonic O-RADS classification are shown in Table I. The image features of ultrasonic O-RADS category 4 are diverse. A tumor with a high proportion of cystic components is not necessarily a benign tumor and a tumor with solid components is not necessarily a malignant one. Careful identification is required to prevent misdiagnosis and missed diagnosis (Fig. 1A-D).

Inter-observer agreement between two gynecological sonographers. O-RADS classifications were assigned by two senior gynecological ultrasonographers who are highly experienced, with ≥5 years of practical experience. They demonstrated favorable inter-observer agreement (κ=0.817), demonstrating favorable reproducibility of the system for ovarian tumor evaluation (Table II).

Results of different diagnostic methods in the differential diagnosis of benign and malignant tumors. Among the 524 cases of ovarian-adnexal tumors, increasing patient age associated with increasing risk of malignant tumors with statistically significance (P<0.0001). According to the O-RADS classification criteria, there were 104 cases in O-RADS category 2, 113 cases in category 3, 81 cases in category 4 and 226 cases in category 5. Among the O-RADS categories 2_5, the proportions of malignant tumors were 0% (0/104), 4.42% (5/113), 53.09% (43/81) and 97.34% (220/226). These results indicated that the higher the ultrasonic O-RADS classification was, the higher the malignant risk of the tumor was, and the difference was statistically significant (P<0.0001). The tumor markers CA125 and HE4 were used respectively as single indicators for the differential diagnosis of benign and malignant tumors. The results showed that single indicators had certain value in the differential diagnosis of benign and malignant tumors. In the present study, the combined indicator ROMA of the two was used to diagnose tumors which could avoid the errors brought by single diagnosis to a certain extent. According to the ROMA diagnostic criteria, there were 291 cases before menopause and 233 cases after menopause and the proportions of malignant tumors were 27.49% (80/291) and 78.11% (182/233). These results indicated that the risk of malignant tumors after menopause was significantly higher when compared with that before menopause and the difference was statistically significant (P<0.0001; Table III).

O-RADS 2-5 tumors: Grouping by menopausal status for analysis. There were 291 cases of tumors before menopause, including 84 cases in O-RADS category 2; 92 cases in category 3; 46 cases in category 4 and 69 cases in category 5, taking pathological diagnosis as the gold standard. Among the O-RADS categories 2_5, the proportions of malignant tumors were 0% (0/84), 3.26% (3/92), 19.56% (9/46) and 97.10% (67/69). There were 233 cases of tumors after menopause, including 20 cases in O-RADS category 2; 21 cases in category 3; 35 cases in category 4 and 157 cases in category 5, taking pathological diagnosis as the gold standard. Among the

Table I. Results of the ultrasound O-RADS classification for ovarian-adnexal tumors.

	O-RADS classification					
	Number of patients					
Pathology	2	3	4	5	Total number	Proportion
Mature teratoma	4	41	9	0	54	10.31
Endometriosis cyst	36	18	4	2	60	11.46
Cystadenoma (serous, mucinous)	10	30	14	0	54	10.31
Simple cyst	15	8	4	0	27	5.15
Fibroma	0	0	1	4	5	0.95
Ovarian lutein cyst	14	1	0	0	15	2.87
Sex cord-stromal tumor	0	4	1	0	5	0.95
Follicular cyst	2	3	0	0	5	0.95
Parovarian cyst	3	0	0	0	3	0.57
Ovarian inclusion cyst	7	2	0	0	9	1.73
Hydrosalpinx	13	1	5	0	19	3.64
Cystadenocarcinoma (serous, mucinous)	0	1	34	172	207	39.51
Borderline cystadenoma	0	2	3	17	22	4.20
Immature teratoma	0	1	0	6	7	1.30
Ovarian carcinoid	0	0	3	2	5	0.95
Clear-cell carcinoma	0	1	2	7	10	1.92
Malignant Brenner tumor	0	0	0	6	6	1.14
Poorly differentiated adenocarcinoma	0	0	1	5	6	1.14
Ovarian sarcoma	0	0	0	2	2	0.38
Moderately differentiated adenocarcinoma of the ovary	0	0	0	3	3	0.57
n	104	113	81	226	524	100

O-RADS, ovarian-adnexal reporting and data system.

O-RADS categories 2_5, the proportions of malignant tumors were 0% (0/20), 9.52% (2/21), 97.14% (34/35) and 97.45% (153/157). Data analysis revealed that the incidence rate of malignant tumors in postmenopausal O-RADS category 4 is similar to that in premenopausal and postmenopausal O-RADS category 5 (Table IV). Since O-RADS category 2 tumors are all benign both before and after menopause, a further comparison was made on O-RADS categories 3_5. Analysis revealed that the malignant risk of patients with O-RADS category 4 after menopause was significantly higher when compared with that before menopause and the difference was statistically significant ($P<0.01$; Table V).

Comparison of the diagnostic efficacy of ultrasonic O-RADS classification, ROMA and their combination for tumors before and after menopause. Among the 524 cases of ovarian-adnexal tumors, there were 291 cases before menopause and 233 cases after menopause. The combined diagnosis improved the sensitivity and specificity of diagnosis compared with the single diagnostic criteria and enhanced the diagnostic efficacy of ovarian-adnexal tumors (Tables VI and VII).

Comparison of the areas under the ROC curves of the ultrasound O-RADS classification, ROMA and the combined diagnostic methods. Among the 524 cases of ovarian-adnexal tumors, ROC curves were plotted for 291 cases of ovarian-adnexal tumors before menopause and 233 cases after menopause by using the O-RADS classification, ROMA and the combined diagnostic methods. The results showed that the area under the ROC curve of the combined diagnosis was larger when compared with that of the single diagnosis. This result indicates that the combined diagnosis can improve diagnostic efficacy (Fig. 2A and B).

Discussion

Ovarian cancer is the seventh most common cancer among women and a leading cause of death in women with gynecological malignancies (20). Ovarian-adnexal tumors vary in their imaging characteristics due to different tissue origins; thus it remains challenging to accurately distinguish between benign and malignant tumors. With the development of imaging techniques, several risk prediction models have been proposed internationally, including the International Ovarian Tumor Analysis simple rules model (21), the Gynecologic Imaging RADS and the Assessment of Different NEoplasias in the adnexa model aiming to improve the diagnosis and treatment management of ovarian-adnexal tumors (22,23). In the present study, 524 lesions were included. The incidences of malignant tumors in the O-RADS 2_5 ultrasound

Table II. O-RADS classification results between physician A and physician B (Unit: cases).

	Physician B				
Physician A	O-RADS 2 classification	O-RADS 3 classification	O-RADS 4 classification	O-RADS 5 classification	Total n
O-RADS 2 classification	91	13	3	0	107
O-RADS 3 classification	16	87	9	1	113
O-RADS 4 classification	2	11	65	5	83
O-RADS 5 classification	0	1	7	213	221
Total n	109	112	84	219	524

O-RADS, ovarian-adnexal reporting and data system.

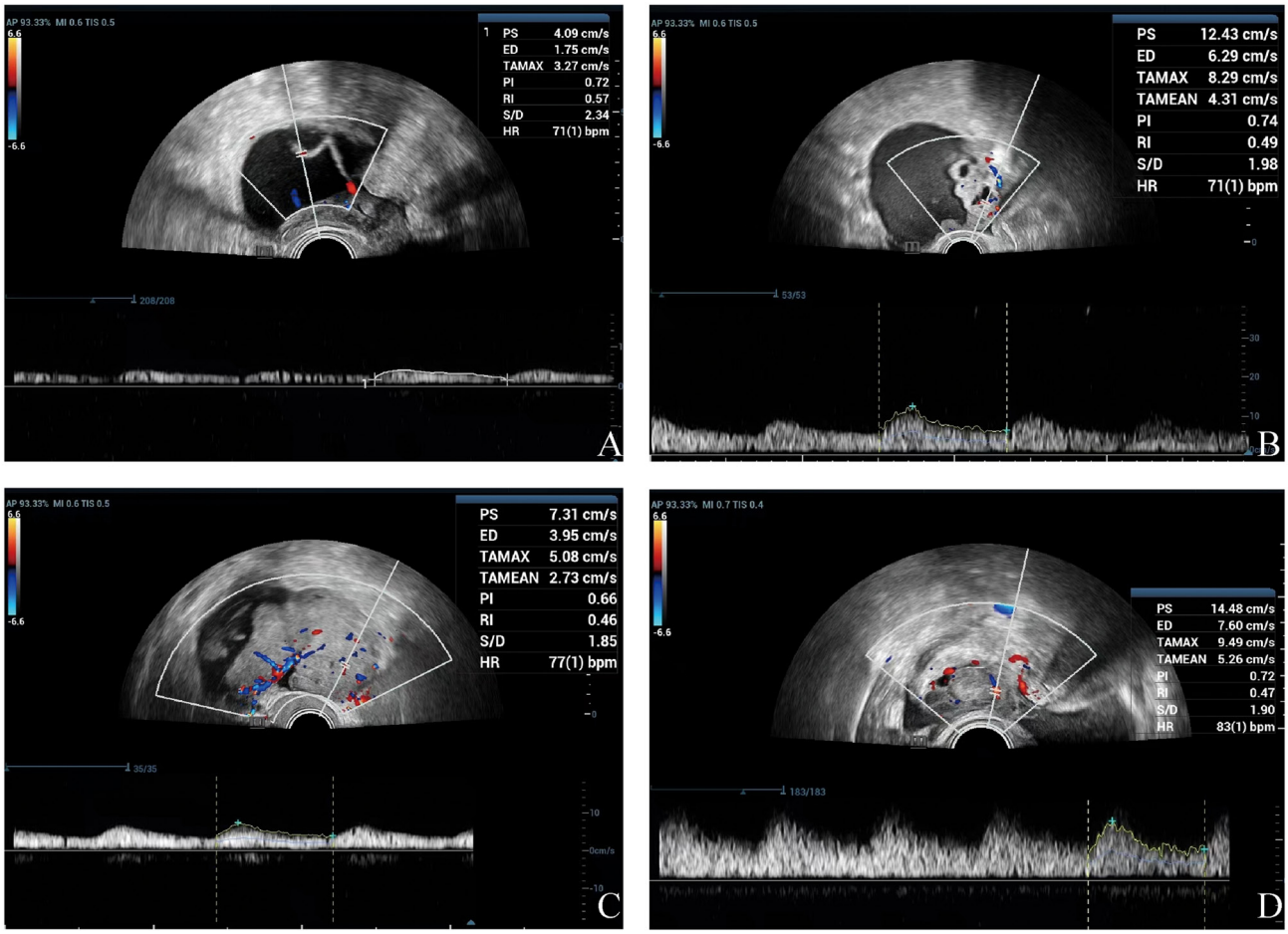

Figure 1. Image features of ultrasonic O-RADS classification. (A) The tumor had a regular contour and was a cystic mass with septa visible inside. A few punctate blood flow signals could be detected within the septa. It was classified as O-RADS category 3 and the pathological diagnosis was serous cystadenoma. (B) The tumor was relatively regular in shape with multiple septa and irregular solid masses visible inside. A few blood flow signals could be detected around it. It was classified as O-RADS category 4 and the pathological diagnosis was high-grade serous cystadenocarcinoma. (C) The tumor had a relatively regular contour was a cystic-solid mass. The cystic part had favorable sound transmission while the solid part had an unclear shape and boundary with irregular in shape and abundant blood flow signals could be detected. It was classified as O-RADS category 4 and the pathological diagnosis was borderline serous papillary cystadenoma. (D) The tumor had a regular contour and was mainly composed of solid components and punctate blood flow signals could be observed around it. It was classified as O-RADS category 4 and the pathological diagnosis was corpus luteum. O-RADS, ovarian-adnexal reporting and data system.

classifications were 0% (0/104), 4.42% (5/113), 53.09% (43/81) and 97.34% (220/226). The higher the ultrasound O-RADS classification is, the higher the detection rate of malignancy, and this result is similar to that of previous studies (24,25). In the present study, the incidence of malignant tumors in the ultrasound O-RADS category 4 was 53.09%. Based on the fact that the incidence of ovarian cancer is relatively high in postmenopausal women, the present study divided the

Table III. Univariate analysis of the differential diagnosis of 524 cases of ovarian-adnexal tumors.

Relevant parameters	Benign	Malignant	n	χ^2	P-value
Age	43.1±13.7	55.9±11.3	524	6.49	<0.001
O-RADS classification				89.08	<0.001
2	104	0	104		
3	108	5	113		
4	38	43	81		
5	6	220	226		
CA125 (U/ml)				237.45	<0.001
≤35	205	0	205		
>35	48	271	319		
HE4 (p mol/l)				432.44	<0.001
≤140	254	68	322		
>140	2	200	202		
ROMA				175.63	<0.001
Premenopausal	211	80	291		
Postmenopausal	51	182	233		

O-RADS, ovarian-adnexal reporting and data system; roma, risk of ovarian malignancy algorithm; CA125, carbohydrate antigen 125; HE4, human epididymis protein 4.

Table IV. Division of O-RADS classification2_5 tumors into premenopausal and postmenopausal groups for statistical analysis.

	Pathology results		
O-RADS classification	Malignant	Benign	Total
2			
Premenopausal	0	84	84
Postmenopausal	0	20	20
Total	0	104	104
3			
Premenopausal	4	88	92
Postmenopausal	2	19	21
Total	6	107	113
4			
Premenopausal	9	37	46
Postmenopausal	34	1	35
Total	43	38	81
5			
Premenopausal	67	2	69
Postmenopausal	153	4	157
Total	220	6	226

research subjects into two groups, the premenopausal group and the postmenopausal group and compared the incidences of malignant tumors between them. Analysis revealed that the incidences of malignant tumors in the O-RADS 4 category in the premenopausal group and the postmenopausal group were 19.56% (9/46) and 97.14% (34/35). Therefore, it can be observed that the risk of malignant tumors in patients in the O-RADS 4 category after menopause is markedly increased when compared with that before menopause and this is similar to that of previous studies (26-28).

According to the data released in the guidelines (17), the range of the malignant risk degree of O-RADS 4 lesions spans from 10 to 50%, which is likely to lead to errors in distinguishing between benign and malignant tumors.

However, in the results of the present study, the incidence of malignancy in postmenopausal patients with ovarian-adnexal tumors in the O-RADS 4 category was 97.14% (34/35) which was similar to that in the O-RADS 5 category (97.45%; 153/157). This result indicates that for postmenopausal lesions classified as O-RADS 4, high vigilance should be exercised as they may be malignant tumors. While the incidence of malignant tumors in the O-RADS 4 category in premenopausal patients was ≤20%, it is hypothesized that the occurrence of benign and malignant ovarian-adnexal tumors is associated with hormones and this result is consistent with that of previous studies (19,29,30).

Taking the O-RADS 4 category as the cut-off value, the sensitivity, specificity and area under the curve of the combined diagnosis for differentiating benign and malignant tumors in premenopausal patients with ovarian-adnexal tumors were 97.5 and 91.9% and 0.989. The difference in benign and malignant tumors in postmenopausal patients with ovarian-adnexal tumors, the sensitivity, specificity and area under the curve were 97.9 and 95.4% and 0.989. The combined diagnosis improved the diagnostic efficacy of ovarian-adnexal tumors compared with a single diagnosis. The ultrasound O-RADS classification can improve the specificity of differentiating between benign and malignant tumors, especially for postmenopausal patients and this result is consistent with that of previous studies (31,32).

Table V. Comparison of ultrasonic O-RADS classification before and after menopause.

O-RADS classification	n	Premenopausal	Postmenopausal	χ^2	P-value
3	113	92	21	2.147	≥0.05
4	81	46	35	38.03	≤0.01
5	226	69	157	0.078	≥0.05

O-RADS, ovarian-adnexal reporting and data system.

Table VI. Diagnostic efficacy of ultrasonic O-RADS classification, ROMA and combined diagnosis for tumors in premenopausal women.

Examination method	Sensitivity (%)	Specificity (%)	ROC-AUC	95% CI	P-value
ROMA	72.5	67.6	0.870	0.817-0.923	0.000
O-RADS	83.8	76.5	0.966	0.943-0.988	0.000
Combined diagnosis	97.5	91.9	0.989	0.980-0.997	0.000

O-RADS, ovarian-adnexal reporting and data system; ROMA, risk of ovarian malignancy algorithm; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

Table VII. Diagnostic efficacy of ultrasonic O-RADS classification, ROMA and combined diagnosis for tumors in postmenopausal women.

Examination method	Sensitivity (%)	Specificity (%)	ROC-AUC	95% CI	P-value
ROMA	83.6	93.2	0.922	0.879-0.964	0.000
O-RADS	81.6	90.9	0.966	0.886-0.996	0.000
Combined diagnosis	97.9	95.4	0.989	0.951-1.000	0.000

O-RADS, ovarian-adnexal reporting and data system; ROMA, risk of ovarian malignancy algorithm; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

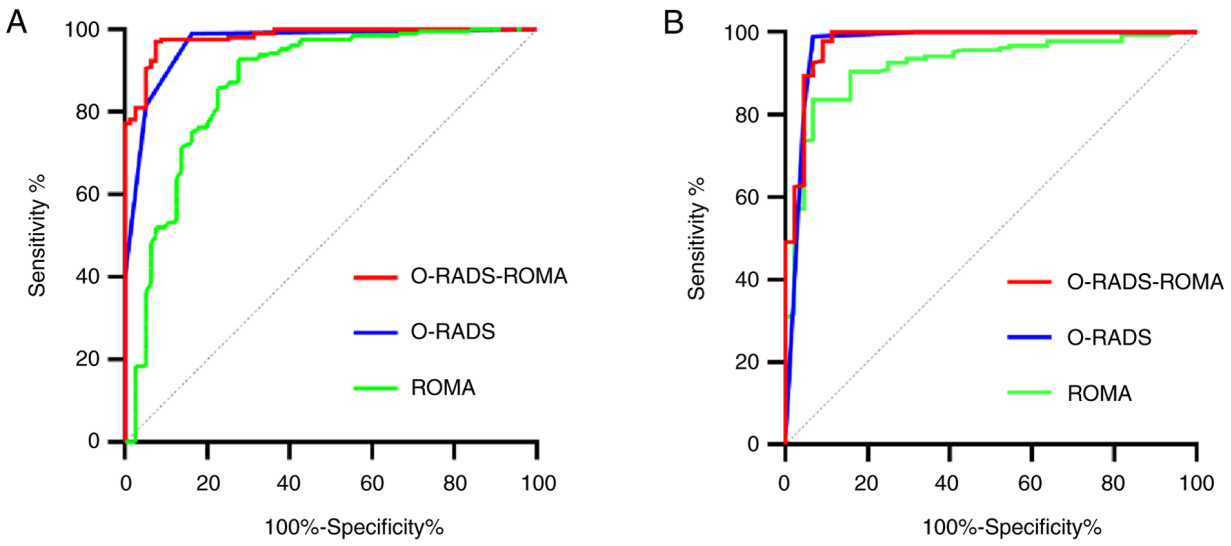

Figure 2. (A and B) By menopausal status, referring to the diagnostic efficacy of O-RADS combined with ROMA, O-RADS classification alone and ROMA alone for benign and malignant ovarian-adnexal masses in premenopausal and postmenopausal women, respectively. The results showed that, regardless of whether the patients were premenopausal or postmenopausal, the diagnostic efficacy of O-RADS classification combined with ROMA for benign and malignant ovarian-adnexal masses was higher compared with that of O-RADS classification used alone and ROMA used alone. O-RADS, ovarian-adnexal reporting and data system; ROMA, risk of ovarian malignancy algorithm.

The lutein cyst is an ovarian tumor-like lesion and generally does not meet surgical indications. In the present study, among the 15 cases of lutein cysts, except for one 15-year-old patient who underwent surgery because their image showed characteristics such as papillary-like echoes and a relatively thick cyst wall and was classified as O-RADS 4, the remaining cases were all two lesions in the adnexal area of patients that were simultaneously included in the present study. Among them, there were 5 cases of lutein cysts combined with endometriotic cysts, 5 cases combined with hydrosalpinx or inflammatory lesions, 3 cases combined with simple cysts or corpus luteum rupture and bleeding, and 1 case combined with serous cystadenoma. In the present study, 5 cases in the O-RADS 3 category were judged as malignant, including 1 case of clear cell carcinoma, 1 case of unilocular serous cystadenocarcinoma, 1 case of immature teratoma and 2 cases of borderline cystadenoma. Among the benign tumors, endometriotic cysts accounted for 11.46% of all tumors (60/524). There were 36 cases in the O-RADS 2 category, 18 cases in the O-RADS 3 category, 4 cases in the O-RADS 4 category and 2 cases in the O-RADS 5 category. The results suggested that the imaging characteristics of ~10% of endometriotic cysts are complex and diverse and need to be differentiated from the images of malignant tumors. In the present study, the combined approach of O-RADS and ROMA was adopted which notably improved the specificity of differential diagnosis and could avoid misdiagnosis caused by using a single diagnostic criterion.

On the ultrasonic image, fibroma may appear as a hypoechoic or isoechoic mass with clear boundaries and a regular shape. This feature is similar to that of some common benign ovarian tumors (33).

In some cases, the ultrasonic manifestations of fibroma may be similar to those of some low-grade malignant ovarian tumors. In the early stage, some malignant tumors may have relatively clear boundaries, regular shapes and relatively uniform internal echoes (34).

If there are some complex echo changes inside the fibroma, such as calcification and a small amount of fluid dark areas, it may be misjudged as the manifestation of a malignant tumor. In the present study, among 5 cases of fibroma, 4 cases were classified as Category 5 and 1 case was classified as Category 4 according to the ultrasound O-RADS classification, which increased the psychological burden on patients. The results of the present study are similar to the study by Valentin *et al* (35) who listed fibroma as one of the most difficult diseases to diagnose in the United States (35,36). In the present study, the combined use of ultrasound O-RADS classification and ROMA has improved the specificity of differential diagnosis and can avoid the psychological pressure on patients and their families caused by misdiagnosis.

In the field of diagnosis of ovarian and adnexal tumors, the ultrasound O-RADS classification is widely used (37).

However, there are still some malignant tumors that are prone to being misdiagnosed as benign tumors in the early stage. The main reasons for misdiagnosis in the present study are summarized as follows: Firstly, the tissues of the ovarian-adnexal tumors are complex and there is an overlap of imaging features. In the early stage of some malignant tumors, they may present relatively regular shapes, clear boundaries and homogeneous internal echoes which are similar to the characteristics of benign tumors in the O-RADS classification. For example, some early-stage epithelial ovarian carcinomas may not show obvious signs of malignancy such as irregular margins, heterogeneous internal structures or significant vascularity. This similarity makes it difficult for ultrasound physicians to accurately distinguish them from benign tumors based solely on the O-RADS classification criteria. Secondly, the resolution of ultrasound is limited and small malignant foci or subtle changes within the tumor may not be clearly visualized therefore resulting in an underestimation of the malignancy of the tumor. For instance, microcalcifications or small areas of necrosis that are typical of malignant tumors may be missed due to the insufficient resolution of the ultrasound equipment. Thirdly, the experience and proficiency of ultrasound operators also play a key role. Inexperienced operators may not be able to detect some subtle but important features that suggest malignancy or may misinterpret the observed features. They may overly rely on the standard O-RADS classification guidelines and overlook some atypical manifestations that could indicate a malignant tumor. The aforementioned situations may delay the condition of a patient and pose a serious threat to the safety of the patient. Through the data analysis of the present study, in order to improve the accuracy of the ultrasound O-RADS classification and reduce the misdiagnosis rate of early malignant tumors as benign tumors, the present study further adopted the combination of O-RADS classification and tumor markers. Analysis revealed that the combined diagnosis is helpful for more precise diagnosis and can avoid misdiagnosis in the early stage of ovarian and adnexal tumors.

The present study has certain limitations. Firstly, the primary limitation of the present study stems from the fact that all enrolled cases were derived from a patient population who opted for surgical treatment. This inclusion criterion may have led to the oversight of physiological masses that could resolve spontaneously during conservative management and may also have limited the full consideration of confounding variables such as hormone replacement therapy, thereby potentially introducing selection bias. Nonetheless, the study protocol employed here remains beneficial, as it helps to mitigate, to some extent, the risk of misdiagnosis associated with relying solely on ultrasound examination, while simultaneously ensuring high diagnostic accuracy for tumors that indeed present with clear surgical indications.

Secondly, the findings of the present study are based on the specific combination of O-RADS and ROMA, and all data were derived from local top-tier tertiary hospitals. It is fully acknowledged that this single-method approach and relatively homogenous data source may affect the generalizability of the current results and represent a potential limitation, which has been clearly addressed in the discussion section. Despite this, the focused design was essential to establish a foundational understanding of the combined diagnostic value. To build upon this work, conducting multi-center, prospective studies that include cases from various levels of healthcare institutions, is proposed. Furthermore, multi-modal data fusion strategies will be actively investigated; for instance, by examining the complementary roles of O-RADS ultrasound and O-RADS MRI or developing integrated models that incorporate

additional serum biomarkers alongside established markers like CA125 and HE4.

Last but not least, the present study was retrospective, and all analyses were based on static images which may have impacted the accuracy of diagnosis. Based on the foundation provided by the present study, future research will try to collect data from prefectural and municipal hospitals in the surrounding areas. To minimize the impact of this limitation, the present study implemented the following measures in the study design: Standardized image selection: A strict image inclusion criteria was established, ensuring that the archived static images contained essential diagnostic views (such as the largest longitudinal and transverse sections of the tumor) and key information (such as color Doppler flow signals). Structured feature extraction: The analysis relied not merely on subjective judgment but, more importantly, on the standardized and structured extraction and recording of sonographic features (such as irregular tumor walls, papillary projection and echogenicity patterns). These features represent key diagnostic elements distilled from the dynamic examination. Emphasis on feasibility: Utilizing retrospective static images made it feasible to train the model on a large-scale dataset.

In conclusion, the present study used the combination of ultrasound O-RADS classification and ROMA to conduct differential diagnosis on the benign and malignant nature of ovarian-adnexal tumors. Taking the O-RADS classification as the research objective, the results revealed that the risk of malignant tumors in postmenopausal patients with ovarian-adnexal tumors was markedly increased when compared with that in premenopausal patients. The results indicated that hormones play an important role in the pathophysiology of ovarian tumors. Taking the O-RADS 4 category as the research objective, it was found that the risk of malignant tumors in postmenopausal patients was markedly increased when compared with the premenopausal group. Compared with using the ultrasound O-RADS classification and ROMA alone, the combined diagnosis notably improved the sensitivity and specificity for the differential diagnosis of benign and malignant tumors, regardless of whether it was for premenopausal or postmenopausal patients with ovarian-adnexal tumors.

Acknowledgements

Not applicable.

Funding

The present study was supported by the National Natural Science Foundations of China (grant no. 8226070416), the Program of Ningxia Hui Autonomous Region science and technology benefit people project (grant no. 2023CMG03025), the Ningxia Natural Science Foundation (grant no. 2022AAC03530) and the Ningxia Natural Science Foundation (grant no. 2023AAC03565).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

LZ, HW and JW participated in the conception and design of the present study. LZ and LX organized the database and statistical analysis and participated in the revision of the manuscript. LZ participated in figure creation and wrote the first draft of the manuscript. LZ and HW confirm the authenticity of all the raw data. HW revised the manuscript for intellectual content and provided financial support. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the General Hospital of Ningxia Medical University (approval no. KYLL-2024-1182; Yinchuan, China). All patients provided written informed consent. The legal guardians/close relatives of the participants provided written informed consent for their participation in the present study.

Patient consent for publication

For any identifiable images or data that may be included in this article, written informed consent was obtained from the legal guardians/close relatives of the individuals (including minors).

Competing interests

The authors declare that they have no competing interests.

References

1. Sambasivan S: Epithelial ovarian cancer: Review article. Cancer Treat Res Commun 33: 100629, 2022.
2. Roett MA and Evans P: Ovarian cancer: An overview. Am Fam Physician 80: 609-616, 2009.
3. Chen GY, Hsu TF, Chan IS, Liu CH, Chao WT, Shih YC, Jiang LY, Chang YH, Wang PH and Chen YJ: Comparison of the O-RADS and ADNEX models regarding malignancy rate and validity in evaluating adnexal lesions. Eur Radio 32: 7854-7864, 2022.
4. Vara J, Manzour N, Chacón E, López-Picazo A, Linares M, Pascual MÁ, Guerriero S and Alcázar JL: Ovarian adnexal reporting data system (O-RADS) for classifying adnexal masses: A systematic review and Meta-analysis. Cancers (Basel) 14: 3151, 2022.
5. Xie WT, Wang YQ, Xiang ZS, Du ZS, Huang SX, Chen YJ and Tang LN: Efficacy of IOTA simple rules, O-RADS, and CA125 to distinguish benign and malignant adnexal masses. J Ovarian Res 15: 15, 2022.
6. Wu M, Zhang M, Cao J, Wu S, Chen Y, Luo L, Lin X, Su M and Zhang X: Predictive accuracy and reproducibility of the O-RADS US scoring system among sonologists with different training levels. Arch Gynecol Obstet 308: 631-637, 2023.
7. Pi Y, Wilson MP, Katlariwala P, Sam M, Ackerman T, Paskar L, Patel V and Low G: Diagnostic accuracy and inter-observer reliability of the O-RADS scoring system among staff radiologists in a North American academic clinical setting. Abdom Radiol (NY) 46: 4967-4973, 2021.
8. Vara J, Pagliuca M, Springer S, Gonzalez de Canales J, Brotons I, Yakcich J, Ajossa S, Pascual MA, Guerriero S and Alcazar JL: O-RADS classification for ultrasound assessment of adnexal masses: Agreement between IOTA lexicon and ADNEX model for assigning risk group. Diagnostics (Basel) 13: 673, 2023.
9. Zhang M, Cheng S, Jin Y, Zhao Y and Wang Y: Roles of CA125 in diagnosis, prediction, and oncogenesis of ovarian cancer. Biochim Biophys Acta Rev Cancer 1875: 188503, 2021.
10. Karam AK and Karlan BY: Ovarian cancer: The duplicity of CA125 measurement. Nat Rev Clin Oncol 7: 335-339, 2010.

11. Yang Q, Zhang H, Ma PQ, Peng B, Yin GT, Zhang NN and Wang HB: Value of ultrasound and magnetic resonance imaging combined with tumor markers in the diagnosis of ovarian tumors. World J Clin Cases 11: 7553-7561, 2023.
12. Nalini N, Kumar A, Sharma S, Singh B, Singh AV, Prakash J and Singh S: The diagnostic accuracy of serum and urine human epididymis protein 4 (HE4) in ovarian cancer in 15,394 subjects: An updated Meta-analysis. Cureus 14: e30457, 2022.
13. Wu L, Dai ZY, Qian YH, Shi Y, Liu FJ and Yang C: Diagnostic value of serum human epididymis protein 4 (HE4) in ovarian carcinoma: A systematic review and meta-analysis. Int J Gynecol Cancer 22, 1106-1112, 2012.
14. Olsen M, Lof P, Stiekema A, van den Broek D, Wilthagen EA, Bossuyt PM and Lok CAR: The diagnostic accuracy of human epididymis protein 4 (HE4) for discriminating between benign and malignant pelvic masses: A systematic review and meta-analysis. Acta Obstet Gynecol Scand 100: 1788-1799, 2021.
15. Lenhard M, Stieber P, Hertlein L, Kirschenhofer A, Fürst S, Mayr D, Nagel D, Hofmann K, Krocker K and Burges A: The diagnostic accuracy of two human epididymis protein 4 (HE4) testing systems in combination with CA125 in the differential diagnosis of ovarian masses. Clin Chem Lab Med 49: 2081-2088, 2011.
16. Jeong TD, Cho EJ, Ko DH, Lee W, Chun S, Kwon HJ, Hong KS, Kim YM and Min WK: A new strategy for calculating the risk of ovarian malignancy algorithm (ROMA). Clin Chem Lab Med 55: 1209-1214, 2017.
17. Andreotti RF, Timmerman D, Strachowski LM, Froyman W, Benacerraf BR, Bennett GL, Bourne T, Brown DL, Coleman BG, Frates MC, *et al*: O-RADS US risk stratification and management system: A consensus guideline from the ACR ovarian-adnexal reporting and data system committee. Radiology 294: 168-185, 2020.
18. Timmerman S, Valentin L, Ceusters J, Testa AC, Landolfo C, Sladkevicius P, Van Holsbeke C, Domali E, Fruscio R, Epstein E, *et al*: External validation of the ovarian-adnexal reporting and data system (O-RADS) lexicon and the international ovarian tumor analysis 2-step strategy to stratify ovarian tumors into O-RADS risk groups. JAMA Oncol 9: 225-233, 2023.
19. Strachowski LM, Jha P, Phillips CH, Blanchette Porter MM, Froyman W, Glanc P, Guo Y, Patel MD, Reinhold C, Suh-Burgmann EJ, *et al*: O-RADS US v2022: An update from the American College Of Radiology's Ovarian-adnexal reporting and data system US committee. Radiology 308: e230685, 2023.
20. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA and Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68: 394-424, 2018.
21. Timmerman D, Valentin L, Bourne TH, Collins WP, Verrelst H and Vergote I; International Ovarian Tumor Analysis (IOTA) Group: Terms, definitions and measurements to describe the sonographic features of adnexal tumors: A consensus opinion from the international Ovarian tumor analysis (IOTA) group. Ultrasound Obstet Gynecol 16: 500-505, 2000.
22. Amor F, Vaccaro H, Alcázar JL, León M, Craig JM and Martinez J: Gynecologic imaging reporting and data system: A new proposal for classifying adnexal masses on the basis of sonographic findings. J Ultrasound Med 28: 285-291, 2009.
23. Van Calster B, Van Hoorde K, Valentin L, Testa AC, Fischerova D, Van Holsbeke C, Savelli L, Franchi D, Epstein E, Kaijser J, *et al*: Evaluating the risk of ovarian cancer before surgery using the ADNEX model to differentiate between benign, borderline, early and advanced stage invasive, and secondary metastatic tumours: Prospective multicentre diagnostic study. BMJ 349: g5920, 2014.
24. Zhang Q, Dai X and Li W: Systematic review and meta-analysis of O-RADS ultrasound and O-RADS MRI for risk assessment of ovarian and adnexal lesions. AJR Am J Roentgenol 221: 21-33, 2023.
25. Thomassin-Naggara I, Poncelet E, Jalaguier-Coudray A, Guerra A, Fournier LS, Stojanovic S, Millet I, Bharwani N, Juhan V, Cunha TM, *et al*: Ovarian-adnexal reporting data system magnetic resonance imaging (O-RADS MRI) score for risk stratification of sonographically indeterminate adnexal masses. JAMA Netw Open 3: e1919896, 2020.
26. Phillips CH, Guo Y, Strachowski LM, Jha P, Reinhold C and Andreotti RF: The Ovarian/adnexal reporting and data system for ultrasound: From standardized terminology to optimal risk assessment and management. Can Assoc Radiol J 74: 44-57, 2023.
27. Xie W, Lin W, Li P, Lai H, Wang Z, Liu P, Huang Y, Liu Y, Tang L and Lyu G: Developing a deep learning model for predicting ovarian cancer in Ovarian-adnexal reporting and data system ultrasound (O-RADS US) category 4 lesions: A multicenter study. J Cancer Res Clin Oncol 15: 346, 2024.
28. Zeng S, Jia H, Zhang H, Feng X, Dong M, Lin L, Wang X and Yang H: Multimodal ultrasound-based radiomics and deep learning for differential diagnosis of O-RADS 4-5 adnexal masses. Cancer Imaging 25: 64, 2025.
29. Khati NJ, Kim T and Riess J: Imaging of benign adnexal disease. Radiol Clin North Am 58: 257-273, 2020.
30. Lin L, Fu L, Wu H, Cheng S, Chen G, Chen L, Zhu J, Wang Y and Cheng J: The value of MRI in differentiating ovarian clear cell carcinoma from other adnexal masses with O-RADS MRI scores of 4-5. Insights Imaging 16: 22, 2025.
31. Heremans R, Valentin L, Sladkevicius P, Timmerman S, Moro F, Van Holsbeke C, Epstein E, Testa AC, Timmerman D and Froyman W: Imaging in gynecological disease (24): Clinical and ultrasound characteristics of ovarian mature cystic teratomas. Ultrasound Obstet Gynecol 60: 549-558, 2022.
32. Zou M, Chen R, Wang Y, He Y, Wang Y, Dong Y and Li J: Clinical and ultrasound characteristics of virilizing ovarian tumors in pre- and postmenopausal patients: A single tertiary center experience. Orphanet J Rare Dis 16: 426, 2021.
33. Moro F, Scavello I, Maseroli E, Rastrelli G, Baima Poma C, Bonin C, Dassie F, Federici S, Fiengo S, Guccione L, *et al*: Women's Endocrinology Group of the Italian Society of Endocrinology. The physiological sonographic features of the ovary in healthy subjects: A joint systematic review and meta-analysis by the Italian Society of Gynecology and Obstetrics (SIGO) and the Italian Society of Endocrinology (SIE). J Endocrinol Invest 46: 439-456, 2023.
34. Chang H, Wang Q, Liu T, Chen L, Hong J, Liu K, Li Y, Yang N, Han D, Mi X, *et al*: A bibliometric analysis for Low-intensity ultrasound study over the past three decades. J Ultrasound Med 42: 2215-2232, 2023.
35. Valentin L, Ameye L, Jurkovic D, Metzger U, Lécuru F, Van Huffel S and Timmerman D: Which extrauterine pelvic masses are difficult to correctly classify as benign or malignant on the basis of ultrasound findings and is there a way of making a correct diagnosis? Ultrasound Obstet Gynecol 27: 438-444, 2006.
36. Nasioudis D, Mastroyannis SA, Ko EM, Haggerty AF, Cory L, Giuntoli RL II, Kim SH, Morgan MA and Latif NA: Delay in adjuvant chemotherapy administration for patients with FIGO stage I epithelial ovarian carcinoma is associated with worse survival; an analysis of the national cancer database. Gynecol Oncol 166: 263-268, 2022.
37. Lee S, Lee JE, Hwang JA and Shin H: O-RADS US: A Systematic review and Meta-analysis of Category-specific malignancy rates. Radiology 308: e223269, 2023.