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ORIGINAL RESEARCH

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Diagnostic value of tumor markers combined with different imaging protocols for ovarian tumors

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Abstract

Background: To investigate the value of ultrasound Gynecological Imaging Reporting and Data System (GI-RADS) classification and Ovarian Reporting and Data System (O-RADS) classifications combined with serum tumor markers for ovarian tumors. **Methods**: A total of 100 patients with ovarian adnexal tumors had serum tumor markers tested and O-RADS and GI-RADS classifications were used for diagnoses. This allowed for a comparison of the diagnostic efficacy of separate and combined diagnostic approaches. **Results**: Among the 100 patients, 62 benign masses and 38 malignant masses were identified. Clinical characteristics showed that age, irregular contour and the presence of ascites were significantly different between the benign and malignant groups. The diagnostic efficacy results showed that the sensitivity, specificity, and accuracy of O-RADS combined with GI-RADS classification, human epididymal protein 4 (HE4) and cancer antigen 125 (CA125) were higher than other separate diagnosis and combined diagnosis schemes. Receiver operating characteristic (ROC) curve analysis also confirmed that this approach had better diagnostic efficacy for ovarian tumors. **Conclusions**: Serum tumor markers HE4, CA125 test, O-RADS classification and GI-RADS classifications provided high diagnostic value for detecting benign and malignant ovarian tumors. However, combining these classifications with HE4 and CA125 further enhanced diagnostic accuracy.

Keywords

Ovarian benign and malignant tumors; O-RADS classification; GI-RADS classification; HE4; CA125; Diagnostic efficacy

1. Introduction

Ovarian cancer is known as the most aggressive malignancy within the category of gynecological cancers, and it has the highest mortality rate among these tumors in China [1]. In recent years, with the improvement of people's living standards and health awareness, the number of patients with ovarian cancer detected through physical examination and other methods has also begun to increase. These ovarian cancer patients are often relatively young, and the cancer is usually detected at an early stage increasing the potential for a cure [1]. Therefore, early identification of ovarian tumors, whether benign or malignant, is crucial for guiding treatment decisions and prognosis [2]. Tumor biomarkers also play a crucial role in preoperative detection of ovarian cancer, with serum carbohydrate antigen 125 (CA125) and human epididymal protein 4 (HE4) serving as important indicators for early diagnosis, as well as assessment of recurrence and metastasis of ovarian tumors [3]. Numerous studies have focused on the combined diagnosis using CA125 and HE4. However, it has also been found that the use of single serum tumor markers has certain limitations in the diagnosis of benign and malignant ovarian tumors [4]. Most females with ovarian cancer experience non-specific symptoms (*e.g.*, abdominal pain or discomfort, urinary frequency, weight changes). Therefore, ovarian cancer is often diagnosed using Computed Tomography (CT) while searching for a cause of these non-specific symptoms or to evaluate the abdomen after worrisome ultrasound findings [5]. The characteristics of ovarian cancer on MR imaging are partly similar to those on CT. A recent meta-analysis showed that Magnetic Resonance Imaging (MRI) had a sensitivity of 91% and specificity of 85% for the diagnosis of ovarian cancer, although CT is most commonly used to stage ovarian cancer patients, MRI and positron emission tomography (PET)-CT are increasingly used in specialized centers to stage advanced cases [5]. As a noninvasive examination method, Doppler ultrasound has significant value in diagnosing intrauterine lesions in perimenopausal and postmenopausal women with vaginal bleeding [6]. The uterine artery Doppler index (UTA) is beneficial in distinguishing malignant from benign endometrial lesions. Additionally, pulsed ultrasound Doppler velocimetry appears to be effective in predicting the advanced stage of endometrial cancer [7]. The Gynecological Imaging Reporting and Data System (GI-RADS) can classify adnexal masses as benign or

malignant, aiding in the clinical selection of optimal treatment strategies [8]. The Ovarian Reporting and Data System (O-RADS) is currently the only system that includes all risk categories and associated management protocols. Its formal release is expected to reduce reporting ambiguities, thereby enhancing the accuracy of benign and malignant risk assessments for ovarian masses [9]. Currently, research indicates that the combination of imaging examinations with tumor marker detection can detect ovarian cancer five months earlier than clinical symptoms [10]. Thus, exploring diagnostic schemes that integrate imaging examinations with tumor marker detection holds significant clinical significance for the screening and detection of ovarian cancer [11]. Therefore, this study investigates the clinical value of the ultrasound GI-RADS system and O-RADS classification combined with serum tumor markers CA125 and HE4 in diagnosing the benign and malignant tumors of the ovaries and adnexa.

2. Methods

2.1 Patients and study design

Retrospective analysis of clinical data of 100 patients with ovarian adnexal tumors admitted to our hospital from January 2022 to December 2023. The age of patients ranged from 34 to 64 years, with a mean age of (49.21 $\pm$ 7.01) years. In cases of multiple masses, the mass exhibiting the most or largest suspicious malignant features was selected. When both benign and malignant masses were present, the mass with the higher classification category was chosen.

The inclusion criteria are as follows: age over 18 years old, determined postoperative pathological stage, clear and complete saved ultrasound images, standardized report writing, and detection of serum cancer antigen 125 (CA125) and HE4 levels one week before surgery. The exclusion criteria are as follows: incomplete clinical or pathological data, and previous ovarian tumor surgery or drug treatment. The study has been reviewed and approved by the Ethics Committee of our institution.

2.2 Study tool

Instrument and Inspection Methods: The Philips iU22 (Philips Healthcare, Andover, MA, USA) and GE Logiq E8 color Doppler ultrasound instruments (GE Healthcare, Wauwatosa, WI, USA) were utilized. The transducer frequency for transvaginal ultrasonography ranged from 3 to 7 MHz. All ultrasonographic examinations were conducted within 30 days prior to surgery. Before starting the image analysis, two sonographers with more than 5 years of work experience received 6 h of special theoretical training and practical experience for the two classification methods. Subsequently, the two physicians independently analyzed the morphological characteristics of each ovarian tumor and completed the classification diagnosis. If their results differed, the diagnosis was unified through consultation. The images were acquired by the same sonographers with over 3 years of experience in the field.

Morphological characteristics of each lesion were recorded, including size, echogenicity, outline, maximum cyst wall and septal thickness, cyst contents, size of solid areas, number and size of papillary projections, presence of ascites and peritoneal nodules, as well as blood flow conditions. All images were archived.

Serum Tumor Markers: Serum CA125 and HE4 levels were measured 1–14 days prior to surgery. The measurements were conducted using the Abbott Architect 2000 fully automated chemiluminescent immunoassay system (Abbott Laboratories, Abbott Park, IL, USA). The reagents used were from Abbott Laboratories' second-generation immunoradiometric assay kits (20113402930, Abbott Park, IL, USA). Normal values for HE4 (per the manufacturer's instructions, Abbott, USA) were 0–70 pmol/mL for premenopausal women and 0–140 pmol/mL for postmenopausal women, while normal values for CA125 (per the manufacturer's instructions, Abbott, USA) were 0–35 U/mL. The cutoff values were $>$35 U/mL for CA125 and $>$66.3 pmol/L for HE4 in premenopausal women and $>$143.26 pmol/L for HE4 in postmenopausal women.

2.3 GI-RADS classification

The GI-RADS classification is based on the Simple Rules (SR) of the International Ovarian Tumor Analysis (IOTA) group [12]. The GI-RADS 5 classification method was used to classify GI-RADS categories 1 to 3 as benign lesions and categories 4a to 5 as malignant lesions [13].

2.4 O-RADS classification

According to the O-RADS classification guidelines [14, 15], malignant risk classification uses six categories. This study only investigated lesions classified as O-RADS 1–5, with O-RADS 1–3 designated as benign lesions and O-RADS 4–5 as malignant lesions. When ultrasound indicates benignity but serum tumor markers CA125 and HE4 are elevated above normal reference values, the tumor classification is upgraded. Conversely, when ultrasound indicates malignancy and serum tumor markers CA125 and HE4 are within normal range, the tumor classification is downgraded [16].

2.5 Statistical analysis

Statistical analysis was performed using SPSS version 26 (SPSS Inc., Chicago, IL, USA). For continuous data conforming to a normal distribution, descriptive statistics were presented as mean $\pm$ standard deviation, and intergroup comparisons were conducted using *t*-tests. For categorical variables, the number of cases (percentage) is used for description, and the Wilcoxon test is used to analyze non- parametric data. Additionally, ROC curves for the subjects' working characteristics in distinguishing benign from malignant ovarian tumors using different classification methods were plotted, and the area under the curve (AUC) was calculated to obtain the corresponding sensitivity and specificity.

3. Results

3.1 Pathological outcome

A total of 100 ovarian adnexal masses were identified among 100 patients. 62 cases (62.00%) were classified as benign,

while 38 cases (38.00%) were classified as malignant. The specific pathological results of the ovarian adnexal masses are shown in Table 1.

3.2 Clinical characteristics of benign and malignant ovarian tumors

General data of patients on the clinical characteristics of patients in the benign and malignant groups are shown in Table 2. The results indicate that the age of patients in the malignant group is significantly higher than that in the benign group, with statistical significance ($t = 3.051$, $p = 0.003$). Additionally, the malignant group exhibits significantly higher rates of maximum lesion diameter, tumor irregular margins and ascites compared to the benign group, with statistical significance ($Z = 2.447$, 3.800, 2.828, $p < 0.001$). There is no significant difference in menopausal status and Body Mass Index (BMI) between the two groups, with no statistical significance ($Z = 0.991$, $t = 1.416$, $p > 0.05$).

3.3 The diagnostic efficacy of serum tumor markers

Compared with pathological results, the accuracy of HE4 diagnosis is 81.00%, with a sensitivity of 84.20% and a specificity of 79.00%. The accuracy of CA125 diagnosis is 76.00%, with a sensitivity of 76.32% and a specificity of 75.81%. The specific detection results are shown in Table 3.

3.4 Comparison of diagnostic efficacy of ultrasound GI-RADS and O-RADS

Compared with pathological results, the diagnostic efficacy of O-RADS classification with an accuracy of 90.00%, sensitivity of 86.80% and specificity of 91.94%. GI-RADS classification with an accuracy of 85.00%, sensitivity of 84.20% and specificity of 85.48%. Specific results are presented in Table 4.

3.5 The diagnostic efficacy of combined diagnosis

Compared with pathological results, the diagnostic results of the scheme combined with O-RADS classification and HE4, CA125 scheme, the scheme combined with GI-RADS classification and HE4, CA125 scheme and the scheme combined with four methods were all higher than those of individual HE4, CA125, O-RADS classification, and GI-RADS classification to varying degrees. Among them, the sensitivity, specificity, and accuracy of the combined diagnosis of the four schemes were the highest. Furthermore, the results of ROC curves showed that the AUC curve areas of all groups were >0.5, indicating that the research methods all had optimal diagnostic efficacy. However, considering that the AUC curve area of the combined diagnosis of the four schemes was the largest, it proves that the diagnostic efficacy of the four combined schemes is the best. Specific results are shown in Table 5 and Fig. 1.

4. Discussion

Malignant ovarian tumors represent the most lethal gynecologic malignancies, presenting a persistent clinical challenge in the diagnosis and management of patients with advanced-stage ovarian cancer [17, 18]. Elderly individuals constitute a high-risk population for ovarian cancer, with most patients experiencing insidious onset, often asymptomatic or presenting with mild symptoms, with approximately 75% diagnosed at an advanced stage [19, 20]. Early detection of ovarian cancer is crucial for devising effective treatment strategies and improving patient prognosis.

Serum tumor marker tests, such as CA125 and HE4, are widely used for differentiating benign from malignant ovarian tumors in patients [21]. Previous studies have confirmed that the combination of CA125 and HE4 can reduce the misdiagnosis rate of ovarian cancer, improve the accuracy of early diagnosis, and exhibit higher sensitivity and specificity. Moreover,

TABLE 1. The specific pathological findings of the patient's ovarian adnexa.

Pathological pattern	Cases (n)	Percent (%)
Benign group (n = 62)		
Ovarian endometrioid cyst	17	27.42
Mature cystic teratoma	22	35.48
Serous (mucinous) cystadenoma	13	20.97
Hemorrhagic corpus luteum cyst	6	9.68
Fibroid	3	4.84
Leiomyoma	1	1.61
Malignant group (n = 38)		
Serous (mucinous) borderline tumor	14	36.84
Endometrioid adenocarcinoma	11	28.95
Ovarian clear cell carcinoma	10	26.32
Immature teratoma	2	5.26
Metastatic carcinoma	1	2.63

TABLE 2. Clinical characteristics of benign and malignant ovarian tumors.

Items	Benign group (n = 62)	Malignant group (n = 38)	*t*/*Z*	*p*
Age (yr)	47.62 ± 6.56	51.82 ± 6.90	3.051	0.003
BMI (kg/m^2)	23.52 ± 4.03	24.11 ± 5.30	1.416	0.160
Parsimonies				
Yes	20 (32.26)	16 (42.11)	0.655	0.513
No	42 (67.74)	22 (57.89)		
Maximum lesion diameter (cm)				
≤3	4 (6.45)	1 (2.63)	2.447	0.014
3~5 or =5	11 (17.74)	4 (10.53)		
5~10	25 (40.32)	15 (39.47)		
≥10	22 (35.48)	18 (47.37)		
Anomalous contour				
Yes	9 (14.52)	25 (65.79)	3.800	<0.001
No	53 (85.48)	13 (34.21)		
Ascites				
Yes	6 (9.68)	16 (42.11)	2.828	0.005
No	56 (90.32)	22 (57.89)		

BMI: Body Mass Index.

TABLE 3. The diagnostic efficacy of HE4 and CA125 (compared with pathological results).

Diagnostic methods	Pathological diagnosis		Accuracy rate (%)
	Benign (n = 62)	Malignant (n = 38)	
HE4			
Benign	49	6	81.00
Malignant	13	32	
CA125			
Benign	47	9	76.00
Malignant	15	29	

HE4: human epididymal protein 4; CA125: cancer antigen 125.

TABLE 4. GI-RADS and O-RADS classifications of diagnostic results.

Diagnostic methods	Pathological diagnosis		Accuracy rate (%)
	Benign (n = 62)	Malignant (n = 38)	
O-RADS			
Benign	57	5	90.00
Malignant	5	33	
GI-RADS			
Benign	53	6	85.00
Malignant	9	32	

O-RADS: Ovarian Reporting and Data System; GI-RADS: Gynecological Imaging Reporting and Data System.

TABLE 5. Diagnostic efficacy of combined diagnosis compared with pathological outcomes.

Diagnosis methods	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC (95% confidence interval)
HE4	84.20	79.00	81.00	0.816 (0.727–0.906)
CA125	76.32	75.81	76.00	0.761 (0.661–0.861)
O-RADS	86.80	91.94	90.00	0.894 (0.815–0.973)
GI-RADS	84.20	85.48	85.00	0.848 (0.775–0.921)
O-RADS + HE4 + CA125	84.20	88.70	87.00	0.865 (0.783–0.946)
GI-RADS + HE4 + CA125	89.50	85.50	87.00	0.875 (0.799–0.951)
O-RADS + GI-RADS + HE4 + CA125	92.10	95.20	94.00	0.936 (0.878–0.995)

HE4: human epididymal protein 4; CA125: cancer antigen 125; O-RADS: Ovarian Reporting and Data System; GI-RADS: Gynecological Imaging Reporting and Data System; AUC: area under the curve.

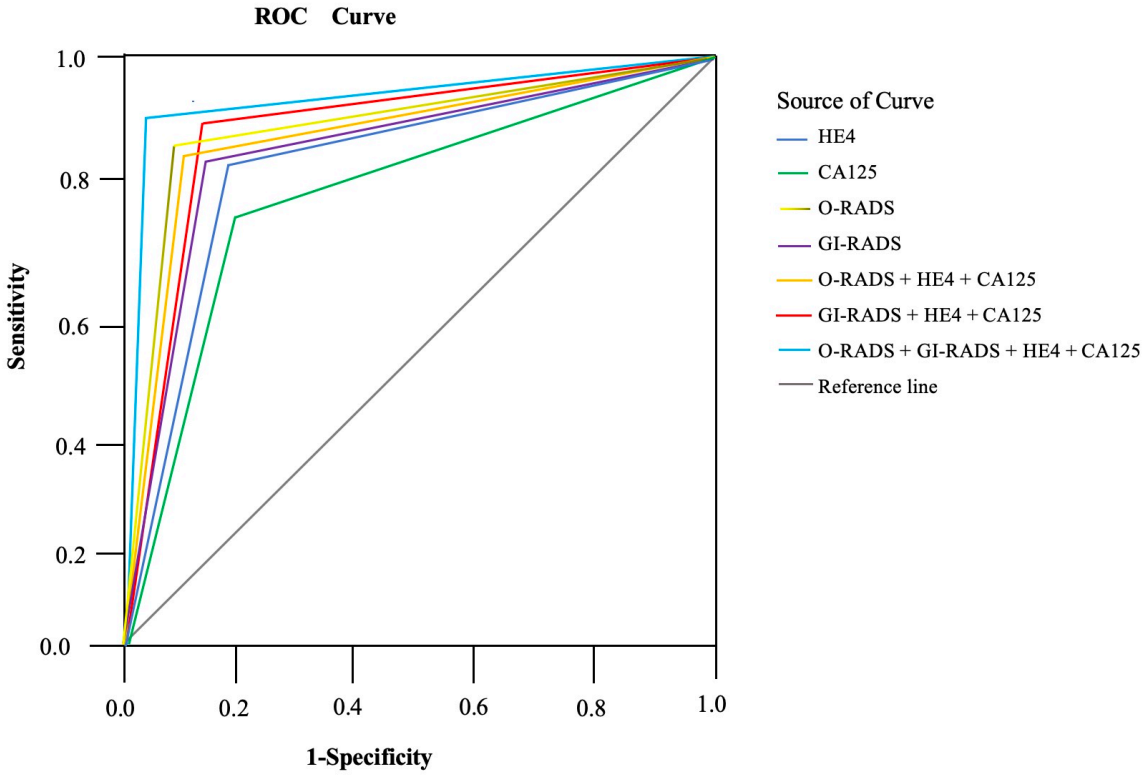

FIGURE 1. ROC curves of single and combined methods for diagnosis. Sensitivity; 1-Specificity; Curve; Reference line. HE4: human epididymal protein 4; CA125: cancer antigen 125; O-RADS: Ovarian Reporting and Data System; GI-RADS: Gynecological Imaging Reporting and Data System; ROC: Receiver operating characteristic.

these markers are not influenced by menopausal status, providing a new diagnostic approach for ovarian cancer. Numerous studies have shown the promising application prospects of combined serum tumor marker testing. The conclusions of related research have been widely accepted and recognized, receiving recommendations from both the U.S. Food and Drug Administration and the Gynecologic Oncology Committee of the Chinese Anti-Cancer Association [22]. However, some studies have indicated the limited diagnostic value of serum tumor markers. For instance, serum CA125 levels can also be elevated in patients with benign conditions such as endometriosis, thus limiting its utility in the diagnosis of ovarian tumors [23]. In this study, HE4 and CA125 were individually used for diagnosing of benign and malignant ovarian tumors. The results demonstrated an accuracy of 81.00%, sensitivity of 84.20% and specificity of 79.00% for HE4, while CA125 exhibited an accuracy of 76.00%, sensitivity of 76.32% and specificity of 75.81%. The ROC curve results indicated an area under the curve (AUC) of 0.816 and 0.761 for HE4 and CA125, respectively, confirming their high diagnostic efficacy. These findings are consistent with previously reported data [24].

To accurately assess the benign and malignant nature of ovarian tumors preoperatively, and to formulate rational clinical management and surgical strategies, numerous guidelines, grading systems and predictive models have been developed, including the GI-RADS and O-RADS classification assessment systems, along with the use of serum markers [25]. The results of this study demonstrate that both GI-RADS and O-RADS classifications have good diagnostic performance in distinguishing between the benign and malignant ovarian

tumors, with sensitivities of 84.20% and 86.80%, respectively, and AUC curve areas of 0.848 and 0.894, respectively. To explore the combined diagnostic performance of these classification assessment systems with serum tumor markers, this study also analyzed the diagnostic schemes of the other three combinations. The results revealed that the diagnostic performance of the O-RADS classification combined with the HE4, CA125 scheme and the GI-RADS classification combined with the HE4, CA125 scheme were significantly higher than that of serum tumor markers alone and evaluation system diagnosis. However, the diagnostic performance of the two classification systems combined with HE4 and CA125 was the best, with a sensitivity of 92.10%, specificity of 95.20%, accuracy of 94.00% and an AUC area of 0.936, which was the highest numerical value. In this study, one case of an ovarian endometriosis cyst was misclassified as a solid component of the tumor, and one case of ovarian serous cystadenoma was classified as class 4 by O-RADS and class 4 by GI-RADS because it appeared as a multilocular cystic mass with irregular septa or cystic-solid mass on sonography. Combining CA125 and HE4 can improve the specificity and accuracy of the diagnosis. The results of the study also confirmed that the specificity of the tumor diagnosis for benign and malignant cases based solely on classification methods is limited and requires the combination of serum tumor markers to improve specificity.

5. Conclusions

In summary, the results of this study indicate that individual serum tumor markers, O-RADS classification, and GI-RADS classification methods all have good diagnostic value for distinguishing ovarian benign and malignant tumors. However, the combined diagnostic scheme of the two classification evaluation systems with serum tumor markers demonstrates superior diagnostic efficacy. The diagnostic results of O-RADS and GI-RADS classifications are more objective, with descriptions of lesion characteristics being more uniform and standardized. When combined with serum HE4 and CA125, this approach not only exhibits higher diagnostic efficiency, but also provides more objective diagnostic results. Therefore, it holds clinical significance for further dissemination. The limitations of this study lie in its nature as a single-center study with a limited sample size, as all patients were selected from those undergoing surgical procedures. This may result in potential selection bias.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

QYD and LPL—designed the study and carried them out, QYD, LPL, JLL and DPH—interpreted the data, QYD, LPL, JLL and DPH—prepared the manuscript for publication, and reviewed the draft of the manuscript. QYD, LPL, JLL and DPH—supervised the data collection. QYD, LPL and JLL—analyzed the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of The Sixth Affiliated Hospital, South China University of Technology (Approval no. NYKY-2024-14-01).

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Xia T, Fang C, Chen Y. Advances in application of circulating tumor DNA in ovarian cancer. Functional & Integrative Genomics. 2023; 23: 250.

[2] Terp SK, Stoico MP, Dybkær K, Pedersen IS. Early diagnosis of ovarian cancer based on methylation profiles in peripheral blood cell-free DNA: a systematic review. Clinical Epigenetics. 2023; 15: 24.

[3] Zhang M, Cheng S, Jin Y, Zhao Y, Wang Y. Roles of CA125 in diagnosis, prediction, and oncogenesis of ovarian cancer. Biochimica et Biophysica Acta: Reviews on Cancer. 2021; 1875: 188503.

[4] Bizoń M, Awiżeń-Panufnik Z, Sawicki W. Comparison of interleukin-6 with other markers in diagnosis of ovarian cancer. Journal of Personalized Medicine. 2023; 13: 980.

[5] Engbersen MP, Van Driel W, Lambregts D, Lahaye M. The role of CT, PET-CT, and MRI in ovarian cancer. British Journal of Radiology. 2021; 94: 20210117.

[6] Nguyen PN, Nguyen VT. Endometrial thickness and uterine artery Doppler parameters as soft markers for prediction of endometrial cancer in postmenopausal bleeding women: a cross-sectional study at tertiary referral hospitals from Vietnam. Obstetrics & Gynecology Science. 2022; 65: 430–440.

[7] Nguyen PN, Nguyen VT. Additional value of Doppler ultrasound to B-mode ultrasound in assessing for uterine intracavitary pathologies among perimenopausal and postmenopausal bleeding women: a multicentre prospective observational study in Vietnam. Journal of Ultrasound. 2023; 26: 459–469.

[8] Alcázar JL, Rodriguez-Guzman L, Vara J, Amor F, Diaz L, Vaccaro H. Gynecologic imaging and reporting data system for classifying adnexal masses. Minerva Obstetrics and Gynecology. 2023; 75: 69–79.

[9] Phillips CH, Guo Y, Strachowski LM, Jha P, Reinhold C, Andreotti RF. The ovarian/adnexal reporting and data system for ultrasound: from standardized terminology to optimal risk assessment and management. Canadian Association of Radiologists Journal. 2023; 74: 44–57.

[10] Bang JI, Kim JY, Choi MC, Lee HY, Jang SJ. Application of multimodal imaging biomarker in the differential diagnosis of ovarian mass:

integration of conventional and molecular imaging. Clinical Nuclear Medicine. 2022; 47: 117–122.

[11] Chen L, Yan L, Chai H, Wang G. Clinical significance of improved gynecologic imaging report and data system in differential diagnosis of benign and malignant ovarian tumors. Minerva Surgery. 2023; 78: 318–319.

[12] Cherukuri S, Jajoo S, Dewani D. The international ovarian tumor analysis-assessment of different neoplasias in the adnexa (IOTA-ADNEX) model assessment for risk of ovarian malignancy in adnexal masses. Cureus. 2022; 14: e31194.

[13] Haliti TI, Hoxha I, Mojsiu R, Mandal R, Goç G, Hoti KD. Diagnostic accuracy of biomarkers and international ovarian tumor analysis simple rules in diagnosis of ovarian cancer. Hematology/Oncology Clinics of North America. 2024; 38: 251–265.

[14] Andreotti RF, Timmerman D, Strachowski LM, Froyman W, Benacerraf BR, Bennett GL, *et al*. O-RADS US risk stratification and management system: a consensus guideline from the ACR ovarian-adnexal reporting and data system committee. Radiology. 2020; 294: 168–185.

[15] Knipprath-Mészáros AM, Tozzi A, Butenschön A, Reina H, Schoetzau A, Montavon C, *et al*. High negative prediction for the Basel sarcoma score: sonographic assessment of features suspicious of uterine sarcoma. Gynecologic Oncology. 2023; 174: 182–189.

[16] Xie WT, Wang YQ, Xiang ZS, Du ZS, Huang SX, Chen YJ, *et al*. Efficacy of IOTA simple rules, O-RADS, and CA125 to distinguish benign and malignant adnexal masses. Journal of Ovarian Research. 2022; 15: 15.

[17] Zhang Q, Ding J, Wang Y, He L, Xue F. Tumor microenvironment manipulates chemoresistance in ovarian cancer (Review). Oncology Reports. 2022; 47: 102.

[18] Chen H, Jiang Q, Yin Y. Increased risk of ovarian and breast malignancies in women with polycystic ovary syndrome: a review article. Cellular and Molecular Biology. 2023; 69: 15–21.

[19] Sessa C, Balmaña J, Bober SL, Cardoso MJ, Colombo N, Curigliano G, *et al*.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline. Annals of Oncology. 2023; 34: 33–47.

[20] Rampes S, Choy SP. Early diagnosis of symptomatic ovarian cancer in primary care in the UK: opportunities and challenges. Primary Health Care Research & Development. 2022; 23: e52.

[21] Luo HJ, Hu ZD, Cui M, Zhang XF, Tian WY, Ma CQ, *et al*. Diagnostic performance of CA125, HE4, ROMA, and CPH-I in identifying primary ovarian cancer. Journal of Obstetrics and Gynaecology Research. 2023; 49: 998–1006.

[22] Janas L, Stachowiak G, Glowacka E, Piwowarczyk I, Kajdos M, Soja M, *et al*. The use of CA125, human epididymis protein 4 (HE4), risk of ovarian malignancy algorithm (ROMA), risk of malignancy index (RMI) and subjective assessment (SA) in preoperative diagnosing of ovarian tumors. Ginekologia Polska. 2024; 95: 321–327.

[23] Dong S, Yu F, Liu Y, Yu X, Sun X, Wang W, *et al*. Comparison of the clinical characteristics and prognosis between clear cell carcinomas and high-grade serous ovarian carcinomas. Ginekologia Polska. 2023; 94: 792–798.

[24] Song L, Qi J, Zhao J, Bai S, Wu Q, Xu R. Diagnostic value of CA125, HE4, and systemic immune-inflammation index in the preoperative investigation of ovarian masses. Medicine. 2023; 102: e35240.

[25] Basha MAA, Metwally MI, Gamil SA, Khater HM, Aly SA, El Sammak AA, *et al*. Comparison of O-RADS, GI-RADS, and IOTA simple rules regarding malignancy rate, validity, and reliability for diagnosis of adnexal masses. European Radiology. 2021; 31: 674–684.

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