DIAGNOSTIC ACCURACY OF ULTRASOUND O-RADS CLASSIFICATION IN DIFFERENTIATION OF BENIGN AND MALIGNANT OVARIAN LESIONS KEEPING MRI PELVIS AS REFERENCE STANDARD

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ABSTRACT

OBJECTIVES

This study aimed to evaluate the diagnostic accuracy of the ultrasound O-RADS classification for distinguishing between malignant and benign ovarian lesions, using MRI of the pelvis as the reference standard.

METHODOLOGY

A cross-sectional study was conducted, enrolling 169 women with suspicious adnexal masses. All participants underwent standardised ultrasound examinations (with O-RADS scoring) and MRI of the pelvis (with O-RADS MRI scoring). Diagnostic performance metrics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall accuracy, and the area under the receiver operating characteristic curve (AUC), were calculated.

RESULTS

The prevalence of malignancy was 29.0%. Ultrasound O-RADS demonstrated a sensitivity of 83.7% (95% CI: 76.2-89.5%), specificity of 85.0% (95% CI: 78.3-90.1%), PPV of 69.5%, NPV of 92.7%, and overall accuracy of 84.6%. The AUC was 0.91 (95% CI: 0.86-0.95). Performance was superior in postmenopausal women and for larger lesions (greater than 5 cm in diameter). False positives occurred primarily with hemorrhagic cysts and endometriomas.

CONCLUSION

Ultrasound O-RADS classification demonstrates high diagnostic accuracy, particularly an excellent NPV, for evaluating adnexal masses. It serves as a reliable first-line triage tool, potentially reducing unnecessary MRI referrals in settings with limited resources.

KEYWORDS: *Ovarian Neoplasms; Ultrasonography; Magnetic Resonance Imaging; O-RADS; Diagnostic Accuracy; Sensitivity and Specificity*

INTRODUCTION

Ovarian cancer remains the most lethal gynecologic malignancy, accounting for the highest mortality rate among female reproductive cancers, particularly in postmenopausal women.[1] The clinical challenge lies in distinguishing between benign and malignant ovarian lesions, as benign masses (64.4%) are far more prevalent than malignant ones (29.4%).[2] Accurate preoperative characterisation is crucial to avoid unnecessary surgical interventions in benign cases while ensuring timely and aggressive management for malignancies.[3]An essential part of the diagnosis process for ovarian masses is imaging. Non-invasive imaging methods such as ultrasonography and magnetic resonance imaging (MRI) are crucial for initial assessments, although histological analysis remains the gold standard. Due to their cost-effectiveness, ease of application, and ability to provide real-time evaluations, both transvaginal and transabdominal ultrasounds are commonly employed. Nevertheless, to enhance diagnostic reliability and risk assessment, standardised scoring systems like the Ovarian-Adnexal Reporting and Data System (O-RADS) have been developed in response to the variability of subjective interpretations and the influence of the operator‘s expertise.[4] Based on morphologic and Doppler characteristics, the O-RADS classification system assigns ratings from 0 (incomplete evaluation) to 5 (verysuggestive of malignancy) to ovarian lesions. The sensitivity (84.8%) and specificity

(81.9%) reported in studies assessing its diagnostic ability differ, with some indicating even better accuracy.[5] These investigations, however, frequently lack a reliable reference standard, like magnetic resonance imaging (MRI), which provides multiplanar imaging and improved soft-tissue contrast, making it highly accurate in distinguishing benign from malignant lesions.[6] Previous studies validating O-RADS have shown variable performance, with sensitivities ranging from 84.8% to 96% and specificities from 81.9% to 93%.[7] However, many studies lack a robust reference standard, such as MRI, or are conducted in well-resourced settings. In developing countries like Pakistan, MRI is not readily accessible, creating a critical need to validate highly accurate and accessible diagnostic tools, such as ultrasound O-RADS. This validation is essential to build clinician confidence in using O-RADS for primary triage, thereby optimising resource utilisation and improving patient care pathways. Moreover, factors such as menopausal status, CA-125 levels, and lesion characteristics may affect diagnostic accuracy, indicating the need for further stratification. This study aims to assess the diagnostic accuracy of ultrasound O-RADS classification in distinguishing between benign and malignant ovarian lesions, with MRI of the pelvis serving as the reference standard. In doing so, we aim to confirm the dependability of ultrasound O-RADS within clinical settings, especially where advanced imaging is not readily available. The results may support the use of O-RADS as a cost-effective initial diagnostic approach, enhancing patient triage and minimising unwarranted referrals for MRI.

METHODOLOGY

Study Design and Setting: This cross-sectional validation study was conducted over six months at the Department of Diagnostic Radiology, PGMI/Hayatabad Medical Complex, Peshawar. The sample size was calculated using the formula for diagnostic test validation [8]. With an expected sensitivity of 84.8%[7], a prevalence of malignancy of 29.4%,[2] a 95% confidence level, and a desired precision (d) of 10%, the required sample size was 169 participants. A total of 169 women aged 18-65 years presenting with suspicious adnexal masses on initial ultrasound were enrolled via non-probability consecutive sampling. Inclusion criteria were: women aged 18-65 years with an adnexal mass deemed suspicious on referral ultrasound. Exclusion criteria were contraindications to MRI (e.g., metallic implants, pacemakers, severe claustrophobia), contraindications to contrast media (impaired renal function with serum creatinine >1.1 mg/dL or known allergy), and a history that could confound results (prior ovarian cancer, extensive prior pelvic surgery). All participants underwent a detailed transabdominal and transvaginal ultrasound examination using a Canon Aplio i800 machine with a 3.5MHz convex and a 7.5MHz endocavitary probe. Doppler flow was assessed for colour score assignment. A consultant radiologist with over 10 years of experience, blinded to the MRI results, assigned an O-RADS score based on the ACR O-RADS US lexicon.[8] Subsequently, all patients underwent a 1.5T MRI of the pelvis with intravenous contrast. A second consultant radiologist, blinded to the US results, assigned an O-RADS MRI score. For analysis, a score of 3 or higher on either system was considered predictive of malignancy. Ethical approval for this study was obtained from the Institutional Review Board of Hayatabad Medical Complex (approval no:1629). Written informed consent was obtained from all participants. Data were analysed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. A 2x2 contingency table was constructed to calculate sensitivity, specificity, PPV, NPV, and overall accuracy. A receiver operating characteristic (ROC) curve was generated to determine the area under the curve (AUC). A p-value of <0.05 was considered statistically significant.

RESULTS

This study evaluated 169 women presenting with suspicious adnexal masses, with a mean age of 48.2 years (±12.4 SD). The cohort comprised 52 postmenopausal women (30.8%) and 117 premenopausal women (69.2%). The average lesion size measured 6.8 cm (±3.2 SD), with 36.7% (n = 62) of patients demonstrating elevated CA-125 levels (greater than 35 U/mL). Using MRI pelvis as the reference standard, 49 lesions (29.0%) were classified as malignant (O-RADS MRI ≥3) while 120 (71.0%) were benign (O-RADS MRI <3). Ultrasound O-RADS classification demonstrated robust diagnostic performance, correctly identifying 41 actual positive malignant cases while misclassifying 18 benign lesions as false positives. The system accurately ruled out malignancy in 102 actual negative cases, though it missed 8 malignant lesions (false negatives). Sensitivity analysis revealed the method correctly detected 83.7% of malignant cases (95% CI: 76.2-89.5%), while specificity measurements showed 85.0% accuracy in identifying benign lesions (95% CI: 78.3-90.1%). The positive predictive value of 69.5% (95% CI: 61.4-76.6%) suggests moderate confidence in positive classifications, whereas the negative predictive value of 92.7% (95% CI: 87.5-96.0%) indicates excellent

reliability in ruling out malignancy. The overall diagnostic accuracy reached 84.6% (95% CI: 79.3-88.9%). Subgroup analyses revealed important variations in test performance. Postmenopausal women showed higher sensitivity (88.2%) but slightly reduced specificity (80.4%) compared to premenopausal counterparts (80.6% sensitivity, 87.2% specificity). Larger lesions (>5 cm) were more accurately detected (89.1% sensitivity) than smaller lesions (76.3% sensitivity). The combination of elevated CA-125 with an O-RADS classification of≥4 significantly improved the positive predictive value to 91.8%. Diagnostic challenges were most frequently encountered with hemorrhagic cysts (accounting for 7 of 18 false positives), endometriomas (5 false positives), and early-stage borderline tumours (representing 5 of 8 false negative cases). These findings demonstrate that ultrasound O-RADS is a clinically valuable tool, with particular strength in ruling out malignancy, while suggesting the need for confirmatory MRI in complex cases or when managing premenopausal patients with smaller lesions.

Table 1: Baseline Characteristics of Study Participants (n=169)

Characteristic	Value
Age (years), mean ± SD	48.2 ± 12.4
Menopausal status, n (%)	
- Premenopausal	117 (69.2%)
- Postmenopausal	52 (30.8%)
Lesion size (cm), mean ± SD	6.8 ± 3.2
CA-125 levels, n (%)	
- Elevated (>35 U/mL)	62 (36.7%)
- Normal (≤35 U/mL)	107 (63.3%)
MRI classification, n (%)	
- Malignant (O-RADS MRI ≥3)	49 (29.0%)
- Benign (O-RADS MRI <3)	120 (71.0%)

Table 2: Diagnostic Performance of Ultrasound O-RADS Classification

Parameter	Value (95% CI)
Sensitivity	83.7% (76.2-89.5%)
Specificity	85.0% (78.3-90.1%)
Positive Predictive Value	69.5% (61.4-76.6%)
Negative Predictive Value	92.7% (87.5-96.0%)
Overall Accuracy	84.6% (79.3-88.9%)

Table 3: Subgroup Analysis of Diagnostic Performance

Parameter	Value (95% CI)	Parameter
Sensitivity	83.7% (76.2-89.5%)	Sensitivity
Specificity	85.0% (78.3-90.1%)	Specificity
Positive Predictive Value	69.5% (61.4-76.6%)	Positive Predictive Value
Negative Predictive Value	92.7% (87.5-96.0%)	Negative Predictive Value
Overall Accuracy	84.6% (79.3-88.9%)	Overall Accuracy
Sensitivity	83.7% (76.2-89.5%)	Sensitivity
Specificity	85.0% (78.3-90.1%)	Specificity
Positive Predictive Value	69.5% (61.4-76.6%)	Positive Predictive Value

Table 4: Analysis of Misclassified Cases

Classification Error Type	Number of Cases	Most Common Lesions (n)
False Positives	18	- Hemorrhagic cysts (7) - Endometriomas (5) - Other benign lesions (6)
False Negatives	08	- Borderline tumours (5) - Early-stage malignancies (3)

Table 5: Receiver Operating Characteristic (ROC) Curve Analysis of O-RADS US

Parameter	Value (95% CI)
Area Under the Curve (AUC)	0.91 (0.86 - 0.95)
Standard Error	0.02
p-value	<0.001

DISCUSSION

The findings of this study demonstrate that ultrasound O-RADS classification provides clinically valuable diagnostic performance in differentiating benign from malignant ovarian lesions, with an overall accuracy of 84.6%. These results align with contemporary literature while providing important insights for clinical practice in resource-limited settings. Our observed sensitivity of 83.7% and specificity of 85.0% compare favourably with those of previous validation studies of the O-RADS system. A 2022 multicenter study by Guo et al. reported similar performance characteristics (sensitivity 84.8%, specificity 81.9%) in their evaluation of 487 adnexal masses.[5] The slightly higher specificity in our study may reflect the standardised application of O-RADS criteria by experienced radiologists in our setting. Importantly, our findings support the growing body of evidence that standardised ultrasound classification systems can approach the diagnostic accuracy of more advanced imaging modalities for characterising ovarian masses. The excellent negative predictive value (92.7%) we observed is particularly clinically relevant. This finding suggests that ultrasound O-RADS can reliably exclude malignancy when lesions are classified as low-risk (O-RADS 1-2), potentially reducing unnecessary MRI referrals in resource-constrained environments. This aligns with the conclusions of a 2021 meta-analysis by Vara et al., which found a pooled NPV of 94% for ultrasound-based risk stratification systems.[9] The high NPV supports the use of O-RADS as an effective triage tool, particularly in premenopausal women, where the prevalence of malignancy is lower. However, our moderate positive predictive value (69.5%) indicates limitations in definitively diagnosing malignancy based solely on ultrasound findings. This is consistent with known challenges in characterising complex adnexal masses, particularly in premenopausal women. Our finding that 38.9% of false positives were either

hemorrhagic cysts or endometriomas echoes the results of a 2023 study by Zhang et al., who reported similar diagnostic pitfalls in their analysis of 632 ovarian masses.[5] These limitations underscore the importance of correlating imaging findings with clinical and biochemical markers, particularly in cases with indeterminate results. The superior performance in postmenopausal women (88.2% sensitivity) compared to premenopausal women (80.6% sensitivity) has important clinical implications. This difference likely reflects both the higher prevalence of malignancy in postmenopausal women and the greater diagnostic challenge posed by physiologic changes in premenopausal ovaries. A study similarly found lower sensitivity (78.5%) in premenopausal populations.[10] These results suggest that additional caution should be exercised when interpreting O-RADS classifications in premenopausal patients, with consideration given to serial follow-up or MRI confirmation for cases that are indeterminate. Our findings regarding lesion size are particularly noteworthy. The significantly higher sensitivity for lesions greater than 5 cm (89.1% vs 76.3% for lesions ≤5 cm) supports existing evidence that smaller lesions pose greater diagnostic challenges. This finding is consistent with a 2022 study by Hack et al., which reported a decrease in diagnostic accuracy with smaller lesion sizes in their evaluation of 354 adnexal masses.[10] This size-dependent performance should be considered when making clinical management decisions, particularly for small complex lesions where the risk of missing early-stage malignancies may be higher. The combination of CA-125 with O-RADS classification significantly improved PPV to 91.8% in our study. This finding supports the growing trend toward multimodal risk assessment in the evaluation of ovarian masses. A study found that combining IOTA simple rules with CA-125 improved specificity from 82% to 91% without compromising sensitivity.[11] Our results suggest that such combined approaches may be particularly valuable in settings where MRI availability is limited. The ultrasound O-RADS system demonstrated strong clinical utility with 84.6% overall accuracy and excellent negative predictive value (92.7%), supporting its role in initial triage of adnexal masses.[12] However, reduced sensitivity in premenopausal women (80.6%) and for small lesions (76.3%) highlights important diagnostic limitations, particularly for borderline tumours.[13] The significant improvement in positive predictive value to 91.8% when combining O-RADS with CA-125 underscores the value of multimodal assessment.[14] These findings suggest O-RADS serves best as part of an integrated diagnostic approach, particularly in resource-limited settings where MRI availability is constrained.[15] The diagnostic challenges we identified with specific lesion types (hemorrhagic cysts, endometriomas, and borderline tumours) have been consistently reported in the literature. A 2022 study by Van Calster et al. specifically highlighted these lesion types as familiar sources of misclassification in ultrasound-based systems.[16] These limitations underscore the importance of: 1) correlating imaging findings with clinical context, 2) considering follow-up imaging for potentially physiologic lesions, and 3) maintaining a low threshold for MRI referral in cases with discordant findings. The performance characteristics we observed compare favorably with MRI-based characterisation in several respects. While MRI generally offers higher specificity (typically 90-95% in recent studies), our results suggest ultrasound O-RADS may be sufficient for initial triage in many cases.[17] This is particularly relevant for low-resource settings where MRI availability is limited. A cost-effectiveness analysis by Chacon et al.,in 2023 concluded that ultrasound-based triage followed by selective MRI was the most efficient strategy for evaluating ovarian masses in resource-limited environments.[18]

LIMITATIONS

The single-centre design may limit generalizability; although our sample size was adequate, it was smaller than that of some recent multicenter studies. Additionally, we did not evaluate inter-observer variability in O-RADS application, which has been shown to impact diagnostic performance in other studies.[20] Future research should address these limitations through multicenter collaborations with standardised imaging protocols.

CONCLUSIONS

The ultrasound O-RADS classification is a highly accurate and validated tool for the preoperative assessment of adnexal masses. Its high NPV makes it an effective first-line triage tool to rule out malignancy. In resource-constrained environments, adopting O-RADS can optimise resource utilisation by confidently stratifying patients, reserving advanced imaging, such as MRI, for indeterminate or positive cases, ultimately streamlining patient care.

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Mehreen Khan - *Concept & Design; Data Acquisition; Data Analysis/Interpretation;Drafting Manuscript; Critical Revision, Final Approval*

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The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.