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REVIEWS AND COMMENTARY • EDITORIAL

MRI Improves the Characterization of Incidental Adnexal Masses Detected at Sonography

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Incidental adnexal masses are common. They occur in 35% of premenopausal and 17% of postmenopausal women (1). While the vast majority are benign, a few prove to be cancer. Although US represents the mainstay for characterization, up to 30% of masses remain indeterminate after US (2). When adnexal masses cannot be characterized as definitively benign with imaging and serum tumor markers, they are triaged for tissue diagnosis. Needle biopsy is usually avoided because of the concern for tumor seeding, and imaging follow-up may delay a diagnosis of ovarian cancer (3). Thus, oophorectomy, the surgical removal of one or both ovaries, with resulting morbidity of decreased fertility and premature menopause, constitutes the major long-term health burden of incidental adnexal masses.

To enable more accurate imaging evaluation, MRI is the preferred modality for evaluating adnexal masses that remain indeterminate after US examination. MRI demonstrates high sensitivity in the diagnosis of ovarian cancer. MRI also reduces the rates of false-positive diagnoses. The Ovarian-Adnexal Reporting and Data System (O-RADS) for MRI (O-RADS MRI), originally described as the ADNEX scoring system in 2013, offers a five-category reporting structure for assessment and risk stratification of incidental adnexal masses (4,5). When dichotomized, a score of 3 or less is considered benign and a score of 4 or greater is considered malignant. The reference standard typically is pathologic examination or follow-up.

In this issue of *Radiology*, Rizzo and colleagues (6) undertook a systematic review and meta-analysis of 12 studies reporting the use of pelvic MRI interpreted with the ADNEX and/or O-RADS MRI systems to characterize US-indeterminate adnexal lesions. A total of 4520 adnexal lesions in 3731 women were analyzed. Of those 4520 lesions, 840 (18.6%) were invasive cancers, 179 (4.0%) were borderline tumors, and 3501 (77.4%) were benign lesions confirmed at pathologic examination or follow-up. Overall estimates of summary sensitivity, specificity, and area under the receiver operating characteristic curve were 92% (95% CI: 88, 95), 91% (95% CI: 89, 93), and 0.97 (95% CI: 0.95, 0.98), respectively. Estimates on the prevalence of malignancy were 0.1% for category 2 (almost certainly benign), 6% for category 3 (low risk), 60% for category 4 (intermediate risk), and 96% for category 5 (high risk) lesions. There were insufficient data to estimate malignancy rates for category 1 lesions, which are comprised of normal ovaries, including those with physiologic, corpus luteum, and hemorrhagic cysts.

One of the challenges in generalizing studies of O-RADS MRI to clinical practice is the heterogeneity of the US-indeterminate adnexal masses referred for MRI. The prevalence of malignancy varies from 12% to nearly 40% in the reported literature. The authors calculated that this range of prevalence would correspond to positive predictive values (PPVs) ranging from 57% to 86%, respectively. In comparison, the PPV for O-RADS US applied to incidental adnexal mass cohorts not enriched for malignancy is 31% (7). The greater PPV of MRI and the corresponding reduction in rates of false-positive cancer diagnoses represents its major added value when compared with US. Thus, while surgical resection of benign adnexal masses will still occur with MRI, the rates will likely be lower than with US. Meanwhile, the negative predictive value with O-RADS MRI remains reassuringly high at 94% or greater for the entire range of cancer prevalence, indicating that cancer is unlikely to be missed with MRI.

The estimates of malignancy rates corresponding to each O-RADS MRI category calculated by Rizzo et al are particularly useful to aid the patient in

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See also the article by Rizzo et al in this issue.

decision-making. Management of an incidental adnexal mass is driven by several factors. One of these is the likelihood of malignancy as assessed with imaging. Fertility and endogenous hormone preservation are also important (1). Thus, the risk estimates provided by O-RADS MRI enable a more informed discussion between the patient and physician to arrive at an appropriate management plan.

Contrast material administration is the standard of care in MRI performed for adnexal mass characterization. The use of contrast material has been shown to improve diagnostic accuracy. O-RADS recommends dynamic contrast-enhanced (DCE) MRI with a time resolution of 15 seconds or less to enable time-intensity curve analysis. However, this protocol does not reflect current general practice. Rizzo et al compared studies where DCE is performed with and without a temporal resolution of 15 seconds or less. They noted a slightly lower specificity with temporal resolution of 15 seconds or less versus without (90% vs 93%, P = .049), with comparable sensitivity (92% vs 92%, P = .96). Thus, the high temporal resolution time-intensity curve analysis recommended by the current O-RADS MRI protocol with its requirement for added technology and image interpretation time may not be warranted.

As with all the standardized reporting paradigms, O-RADS MRI is a work in progress. Although the necessary imaging technology is widely available, radiologist expertise is less so. To date, evidence on O-RADS MRI performance has relied primarily on readers at subspecialty and academic centers. Moreover, a study evaluating the cause of the misclassification of 1502 adnexal masses indicated that 75% of errors were interpretative (8). An overall 17% misclassification rate was reported in the low (O-RADS MRI 3) and intermediate (O-RADS MRI 4) risk categories that represent the cutoff between benign and malignant. Thus, whether O-RADS MRI propagates into the community and generalist practices with comparable accuracy remains an open question.

As most incidental adnexal masses will likely prove benign and may require longitudinal follow-up with multiple imaging visits, minimizing both the morbidity and cost of O-RADS MRI–based management is also a priority. The patient population presenting with incidental adnexal masses are in general healthy, and many have yet to complete childbearing. Imaging protocols that use widely available scanner technology, minimize the need for repeated doses of gadolinium-based contrast material, and involve short scanning times for patient comfort would be desirable. Thus, studies are underway to identify simpler and more robust protocols while maintaining high image quality and diagnostic accuracy.

Diffusion-weighted imaging (DWI) is now the standard of care in pelvic MRI of the intra-abdominal organs, especially when cancer is known or suspected. O-RADS MRI specifies that solid tissue with a low signal intensity at DWI indicates a benign lesion. However, a high signal intensity on DWI scans with a corresponding low signal intensity on apparent diffusion coefficient maps is not incorporated into the O-RADS MRI assessment. Such features would indicate diffusion-restricted tissue, which increases the likelihood of malignancy. Whether the qualitative or quantitative assessment of diffusion restriction could improve discrimination for cancer risk or eliminate the need for routine contrast material administration without sacrificing diagnostic accuracy are questions undergoing active investigation (9,10).

While O-RADS MRI has been studied by multiple investigators, the available evidence has accumulated over a number of years, at disparate centers, and using varied study designs. Thus, the systematic review and meta-analysis reported by Rizzo and colleagues (6) is of added value beyond summarizing the available evidence. It focuses on the issues directly relevant to clinical practice using a multicenter cohort that would not be feasible in a clinical trial. The strength of a systematic review lies in its comprehensive and objective assessment of all published studies. Compared with individual studies, summarization of the diagnostic performance of a decision rule or test using sufficiently high-quality literature allows more insight into generalizability. Diagnostic test accuracy in particular lends itself to meta-analysis without the randomized design that is so essential for meta-analysis of treatment effects. Such methodology enables the authors to offer high level of evidence on O-RADS MRI that includes reliable measurements of diagnostic accuracy and category-specific disease prevalence.

To provide guidance with objectivity and stringency, diagnostic performance systematic reviews are reported strictly according to guidelines using recommended hierarchical modeling methods and an assessment of risks of bias. Notably, Rizzo and colleagues present a meta-analysis after excluding two studies with a high risk of selection bias. Due to the heterogeneity of patient ages across the original studies, one may wonder whether a subset of studies with specific patient demographics would apply best to a local practice setting. The authors do present PPV and negative predictive value for settings with both low and high prevalence of cancer. This information is useful given a reasonably strong positive likelihood ratio of 10 and a negative likelihood ratio of 0.09. The authors report that subgroup analysis and examination of covariates associated with greater false-positive or false-negative results was mostly not possible. Most studies were clustered in specialized centers (reflecting the early stage of dissemination). Allowing for an experience that remains concentrated, for now, the O-RADS MRI threshold score of 4 or higher likely offers excellent sensitivity and specificity for clinical practice.

In summary, the systematic review and meta-analysis by Rizzo et al provides an objective summary of the evidence on the diagnostic performance of O-RADS MRI for US-indeterminate adnexal masses that we can apply to clinical practice. Radiologists are now in a better position to offer more precise risk assessments to our patients and referring physicians. These results will also prove useful to the O-RADS MRI group in their development of management recommendations for the scored categories. Whether MRI impacts patient outcomes at a population level by decreasing mortality or morbidity has yet to be demonstrated. A trial to address this issue would require investments in patient recruitment, referral base buy-in, and radiologist training. But given the current state of the evidence, we are now poised to directly ask, "Does MRI improve health outcomes in women with incidental adnexal masses?"

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References

1. Sisodia RC, Del Carmen MG. Lesions of the Ovary and Fallopian Tube. N Engl J Med 2022;387(8):727–736.
2. Meys EM, Kaijser J, Kruitwagen RF, et al. Subjective assessment versus ultrasound models to diagnose ovarian cancer: A systematic review and meta-analysis. Eur J Cancer 2016;58:17–29.
3. Thabet A, Somarouthu B, Oliva E, Gervais DA, Hahn PF, Lee SI. Image-guided ovarian mass biopsy: efficacy and safety. J Vasc Interv Radiol 2014;25(12):1922–1927.e1.
4. Thomassin-Naggara I, Poncelet E, Jalaguier-Coudray A, 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 2020;3(1):e1919896.
5. Sadowski EA, Thomassin-Naggara I, Rockall A, et al. O-RADS MRI Risk Stratification System: Guide for Assessing Adnexal Lesions from the ACR O-RADS Committee. Radiology 2022;303(1):35–47.
6. Rizzo S, Cozzi A, Dolciami M, et al. O-RADS MRI: A Systematic Review and Meta-Analysis of Diagnostic Performance and Category-wise Malignancy Rates. Radiology 2023;307(1):e220795.
7. Jha P, Gupta A, Baran TM, et al. Diagnostic Performance of the Ovarian-Adnexal Reporting and Data System (O-RADS) Ultrasound Risk Score in Women in the United States. JAMA Netw Open 2022;5(6):e2216370.
8. Thomassin-Naggara I, Belghitti M, Milon A, Abdel Wahab C, Sadowski E, Rockall AG; EURAD study group. O-RADS MRI score: analysis of misclassified cases in a prospective multicentric European cohort. Eur Radiol 2021;31(12):9588–9599.
9. Sahin H, Panico C, Ursprung S, et al. Non-contrast MRI can accurately characterize adnexal masses: a retrospective study. Eur Radiol 2021;31(9):6962–6973.
10. Hottat NA, Badr DA, Van Pachterbeke C, et al. Added Value of Quantitative Analysis of Diffusion-Weighted Imaging in Ovarian-Adnexal Reporting and Data System Magnetic Resonance Imaging. J Magn Reson Imaging 2022;56(1):158–170.