



New Frontiers in Endometriosis: Imaging and Beyond

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Citation: EMJ Repro Health. 2025;11[1]:32-36.
<https://doi.org/10.33590/emjreprohealth/NRUM8961>



A DEDICATED session on endometriosis at the 41st Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE) highlighted the significant progress being made in both imaging technologies and emerging diagnostic biomarkers. Experts explored how clinical tools are evolving to support earlier, more accurate, and more patient-friendly diagnosis, redefining the way endometriosis is detected and managed.

FROM INVASIVE PROCEDURES TO IMAGING FIRST

The session opened with Mee Kristine, Oslo University Hospital, Norway, who traced the diagnostic evolution from invasive laparoscopy to the current use of non-invasive imaging. Today, transvaginal sonography (TVS) and MRI are at the heart of diagnosis and disease mapping, helping to identify the three main phenotypes of endometriosis: superficial peritoneal, ovarian (endometriomas), and deep infiltrating endometriosis.

TVS remains the first-line imaging modality. It is widely available, cost-effective, and environmentally friendly, with excellent test performance. As a dynamic tool, TVS allows real-time interaction with the patient, enabling the clinician to assess site-specific tenderness and gain immediate insight. However, TVS has limitations, particularly in detecting peritoneal lesions and disease in the lateral pelvic compartments.

MRI serves as a valuable second-line tool when TVS is inconclusive or negative in patients who are symptomatic. It is also used preoperatively and postoperatively if symptoms persist. Its strengths include the ability to generate multiplanar images and better visualisation of lateral and

extra-pelvic disease, which are crucial for identifying issues such as ureteral involvement. However, MRI lacks dynamic interaction with the patient and, like TVS, has limited ability to detect superficial peritoneal lesions.

IMAGING AT THE CENTRE OF DIAGNOSIS AND MANAGEMENT

The 2022 ESHRE guideline¹ formally placed imaging at the forefront of the endometriosis diagnostic pathway, recommending it alongside clinical examination as the first-line assessment for suspected endometriosis. Importantly, a negative ultrasound does not rule out the condition. In cases where empirical medical therapy is ineffective or inappropriate, particularly in infertility, diagnostic laparoscopy may still be necessary, especially to assess peritoneal involvement.

Imaging now plays a critical role beyond diagnosis, guiding treatment decisions, surgical planning, and long-term management. It provides essential information about lesion location, size, and complexity, which informs surgical strategy, risk evaluation, and the required level of surgical expertise.

“Both TVS and MRI have limited sensitivity for detecting gastrointestinal, diaphragmatic, and superficial peritoneal disease”

FERTILITY AND IMAGING

Endometriosis often affects fertility, being linked to reduced ovarian reserve and elevated oxidative stress in the pelvic environment. Here, imaging is essential: it supports fertility preservation, guides egg retrieval in assisted reproductive technology (ART), and helps tailor treatment protocols based on uterine and ovarian accessibility.

A recent Australian study showed the importance of early endometriosis diagnosis.² Women diagnosed with endometriosis after their first ART cycle required more treatment cycles, had higher rates of intrauterine insemination, and reported lower live birth rates than women without endometriosis. In contrast, women diagnosed prior to initiating ART had outcomes similar to those without endometriosis. This highlights how timely imaging and diagnosis can improve fertility success rates.

DIAGNOSTIC GAPS AND THE NEED FOR EXPERTISE

Despite its advantages, imaging still faces challenges. Both TVS and MRI have limited sensitivity for detecting gastrointestinal, diaphragmatic, and superficial peritoneal disease. Operator expertise is also a major factor, though standardised protocols and key signs (such as the ‘negative sliding sign’ or ovarian immobility) can assist in detection in less specialised settings.

Surgical treatment continues to play an important role, particularly for women with severe symptoms, anatomical distortion, or fertility concerns. The goals of surgery include symptom relief, anatomical restoration, function preservation (such as bowel and ureteral integrity), and recurrence prevention.

The latest ESHRE Guidelines support surgery for endometriosis-related infertility in cases of minimal-to-mild disease and ovarian endometriosis, where evidence suggests improved spontaneous pregnancy rates postoperatively.¹ However, surgery before ART is not recommended for superficial or ovarian endometriosis. In deep disease, decisions should be individualised based on pain severity and patient preference.





Surgical technique is also evolving. For superficial peritoneal disease, the standard approach is shifting from ablation, which destroys the lesion with heat, to excision, which involves removing the lesion along with the affected peritoneum. This method is more complex and demands advanced surgical planning, once again highlighting the indispensable role of accurate imaging.

IMAGING INNOVATIONS

Future directions in imaging aim to overcome current limitations. 3D TVS offers better spatial visualisation and could improve the detection of deep or even superficial lesions. Though difficult to identify on current imaging, superficial lesions may be visible if there is some fluid in the posterior cul-de-sac. New methods are under investigation to enhance the detection of these subtle findings.

In 2024, the International Deep Endometriosis Analysis (IDEA) group consensus expanded its guidelines to include routine evaluation of the parametrium, helping to improve identification of lateral compartment disease.³ Another exciting development is pelveoneurosonography, which enables

visualisation of the sacral nerve roots and plexus, structures often involved in chronic pelvic pain but difficult to assess with traditional imaging.

Additionally, molecular imaging is showing promise. The University of Oxford's DETECT study⁴ is evaluating ^{99m}Tc-maraciclalide, a radiolabelled tracer that binds to the $\alpha v \beta 3$ integrin, a protein expressed on the surface of endometriotic lesions. This novel agent may allow non-invasive detection of early-stage endometriosis, a major breakthrough if successfully validated. The tracer offers the potential for functional imaging of active lesions and could complement conventional anatomical imaging modalities.

AI: SUPPORTING DIAGNOSIS AND ACCESS

AI is also making its way into endometriosis diagnostics, offering opportunities to improve early detection and overcome workforce shortages. AI could be used for triage, helping to identify patients who need further imaging, as well as to accelerate diagnosis in adolescents or those experiencing infertility.

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However, challenges remain. MRI data are complex, requiring substantial computational power. TVS images, by contrast, are highly operator-dependent and variable. AI model development is also limited by small and non-representative datasets, a lack of validation, and inconsistent data quality.⁵

Despite these hurdles, AI holds long-term promise. It could support less experienced clinicians, reduce diagnostic delays, and streamline patient access to expert care, particularly in underserved regions.

BEYOND IMAGING: THE RISE OF BIOMARKERS

In the second part of the session, Arne Vanhie, Leuven University Fertility Centre and University Hospital Leuven, Belgium, addressed the growing interest in non-invasive biomarkers as a complement, or potential alternative, to imaging.

He began by distinguishing between biomarkers and diagnostic tests. While biomarkers may correlate with the presence of disease, true diagnostic tests must demonstrate measurable performance using metrics such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Vanhie also highlighted the crucial role of prevalence in determining a test's utility, as lower prevalence dramatically reduces PPV, meaning tests are more reliable in specialist settings than in general practice.

To meet the diverse needs in endometriosis diagnosis, he identified three types of diagnostic tests, each with a different aim, population, and expected outcome. A referral test aims to triage patients who are symptomatic more effectively for imaging,

and must prioritise high sensitivity to avoid missed cases. A replacement test could eventually obviate the need for laparoscopy in patients with negative imaging, requiring a high NPV or PPV, and should reduce healthcare costs. A 'red flag' test would identify patients likely to have deep disease and ensure they are referred to expert centres. This type of test must offer a high PPV and contribute to increased detection of deep endometriosis.

PROMISING BIOMARKER RESEARCH

Recent advances have yielded some exciting candidates for the diagnosis of endometriosis. One area of promise lies in salivary microRNAs. A 2022 study involving 153 patients with various disease stages used a random forest model based on 109 salivary microRNAs.⁶ Interim data from a multicentre validation study are highly encouraging, showing 96.2% sensitivity, 95.1% specificity, and a PPV of 95.1%.⁷ These results suggest real potential for clinical application, although full validation is still ongoing.

Another line of research has identified plasma protein biomarkers, including proteins involved in the coagulation cascade, complement system, and protein-lipid complexes.⁸ One model, trained specifically to detect Stage III–IV disease, showed excellent sensitivity and specificity and could be a promising candidate for a red flag test. Even when applied across all

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disease stages, the model performed well, with 87% sensitivity and 72% specificity for early-stage (Stage I) endometriosis. As with the salivary test, further independent validation is needed.

A FUTURE WITHIN REACH

The ESHRE 2025 session made it clear that the future of endometriosis diagnosis lies in integrated, non-invasive, and personalised care. Imaging has become central not just for diagnosis but also for surgical planning, fertility management, and

disease monitoring. Molecular imaging and AI are adding new layers of insight, while biomarkers are approaching clinical readiness.

Though challenges remain in validation, standardisation, and access, the combination of advanced imaging, AI, and biomarkers offers a path toward earlier detection, fewer diagnostic delays, improved surgical outcomes, and better quality of life for patients. As Vanhie concluded, “Are we there yet? Not quite, but we may be closer than ever.”

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