Challenges and opportunities in endometriosis diagnosis and management: time to disrupt, not double down

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Endometriosis is a complex and heterogeneous disease that affects 1:7 women and individuals assigned female at birth[1] with a variety of symptoms including pain, infertility and systemic issues such as severe fatigue and migraine resulting[2]. The diagnosis has traditionally hinged on the histological findings of endometrial glands and stroma outside of the endometrial cavity. This necessitates invasive surgery, although this has been used as a treatment for removal of endometriosis lesions[3]. The disease has been understudied given its prevalence and the substantive impact on women and girls. Apart from surgery, hormonal menstrual suppression or control has been the other mainstay of traditional medical management[4], with symptomatic treatments using analgesics or assisted reproductive technologies utilised where appropriate but not directed at disease control or reversal. There has not been a major therapeutic improvement in endometriosis care for more than 40 years.

Challenges in this space include diagnostic issues, with imaging missing 50% of disease. Recent technologies include salivary miRNA or blood biomarkers, with external validation studies pending. An accurate non- or low invasive diagnostic test would be transformational. Following diagnosis, considerable disease heterogeneity, and classification difficulties exist. Of the 22 published classification systems only 1 has any clinical correlation and that is for fertility and the chance of live birth and need for assisted reproduction[5]. Since endometriosis lesions are similar to the eutopic endometrium, targeted destructive treatments risk damage to future fertility in a young population, and this considerably complicates potential therapeutics. Considerable intra- and inter-patient patient lesion variability may occur with menstrual cyclicity variations a further confounding complication. Fibrosis often occurs in deeply invasive lesions and may represent a specific subtype of disease, with structural changes complicating presentations due to invasion into the gastrointestinal, urinary and even respiratory tracts.

To address this disease, a new approach must be taken. Diagnostic pathways must address the heterogeneity and be specifically sensitive that initiation of management has the opportunity to change disease course before the end-stage processes of fibrosis and organ invasion necessitate major surgery. Classification based on biology, rather than surgical appearance is required to potentiate precision-medicine based therapeutic approaches. Finally, delivery systems must be adaptable and consider trans-uterine, trans-tubal and other novel approaches. These treatments should not interfere with fertility (i.e., not be hormonally based) and must recognise the chronic nature of endometriosis variations with long-term safety, efficacy and patient acceptability critical.

References:

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