RESPONSE to the EDITOR

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Facts Views Vis Obgyn

Reply: Iatrogenic breaching of the junctional zone: the unintended path to placenta accreta spectrum?

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Dear Editor,

Our study concerns a highly selected group of patients with longstanding infertility and recurrent implantation failure, all of whom had exhausted conventional treatment strategies before referral. The article does not present any of the described interventions -such as gonadotropin releasing hormone suppression, platelet-rich plasma, or adjuvant medications- as validated therapies; these were clearly documented as part of patients' prior management. We fully agree that such approaches currently lack robust evidence and should be confined to research settings.

The statement that patients showed "no major pathology" refers exclusively to transvaginal ultrasound findings. Ultrasound and magnetic resonance imaging (MRI) assess fundamentally different aspects of myometrial structure and cannot be used interchangeably. Whereas ultrasound evaluates macroscopic echotexture and gross anatomical irregularities, MRI provides detailed insight into tissue composition, water diffusion, iron distribution, and the microstructural integrity of the junctional zone (JZ). In our cohort, many women with recurrent implantation failure had reassuring ultrasound and hysteroscopic findings, yet MRI consistently demonstrated complete loss of JZ differentiation -a pathological feature that would otherwise have remained undetected. This discrepancy cannot be attributed to transient physiological changes, which do not mimic a diffuse global absence of JZ structure. Rather, it underscores MRI's superior sensitivity for detecting diffuse JZ disruption, a finding that in our experience correlates strongly with impaired reproductive outcomes.

All MRIs were performed before any procedures at our centre. In over 90% of cases, diffuse loss of JZ differentiation corresponds histologically to adenomyosis; these data will be published soon. Focal adenomyosis is more heterogeneous, and while a causal relationship with intrauterine procedures cannot be excluded, it remains unproven. The fact that not all women develop adenomyosis despite universal uterine peristalsis suggests that genetic or epigenetic contributors, such as KRAS mutations, likely play a substantial role.

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Contractions may confound assessment of focal JZ thickness but do not account for the complete absence of JZ definition, in which all myometrial cells display similar water and iron content. No significant variations in JZ thickness across menstrual phases have been reported.[1-2]

Hysteroscopic sub-endometrial exploration is not an indiscriminate "breaching" technique. In carefully selected patients with recurrent failure or pregnancy loss, a standardized full-thickness biopsy is performed using a bipolar resectoscope designed to minimize thermal injury. Postoperative evaluation shows no adhesion formation or changes in MUSA criteria.

We thank you for raising the concern that targeted biopsies might increase placenta accreta spectrum (PAS) risk. Our recent data indicate proper healing after cytoreductive surgery, high pregnancy rates, and acceptable obstetric outcomes, with no evidence thus far of elevated PAS risk.[3] Observed differences appear more closely linked to maternal age and donor-oocyte use.

We agree that meticulous follow-up and prospective registration are essential. Our intention is not to establish a new routine intervention but to stimulate further investigation into recurrent implantation failure within centres of excellence.

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Informed consent: Informed consent was obtained from all individual participants included in this study.

Data sharing: All data is available to be shared upon request to the corresponding author.

Transparency: The authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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