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Correspondence

Letter to the editor/comments on “the conversion to IUI versus continuance with IVF in low responder patients” by Fujii et al. Eur J Obstet Gynecol Reprod Biol 2018 Aug; 227:35–40



To the editor,

We have read with great interest the systematic review by Fujii et al. [1] which compares conversion to IUI to continuation with IVF in poor responders (POR) to controlled ovarian stimulation (COS). The authors thoroughly reviewed all studies comparing the two strategies in patients with ≤ 4 follicles following COS, and concluded that “continuation with IVF offers the best chance at live birth (LB) but not clinical pregnancy when ≥ 2 follicles develop”. We would like to thank the authors for the extensive review of an important issue that could be helpful for everyday practice, but we believe the results should be interpreted with caution.

First of all, the quality of the available evidence is too low to be able to draw conclusions and guide clinical practice. Indeed, only eight studies were included, and seven were retrospective and observational in design, thus associated with multiple biases, while only five reported LB rates (LBR). Moreover, several aspects should be pointed out in the studies that reported higher LBR with IVF. In the study by Quinquin et al. [2], the choice between IVF and IUI was made in collaboration with the couples, which could have influenced the outcomes, and the 16 mm threshold used to define a mature follicle is different from the one used in most studies. Moreover, the authors do not mention the number of smaller follicles (14–15 mm) and whether they were aspirated or not, nor the number of mature oocytes, embryos available and embryos transferred in the “2 follicles ≥ 16 mm” group. Finally, the miscarriage rate was abnormally high in the IUI group: out of 5 clinical pregnancies confirmed on ultrasound at 7 weeks, 4 did not result in a LB (4/5, 80%). An 80% miscarriage rate is extremely high for a patient population with a mean age of 36 years, especially that the IVF group had a comparable mean age but a miscarriage rate of 30% (6/20).

In the study by Reichman et al. [3], the inclusion criteria were not well defined, and the distribution of patients between groups was quite disparate. Indeed, in the “2 follicles” group, there were 208 IVF compared to 146 IUI (1.5 times higher), and in the “3 follicles” group, 312 had IVF compared to 61 IUI (5 times higher). On the other hand, in the “1 follicle” group, 267 had IUI compared to 104 IVF (2 times higher). As the authors mentioned, patients with 3 follicles were encouraged to undergo IVF whereas patients with one follicle were encouraged to undergo IUI. Moreover, the authors found a significantly higher LBR with IVF in the “2 follicles” group, but there was no

difference between IVF and IUI in the “3 follicles” group. These counterintuitive findings were not explained by the authors.

Finally, the authors did not include a large 2009 retrospective study by Shahine et al. [4] in their analysis, despite filling the inclusion criteria. The study showed no difference in clinical pregnancy and LBR between IUI and IVF in women with < 5 follicles.

Overall, we believe that, despite some evidence suggesting better outcomes with IVF, it is not enough to conclude that “continuation with IVF offers the best chance at live birth but not clinical pregnancy when ≥ 2 follicles develop”. Randomized Controlled Trials (RCT) using strict definitions of POR are needed to compare continuation with IVF and IUI, in order to offer guidelines for the management of this commonly encountered problem. A French multicentric RCT has started in December 2017 (NCT03362489) with the objective of assessing which strategy offers the best outcomes in poor responders, and it includes with a cost-effectiveness analysis.

References

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