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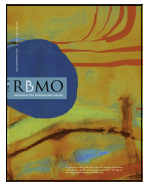

LETTER

Modified natural cycle IVF is a reasonable alternative in women of advanced maternal age

We appreciate the interest of colleagues *El Tokhy and El-Toukhy (2020)* in our study regarding the role of modified natural cycle (MNC)-IVF versus conventional stimulation in advanced-age Bologna poor responders (*Drakopoulos, et al., 2019*). However, we humbly disagree with their concerns regarding the main conclusions of the paper. Specifically, El Tokhy and El-Toukhy argue that the number of oocytes and embryo availability should not be considered as potential confounders and, therefore, should not have been included in the multivariate regression model.

Although we agree that true confounders should not be directly related to the exposure (namely mode of ovarian stimulation), one ought not overlook the fact that MNC-IVF may also result in more than one oocyte being retrieved. To that extent, the crude analysis according to number of oocytes showed non-significant difference in ongoing pregnancy rate/cycle (OPR) between the two groups. Secondly, the claim that embryo availability was part of the regression model is inaccurate. In fact, the variable 'top quality embryo' was the confounder included and evidence supports that embryo quality is not related to ovarian stimulation regimen (*Ziebe, et al., 2004*, *Ho and Paulson, 2017*).

Nonetheless, in order to assuage these concerns, we performed a new regression analysis after excluding the number of oocytes from the model, in which the results remained approximately the same: OR conventional stimulation versus MNC-IVF = 2.32 95%CI 0.81-6.7, $P = 0.11$).

We acknowledge that the retrospective nature of our study preclude any establishment of causality. That said, this study is currently the largest to evaluate the role of MNC-IVF in older poor responders and, according to its results, even after taking into consideration the above-mentioned concerns, MNC-IVF remains a reasonably valid alternative in women of advanced maternal age.

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