

# ICSI has no outcome benefits over conventional IVF in routine non-male infertility cases

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Intracytoplasmic sperm injection (ICSI), the world's favoured means of fertilisation in assisted reproduction, offers no benefit over conventional in vitro fertilisation in fertility treatments without a male factor indication, according to results of a large multicentre study.

ICSI was developed throughout the 1990s as a specific treatment for infertility of male cause. Until then, men with poor quality or insufficient sperm cells in their ejaculate had little chance of fathering their own children. But now, in the hands of the ICSI embryologist and beneath powerful microscopes, just one sperm cell might be enough for conception.

Since its development, however, ICSI has been adopted as a fertilisation technique for all types of sub-fertility, and not just of male cause. Globally, ICSI cycles now outnumber conventional IVF cycles by around two to one, and in some countries—in the Middle East, for example—assisted reproduction cycles are entirely ICSI.

Now, a large population-based study of almost 5000 patients in Belgium and Spain being treated with ICSI or standard IVF has found no benefit from ICSI in terms of fresh and cumulative live birth rate in non-male factor cases. The results of the study are presented today at the Annual Meeting of ESHRE by Dr. Panagiotis Drakopoulos from UZ Brussels, the pioneering Belgian centre at which ICSI was developed more than 25 years ago. The study was a collaboration between the Brussels centre and 14 IVI clinics in Spain.

This important study did not just compare outcomes in ICSI and IVF in non-male factor cases but also in different kinds of patient response to ovarian stimulation. "There has been a worldwide increase in the use of ICSI for all causes of

infertility," explained Dr. Drakopoulos. "The rationale for this seems to be that ICSI is associated with a higher likelihood of fertilisation and an increased number of embryos—but this is controversial. For example, ICSI is the first choice for fertilisation in many centres in patients who respond mildly to ovarian stimulation and have few eggs retrieved. But there is currently no evidence on the comparative effectiveness of ICSI and IVF according to the number of oocytes retrieved in patients with non-male factor infertility. This study for the first time aimed to provide that evidence using a large sample size."

Results firstly showed no overall difference in outcome (fertilisation rate, live birth rate and cumulative live birth rate) in the ICSI or standard IVF cycles. Moreover, these comparable findings were also evident in four different patient response categories ranging from poor responders (1-3 eggs retrieved) to high responders (more than 15 eggs retrieved). "It's clear from these results," said Dr. Drakopoulos, "that the number of oocytes retrieved has no value in the selection of the insemination procedure in cases of non-male infertility," confirming that ICSI will not improve outcome in cycles in which only a few eggs are retrieved.

Both global and European registry figures show that around 70% of all reported cycles were ICSI in 2015, with a slightly higher pregnancy rate found in the IVF cycles (27.7% IVF and 25.5% ICSI). However, these usage rates varied from region to region, with high rates of ICSI evident in many countries of Eastern and Mediterranean Europe. More modest use, with a roughly 50-50 split between IVF and ICSI, was found in some Nordic countries, UK and France. In its latest review of treatment trends in the UK, the HFEA reported that ICSI use 'continued to increase until 2014, but it is now in decline, possibly due to clinical opinion that

it's not needed in all contexts of IVF."

This is indeed the clinical message from this study, which, according to Dr. Drakopoulos, found 'no justification for the use of ICSI in non-male factor infertility.' He added that the number of eggs retrieved 'should not play any role in selecting the insemination method.'

"The rationale for the high use of ICSI in non-male factor cases," he said, 'is based on a wrong assumption that ICSI may be associated with a higher likelihood of fertilisation and an increased number of available embryos. However, our results show that this assumption is misplaced.'

Dr. Drakopoulos described these results as sufficiently robust 'to convince clinicians not to propose ICSI in all infertile patients,' adding that the extra financial cost of ICSI over IVF should also be considered in the absence of male factor infertility.

**More information:** Abstract O-228, Wednesday 26 June 2019: ICSI does not offer any benefit over conventional IVF across different ovarian response categories: a European multicenter analysis

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