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Associate Editor

## Avoiding type II errors—simulation studies?

To the Editor:

We read with interest the paper by Gozlan et al. (1) regarding the comparison of intracytoplasmic sperm injection (ICSI) versus in vitro fertilization (IVF) in poor-responder patients. This issue is an extremely important and unsolved subject to all human reproduction centers. However, we have some comments regarding this paper.

The proper design to study and accurately conclude any treatment topic, in this case ICSI versus IVF, is a randomized clinical trial, not the retrospective design used. Using a retrospective design, there are several biases that could be present and could interfere in all outcomes, which makes all conclusions nonviable.

Nevertheless, the main problem for the majority of papers concerning human reproduction that tried to compare pregnancy rates is the power calculation and, consequently, an adequate sample size.

If we include, in any research protocol, a low number of subjects, hypothetically we will have some (calculated) risk to not achieve statistical power to detect a true difference between those subjects. Therefore, we can erroneously have a false conclusion (type II error) if we did not detect any difference among the studied groups.

Using the presented data of the authors, we calculated the power and the sample size needed to achieve a  $P$  value  $\geq 90\%$ . The appropriate sample sizes for ICSI versus conventional IVF in patients  $\leq 39$  years old were 440 for the fertile sperm group and 486 for the subfertile sperm group. Moreover, the adequate sample sizes for patients  $>39$  years old was 3,264 for the fertile sperm group and 308 for the subfertile group (chi-squared test with continuity correction). In addition, using their data in all analysis the power calculation was lower than 50%.

Unfortunately, this paper did not include a sufficient number of patients to reach any conclusion regarding the best treatment (ICSI vs. IVF) using pregnancy rates as an outcome.

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## REFERENCE

1. Gozlan I, Dor A, Farber B, Meirow D, Feinstein S, Levron J. Comparing intracytoplasmic sperm injection and in vitro fertilization in patients with single oocyte retrieval. *Fertil Steril* 2007;87:515–8.

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## Reply of the Authors:

We thank Dr. João Sabino Cunha-Filho and his colleagues for their interest in our work. The data presented in our work was collected during a period of 5 years. Often we refer to such patients as if they have an “ovarian” or “egg” factor problem. In most centers worldwide, such patients are discouraged from undergoing IVF trials other than egg donation.

There is no doubt that ideally, every clinical research should be conducted as a prospective randomized one. However, as important as it may be, it is almost impractical to conduct such a prospective project, which may last for more than 10 years to complete, just for the sake of getting an appropriate statistical power.

Much of our clinical experience is still gained through retrospective analysis of our patients' medical records. These worldwide research activities usually enable us to make prudent decisions while keeping in mind the limitations that type II errors impose on us. Usually such research activities inspire authors to design further prospective research projects to settle disputes or clarify more specific issues.

In terms of fertilization rates, our data have enabled us to draw valid statistical results and conclusions. The pregnancy rate, however, in this group of patients is obviously low, and therefore we were not able to consider this end point in our study. Nevertheless, careful evaluation of the results, even though the power is less than 50%, may provide some hints for the appropriate practical clinical approach in such patients even in this respect.

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