Letters to the Editor


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WHO grade ‘a’ sperm motility and zona pellucida-binding test predict IVF outcome

Sir,
I have read with great interest the article by Sifer et al. (2005) on the combination of a newly developed sperm–zona pellucida-binding assay and WHO grade ‘a’ sperm motility to predict sperm fertilizing ability in IVF. The authors have to be commended for developing a— theoretically very appealing—new sperm function test, and it is easy to understand how they could get carried away by their enthusiasm about the clinical applicability of this new test. In fact, the authors are so positive about the results of their combination test that they consider it ‘an excellent predictor of sperm fertilizing potential in cases of mild male-factor infertility’, and they recommend that it ‘should be incorporated as a functional test to direct patients to IVF or ICSI at their first attempt’. They continue by stating that ‘the positive LR of 1.67 (95% CI 1.07–2.59) allowed us to use this test in these cases’ (i.e. in patients with unexplained infertility).

I beg to disagree. Likelihood ratios (LRs) measure the power of a test to change the pre-test into the post-test probability of a disease being present. An LR of 1.67 will change the likelihood of disease in a clinically not very relevant way (the likelihood of fertilization e.g. would increase from 50 to 62.5%). LRs between 2 and 5 cause only small changes, LRs between 5 and 10 cause moderate changes and only LRs >10 cause clinically important changes (Sackett et al., 2000). In male infertility, the authors found an LR of 6.0 indeed, suggestive of a clinically moderately useful test. However, in contrast to unexplained infertility, they fail to include the 95% confidence interval (CI) of this LR. Using the figures from their Tables 3 and 4, however, this 95% CI can be calculated. For the LR of 6.0, it results in 0.9–41, which not only includes 1.0 (so the test may even be more likely to be abnormal in those who fertilize their oocytes than in those who do not) but also is so wide that it lacks the precision to contribute in a meaningful way to the clinical decision-making process [based on the results of this study, in case of a positive test outcome, a pre-test chance of fertilization of e.g. 50% may (with 95% certainty) decrease to as low as 47%, but at the same time increase to as high as 98%].

I do agree with the authors that the test ‘needs to be confirmed on a larger, external series of patients’, but I suggest that, in fact, validation of a newly proposed clinical diagnostic test (either in an independent new group of patients or in a split sample) should always be included in the original article. This would have restrained the authors from concluding that ‘we thought that it would not be ethical still to perform IVF rather than ICSI, especially in cases of male factor presence, when a sperm–zona pellucida-binding test was determined as negative’. This, when true, would effectively make further research into this exciting test unethical, which is not, I hope, what the authors would want.

References

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Reply: WHO grade ‘a’ sperm motility and zona pellucida-binding test predict IVF outcome

Sir,
We thank Professor Evers for his interest in our preliminary work (Sifer et al., 2005). We agree that a positive likelihood ratio (LR+) of 1.67 will change the likelihood of disease in a clinically not very relevant way. Indeed, we have moderated our purpose saying that an LR+ of 1.67 indicated a small impact on the post-test probability of successful IVF. However, this change was statistically significant as our study showed. Thus, we believe that in the lack of other predictive tests that could be performed routinely, this new combined test is helpful to decrease the risk of fertilization failure during IVF therapy in the case of unexplained infertility.

Concerning male factor, we have found an LR+ of 6.0, which indicated a better, though moderate, post-test impact, as we have said in our study and accordingly to Professor Evers’ letter. However, we effectively did not include the 95% confidence interval (CI) of this LR in our study, and we agree that...