Higher pregnancy rate of embryos with synchronous transition from the 2-cell stage to the 4-cell stage (t4-t3)

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Study question
How do different morphokinetic parameters affect the pregnancy rate? Is there any difference between agonist and antagonist protocols for controlled ovarian stimulation?

Summary answer
The duration of the 3-cell stage (t4-t3) is significantly shorter in embryos that lead to a pregnancy in both the agonist and the antagonist group.

What is known already
The EmbryoScope™ allows for the selection of embryos with the highest implantation potential based on different morphokinetic markers [1]. Some of them, like the time of cleavage from the 2- to the 3-cell stage (t3), the time of cleavage from the 3- to the 4-cell stage (t4) and the duration of the 3-cell stage (t4-t3) are associated with high blastulation or implantation rates after transfer on day 3 [2,3].

Study design, size, duration
We performed a retrospective analysis of the time-lapse annotations of 203 IVF/ICSI cycles with embryo transfer predominantly on day 5 from September 2013 to May 2015.

Table 1: Different morphokinetic parameters according to stimulation protocol.

<table>
<thead>
<tr>
<th></th>
<th><strong>Antagonist protocol</strong></th>
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<th><strong>Agonist protocol</strong></th>
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<tbody>
<tr>
<td></td>
<td>pregnant mean ± SEM [h]</td>
<td>not pregnant mean ± SEM [h]</td>
<td>Sig.</td>
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<tr>
<td>t3</td>
<td>38.4 ± 4.61</td>
<td>38.1 ± 4.80</td>
<td>n.s.</td>
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<tr>
<td>t4</td>
<td>40.0 ± 4.87</td>
<td>41.8 ± 6.62</td>
<td>n.s.</td>
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<tr>
<td>t4-t3</td>
<td>1.6 ± 2.1</td>
<td>3.7 ± 4.7</td>
<td>p = 0.039</td>
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</tbody>
</table>

Participants/materials, settings, methods
Using the EmbryoScope™ (Unisense Fertilitech, Denmark) as a time lapse imaging device, we analysed different morphokinetic parameters (t3, t4 and t4-t3) of all transferred embryos stratified by stimulation protocol (antagonist vs. agonist). Transfers were performed either on day 3 or 5.

Main results and the role of chance
Embryos with a high implantation rate show a significantly shorter duration of the 3-cell stage both in the antagonist (1.6±2.1 hours vs. 3.7±4.7 hours, p=0.039) and the agonist group (1.9±2.2 hours vs. 2.6±2.9 hours, p=0.039). In the agonist group, significantly shorter times of cleavage to the 3- t3 and 4-cell stages (t4) were observed in embryos with a high implantation potential (38.2±3.76 hours vs. 39.7±5.61 hours, p=0.026 for t3 and 40.1±4.48 hours vs. 42.3±5.97 hours, p=0.002 for t4).

The mean age of patients in the antagonist group was distinctively lower than in the agonist group (34.2 years vs. 37.4 years).

Wider implications of the findings
The analysis of morphokinetic parameters during early embryonic development allows for non-invasive selection of embryos with high implantation potential, offering a clear advantage over the conventional static evaluation. In our study, the best predictive morphokinetic parameter was the duration of the 3-cell stage being significantly shorter in embryos with a high implantation potential, regardless of the stimulation protocol.

Limitations, reasons for caution
The numbers of embryos analysed are low and the study results are based on a retrospective time lapse movie evaluation that can be associated with certain inter and intra-observer variation.

References: