Reviewer’s report

Title: D6 blastocyst transfer on day 6 in frozen-thawed cycles should be avoided: a retrospective cohort study

Version: 0 Date: 17 Feb 2020

Reviewer's report:

The manuscript discussed the timing of day 6 blastocyst transfer in FET cycles. Within 518 FET cycles with D6 blastocysts, they found that the pregnancy rates in D6-on-D5 group were significantly higher than those in D6-on-D6 group. The topic is potentially clinical important. However, the authors should also make further efforts to control the potential bias.

Specific
1) The title should be shortened and focused.
2) Patients:
The authors stated that "D6 blastocysts are transferred on day 6 in natural FET cycles to avoid transfer on weekend. While in some other in vitro fertilization (IVF) clinics, including our center, D6 blastocysts were planned to be transferred on day 6 according to the synchronization between the endometrium and the embryos" in the Introduction section. They may also declare how the time of D6 embryo transfer was planned in their dataset in the Materials and Methods section.
The authors suggested a "day 6 according to the synchronization between the endometrium and the embryos". How did they determine the synchronization and the timing? It should be detailed in the Materials and Methods.
In Table 1, data shown that the proportion of NC/HRT cycles was comparable between day6 on day 5 and day 6 on day 6 group. How many day 6 on day 6 cycles are due to logistic reason and many are due to endometrial synchronization?
3) Statistics:
The authors used multivariate analyses in the study. The selection of the covariates should be detailed in the Materials and Methods section.
Because the pregnancy rates are related to many factors and day 6 FET is related to several biases, I suggest the authors consider additional confounders and biases.
For instance, the D5 embryos were transfer in priority in the present study. It may suggest that patients with D6 FET have more previous failures and therefore have poor prognosis. Important predictors for pregnancy such as age and endometrial thickness should also be included in the multivariate model, regardless they are significant or not in the univariate analysis.
In addition, the authors considered the "Day of blastocyst formation" and "Timing for blastocyst transfer" as independent factors. However, timing and day of blastulation are closely related in the present study. D6 transfer was only for day 6 embryos. It may be problematic to consider these two factors independent. One may replace them with a three-level parameter (eg. day 6 on day6, day 6 on day5 and day 5 on day 5).
4) Tables:
I suggest the authors integrate the CPR/IR into the Tables.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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