In vitro fertilization oocyte retrieval: to "flush" or not?

The use of follicle "flushing" during transvaginal oocyte retrieval in in vitro fertilization (IVF) has been debated for many years. The theoretical advantage of using a double-lumen retrieval needle to aspirate the follicular fluid is that this process should "flush" out the oocyte and optimize oocyte retrieval yield (oocytes retrieved divided by follicles aspirated) when compared with direct follicle aspiration. There are now multiple randomized controlled trials in the scientific literature, which can help us objectively analyze the current data and come to some conclusions.

An older systematic review and meta-analysis, from the NIH group led by Levy et al. (1), assessing 6 randomized controlled trials (RCTs) (N = 518) in healthy responders undergoing IVF, found no positive impact of follicle flushing on oocyte yield or total oocytes retrieved and demonstrated an actual increase in the operating time with follicle flushing compared with direct follicle aspiration. A recent Cochrane systematic review of 10 RCTs (N = 928) concluded that follicle flushing during IVF oocyte retrieval does not increase the oocyte yield but increases the retrieval time in both healthy and poor responder patients (2). More importantly, the Cochrane review did not find any improvement in the primary outcome, live birth rate (direct follicle aspiration 41% vs. follicular flushing 29%–52%; OR 0.95, 95% CI 0.58–1.56, P= .84) (2).

The follow-up systematic review and meta-analysis in this issue of *Fertility and Sterility* by the NIH group, led by Martini et al. (3), reported 11 RCTs with 1,178 retrievals. The primary outcome, live birth rate, did not significantly increase with follicle flushing compared with direct follicle aspiration (RR 1.03, 95% CI 0.79–1.34, P= .93). The investigators also found no improvement with follicular flushing on the total number of oocytes and mature oocyte yield (secondary outcomes). They also confirmed a significant increase in the IVF procedure time, by an average of 2 minutes in poor responders (mean difference 2.03, 95% CI 1.29–2.77, P< .00001) and 9 minutes in healthy responders (mean difference 4.10, 95% CI 2.51–5.66, P< .00001). Interestingly, post hoc sensitivity analyses evaluating the impact of study differences in double-lumen retrieval needle type, the volume of media used, and the number of flushes, did not demonstrate any significant differences in live birth rate, total oocytes, or mature oocyte yield. Some notable limitations of this meta-analysis related to the inclusion of open-label studies, and high heterogeneity across studies in IVF poor responders and in those comparing procedure times between follicle flushing and direct follicular aspiration (3). In addition, the 5 RCTs which assessed IVF poor responders varied in their definition between ≤4–8 follicles >12 mm on the day of the trigger injection). Another limitation of this study was that the 11 RCTs did not assess the impact of follicle flushing in patients undergoing IVF natural cycles, minimal stimulation cycles, or in vitro maturation cycles. A recent RCT (N = 164) evaluated the impact of follicular flushing vs. direct follicle aspiration in minimal stimulation monofollicular IVF cycles only (4). They found a significant increase in the mature oocyte yield in the follicular flushing group compared with the direct follicle aspiration group (adjusted risk difference 18.2%, 95% CI 3.9–31.7, P< .02). However, there was no significant difference in the live birth rate, and there was a significant increase in the median duration of the procedure in the flushing group compared with direct follicle aspiration (2.38 minutes vs. 0.43 minutes, P< .01) (4).

In summary, the results of the Martini et al. (3) systematic review and meta-analysis of 11 RCTs confirmed that the use of follicular flushing in both healthy and poor responder IVF patients should be abandoned because it does not increase the live birth rate or the oocyte yield, and significantly increases the procedure time. When attempting monofollicular IVF oocyte retrieval, it is possible that follicular flushing may improve mature oocyte yield compared with direct follicle aspiration. However, it did not improve the live birth rate.

Humberto Scoccia, M.D.
Division of Reproductive Endocrinology and Infertility, University of Illinois at Chicago, Chicago, Illinois

https://doi.org/10.1016/j.fertnstert.2021.01.033

You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/posts/32274

REFERENCES

1. Levy G, Hill MJ, Ramirez CI, Correa L, Ryan ME, DeCherney AH, et al. The use of follicle flushing during oocyte retrieval in assisted reproductive technologies: a systematic review and meta-analysis. Hum Reprod 2012;27:2373–9.
2. Georgiou EX, Melo P, Brown J, Granne IE. Follicular flushing during oocyte retrieval in assisted reproductive techniques. Cochrane Database Syst Rev 2018;4:CD004634.
3. Martini AE, Dunn A, Wells L, Rollene N, Saunders R, Healy MW, et al. Follicle flushing does not improve live birth and increases procedure time: a systematic review and meta-analysis of randomized controlled trials. Fertil Steril 2021;115:974–83.
4. Kohl Schwartz AS, Calzaferri I, Roumet M, Limacher A, Fink A, Wueest A, et al. Follicular flushing leads to higher oocyte yield in monofollicular IVF: a randomized controlled trial. Hum Reprod 2020;35:2253–61.