Thickness or pattern: that is the question

We developed the concept of endometrial "compaction" to denote endometrial thinning in response to progesterone during the follicular/luteal transition. In the study by Jin et al. (1) in this issue of *Fertility and Sterility*, endometrial compaction is evaluated in 508 blastocyst transfer cycles monitored by transvaginal ultrasound at the end of estrogen administration and on the day of embryo transfer. The investigators used preimplantation genetic testing for aneuploidy to select single euploid blastocysts for transfer and chose the same hormone replacement therapy regimen with exogenous estrogen and progesterone to ensure cycle uniformity in the study. Two ultrasound technicians measured the endometrial thickness using a vaginal transducer and stored the images electronically so that two of the investigators, blinded to the outcomes, were able to confirm the accuracy of the measurements. The difference in endometrial thickness between the two ultrasound measurements was calculated. They found that 19.5% (99/508) of the patients had decreased endometrial thickness on the blastocyst transfer day, 47.2% (240/508) of the patients had increased endometrial thickness, and the remaining 33.3% (169/508) had no change in endometrial thickness. In contrast to our studies (2, 3), which showed increased pregnancy rates with endometrial compaction, there was no statistically significant difference in the clinical pregnancy, miscarriage, or live birth rates among the three groups.

Our concept of comparing endometrial ultrasound measurements at two different times during an embryo transfer cycle was based on the hypothesis that we could use ultrasound measurements as a bioassay of progesterone activity on the basis of known physiologic changes of the endometrium during the menstrual cycle. In the follicular phase, estrogen increases endometrial thickness by stimulating the linear growth of endometrial glands and blood vessels. As a result, there is little reflection back of ultrasound waves between the myometrial/endometrial junctions and the midline luminal endometrial layers, resulting in the typical trilaminar appearance of the endometrium in the longitudinal view of the uterus. The linear growth of the endometrium slows down 2–3 days after ovulation, but the continuing growth of glands and vessels under the influence of progesterone within the endometrium results in coiling of the glands and vessels and accumulation of glycogen in the gland lumens and increased proliferation of T cells, macrophages, and lymphoid nodules. Together, these changes result in an increased endometrial density that reflects ultrasound waves, resulting in a homogeneous bright pattern on two-dimensional ultrasound. Therefore, the ultrasound change from a trilaminar pattern to a bright homogeneous pattern is characteristic of the follicular/luteal transition that occurs before and after ovulation.

Our premise was that the follicular/luteal transition may be detected simply by measuring the change in endometrial thickness from the end of the estrogen phase to the day of embryo transfer. The measurement of endometrial thickness should be more objective than the determination of the endometrial pattern. This hypothesis appeared to be correct from the results of our two previous publications. However, a criticism of our studies was that we used transvaginal ultrasound for the measurement of endometrial thickness in the estrogen phase and less accurate abdominal ultrasound measurements on the day of embryo transfer. We are now concerned that this criticism may be partially correct, not because of accuracy of the ultrasound measurement but rather because of the mechanical forces involved in abdominal ultrasound. We believe that the combination of a full bladder and pressure from the abdominal ultrasound transducer over the bladder may have compressed the uterus and endometrium to give an artifactually thinner lining measurement compared with vaginal ultrasound. As a result, we detected a higher percentage of cycles with compaction (approximately 30%–40%) (2, 3) compared with the results of Jin et al. (1) with approximately 20% of the embryo transfer cycles showing endometrial compaction. In the present study (1), the investigators did not find that a decrease in thickness predicted an increase in pregnancy, nor did they confirm that an increase in thickness was associated with improved pregnancy rates as published earlier by this same group (4).

A weakness of the study by Jin et al. (1) is the failure to specify that both a trilaminar pattern and endometrial thickness of >7 mm were required as inclusion criteria in their study. We still believe that a transition from a trilaminar pattern to a homogeneous bright pattern reflects the appropriate progesterone action in the endometrium to open the window of implantation. Endometrial thickness itself may not reflect this transition, although if the lining does get thinner, it is likely to be denser and probably does confirm the normal transition. On the other hand, if the follicular/luteal transition occurs, whether the lining stays the same or increases in thickness may not matter. There are enough conflicting data from retrospective case–control studies that we believe a large prospective study is the only way to really answer the question of whether endometrial compaction is significant or not for pregnancy outcome. Nonetheless, it is encouraging that a raft of new publications is looking at dynamic changes in the endometrium as a noninvasive marker of endometrial receptivity that may lead to improved pregnancy outcomes in the future.

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