The use of ultrasonography has improved the care of the infertility patients [1]. Ultrasonography is used for diagnostic purposes during the evaluation of the patient and also during the treatment of the infertility patient: monitoring follicular development during ovarian stimulation, visualization during oocyte retrieval for in vitro fertilization (IVF), visualization during embryo transfer for IVF, and, should the patient become pregnant from the treatment, to follow the pregnancy for viability (fetal cardiac activity), to determine the location of the pregnancy, to determine whether the pregnancy is a singleton gestation or a multiple gestation and to follow the progress of the pregnancy should there be a threatened miscarriage. It is also useful to monitor for complications of infertility treatment, such as ovarian hyperstimulation syndrome (OHSS).

The Antral Follicle Count (AFC) is a tool that could help determine a patient’s ovarian reserve. An AFC is the measurement of the follicles in the two ovaries that measure between 2 to 9 mm in diameter [2, 3]. The AFC is the sum of the 2-9 mm follicles in both ovaries. The AFC is considered a reliable measurement of ovarian reserve for patients undergoing IVF. The normal range of the antral follicle count is 9-19 antral follicles [2]. If the AFC is 0-4 antral follicles, it is considered “very low functional ovarian reserve”. With AFC between 5-8 antral follicles, this is considered “low functional reserve”, with high risk of poor response to ovarian stimulation. If the AFC is equal or greater than 20 antral follicles, this is considered “high functional ovarian reserve” and the patient is at high risk of excessive ovarian response and OHSS.

Studies of the AFC in infertile patients reveal that this biophysical measurement is useful in specific contexts. Generally speaking, the AFC is a marker of ovarian reserve [4, 5]. Another useful marker of ovarian reserve is the serum peptide antimullerian hormone (AMH), which is secreted by developing preantral follicles and small antral follicles. As such, the ovarian reserve information is useful for patients undergoing ovarian stimulation for IVF. However, the ovarian reserve predictive ability of AFC and AMH may not be as accurate for patients who are attempting pregnancy, and who are not currently undergoing ovarian stimulation for IVF. Furthermore, the AFC does not necessarily predict the success of ovarian stimulation in the oral agent treatment cycles. Thus, while the AFC is currently considered a standard diagnostic test for infertile patients, there are still significant gaps in being able to use this test to generate data that benefits a greater range of infertile patients.

GAPS THAT NEED TO BE ADDRESSED

The improvements in using AFC to make this test more useful for the prognosis of infertile patients in general and to make it more personalized to specific infertile patients could come from focusing in these three areas: advances in technology, advances in understanding the optimal timing of the AFC information gathered and advances in understanding the origins of discordance between the AFC and AMH and/or day 3 FSH levels.

The first area is advancing technology for the AFC. In addition to the standard 2D and 2 D cine-loop measurements of AFC, additional technologies could be considered. 3D measurements could be made, with volume information potentially providing about the relationship between the antral follicle volume and ovarian reserve status. A second technology that might assist is color Doppler flow to look at the vascularity of the antral follicles. Do patients with good prognosis have a different microscopic vascular flow pattern compared to the other patients? In addition, the new technology of photoacoustics could enhance the information obtained; if, for example, the oxygen levels are determined for the antral follicles and a correlation is able to be made between good outcome patients and poor outcome patients [6]. Another area in which there is potential for technology advancement is the use of machine learning-Artificial Intelligence (AI). With the AFC data available for large numbers of infertility patients, algorithms could be created to predict the factors resulting in good prognosis, based on the AFC and patient age, infertility factors, other ovarian reserve parameters and prior live births of patients with similar parameters. Furthermore, the AI algorithm involving AFC may assist with projecting the trajectory of the ovarian stimulation cycles that the patients may undergo. In addition, AI may be used to predict difference in the outcomes for general infertility treatments versus IVF treatments using the AFC information for these patients.

Another area that needs more investigation is the timing of AFC measurement in relation to the menstrual cycle [2]. Many infertility practices use a Day 3 AFC. Getting AFC ultrasound scan on Day 3 has been straightforward, as other tests are performed on this day. However, if it is not practical to do so, then how much of a discrepancy is there between a day 3 AFC and an AFC in other parts of the menstrual cycle? In some centers, the discrepancy may be about 10%. For the good prognosis patients, the 10% difference may not significantly alter the fertility treatment plan. However, in the patients with poor ovarian reserve and low AFC, with repeating the AFC on Day 3 of the menstrual cycle improve the prognostic capability of the AFC? Is this AFC information helpful for both general infertility patients and IVF patients? An important tool to be able to help patients is a table of the variation of the AFC throughout the menstrual cycle and to determine the variation of the AFC between menstrual cycles. This information will allow patients to be able to have AFC scans either at any time during the menstrual cycle, which provides more latitude for timing of the patient diagnostic tests, or at specific and optimized times of the menstrual cycle.
cycle. Furthermore, information about the AFC variation between menstrual cycles will also increase the predictive ability of a single AFC during the diagnostic evaluation of an infertile patient.

A third area of investigation is to further understand the implications of the discordance between an AFC and other markers of ovarian reserve [7]. For example, some patients have normal AFC while the AMH and days 3 FSH are abnormal and are consistent with poor ovarian reserve. Conversely, some patients have low AFC while having normal AMH and day 3 FSH. Thus, it would be helpful to have data about the different situations where the patient ovarian reserve discrepancies are present and the outcomes of patients undergoing infertility treatment in these situations. Could these more detailed data help define the most useful ovarian reserve test? In addition, could the AFC ovarian reserve discrepancies have different prognostic outcomes, depending on whether the patient is undergoing general infertility treatment, as opposed to IVF treatment?

CONCLUSION

The advancements in the ultrasound technology have made the capacity for the determination of AFC in patients more widely available. However, the ability to make the next jumps using the basic information hinges on advancing technology and getting more information about the AFC data generated. Three important considerations for the next steps forward are to enhance the technology associated with the collection of the AFC, to be able to create a table about variations of the AFC during the menstrual cycle so that the AFC could be performed at any time in the menstrual cycle and to be able to determine the best steps for the patient when there is discordance between the AFC and AMH levels when measuring ovarian reserve. All the potential avenues of advances can result in improved prognosis and treatment options for the infertile couple.

REFERENCES


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