Timing intrauterine inseminations: Do we need an ultrasound, or can artificial intelligence do the trick?

Cost. Convenience. Access. These are 3 of the main factors that limit the reach and impact of assisted reproductive technology (ART). For many patients, the first step in the treatment algorithm is intrauterine insemination (IUI). Although we commonly use a combination of hormonal testing and ultrasound imaging to determine ovulation time, there is no clear best approach (1). The lack of standardization is apparent in the haphazard combination of one or more costly ultrasounds, daily qualitative urinary luteinizing hormone (LH) testing, and the seemingly arbitrary collection of serum labs that different clinics draw. The average natural IUI cycle costs between $500 and $4000, with most of this cost burden ascribed to ultrasounds and bloodwork (2).

Artificial intelligence (AI) has recently become a proposed tool to synthesize multiple data sources to aid a given decision or predict an optimal outcome. Previous studies of the applications of AI in ART, such as optimizing the timing of the trigger shot, have focused on vitro fertilization stimulation or embryo selection (3). Furthermore, these studies have solely focused on optimizing existing steps in the process, rather than removing any, which could lead to reduced costs for the patient and system. Youngster et al. (4) are unique in their approach to this problem in 2 ways: they selected a unique problem in IUI cycle timing, and they sought to solve it in a way that would improve efficiency and directly reduce costs.

In their study, Youngster et al. (4) designed a machine learning algorithm that utilizes a few laboratory values alone to recommend both timing of ovulation and of insemination without the need for any imaging. This algorithm was astutely trained on a dataset of natural cycles that included all cycle data, including ultrasounds, and then tested against 2 separate test sets to minimize bias: one in which ovulation timing was determined by a trio of expert physicians and another in which ovulation timing was determined on the basis of the disappearance of the leading follicle on 2 consecutive ultrasounds. Remarkably, the algorithm correctly suggested insemination 1 or 2 days before its predicted ovulation time in 93% of cases using, on average, less than 3 lab draws.

As with any newly developed AI solution, this algorithm only operates within specified confines. Trained with natural cycle IUI, the algorithm also relies on regular menstrual cycles, which ultimately limits its applicability to subfertile patients who would benefit from stimulated IUI cycles. Although the algorithm ended up missing ovulation and/or the correct timing of insemination in only 7% of cases, it did end up recommending same-day IUI in 12% of cases. Although same-day IUI may be a possibility in some clinics globally, in the United States, very few, if any, clinics would have the infrastructure and logistic capability to reliably perform a same-day IUI, even if the patient was willing and available. Training the model on stimulated IUI cycles and irregular menses as well as evaluating the feasibility of using a human chorionic gonadotropin trigger injection without a prior ultrasound would be welcome next steps to further increase the applicability of the algorithm to a broader number of clinical situations. Furthermore, in patients at high risk for multiples, ultrasounds may be desired to minimize the risk of twins and higher order multiples. Nonetheless, this study proves that this approach is feasible if the appropriate large datasets are available to train the AI models.

Despite these constraints, the investigators demonstrate a tool with far-reaching potential. Eliminating or even reducing the use of ultrasound for IUI cycles would not only substantially reduce cost, but it would also reduce the burden on patients, especially those who reside far away from their clinics. On the clinic side, it lowers the cost needed to care for these patients because most of this comes from the cost of administering an ultrasound. We hope to see a formal cost-effectiveness analysis to compare outcomes from use of this algorithm to current clinical practice once it is deployed.

The most exciting prospect for such an AI tool is a potential marriage with at-home fertility hormone testing. This algorithm relies only on LH, estradiol, and progesterone levels to predict ovulation and insemination timing. If the patients do not need to come to clinic for ultrasounds, they may not need to come to clinic at all. At-home spot urinary measurements of LH and metabolites of estrogen and progesterone have already been shown in preliminary studies to have comparable accuracy to serum measurements and are able to predict cycle timing with marked accuracy (5). If these at-home tests are combined with the algorithm described by Youngster et al. (4), it would allow patients to undergo IUI without having to step foot in a clinic before the insemination.

As we envision the various scenarios in which this algorithm could be implemented, it is difficult to ignore the wider implications that a tool like this could have on our field. It holds the capability to alleviate the bottleneck faced by the ART industry, namely, limited access to clinicians, while simultaneously enhancing accessibility through cost reduction. Although there is a considerable journey from a conceptual algorithm to a rigorously tested and prospectively validated product, advancements of this nature ought to be embraced and encouraged.

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