IVF WORLDWIDE ONLINE CONGRESS

Luteal Phase oocyte retrieval and indications of successful practice

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INTRODUCTION

The second follicular wave (1,2) has been introduced as an encouraging means towards optimizing the context of in vitro fertilization (IVF) success rates for infertile women and especially for those who present as time-sensitive groups-namely women with poor ovarian response (POR). The prevalence of POR ranges between 5 and 35% in infertile women (3). POR may lead to a significantly low live-birth rate (4), while 50% of cancelled IVF cycles originate from poor responders' treatment according to the Society for Assisted Reproductive Technology (SART) (5,6). Aiming to efficiently address the demanding pathophysiology of POR, new protocols have been suggested, combining conventional follicular phase oocyte retrieval (FoPOR) with luteal phase oocyte retrieval (LuPOR) (7), known as "DuoStim", (8). Numerous studies attempted to compare the developmental potential between oocytes retrieved from the follicular phase and those from the luteal phase. Their observations have indicated that there are no statistically significant differences in maturation status, fertilization rate, embryonic development and live-birth rates (9). The rationale of this study stems from the fact that the newly introduced practice of LuPOR is still under investigation in spite of the promising data sourced to date. In the era of personalized and precision medicine, relying solely on a rather generic diagnosis such as POR to guide practice towards effective treatment may not be enough. In light of the fact that hitherto published data fails to conclusively indicate grounds for decision-making in application of LuPOR, the present study aims to investigate and identify patient characteristics that may indicate successful application of LuPOR, defined as the retrieval of at least one oocyte. The clinical end point of this study aiming to report back to the practitioner, is development of a predictive model identifying the optimal poor responders' population benefiting from LuPOR practice.

RESULTS

A total of 4739 medical records of women undergoing natural cycle IVF, between 2012 and 2020, were screened, and 1688 medical records fulfilled the inclusion criteria for this retrospective observational study. The inclusion criteria for this study were normal ovulation, poor ovarian response according to Bologna criteria (10), with at least one previous failed IVF-Controlled Ovarian Stimulation (COS) cycle yielding 3 or less oocytes. Only the first cycle from each couple was considered eligible for inclusion. For this retrospective analysis study, a further inclusion criterion was performance of ICSI for all couples, enabling identification of the oocytes' maturation status following retrieval. ICSI was performed on the grounds of male factor infertility and abnormal semen analysis parameters. The study aimed to associate patient characteristics with the probability of retrieving at least one oocyte. Thus, the MII outcome was transformed into a dichotomous outcome representing the efficiency of LuPOR practice in resulting to retrieval of an MII oocyte – or LuPOR's failure to result to retrieval of an MII oocyte. To achieve this, the receiver operating characteristics (ROCs) curve was calculated and the area under the curve (AUC) was employed for the determination of the predictive value of each characteristic. The youden index was employed in order to determine the threshold value. Thus, AUC of the ROC is calculated by plotting the true positive rate (sensitivity) against the false positive rate (1-specificity) across all possible thresholding values. Patients that failed to reach the follicular developmental stage of >17mm diameter were not subjected to LuPOR. Nonetheless they were recorded and respective data was included in the prediction model representing retrieval of zero oocytes. Patient dataset was stratified according to age in quantiles. A random 20% of each quantile was employed to validate the model. The remaining 80% was employed to develop the model.

Patients' age, number of previous failed IVF attempts, BMI, basal levels of FSH, LH, AMH, prolactin and progesterone failed to be predictive of the retrieval of at least one oocyte following LuPOR as the AUC was below 0.6. AFC, estradiol (E_2) levels on both trigger days, as well as number of small (8-12mm) non aspirated follicles were observed to also be predictive of the retrieval of an oocyte irrespectively of maturity status following LuPOR, however the predictive value was significantly lower when compared to the number of MII oocytes. More specifically, AFC with a threshold of 3.92, presented with an AUC at 0.64 with specificity at 0.52, sensitivity at 0.69 and accuracy at 0.68. E_2 at the day of trigger during FoPOR presented with a threshold of 222.92 pg/ml, presented with an AUC at 0.65 with specificity at 0.45, sensitivity at 0.77 and accuracy at 0.75. E_2 at the day of trigger during LuPOR presented with a threshold of 174.38 pg/ml, presented with an AUC at 0.62 with specificity at 0.46, sensitivity at 0.93 and accuracy at 0.89. The number of small follicles, with a threshold value of 1.93, presented with an AUC at 0.62 with specificity at 0.28, sensitivity at 0.91 and accuracy at 0.86. When combining the above characteristics into a single predictive model the AUC was 0.64, specificity 0.56, sensitivity 0.65 and accuracy was 0.65. The positive predictive value was 94.61%, whereas the negative predictive value was 10.46%.

CONCLUSION

Concurring on the validity of LuPOR practice as an IVF add-on has served as the main driver to conduct this study. Initial employment of LuPOR pertained to emergency fertility preservation (11). Nonetheless, its application appears to address patients with diminished ovarian reserve and POR. A recent meta-analysis in LuPOR, based on cohort studies, reported a significantly high heterogeneity in the results, despite the authors' attempt to perform a subgroup analysis, thus homogenizing the population (9). This level of heterogeneity may be attributed to the fact that the POR population is highly heterogenous and possibly DuoStim and LuPOR may not be the optimal strategy nor benefit all POR patients catholically. According to the results of our study, AFC, estradiol levels on both trigger days as well as the number of small follicles observed may be predictive of a successful LuPOR. When combining the above-mentioned characteristics associated with LuPOR success in a single model, the resulting model appears to be accurate. The high positive predictive value of this model may assist clinicians in identifying poor responders who will benefit from double oocyte retrieval in the same cycle.

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