DOES EARLY VERSUS DELAYED LETROZOLE START DURING CONTROLLED OVARIAN STIMULATION (COS) AFFECT OOCYTE MATURATION RATE?

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Background:
Oocyte and embryo cryopreservation are often utilized for oncology and BRCA patients who desire fertility preservation. COS often requires high doses of gonadotropins to stimulate the ovaries and maximize the number of oocytes retrieved. The resultant supraphysiologic levels of estrogen raises concern in some cancer patients with hormone sensitive cancer [1]. Letrozole, an aromatase inhibitor, has been used as an effective modality for lowering estrogen levels in cycles where supraphysiologic levels of estrogen are of concern [1]. Most studies have shown minimal effect on the oocyte maturation rate with letrozole use during COS, however the impact of varying letrozole start times during COS has not yet been studied [2].

Objective:
To determine whether there is a difference in the oocyte maturation rate from COS cycles that utilize early versus delayed letrozole starts.

Methods and Materials:
This was a retrospective cohort study of all oocyte and embryo cryopreservation cycles that utilized letrozole at a single academic fertility center from October 2019 to October 2023. Early letrozole start (ES) was defined as letrozole start on day 1 or 2 of COS and delayed start (DS) was defined as letrozole start on day 3-6 of COS. Letrozole 5mg was administered daily until day of trigger. Primary outcome was the % oocyte maturation which was defined as the number of metaphase II oocytes (MII)/ oocytes retrieved. Statistical significance of our primary outcome was assessed in IBM SPSS Statistics (version 29.0.1.0). T-tests were used to compare patient-specific variables between ES and DS cycles.

Results:
Of the 67 patients included in the study, 43 (64%) used ES and 24 (36%) used DS. There was no significant difference in average age (p=0.57), AMH (p=0.08) or total FSH dosage (p=0.67) between ES and DS groups (Table 2). There was no significant difference in oocyte maturation rates between ES (M=72%, SD=33%) and DS (M=67%, SD=29%, p=0.32) When stratified by age, there was no difference in oocyte maturation rate for ES and DS cycles for patients <35 (p=0.12) and >35 (p=0.29) (Table 1).

Table 1: Maturation Rate Stratified by Age

	ES (n=43)	DS (n=24)
Age < 35 (n=41)	73% (+/- 35%)	63% (+/- 31%)
Age > 35 (n=26)	70% (+/- 32%)	77% (+/- 25%)

Table 2: Descriptive Statistics by Group

	ES (n=43)	DS (n=24)	P-Value
Mean Age at Retrieval	33.3 (+/- 4.7)	32.5 (+/- 7.1)	0.57
Mean AMH Level	2.5 (+/- 2.0)	4.5 (+/- 6.4)	0.08
Mean Total FSH Dosage	4453.5 (+/- 1714.9)	4253.6 (+/- 1982.6)	0.67

Conclusions:
The timing of letrozole start during controlled ovarian stimulation does not affect oocyte maturation rate. A larger, prospective analysis is needed to confirm our findings.

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