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Evaluating the role of endometrial thickness on hCG injection day: a predictive marker for reproductive success in clomiphene-IUI cycles

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ABSTRACT

Objective. Endometrial thickness (EMT) on the day of hCG administration is critical for predicting reproductive success in intrauterine insemination (IUI) cycles with clomiphene citrate (CC). However, the optimal EMT for clinical pregnancy and live birth outcomes remains unclear. In this study, the influence of EMT on reproductive outcomes in CC+IUI cycles is investigated.

Materials and Methods. This retrospective analysis included 640 IUI cycles performed at a tertiary reproductive endocrinology centre between February 2019 and February 2020. Participants were couples with unexplained infertility or WHO category 2 anovulation. All underwent ovulation induction with CC, and EMT was measured via transvaginal ultrasound on the day of the hCG trigger. Outcomes included clinical pregnancy and live birth rate.

Results. Of 640 cycles, 80 (12.5%) achieved clinical pregnancy, with 52 (8.1%) resulting in live births. Spontaneous abortion occurred in 23 cases (3.6%). Age, duration of infertility and CC dose had a significant impact on clinical pregnancy and live birth rates. The optimal EMT threshold for predicting clinical pregnancy was 8.45 mm (sensitivity 49.4%, specificity 55.3%). An EMT between 8-9 mm was associated with higher clinical pregnancy ($p = 0.010$) and live birth rates ($p = 0.002$).

Conclusions. EMT has a significant impact on pregnancy outcome in CC+IUI cycles, with 8-9 mm being the optimal range for better outcomes. However, EMT alone shows moderate predictive accuracy and should be combined with other clinical factors in decision making. Further research is needed to refine prediction models that integrate EMT, patient age and duration of infertility to improve outcomes.

INTRODUCTION

Infertility affects an estimated 8-12% of couples of reproductive age and has an increasing trend. It is estimated that 1 in 7 couples in Western countries is affected by infertility, compared to 1 in 4 couples in developing countries [1-4]. Unexplained infertility (UI) occurs in 15% of all cases of infertility. In

women, UI is associated with older age, lower BMI, lower endometrial thickness, and poorer ovarian reservation testing [1-4]. The World Health Organization (WHO) task force on Diagnosis and Treatment of Infertility performed a study on 8,500 infertile couples utilizing standard diagnostic criteria and reported female factor infertility in 37%, male factor infertility in 8% of the couples while both male and female factor infertility was present in 35% of the couples in developed countries. Meanwhile, 5% of the couples had unexplained infertility and 15% became pregnant during the study [5].

Clomiphene citrate (CC), a selective estrogen receptor modulator (SERM), has been widely used for 40 years as it is the first agent used for ovulation induction. CC is used for ovulation induction in combination with intrauterine insemination (IUI) in normogonadotropic anovulatory women and women with unexplained infertility. When endogenous estrogen levels are sufficient, CC acts as a competitive estrogen antagonist, whereas at low endogenous estrogen levels it exhibits estrogenic properties. CC binds to the nuclear estrogen receptors (ER) in the subthalamic area and thus depletes hypothalamic ERs by blocking the negative feedback effect of circulating endogenous estradiol (E2) [6]. This leads to stimulation of the pulse rate of hypothalamic gonadotropin-releasing hormone (GnRH), resulting in increased serum concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [7]. The elevated FSH and LH concentrations stimulate follicular development in the ovaries. CC acts primarily as an anti-estrogen on the uterus, cervix and vagina, so the expected normal increase in uterine volume and endometrial thickness (EMT) that occurs in spontaneous menstrual cycles is largely absent during clomiphene-induced cycles, although E2 levels are high [8]. The use of clomiphene citrate (CC) is associated with the development of a thinner endometrium in 15% to 50% of patients [9]. The thinner endometrium is one of the factors blamed for the discrepancy between the ovulation rate and the pregnancy rate in CC-induced cycles [10].

The role of the EMT and normal trilaminar appearance evaluated during ultrasonographic examination have been extensively studied in *in vitro* fertilization-embryo transfer (IVF-ET) cycles as these parameters have been proposed to be predictors of endometrial receptivity and thus reproductive outcome [11].

In the presented study we aimed to evaluate the effect of EMT on the day of Human Chorionic Gonadotropin (hCG) administration on the reproductive outcomes and determine the threshold value for EMT for achieving clinical pregnancy in CC + IUI cycles.

MATERIALS AND METHODS

Study design

The results of the 640 cycles in couples who received CC+IUI treatment at Reproductive Endocrinology Department of Health Sciences University Etlik Zübeyde Hanım Women's Training and Research Hospital between February 2019 and February 2020 for unexplained infertility or WHO Category 2 anovulation (normogonadotropic anovulatory women) and met the inclusion criteria were analysed retrospectively. Our study was approved by the Ministry of Health, Health Sciences University Etlik Zübeyde Hanım Women's Institutional Board (30/12/2020-90057706-799).

Day-3 FSH (Elecsys FSH, Roche), LH (Elecsys LH, Roche), Prolactin (Elecsys Prolactin II, Roche), thyroid-stimulating hormone (TSH) (Elecsys TSH, Roche) levels and Day-21 progesterone (Elecsys Progesterone, Roche) levels are analysed. Basal transvaginal ultrasonography (TVUSG), basal antral follicle count (AFC), and hysterosalpingography (HSG) were performed as a part of the routine infertility workup. Two sperm samples of the partners were examined after urological examination, and the presence of male factor was evaluated according to the WHO criteria [12].

Inclusion-Exclusion criteria

During the assessment phase, the causes of infertility were carefully evaluated for each patient. This evaluation included a thorough review of medical histories, physical examinations, and diagnostic tests to identify any underlying factors contributing to infertility. Based on these findings, any necessary adjustments were made to the treatment protocol, including modifications to the doses of medications used or alterations in the duration of follicular growth stimulation. These adjustments were personalized to optimize the chances of a successful outcome. Women with under 40 age, ovulatory dysfunction (WHO Category 2) or unexplained infertility (ovulatory women with at least one patent tube on HSG and follicular growth on the

side of the patent tube and absence of male infertility) were included in the study. Women with the duration of infertility less than a year, bilateral tubal occlusion, a basal FSH ≥ 15 mIU/ml, basal estradiol ≥ 80 pg/ml or ≤ 20 pg/ml, additional endocrine disease (such as Cushing, diabetes, thyroid dysfunction, hyperprolactinemia, androgen-synthesizing tumour, 21-hydroxylase enzyme defect) and who failed to demonstrate follicular growth during the CC treatment cycle or did not receive intrauterine insemination were excluded from the study.

Treatment protocol

CC (Klomen®; Kocak Farma / Turkey, Serophene®; Merck Serono / Italy) was commenced on Day-3 and was continued for five days after the onset of spontaneous menses after a TVUSG evaluation. A standard dose of 50 mg/day was used for the first treatment cycle, but the treatment doses were increased by 50 mg increments if the patients failed to achieve follicular growth with the given dose during the previous treatment cycle. The maximum CC dose was 150 mg/day according to our protocol. The women were scheduled for IUI 36 hours after subcutaneous hCG injection (250 μg recombinant hCG Ovitrelle®; Merck-Serono / Italy) when a follicle reached to a diameter > 17mm. hCG was used to trigger ovulation because it allows for the optimization of timing in terms of follicle development and endometrial preparation. The main reason for using hCG instead of monitoring natural ovulation is that the timing of the LH surge and natural ovulation is unpredictable, which can make IUI timing difficult. Triggering with hCG allows for the best timing of sperm to egg, allowing for controlled ovulation. Additionally, the use of hCG is more consistent compared to the LH surge observed in natural cycles, which can improve pregnancy rates. The patients who had more than 2 follicles with a diameter >17 mm were not scheduled for intrauterine insemination in order to avoid multiple pregnancies. Estradiol levels were measured in all participants before hCG injection. The mean estradiol level was determined as 362 pg/ml. The estradiol threshold determined for hCG triggering was accepted as 1,500 pg/ml; hCG was not administered to induce ovulation in patients below this threshold. This threshold value, together with endometrial thickness and follicle development, was used to determine the optimal timing. EMT was measured on the day of hCG injection in the midsagittal plane of the uterus as the maximum distance between the two inner faces of the endometrial myometrial junction and recorded.

Semen samples were collected by masturbation following 3-5 days of sexual abstinence. The seminal parameters were analysed by a single observer and categorized according to the 2021 WHO criteria [12]: complete liquefaction within 60 minutes; sperm concentration ≥ 15 million per ml; progressive motility (PR) ≥ 32%; total motility (progressive + non-progressive, PR + NP) ≥ 40%; and normal morphology ≥ 4%. The ejaculate was prepared using a swim-up technique. IUI was performed by injecting the prepared semen into the intrauterine cavity using a soft insemination catheter (AINSEBLUE-R RI. MOS. ITALY). For luteal phase support, a standardized protocol was employed, which involved the administration of vaginal 200 mg progesterone twice a day. This was initiated following the insemination procedure and continued throughout the luteal phase to support the endometrium and enhance the likelihood of implantation. Success criteria after IUI were taken as clinical pregnancy (CP) and live birth (LB). CP was diagnosed with a positive β-hCG (> 10 mIU/ml) on the 14th day after IUI followed by observing an intrauterine gestational sac during TVUSG in the 5th week as described by Zhang *et al*. [13]. LB was defined as the delivery of a viable infant at 24 weeks gestation or later. The absence of a gestational sac on TVUSG despite an elevated β-hCG was defined as biochemical pregnancy [14]. The findings were compared by comparing the variables of the group with CP with the ones without CP.

Statistical analysis

SPSS 21.0 package program was used to analyse the data. Numerical data are mean ± standard deviation, data on categorical variables number (percentage). The compliance of numerical variables to normal distribution was checked by the Shapiro Wilk test. The numerical data conforming to the normal distribution assumption were compared with the independent sample t-test, the numerical data not compatible with the normal distribution assumption with the Mann-Whitney U test, and the categorical variables with the Pearson's Chi-square test. Statistical significance was accepted as $p < 0.05$. The sample size was determined based on the statistical power analysis of previous similar study [15]. The minimum sample size required to detect a significant difference with 90% power and 5% margin of error was calculated as 600. However,

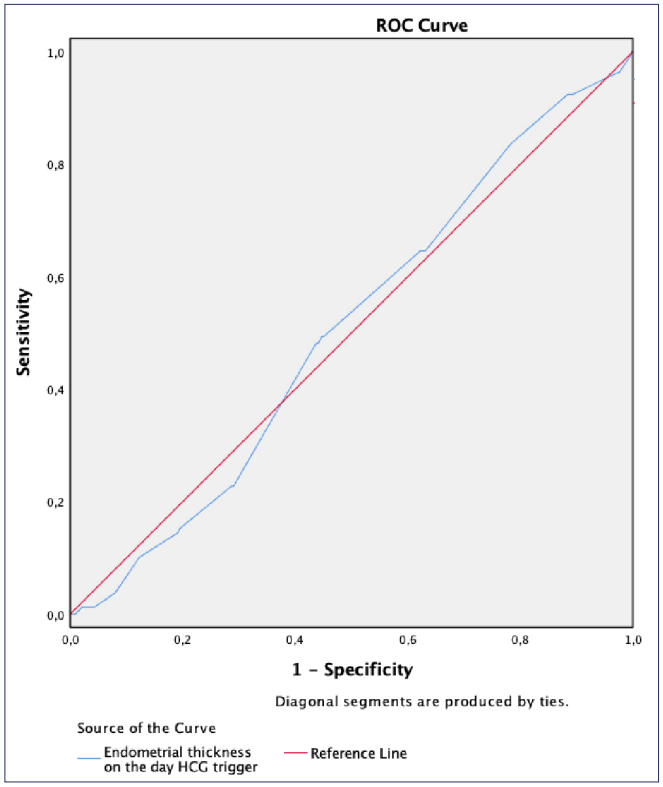

Figure 1. *Receiver operator characteristic (ROC) curve of endometrial thickness on the day of hCG trigger.*

The ROC curve illustrates the diagnostic ability of endometrial thickness (EMT) on the day of hCG trigger for predicting clinical pregnancy in CC+IUI cycles. The optimal cut-off value for EMT was determined to be 8.45 mm, with a sensitivity of 49.4% and specificity of 55.3%. Despite its moderate predictive accuracy, the results suggest that EMT can serve as a useful biomarker for assessing uterine receptivity, although it should not be used as a sole criterion for cycle continuation or cancellation. The analysis emphasizes the importance of considering other factors, such as female age and duration of infertility, in conjunction with EMT for clinical decision-making.

Table 1. *The demographic characteristics and clinical features of the patient group compared according to the presence of live birth.*

	Live Birth		P-value
	None (n = 588)	Yes (n = 52)	
Age	28.01 ± 4.95	26.31 ± 5.02	0.018*
Infertility type			
Primary	407 (69.22%)	35 (67.31%)	0.775
Secondary	181 (30.78%)	17 (32.69%)	
Duration of marriage	4.37 ± 3.28	4.17 ± 3.82	0.682
Duration of infertility	3 ± 1.94	2.52 ± 2.06	0.086
AMH (ng/ml)	4.45 ± 3.09	4.83 ± 3.39	0.436
FSH (mIU/ml)†	7.04 ± 2.06	6.94 ± 1.71	0.740
LH (mIU/ml)†	5.8 ± 4.46	5.49 ± 3.04	0.628
E2 (pg/ml)†	48.7 ± 20.13	46.1 ± 14.03	0.125
PRL (mg/dl)†	14.19 ± 7.96	13.08 ± 7.32	0.348
TSH (µg/dl)†	1.99 ± 1.22	2.14 ± 1.16	0.375
Body mass index (kg/m^2)	24.8 ± 4.33	25.02 ± 5.32	0.734
Basal USG EMT (mm)	4.61 ± 1.79	4.3 ± 1.68	0.236
Daily CC dose (mg)	57.48 ± 20.31	62.5 ± 25.96	0.180
Ovarian Response			
Duration of follicular growth (day)	11.11 ± 2.81	12.04 ± 2.92	0.024*
Number of Follicle	1.23 ± 0.52	1.1 ± 0.36	0.014 *
Diameter of the dominant follicle (mm)	19.34 ± 1.85	19 ± 1.36	0.203
EMT on the day HCG trigger (mm)	8.47 ± 2.55	8.38 ± 2.11	0.802

EMT: Endometrial Thickness; TSH: Thyroid-stimulating hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; E2: Estradiol; PRL: Prolactin; AMH: Anti-mullerian hormone; CC: Clomiphene citrate; USG: Ultrasonography; *P-value < 0.05 statistically significant; †Measurement on the day of the early follicular phase.

a total of 640 cycles were analysed throughout the study, which increases the statistical power of our study and reinforces the reliability of the findings.

RESULTS

Out of the 640 cycles evaluated, elevated β-hCG (> 10 mIU/ml) was observed in 92 (14.4%). Twelve (1.8%) of these cases were biochemical pregnancies as the β-hCG level declined and a gestational sac was not observed while 80 of the cases (12.5%) achieved clinical pregnancy. Ectopic pregnancy was not observed in the study group. While 23 (23/640, 3.6%) of the cases with CP had spontaneous abortion (SA), 52 (52/640, 8.1%) resulted in live birth (LB) (**Table 1**). 5 cases were not followed-up till the end of pregnancy. The patients with CP were significantly younger (p = 0.002), the duration of infertility was significantly shorter (p = 0.002), and the CC dosage was statistically significantly higher (p = 0.034) when compared to the group who failed to achieve a CP (**Table 2**). The age was statistically lower in patients who had an LB (p = 0.018).

We compared biochemical pregnancy, CP, SA, and LB. The incremental EMT measurement results were starting to ≤ 6 up to > 15 mm. The rate of clinical pregnancy (CPR), live birth (LBR), and spontaneous abortion (SAR) were evaluated in relation to the endometrial thickness (**Table 3**).

The mean EMT was found to be 8.38 mm in cases with a CP, and the cut-off point for EMT on the day hCG trigger was 8.45 (sensitivity of 49.4.% and specificity of 55.3%) for CP (**Figure 1**). When we compare the EMT the incidence of biochemical pregnancy was lower (p = 0.013), and CPR (p = 0.010) and LBR (p = 0.002) were higher in cases with an EMT was between 8 -9 mm on the day of β-hCG injection. There was no significant difference in the EMT in terms of the incidence of SA (p = 0.579) (**Table 3**). The distribution of statistically significant data was given in **Table 4**. A multivariate

Table 2. *The demographic characteristics and clinical features of the patient group compared according to the presence of clinical pregnancy.*

	Clinical Pregnancy		P-value
	None (n = 560)	Yes (n = 80)	
Age	28.1 ± 4.99	26.29 ± 4.62	0.002*
Infertility type			
Primary	387 (69.11%)	55 (68.75%)	0.948
Secondary	173 (30.89%)	25 (31.25%)	
Duration of marriage	4.41 ± 3.3	3.95 ± 3.49	0.245
Duration of infertility	3.04 ± 1.96	2.44 ± 1.81	0.011*
AMH (ng/ml)	4.44 ± 3.1	4.79 ± 3.16	0.368
FSH (mIU/ml)†	7.07 ± 2.06	6.77 ± 1.83	0.218
LH (mIU/ml)†	5.71 ± 3.8	6.25 ± 7.19	0.303
E2 (pg/ml)†	48.3 ± 20.19	46.6 ± 17.01	0.495
PRL (mg/dl)†	14.09 ± 7.9	14.15 ± 7.97	0.955
TSH (µg/dl)†	1.98 ± 1.2	2.15 ± 1.26	0.252
Body mass index (kg/m^2)	24.82 ± 4.33	24.77 ± 5.02	0.920
Basal USG EMT (mm)	4.61 ± 1.81	4.38 ± 1.61	0.283
Daily CC dose (mg)	57.23 ± 20.21	62.5 ± 24.52	0.034*
Ovarian Response			
Duration of follicular growth (day)	11.11 ± 2.82	11.75 ± 2.88	0.058
Number of Follicle	1.24 ± 0.53	1.11 ± 0.36	0.007*
Diameter of the dominant follicle (mm)	19.34 ± 1.84	19.1 ± 1.68	0.275
EMT on the day HCG trigger (mm)	8.47 ± 2.56	8.38 ± 2.16	0.766

EMT: Endometrial Thickness; TSH: Thyroid-stimulating hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; E2: Estradiol; PRL: Prolactin; AMH: Anti-mullerian hormone; CC: Clomiphene citrate; USG: Ultrasonography. *P-value < 0.05 statistically significant; †Measurement on the day of the early follicular phase.

logistic regression analysis was performed to evaluate the independent effects of various variables on live birth rates. The results showed that age was a statistically significant predictor (OR 0.91, 95%CI 0.86-0.98, p = 0.019), with increasing age negatively affecting the likelihood of live birth. However, endometrial thickness (EMT) did not demonstrate independent predictive significance for live birth outcomes (OR 0.99, 95%CI 0.88-1.11, p = 0.86). Similarly, the duration of follicular growth and the number of dominant follicles were not significant predictors of live birth rates in this model (**Table 5**).

Our results demonstrate that an optimal EMT of 8-9 mm is associated with significantly higher clinical pregnancy and live birth rates, suggesting that EMT could be a useful biomarker for assessing uterine receptivity in CC+IUI cycles, despite its moderate predictive accuracy (sensitivity of 49.4% and specificity of 55.3%) (**Figure 1**).

DISCUSSION

This study aimed to evaluate the relationship between endometrial thickness (EMT) on the day of hCG injection and reproductive outcomes in patients undergoing ovulation induction with clomiphene citrate (CC) combined with intrauterine insemination (IUI). Our findings indicate that an

Table 3. *Endometrial Thickness (EMT) on the day of hCG administration.*

EMT (mm)	Number of patients (n = 640)	Biochemical Pregnancy (n = 12)	Clinical Pregnancy (n = 80)	Spontaneous Abortion (n = 23)	Live Birth (n = 52)
≤6	135	3 (2.22%)	13 (9.63%)	4 (2.96%)	8 (5.93%)
>6 - ≤7	100	4 (4%)	15 (15%)	5 (5%)	9 (9%)
>7 - ≤8	113	1 (0.88%)	12 (10.62%)	5 (4.42%)	7 (6.19%)
>8 - ≤9	111	0 (0%)	22 (19.82%)	3 (2.7%)	17 (15.32%)
>9 - ≤10	60	2 (3.33%)	6 (10%)	2 (3.33%)	4 (6.67%)
>10 - ≤11	44	0 (0%)	4 (9.09%)	1 (2.27%)	3 (6.82%)
>11 - ≤12	2	1 (3.45%)	5 (17.24%)	2 (6.9%)	3 (10.34%)
>12 - ≤13	23	0 (0%)	2 (8.7%)	1 (4.35%)	0 (0%)
>13 - ≤14	12	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>14 - ≤15	8	0 (0%)	1 (12.5%)	0 (0%)	1 (12.5%)
>15	5	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Distribution of results by endometrial thickness (> 8 & 9) on the day of HCG					
8 - 9 mm	111	0 (0%)	22 (19.82%)	3 (2.7%)	17 (15.32%)
<8 - >9 mm	539	12 (2.27%	58 (10.96%)	20 (3.78%)	35 (6.62%)
p	N/A	0.013*	0.010*	0.579	0.002*

EMT: Endometrial Thickness; HCG: Human Chorionic Gonadotropin. Data are shown as numbers (percentages). *Statistically significant; P-value < 0.05 statistically significant.

Table 4. *Distribution of statistically significant data.*

	Age	Duration of infertility	Daily clomiphene citrate dose (mg)	Number of Follicle	Duration of Follicular growth
Clinical Pregnancy (+) (n = 80)	26.29	2.44	62.5	1.11	11.75
Clinical pregnancy (-) (n = 560)	28.1	3.04	57.23	1.24	11.11
P-value	**0.02***	**0.011***	**0.034***	**0.007***	**0.058**
Live Birth (+) (n = 52)	26.31	2.52	62.5	1.1	12.04
Live Birth (-) (n = 588)	28.01	3	57.48	1.23	11.11
P-value	**0.018***	**0.086**	**0.180**	**0.014***	**0.024***
Spontaneous abortion (+) (n = 23)	26.57	2.39	65.22	1.09	10.96
Spontaneous abortion (-) (n = 57)	26.31	2.52	62.50	1.10	12.04
P-value	**0.704**	**0.631**	**0.001***	**0.903**	**0.138**

*Statistically significant; P-value < 0.05 statistically significant.

Table 5. *Variables associated with live birth analysed by multivariate logistic regression.*

		Standardized Coefficients		
Variable	**Beta**	**Standardized Error**	**Odds ratio (CI)**	**P-value**
Age	-0.95	0.002	0.91 (0.86-0.98)	0.019*
Duration of Follicular Growth	0.74	0.007	0.51 (0.22-1.17)	0.72
Number of Dominant Follicile	-0.53	0.021	0.93 (0.81-1.07)	0.186
Endometrial Thickness	-0.01	0.59	0.99 (0.88-1.11)	0.86

OR: Odds ratio; CI: Confidence interval; P-value < 0.05 statistically significant; *statistically significant.

EMT of 8-9 mm is associated with significantly higher clinical pregnancy and live birth rates, suggesting that EMT could serve as a useful biomarker for uterine receptivity in CC+IUI cycles, albeit with moderate predictive accuracy.

Several studies have explored the predictive value of EMT in assisted reproductive techniques. Our results align with previous research indicating that certain EMT thresholds, particularly between 8 and 9 mm, are associated with higher pregnancy success rates [16, 17]. This threshold is consistent with the findings of Huniadi *et al*. [18], who also reported that EMT, along with other factors such as the duration of infertility and patient age, significantly predicts the success of IUI procedures. They emphasized that integrating these factors into a prognostic model could enhance patient counselling and improve treatment outcomes [18].

Our findings also reveal that EMT alone may not be sufficient to predict IUI outcomes reliably, as its sensitivity and specificity were moderate. This is consistent with studies by. Masrour *et al*. and Kolibianakis *et al*, which found no significant difference in EMT between women who achieved pregnancy and those who did not [15,19]. These results suggest that while EMT is a useful indicator, it should be evaluated alongside other factors such as age, hormonal levels, and ovarian response to provide a more comprehensive prediction model [20].

Additionally, the multivariate analysis revealed that age was the only variable significantly associated with live birth rates, with a negative impact observed as age increased. This finding aligns with previous studies that highlight the detrimental effects of advanced maternal age on reproductive outcomes due to factors such as reduced oocyte quality and increased aneuploidy rates [21, 22]. Contrary to expectations, EMT did not independently predict live birth in our model. This may reflect the moderate predictive accuracy of EMT observed in univariate analyses, emphasizing its limited standalone utility. Furthermore, neither the duration of follicular growth nor the number of dominant follicles showed significant associations with live birth outcomes, suggesting that these factors may play a secondary role compared to age [23, 24]. Besides, our study highlighted that shorter infertility duration was associated with higher clinical pregnancy rates, which aligns with other studies reporting similar findings [25, 26]. However, there is no consensus on the ideal duration of infertility for achieving favourable outcomes during treatment cycles.

In conclusion, while EMT remains a valuable biomarker for assessing uterine receptivity in CC+IUI cycles, it should not be the sole criterion for clinical decisions. The moderate predictive accuracy of EMT underscores its limitations as a standalone biomarker. While our findings suggest that an EMT of 8-9 mm improves reproductive outcomes, its clinical utility must be contextualized within a broader framework of patient-specific factors. These findings highlight the need for multifactorial prediction models to improve decision-making in clinical practice. A multifactorial approach that includes patient age, infertility duration, ovarian response, and specific infertility conditions should be adopted to enhance the predictive accuracy of IUI outcomes and optimize treatment strategies. Future research should focus on developing and validating comprehensive predictive models that incorporate these variables to better guide clinical practice.

Strengths and limitations

To the best of our knowledges, this study is one of the largest retrospective study which is searching only CC-IUI from the assisted reproductive technique. In addition, one of the strongest aspects of this study is that it is one of the few studies that tried to find a threshold value for EMT on the day of the hCG trigger in infertile couples who underwent CC-IUI, and also gave concretely viable pregnancy and spontaneous abortion rates according to the threshold value. Inclusion of only those with unexplained infertility and WHO category 2 normogonodotropic anovulatory patients in the study resulted in a more homogeneous patient group.

There are also many limitations. One of these limitations is the retrospective design. The retrospective nature of this study limits its ability to establish causality. Biases in data collection, including incomplete medical records and variability in ultrasound measurements, may have influenced the findings. Furthermore, the homogeneity of the study population, while providing consistency, limits the generalizability of the results to more diverse populations. Apart from this, although this study has a sufficient sample size to give an EMT threshold value, the low sensitivity and specificity of the threshold value obtained indicate that prospective studies with larger sample sizes are needed to give a threshold value with higher sensitivity and specificity. In addition, ultrasound measurements are inherently subjective even though the technique is standardized across the reproductive endocrinology clinics as mentioned in the method section. Among the possible limitations of the present study, endometrial receptivity is not only influenced by EMT, but also by factors such as endometrial pattern and vascularity, which were not evaluated in this study. The absence of these parameters is a limitation, as their inclusion would allow a more comprehensive assessment of uterine receptivity. Another limitation of this study was that endometrial thickness was not measured in 2-3 day cycles. Perhaps midcycle endometrial thickness is related to early follicular phase thickness.

Given these discrepancies, further prospective, large-scale studies are necessary to validate the role of EMT as a reliable predictor of reproductive outcomes in IUI cycles. Such research should aim to control for the various confounding factors that may influence EMT, including patient demographics, treatment protocols, and ultrasound measurement techniques. Moreover, exploring the interaction between EMT and other factors, such as ovarian response and hormonal profiles, could help develop a more comprehensive predictive model for IUI success.

CONCLUSIONS

In conclusion, our study found that an endometrial thickness (EMT) of 8-9 mm on the day of hCG trigger is associated with higher clinical pregnancy and live birth rates in CC+IUI cycles. However, due to the low sensitivity and specificity, and successful pregnancies occurring outside this range, setting a strict EMT threshold for cycle decisions is not advisable. Other factors such as female age and duration of infertility should also be considered. These findings can help optimize patient selection and treatment regimens, reducing unnecessary interventions and costs.

COMPLIANCE WITH ETHICAL STANDARDS

Authors' contribution

A.A.: Conceptualization. A.A., G.A.E., D.S.: Data curation, formal analysis. A.A., B.D., A.G.E., S.D..: Investigation, project administration, visualization. A.A., B.D.: Methodology. B.D, S.D.: Supervision, validation. A.A.: Writing – original draft. A.A., B.D., S.D.: Writing – review & editing.

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Study registration
N/A.

Disclosure of interests
The authors declare that they have no conflict of interests.

Ethical approval
This study was approved by Ministry of Health, Health Sciences University Etlik Zübeyde Hanım Women's Institutional Board (30/12/2020-90057706-799) and all the patients consented to the use of their clinical data anonymously for scientific studies prior to the treatment cycles.

Informed consent
As this study was retrospective and all data were anonymized prior to analysis, the Institutional Review Board waived the requirement for informed consent.

Data sharing
Data are available under reasonable request to the corresponding author.

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