Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2023;12(4):1306-9

Evaluation of the IVF success in frozen-thaw in vitro fertilization cycles in terms of endometrial thickness

Mustafa Bertan Demir[1], Davut Guven[2], Ilhami Ersoy[2]

[1]Health Sciences University, Kayseri City Health Application and Research Center, Department of Obstetrics and Gynecology, Kayseri, Türkiye
[2]19 Mayıs University, Medical Faculty Training and Research Hospital, Department of Obstetrics and Gynecology, Samsun, Türkiye

Received 27 August 2023; Accepted 20 October 2023
Available online 22.10.2023 with doi: 10.5455/medscience.2023.08.153

Abstract

The aim of this research was to analyze the link between endometrial thickness (EMT), as measured during progesterone administration, and the results observed in individuals who underwent frozenthawed embryo transfer. A retrospective analysis was performed on 233 hormone replacement therapy (HRT) methods of endometrial preparation in frozen-thawed embryo transfer (FET) cycles (HRT-FET). HRT-FET cycles that were conducted between January 2021 and December 2022 at the In vitro fertilization (IVF) Clinic of 19 May University Medical Faculty Training and Research Hospital. The patients' age, infertility duration, basal follicle-stimulating hormone (FSH) level, body mass index (BMI), number and day of embryos transferred, and pregnancy rates were evaluated. Endometrial thickness was measured using transvaginal ultrasound (TV USG) on the day of progesterone administration. The endometrial thickness of patients who achieved clinical pregnancy and those who did not were analyzed. No significant differences in demographic factors were found between the groups in terms of age, infertility duration, basal FSH level, and BMI (p=0.209, p=0.959, p=0.866 and p=0.685, respectively) . The success rates of clinical pregnancy did not strongly correlate with endometrial thickness. The study found that EMT is not a valid indicator for clinical pregnancy in frozen-thawed embryo transfer cycles.

Keywords: Endometrial thickness, in vitro fertilization, frozen embryo transfer, clinical pregnancy

Introduction

FET and "freeze-all" cycles have markedly increased globally over the past ten years due to effective and secure vitrification techniques [1]. Successful embryo implantation and pregnancy require communication between the endometrium and the embryo. In assisted reproductive technology (ART), coordination between endometrial and embryo development is necessary for success [2]. Normal endometrial receptivity is crucial for embryo attachment, implantation, placental invasion, and development [3]. In FET cycles, endometrial receptivity is thought to be more critical than embryo quality for successful ART outcomes. HRT commonly uses progesterone and exogenous estrogen to condition the endometrial lining for successful embryo implantation in FET cycles. In HRT-FET cycles, the start of progesterone administration is the key factor in preparing the endometrium for the implantation window. Endometrial thickness is one of the superior markers that indicate the readiness of the endometrium for embryo implantation. However, the effect of endometrial thickness on IVF success is controversial and unclear despite many studies [4]. Nevertheless, most studies have found a pronounced correlation between endometrial thickness and the achievement of clinical pregnancy in HRT-FET cycles [5].

Clinicians generally agree that inadequate endometrial thickness adversely affects the rate of successful pregnancies. However, experts suggest that the most suitable values for endometrial thickness for pregnancy are between 9-10 mm [6].

The current study aims to evaluate the significance of endometrial thickness on reproductive results in women undergoing HRT-FET cycles with frozen-thawed embryo transfer.

Material and Methods

A retrospective comparative study was conducted at the 19 May University Medical Faculty Training and Research Hospital IVF Clinic archive. The study involved scanning the file information of HRT- FET cycles between 2021-2022 and retrospectively

CITATION
Demir MB, Guven D. Ersoy I. Evaluation of the IVF success in frozen-thaw in vitro fertilization cycles in terms of endometrial thickness. Med Science. 2023;12(4):1306-9.

Corresponding Author: Mustafa Bertan Demir, Health Sciences University, Kayseri City Health Application and Research Center, Department of Obstetrics and Gynecology, Kayseri, Türkiye
Email: bertandemir@hotmail.com

DOI: 10.5455/medscience.2023.08.153

recording the progesterone administration day, endometrial thickness, and transfer successes as clinical pregnancy. The protocol used to prepare the endometrium was also evaluated, along with age, duration of infertility, FSH level, BMI, and pregnancy rates.

Patients were started on oral estradiol using the Novo Nordisk product Estrofem® at a daily dose ranging from 4 to 8 mg. This regimen began on days 2-3 of the menstrual cycle and was modified based on the endometrial lining thickness. Supplementation with progesterone began upon reaching an endometrial thickness of approximately 8 mm, typically between days 12 and 20 of the cycle. The dosage and length of estrogen therapy were increased for individuals with a thinner endometrial lining. Progesterone was administered once the endometrium measured 7 mm or higher in thickness. Endometrial thickness was documented via transvaginal ultrasound examination on the day of progesterone administration. Embryos in cleavage stage 3 or 5 were transferred on the same day, and the transfer of embryos, guided by transabdominal ultrasound, was restricted to a maximum of two.

Statistical analysis

Data analysis was performed using SPSS version 27.0. Descriptive statistics were represented using mean, standard deviation, number (n), and percentage (%). The Kolmogorov-Smirnov test and Q-Q Plots analysis were used to determine whether numerical data were in accordance with the normal distribution. The Student's t-test was used to compare numerical data between groups, while categorical variable comparisons were made using the chi-square test. The accepted significance level was 0.05.

Results

The clinical pregnancy rate in this report is 31.33%, based on the analysis of 233 HRT-FET cycles. All patients were grouped according to their clinical pregnancy outcomes. A total of 73 patients were observed to have clinical pregnancy as a result of transfer within the specified group. The mean age for this group was 31.6±4.7 years, and 32.4±5.2 years for the non-pregnant group. Pregnancy occurred in 25.3% of the 87 patients with 2 embryos transferred. The quantity of transferred embryos showed no discernible variance . Table 1 displays the demographics and traits of patients. Age, length of infertility, basal FSH levels, and BMI values did not significantly differ between the groups ($p=0.209$, $p=0.959$, $p=0.866$, $p=0.685$ respectively and $p<0.05$). Count and characteristics of transferred embryos did not significantly differ between the groups.

The factors contributing to infertility were similar in both groups, and unexplained infertility was found to be the most common etiology (Table 1). The quantity of embryos transferred on day 3 and day 5 was comparable in both groups (Table 2). The endometrial thickness in patients who achieved pregnancy was 9.01±1.29, while the endometrial thickness in the non-pregnant group was 8.98±1.30. A statistically significant difference was not found in endometrial thickness in both groups ($p=0.891$and $p<0.05$) (Table 2).

Table 1. Comparison of demographic and causes of infertility characteristics between groups. (Group 1: Pregnant patients; Group 2: Non pregnant patients)

	Group 1 (n: 73)	Group 2 (n: 160)	p value
Maternal age	31.6±4.7	32.4±5.2	0.209
Duration of infertility	4.72±2.32	4.74±2.58	0.959
BMI	26.1±5.4	25.5±6.2	0.685
FSH	6.337±7.341	32.4±5.2	0.866
Unexplained (%)	52.2 (38/73)	50.7 (81/160)	0.998
Diminished ovarian reserve (DOR) (%)	8.2 (6/73)	8.7% (14/160)	0.852
Male Factor (%)	21.9 (16/73)	22.5 (36/160)	0.746
Polycystic Ovarian Syndrome (PCOS) (%)	8.2 (6/73)	9.4 (15/160)	0.857
Tubal Factor (%)	9.5 (7/73)	8.7 (14/160)	0.561

BMI: body mass index; FSH: Follicle-stimulating hormone. To test the normality assumption of the demograhic data Student's t-test was used. Values are expressed as mean±standard deviation, median (25th percentile—75 percentile). p<.05 probability value was considered as statistically significant. To test the normality assumption of the causes of infertility data Pearson Chi-Squared test was used. Values are expressed as mean±standard deviation, median (25th percentile—75 percentile) or n (%). p<.05 probability value was considered as statistically significant.

Table 2. Comparison of transferred embryo day, number of transferred embryo and endometrial thickness between groups. (Group 1: Pregnant patients; Group 2: Non pregnant patients)

	Group 1 (n: 73)	Group 2 (n: 160)	p value
Day 3 (%)	8.2 (6/73)	15 (24/160)	0.072
Day 4 (%)	6.9 (5/73)	9.4 (15/160)	0.128
Dayv5 (%)	84.9 (62/73)	75.6 (121/160)	0.221
1 embryo (%)	69 (51/73)	60 (95/160)	0.125
2 embryos (%)	31 (22/73)	40 (65/160)	0.247
Endometrial thickness	9.01±1.29	8.98±1.30	0.891

To test the normality assumption of the data Pearson Chi-Squared test was used. Values are expressed as mean±standard deviation, median (25th percentile—75 percentile) n (%). p<.05 probability value was considered as statistically significant. To test the normality assumption of the endometrial thickness data Student's t-test was used. Values are expressed as mean±standard deviation, median (25th percentile—75 perc entile). p<.05 probability value was considered as statistically significant.

DOI: 10.5455/medscience.2023.08.153

Discussion

Achieving successful pregnancy outcomes in embryo transfer cycles hinges on the readiness of the endometrium [7]. While endometrial thickness is often considered a reliable marker for endometrial receptivity, research attempting to establish a definitive correlation has produced conflicting findings [8,9]. Discrepancies in outcomes among published studies can be attributed to various factors, including variations in protocols for controlled ovarian stimulation, frozen embryo transfer procedures, and the number of embryos transferred [10]. Previous investigations have encompassed diverse prospective and retrospective studies, employing different criteria to define a thin endometrium. These studies have yielded inconclusive findings regarding the impact of endometrial thickness below 8 mm on outcomes related to ART [11,12]. Furthermore, most previous research has involved a limited sample size of individuals with less than 7 mm endometrial thickness [13].

In a retrospective assessment of FET cycles conducted by Tarek El-Toukhy et al. , individuals with endometrial thicknesses less than 7 mm, ranging from 7 to 8 mm, 9 to 14 mm, and greater than 14 mm, were compared. The research findings indicated that individuals with endometrial thickness between 9 and 14 mm during progesterone supplementation experienced increased rates of implantation and pregnancy. According to Gallos et al., EMT displays a robust connection with both pregnancy losses and births that were successful in the context of IVF [14]. Similarly, Ma et al.'s investigation revealed a direct relationship between increased endometrial thickness and higher rates of successful live births and clinical pregnancies [15]. Additionally, a comprehensive meta-analysis, comprising 9 prospective and 21 retrospective studies, demonstrated that lower endometrial thickness was associated with reduced pregnancy rates compared to cases with greater thickness [16]. However, conflicting interpretations still exist. Research conducted by Craciunas et al. and Huang J et al. [17,18] concluded that biomarkers such as endometrial thickness have limited predictive capability for clinical pregnancy. Deger U et al.'s investigation revealed, if the endometrial thickness is between 11-12 mm in both fresh and frozen-thawed embryo transfers clinical pregnancy and live birth rates are affected positively [19]. According to the results of Yaprak E et al.'s study, in FET cycles the rate of live birth was significantly higher in cycles with endometrial compaction (9.25 mm endometrial thickness at the end of oestrogen phase) [20]. Baris Ata et al. showed that the EMT was not predictive for live birth with total of 560 ET cycles in either fresh or frozen-thawed ET cycles like our findings [21]. Dain et al. analyzed 737 oocyte donation cycles and investigated whether recipient EMT <6 mm and >6 mm had similar live birth rates [22]. In another study, Women had similar mean EMTs, 9.0 vs. 8.8 mm, respectively to obtain pregnancy in a retrospective research from 463 modified natural cycle FET to investigate the predictive value of EMT to obtain pregnancy [23]. Although many studies have noted a decreasing pregnancy outcomes with decreasing EMT at the time of embryo transfers, live births with EMT of <4.9 mm have been reported [24]. Some authors claim that decreasing vascular endothelial growth factor in a thin endometrium causes poor vascularization of the endometrium and placentation defects [25].

Our research promotes that EMT is not predictive for live birth in FET cycles.

Conclusion

Consequently, the purpose of this study was to assist in predicting the endometrial thickness required for successful embryo transfer. In our study, endometrial thickness did not have a significant impact on the clinical fertility rates. Further research is needed to explore the relationship between the thickness of the endometrial lining.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The study protocol was approved by the 19 Mayıs University, Faculty of Medicine Ethics Committee (OMÜ-KAEK-266/2023-2023000266).

References

1. Kasius A, Smit JG, Torrance HL, et al. Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis. Hum Reprod Update. 2014;20:530-41.
2. Tabibzadeh S. Molecular control of the implantation window. Hum Reprod Update.1998;4:465-71.
3. Gursu T, Goksever Celik H, Eraslan A, et al. Impact of endometrial thickness change in response to progesterone on live birth rates embryo transfers with fresh oocyte donation cycles. J Obstet Gynaecol. 2022;42:3260-7.
4. Check JH, Dietterich C, Graziano V, et al. Effect of maximal endometrial thickness on outcome after frozen embryo transfer. Fertil Steril. 2004;81:1399-400.
5. Richter KS, Bugge KR, Bromer JG, Levy MJ. Relationship between endometrial thickness and embryo implantation, based on 1,294 cycles of in vitro fertilization with transfer of two blastocyst-stage embryos. Fertil Steril. 2007;87:53-9.
6. Wu Y, Gao X, Lu X, et al. Endometrial thickness affects the outcome of in vitro fertilization and embryo transfer in normal responders after GnRH antagonist administration. Reprod Biol Endocrinol. 2014;12:96.
7. Lamanna G, Scioscia M, Lorusso F, et al. Parabolic trend in endometrial thickness at embryo transfer in in vitro fertilization/intracytoplasmic sperm injection cases with clinical pregnancy evidence. Fertil Steril. 2008;90:1272-4.
8. De Geyter C, Schmitter M, De Geyter M, et al. Prospective evaluation of the ultrasound appearance of the endometrium in a cohort of 1186 infertile women. Fertil Steril. 2000;73:106-13.
9. Dietterich C, Check JH, Choe JK, et al. Increased endometrial thickness on the day of human chorionic gonadotropin injection does not adversely affect pregnancy or implantation rates following in vitro fertilization-embryo transfer. Fertil Steril. 2002;77:781-6.
10. Casper RF. It's Time to Pay Attention to the Endometrium. Fertil Steril. 2011;96:519-21.

DOI: 10.5455/medscience.2023.08.153

11. Vaegter KK, Lakic TG, Olovsson M, et al. Which factors are most predictive for live birth after in vitro fertilization and intracytoplasmic sperm injection (IVF/ICSI) treatments? Analysis of 100 prospectively recorded variables in 8,400 IVF/ICSI single-embryo transfers. Fertil Steril. 2017;107:641-8.e2.

12. Gingold JA, Lee JA, Rodriguez-Purata J, et al. Endometrial pattern, but not endometrial thickness, affects implantation rates in euploid embryo transfers. Fertil Steril 2015;104:620-8.e5.

13. Noyes N, Liu HC, Sultan K, et al. Endometrial thickness appears to be a significant factor in embryo implantation in in-vitro fertilization. Hum Reprod 1995;10:919–922.

14. Gallos ID, Khairy M, Chu J, et al. Optimal endometrial thickness to maximize live births and minimize pregnancy losses: analysis of 25,767 fresh embryo transfers. Reprod Biomed Online. 2018;37:542-8.

15. Ma NZ, Chen L, Dai W, et al. Influence of endometrial thickness on treatment outcomes following in vitro fertilization/intracytoplasmic sperm injection. Reprod Biol Endocrinol RB&E. 2017;15:5.

16. Gao G, Cui X, Li S, et al. Endometrial thickness and IVF cycle outcomes: a meta-analysis. Reprod Biomed Online. 2020;40:124-33.

17. Huang J, Lin J, Gao H, et al. Value of endometrial thickness change after human chorionic gonadotrophin administration in predicting pregnancy outcome following fresh transfer in vitro fertilization cycles. Arch Gynaecol Obstet. 2021;303:565-72.

18. Craciunas L, Gallos I, Chu J, et al. Conventional and modern markers of endometrial receptivity: a systematic review and meta-analysis. Hum Reprod Update. 2019;25:202-23.

19. Değer U, Kalı Z, Çağıran F. Endometrial thickness is a good predictor of clinical pregnancy and live birth rates in fresh and frozen-thawed embryo transfer cycles. Eur Rev Med Pharmacol Sci. 2023;27:6351-8.

20. Yaprak E, Şükür YE, Özmen B, et al. Endometrial compaction is associated with the increased live birth rate in artificial frozen-thawed embryo transfer cycles. Hum Fertil (Camb). 2021 Aug 18. doi: 10.1080/14647273.2021.1966703. [Epub ahead of print].

21. Shakerian B, Turkgeldi E, Yildiz S, et al. Endometrial thickness is not predictive for live birth after embryo transfer, even without a cutoff. Fertil Steril. 2021;116:130-7.

22. Dain L, Bider D, Levron J. Thin endometrium in donor oocyte recipients: enigma or obstacle for implantation? Fertil Steril. 2013;100:1289-95.

23. Groenewoud ER, Cohlen BJ, Al-Oraiby A, et al. Influence of endometrial thickness on pregnancy rates in modified natural cycle frozen-thawed embryo transfer. Acta Obstet Gynecol Scand. 2018;97:808–15.

24. Liu KE, Hartman M, Hartman A, et al. The impact of a thin endometrial lining on fresh and frozen–thaw IVF outcomes: an analysis of over 40000 embryo transfer. Hum Reprod. 2018;33:1883-8.

25. Miwa I, Tamura H, Takasaki A, et al. Pathophysiologic features of “thin” endometrium. Fertil Steril. 2009;91:998-1004.