IMPACT STATEMENT: Among patients undergoing infertility treatment with assisted reproduction, when provided the option for sex-selection or best quality transfer, more than half will transfer the best quality embryo and the rest will prefer sex selection with male embryos being slightly more preferred than female embryos.

SUPPORT: None

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DO IMPLANTATION AND LIVE BIRTH RATES WITH TRANSFER OF SINGLE EUPLOID BLASTOCYSTS CORRELATE TO THEIR MITOSCORE?

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OBJECTIVE: To examine data from single embryo transfer (SET) cycles with preimplantation genetic screening and Mitoscore assessment to better understand the value of Mitoscore in ranking euploid embryos for transfer.

MATERIALS AND METHODS: Patients undergoing in vitro fertilization (IVF) with preimplantation genetic testing (PGT) for aneuploidy had their zygotes culture in the Embryoscope time lapse incubator. Morphokinetic (MK) data on embryos development was collected. Blastocysts were biopsied and subsequently frozen, awaiting PGT testing. This study is a retrospective review of prospectively collected data of patients that continued on to a frozen embryo transfer cycle. The euploid embryo for transfer was selected strictly on basis of development , morphology and patient gender preference. For each transferred embryo, timing in hours post insemination for cleavage events, start of compaction (tSC), morula (tM), start of blastulation, blastocyst (tB), expanded blastocyst (tEB), and hatched blastocyst (tHB) were analyzed along with Mitoscore. Statistical analyses were performed using Chi square and Pearson correlation tests. A p-value of <0.05 was considered statistically significant.

RESULTS: A total of 49 vitrified–thawed blastocysts diagnosed as euploid were singly transferred. Mitoscore was significantly associated with kinetic parameters in developing embryos. A positive correlation was found between Mitoscores and t4 (0.33 [0.05, 0.56]; p=0.022), and the second synchronous division t4-t3 (0.51 [0.27, 0.69]; $p<0.001$). A positive correlation was also found for tSC (0.32 [0.04, 0.55]; p=0.024), tM (0.44 [0.18, 0.64]; p=0.001), tSB (0.40 [0.13, 0.61]; p=0.004), tB (0.42 [0.16, 0.63]; p=0.002), tEB (0.50 [0.24, 0.69]; $p<0.001$), and tHB (0.44 [0.10, 0.68]; p=0.012). Blastocysts sufficiently expanded to biopsy on day 5 had significantly lower Mitoscores than D6 biopsied blastocysts ($p<0.001$).

CONCLUSIONS: Mitoscore was clearly reflective of embryo growth kinetics and timing of blastulation. Mitoscores did not differ between pregnant and non-pregnant patients. Whereas a trend towards lower implantation was observed with higher Mitoscores, this did not reach significance.

IMPACT STATEMENT: More data is needed from different centers to determine the value of Mitoscore for ranking of euploid blastocyst for transfer.

Factor	SET Cycles	Mitoscore (Mean ± SD)	p-value
Day of Biopsy			
5	33	23.0 ± 5.7	***<0.001***
6	16	30.8 ± 5.3	
Implantation (sac)			
Yes	31	25.0 ± 6.9	NS
No	16	27.1 ± 6.4	
Implantation (fetal heart)			
Yes	28	25.9 ± 6.6	NS
No	19	25.4 ± 7.1	
Live Birth			
Yes	27	25.7 ± 6.7	NS
No	20	25.7 ± 7.0	
Mitoscore Rank	**N**	**Implantation Rate**	**p-value**
<21	15	80% (12/15)	NS
21-26	12	67% (8/12)	
>26	20	55% (11/20)	

SUPPORT: None

REFERENCES:

Hur, Christine et al. INCREASED MITOCHONDRIAL DNA CONTENT IS ASSOCIATED WITH DELAYED EMBRYO DEVELOPMENT AND ANEUPLOIDY [abstract]. In: Fertility and Sterility Vol. 116, Issue 3, Supp.; ASRM 2021. Abstract nr. e173.

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NON-MEDICAL EMBRYO SEX SELECTION RESULTS IN REDUCED IMPLANTATION COMPARED TO THE TRANSFER OF THE HIGHEST MORPHOLOGICAL GRADE BLASTOCYST.

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OBJECTIVE: Non-medical embryo sex selection has become more accessible to infertile couples undergoing preimplantation genetic testing for aneuploidy (PGT-A). Couples report a combination of motivations for pursuing non-medical embryo sex selection, including a desire to limit family size, family balancing and financial concerns about multiple subsequent pregnancies. The aim of this study was to evaluate the clinical impact of performing euploid embryo selection based on sex chromosomes in preference to the highest morphological grade blastocyst.

MATERIALS AND METHODS: Infertile patients (n=132; mean maternal age = 35.4 ±3.3 years) who chose non-medical embryo sex selection following PGT-A were compared to a maternal age-matched control group of frozen embryo transfers (n=904; mean maternal age = 35.5 ±0.5 years) where a single euploid blastocyst of the best morphological grade, independent of sex chromosomes, was selected. Primary outcomes included clinical pregnancy with fetal heart tone (FHT), implantation with FHT, miscarriage and live birth rates. A two-sided Fisher's exact test with odds ratio calculated significance at $p<0.05$.

RESULTS: There was no significant gender preference observed in this cohort of non-medical embryo sex selection IVF cycles, however there was a potential trend towards a skewed gender ratio (male sex chromosomes = 42.4%, female sex chromosomes = 49.2% and double embryo transfer of both genders = 8.3%). Upon comparison to the control group FETs with euploid embryo selection based on the best morphological grade blastocyst, implantation with FHT after non-medical embryo sex selection was significantly reduced (63.3% vs. 72.1% control; $p<0.05$, OR 0.67). Other clinical outcomes including pregnancy with FHT (65.2% vs 70.8% control) and live birth rates (60.6% vs 65.4% control) also displayed a trend downwards following FET based on non-medical embryo sex selection but were not statistically significant. In contrast, miscarriage rates were comparable between the two euploid embryo selection groups (7.0% non-medical embryo sex selection vs. 7.5% control).

CONCLUSIONS: The debate over the accessibility of non-medical embryo sex selection in IVF is dynamic and complex**.** Some of the arguments against the practice include the likely disruption in the gender ratio and the inequality of access. Our data echoed a potential trend towards a skewed gender ratio but more importantly revealed a significantly reduced implantation rate when choosing euploid embryos based on a priority for sex chromosomes over the highest morphological grade.

IMPACT STATEMENT: The best morphological-grade euploid blastocyst, independent of sex chromosomes, will always result in the most successful clinical outcomes for infertility patients.

SUPPORT: None

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DOES INDIVIDUALIZED PRE- AND POST-EMBRYO TRANSFER ACUPUNCTURE AFFECT LIVE BIRTH RATES?

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OBJECTIVE: To assess the effect of individualized, day of embryo transfer acupuncture on Frozen Embryo Transfer (FET) live birth rates compared with no acupuncture.

Table 1. Acupuncture and FET characteristics and outcomes.

	ACU	FET	*p value*
N	579	1751	
Age (mean±SD)	35.2±4.4	33.9±4.7	<0.0001
Primary diagnosis, N (%)			
Advanced Maternal Age	2 (0.2)	4 (0.2)	1.0
Diminished Ovarian Reserve	175 (30.2)	348 (19.9)	<0.001
Ovulatory	120 (20.7)	240 (13.7)	<0.001
Uterine	12 (2.1)	17 (1.0)	0.04
Tubal	16 (2.8)	67 (3.8)	0.23
Unexplained	37 (6.4)	58 (3.3)	0.001
Recurrent Pregnancy Loss	26 (4.4)	89 (5.1)	0.57
Endometriosis	16 (2.8)	42 (2.4)	0.63
Fertility Preservation	2 (0.2)	4 (0.2)	1.0
Male Factor	74 (12.8)	228 (13.0)	0.88
Other	28 (4.8)	160 (9.1)	0.001
Multiple diagnoses	73 (12.6)	494 (28.2)	<0.001
Number of previous cycles			
First cycle	248 (42.8)	654 (37.4)	0.02
One or more previous cycles	331 (57.1)	1097 (62.6)	0.02
Day of Embryo Transfer			
3	10 (1.7)	17 (1.0)	NS
4	0	9 (0.5)	NS
5	460 (79.6)	1519 (89.6)	0.047
6	99 (17.1)	143 (8.4)	<0.001
7	9 (1.6)	7 (0.4)	NS
Total number embryos transferred (mean±SD)	1.14±0.3	1.17±0.4	0.17
Birth outcomes			**Odds Ratio**
Live Birth	277 (47.8)	650 (37.1)	1.55 (1.29-1.88) p<0.00001
Miscarriage	56 (9.7)	161 (9.2)	1.05 (0.77-1.46) p=0.73
Biochemical	39 (6.7)	193(11.0)	0.58 (0.41-0.83) p=0.002
Ectopic	3 (0.5)	8 (0.5)	1.13 (0.30-4.29) p=0.85

MATERIALS AND METHODS: In this retrospective cohort study, 2,330 patients completed an FET at Vios Fertility Institute, Chicago, IL, from May 2018 – May 2021. Individualized acupuncture therapy was provided on-site, for 30 minutes before and immediately after embryo transfer (ET) by licensed acupuncturists (ACU group) in 579 records, and 1,751 elected FET alone (FET group). Our main outcome measure was live birth rate. Secondary outcomes included biochemical, miscarriage, and ectopic rates. Groups were compared by age, diagnosis, number of cycles, ET day, and number of autologous embryos transferred. Means were compared using analysis of variance and proportions with Chi-square and logistic regression.

RESULTS: Demographics differed between groups on several variables. See Table 1. Individualized acupuncture pre- and post-ET was associated with more live births [Odds Ratio (OR)=1.55, 95% Confidence Interval (CI) 1.29-1.88, p<0.00001] and fewer biochemical pregnancies (OR=0.58, 95% CI 0.41-0.83, p=0.002). There was no difference between groups on the outcomes of miscarriage and ectopic pregnancy.

CONCLUSIONS: Individualized acupuncture on the day of embryo transfer was associated with 55% increase in FET live births and 42% reduction in biochemical pregnancies compared with FET alone.

IMPACT STATEMENT: Individualized day of embryo transfer acupuncture was associated with significant benefit to patients undergoing FET.

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A COMPREHENSIVE MODEL FOR PREDICTING THE PROBABILITY OF LIVE BIRTH PRIOR TO THE START OF PROGESTERONE DURING ARTIFICIAL FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: To develop a comprehensive model for predicting the probability of live birth prior to the start of progesterone during artificial frozen embryo transfer (FET) cycles that can identify at-risk cycles and set expectations.

MATERIALS AND METHODS: Historical, de-identified EMR data was collected from a single IVF clinic in the United States. Records were filtered for autologous cryo-synthetic frozen embryo transfers (FETs) resulting in 5,813 cycles from 4,133 patients between 2014-2021. For endometrial response we extracted measurements from the end of the proliferative phase, a common decision point. Parameters with high variance inflation factor were dropped for accurate interpretation of regression results. We developed a mixed effects logistic regression model using parameters from the embryo, patient, and endometrial response for the primary outcome of live birth.

RESULTS: 13 parameters were found to be significant (P<0.01) with respect to live birth outcomes. The most important parameters positively associated with live birth were higher endometrial thickness (OR 4.22) and embryo ICM grade A (OR 2.00). Parameters negatively associated with live birth included BMI (OR 0.51) and number of previous failed FETs (OR 0.29). Calibration curves showed predicted probabilities closely matched observed live birth rates, with an expected calibration error of 0.028 on a 25% hold-out test set.

CONCLUSIONS: We developed a comprehensive and well-calibrated model to predict live birth probabilities prior to the start of progesterone during artificial FET cycles. Future work will expand the dataset and develop additional tools for clinical decision support.

IMPACT STATEMENT: Successful outcomes in artificial FET cycles are dependent upon parameters related to the patient, embryo, and endometrial response, and modeling all parameters together enables accurate predictions of live birth rate for identifying at-risk cycles and setting expectations.