DESIGN: Retrospective, single center study performed from 2017 to 2019.

MATERIALS AND METHODS: A total of 561 patients who became pregnant after fresh and frozen embryo transfers. A first study group included all IVF cycles where fresh embryo transfer resulted in a singleton live birth (fresh group n=254). A second cohort included FET that led to a singleton live birth (FET group n= 307). All embryos were transferred at a blastocyst stage and vitrification was the only cryopreservation method. In all FET the endometrium was artificially prepared through the administration of exogenous estrogen and progesterone. Data was collected from telephone surveys. We compared the number of LGA newborns and weight differences in both groups. z-test was applied for statistical analysis. A p value <0.05 was considered significant.

RESULTS: The median gestational age in both groups was 38 weeks. The mean adjusted birth weight after FET group was higher by 109.26 g, than the fresh group (3269.32 g vs 3160.13 g respectively, p=0.285). The incidence of newborns that weighted $\geq$ p50 was significantly higher for FET group (142 vs 75 for FET and fresh respectively, p= 0.000048). Moreover, the incidence of LGA livebirths was significantly higher in the FET group (p=0.0226) (23 from the FET group vs 8 from fresh ET). No difference in female to male ratio for LGA newborns or preterm birth rate was identified between groups.

CONCLUSIONS: FET is associated with increased risk of LGA in our population. FET has become an important technique in IVF; however, whether it should be the first choice for ET requires further analysis. An individual approach should remain when deciding between fresh or frozen embryo transfers. Longer-term potential health effects remain to be evaluated.

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OOCYTE MATURITY AS A PREDICTOR OF IVF OUTCOME. Michelle L. Krohn, D.O.,[1] Amy E. Sparks, PhD,[2] Bradley J. Van Voorhis, MD,[3] [1]Monument Health, Spearfish, SD; [2]University of Iowa Center for Advanced Reproductive Care, Iowa City, IA; [3]University of Iowa, Iowa City, IA.

OBJECTIVE: Oocyte maturity after retrieval during IVF can vary significantly and is important in fertilization and development of embryos. Our purpose was to determine if low oocyte maturity from a retrieval cycle is a predictor of poor outcomes from IVF. Secondary objectives were; to identify factors predictive of low oocyte maturity, to assess oocyte maturity across cycles, and to determine if oocyte maturity is affected by the length of ovarian follicular stimulation or the total dose of gonadotropins used.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1451 autologous IVF cycles from 1/2016- 7/2019 at our center were evaluated. Oocyte maturity was initially assessed upon retrieval (M1 + M2 oocytes/total oocytes). The final oocyte maturity assessment was made 5 hours post retrieval, prior to ICSI (oocytes inseminated at ICSI/total oocytes). As the maturity score at the time of retrieval was correlated with score at ICSI (Pearson's r=.848, $p \leq .001$), we used maturity at retrieval as our measure of maturity, allowing inclusion of all cycles. Maturity designation as suboptimal vs. optimal was derived from previously established classifications (1). Statistical tests utilized included Pearson's correlation, independent samples t-tests, and generalized estimating equations.

RESULTS: There was no correlation between female age at retrieval and oocyte maturity (Pearson's r= .131, $p \leq .001$). A diagnosis of polycystic ovarian syndrome (PCOS) was associated with a slightly reduced maturity (81.9% $\pm$ 14.6 vs. 85.5% $\pm$ 14.0, p=.002). There was no association with diminished ovarian reserve (defined as AFC< 10; DOR) and oocyte maturity (p=.172). Increasing oocyte maturity was associated with increased clinical pregnancy rates, age adjusted odds ratio (AOR) 2.5 (1.1-5.8). Oocyte maturity was not found to be associated with miscarriage rates. When cycle 1 was compared to cycle 2 in the same patient, there was a fair correlation between oocyte maturity scores (Pearson's r=.339, $p \leq .001$) with 44% of those classified as suboptimal maturity also classified as suboptimal maturity within their second cycle. In contrast, only 22% of cycles classified as optimal maturity in cycle 1 had suboptimal maturity if a second cycle was performed. There was no evidence of correlation between days of stimulation prior to the trigger shot or total gonadotropins used and maturity scores (Pearson's r=0.43, p=0.149).

CONCLUSIONS: There is no correlation between oocyte maturity and female age or diagnosis of DOR. The diagnosis of PCOS is associated with a slight but statistically significant reduced oocyte maturity at retrieval; however this is unlikely to be clinically significant given that these patients most often have an increased number of total oocytes retrieved. Low oocyte maturity was associated with decreased clinical pregnancy rates but did not impact miscarriage rates. Cycles complicated by low oocyte maturity can be repetitive, and maturity did not appear to correlate with the duration of ovarian stimulation or total gonadotropin dosage used.

References: Parrella, A., Irani, M., Keating, D., Chow, S., Rosenwaks, Z., Palermo, G.D. High proportion of immature oocytes in a cohort reduces fertilization, embryo development, pregnancy and live birth rates following ICSI. Reprod. Biomed. Online.Â 2019; 39: 580-587.

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EVALUATION OF DUAL TRIGGER EFFICACY FOR FINAL OOCYTE MATURATION IN HIGH COMPLEXITY ASSISTED REPRODUCTION TECHNIQUES: A SYSTEMATIC REVIEW AND META-ANALISYS. Luciana Carvalho Delamuta, MD, Alexandre LS. Lobel, MD, PhD, Pedro AA. Monteleone, MD, PhD, Jose Maria Soares, Jr., MD, PhD, Edmund Chada Baracat, MD, PhD University of São Paulo, São Paulo, Brazil.

OBJECTIVE: To compare the number of mature oocytes, number of total oocytes and clinical pregnancy rate in assisted reproductive techniques that used dual trigger (gonadotropin releasing hormone agonist + human chorionic gonadotropin) or human chorionic gonadotropin (hCG) alone for oocyte final maturation.

DESIGN: Systematic review an meta-analysis.

MATERIALS AND METHODS: A systematic review was conducted to compare the number of mature oocytes, number of total oocytes and clinical pregnancy rate in assisted reproductive techniques that used dual trigger or human chorionic gonadotropin alone. For this evaluation, randomized clinical trials (RCT) and retrospective cohort studies were included. We comprehensively searched PubMed, EMBASE and Cochrane Library with the last search made in December 2019. Bibliographies of relevant studies identified by the search strategy and relevant reviews/meta-analyses were also searched for identification of additional studies. The following MeSH terms (gonadotropin-releasing hormone, human chorionic gonadotropin, oocyte maturation, in vitro fertilization) and their combinations were searched. Inclusion and exclusion of the studies were completed according strict criteria. The methodological quality of RCT and retrospective cohorts was assessed using the Review Manager software and the modified Newcastle-Ottawa scale respectively. Data from the included studies were extracted to define whether dual trigger improves the number of total and mature oocytes retrieved and the clinical pregnancy rate. The meta-analysis was performed using *software* R 3.6.1 (R Core Team, 2019) and *meta* package (Schwazer, 2013).

RESULTS: A total of 18 studies were included (8 RCT and 10 retrospective cohorts) with a total of 2798 patients in the dual trigger group and 2649 patients in the hCG trigger group. In six of the studies the patients had a prior failure in an assisted reproductive treatment (ART) and in the other 12 studies it was the first treatment. For the pregnancy rate the relative risk (RR) was 1,24 [CI 95% 1,14 – 1,36], for the number of mature oocytes the mean difference (MD) was 1,41 [CI 95% 0,63 – 2,19], and for the number of total oocytes the MD was 1,07 [CI 95% 0,40 – 1,73]. A subgroup analysis separating RCT from retrospective cohorts showed no difference between the types of study for all the outcomes analyzed. Another subgroup analysis separating patients who had the first ART from patients who had prior failure showed pregnancy rate RR 1,31 [CI 95% 1,06 - 1,62] for "previous failure" and 1,23 [CI 95% 1,12 – 1,34] for "first treatment". For the number of mature oocytes MD was 3,15 [CI 95% 2,39 – 3,91] for "previous failure and 0,81 [CI 95% 0,20 – 1,42] for "first treatment". For the number of total oocytes MD was, respectively, 1,60 [CI 95% 0,60 – 2,60] and 0,93 [CI 95% 0,20-1,66].

CONCLUSIONS: We can conclude that dual trigger for final oocyte maturation results in higher pregnancy rate and higher number of total and mature oocytes when compared to hCG alone. Patients who had a previous ART failure seem to be the subgroup that benefits the most from dual trigger use.

SUPPORT: None.

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THE IMPACT OF DOUBLE-STRANDED SPERM DNA BREAKS ON ICSI OUTCOME. Derek Keating, B.A., Alessandra Parrella, M.Sc., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We sought to evaluate specific sperm DNA damage, double-stranded DNA breaks (dsDNA), and its effect on embryo development and implantation.

DESIGN: Over a year-long period, a prospective pilot study was carried out on sperm samples to evaluate the proportion of dsDNA on samples screened by terminal deoxynucleotidyl dUTP transferase nick-end labeling (TUNEL) to assess total DNA fragmentation. Once a correlation was established, we extrapolated dsDNA values retrospectively onto patients who had their ejaculates screened by TUNEL to evaluate clinical outcome.

MATERIALS AND METHODS: Samples from consenting couples were screened for dsDNA rates by neutral Comet assay using an in-house protocol; 200 spermatozoa were assessed per patient. These samples were also assessed by TUNEL using a commercially available kit, analyzing at least 500 spermatozoa per patient. ICSI was performed in the standard fashion.

RESULTS: The pilot study reported an average total DNA fragmentation of 11.3±6% by TUNEL and an average dsDNA of 2.2±3% by neutral Comet. The results showed a linear relationship between the overall SCF and dsDNA rates (R^2=0.96). This equation was applied to extrapolate the dsDNA levels from 573 normozoospermic men (volume of 2.6±1 mL, concentration of 42.3±33x10^6/mL, 43.1±10% motility, and 4.2±1% normal morphology) with an average SCF of 14.2±8%. Therefore, on the basis of this preliminary test, we established a dsDNA threshold of 3%.

A total of 417 couples (maternal age, 37.0±4 yrs; paternal age, 38.6±5 yrs) underwent 777 ICSI cycles and presented with dsDNA levels of 1.8±0.6%. These cycles had a 73.0% fertilization rate, a 12.7% (123/966) implantation rate, and a 23.2% (102/440) clinical pregnancy rate (CPR), of which 15 were lost (14.7%), leaving a 19.7% (87/440) ongoing/delivery rate.

There were 155 couples with dsDNA levels of 4.2±1%. These couples underwent 268 ICSI cycles with a comparable maternal age of 37.3±5 years, but with older male partners at 41.3±8 years of age (P<0.001). These cycles had a comparable fertilization rate of 71.0%, implantation rate of 11.4% (53/464), and clinical pregnancy rate of 24.3% (44/181). However, these couples were much more likely to lose their pregnancy at 29.5% (13/44; P = 0.03), leaving an ongoing/delivery rate of 17.1% (31/181).

CONCLUSIONS: These findings provide further evidence that dsDNA has an important role in the success of a pregnancy generated by ICSI. dsDNA damage has been linked to aneuploidy and consequent pregnancy loss. The use of an assay in a laboratory setting to screen exclusively for dsDNA would help to identify paternally linked aneuploidy that traditional screening would only report as total SCF.

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PREDICTORS OF EMBRYO ANEUPLOIDY AND MOSAICISM: INSEMINATION METHOD, SPERM AND PATIENT CHARACTERISTICS. Gabriela M. Grant, MSc,[1] Jessica R. Walter, MD,[1] Helena I. Russell, MSc,[2] Dara S. Berger, PhD,[1] [1]University of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; [2]Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: Intracytoplasmic sperm injection (ICSI) is often the insemination method used with pre-implantation genetic testing (PGT). We studied the effects of insemination method on aneuploidy and mosaicism rates in a clinical setting.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Embryos created during an IVF cycle and biopsied using next-generation sequencing between 1/1/2016 to 12/21/2019 were included in this study. Embryos were categorized by insemination method, ICSI versus conventional insemination. Age of the patient, infertility diagnosis, stimulation protocol, and biopsy results were examined. Semen analysis performed using Krueger strict criteria to determine morphology (normal morphology defined as $\geq$ 4). Univariate statistical analyses were performed using the student t-test and chi-square test. Multinomial logistic regression with cluster standard error was performed to identify determinants of a normal, abnormal or mosaic biopsy outcome. Euploidy was the base outcome and all results are explained in terms of aneuploidy and mosaicism.

RESULTS: A total of 3522 embryos were biopsied from 818 IVF cycles. 2667 embryos (75.7%) were fertilized by ICSI. Oocytes inseminated by ICSI were from younger patients (36.3 years compared to 38.0 years, p<0.001), with a significantly higher percentage originating from abnormal morphology (32.0 % compared to 13.7%, p<0.001). Couples with ICSI embryos were more likely to have a reported component of male factor infertility (23.7 versus 2.1%, p <0.001). Female diagnoses of ovulatory dysfunction, structural (uterine/tubal disease), and advanced maternal age were more common in the conventionally inseminated group. Among embryos biopsied, 1758 (53.3%) were aneuploid and 530 (16.1%) demonstrated mosaicism. There were higher rates of aneuploidy among ICSI inseminated embryos (55.2% versus 47.6%; p<0.001) and higher rates of mosaicism among conventionally inseminated embryos (20.5% versus 14.8%, p<0.001). ICSI insemination was found to be an independent risk factor for aneuploidy (RR 1.38 95% CI 1.07-1.77, p= 0.01), when adjusting for oocyte age and female infertility diagnosis. Female infertility diagnosis, specifically ovarian pathology (diminished ovarian reserve, ovulatory dysfunction, and endometriosis), not presence or severity of male infertility, demonstrated an increase in the relative risk of mosaicism. Sperm morphology did not influence the relative risk of a specific biopsy results.

CONCLUSIONS: The influence of laboratory techniques and patient characteristics on aneuploidy and mosaicism rates, are not well understood. While semen parameters and male factor infertility were not shown to affect biopsy results irrespective of insemination method, we demonstrate in this large study that aside from oocyte age, ICSI may adversely affect euploid rate when controlling for relevant confounders, but neither meaningfully seem to influence mosaicism. Future studies are needed to examine the potential relationship between infertility diagnosis, specifically of ovarian origin, and mosaicism rates.

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MICROFLUIDIC SPERM SELECTION IS AN EFFECTIVE METHOD FOR IMPROVING EMBRYO DEVELOPMENTAL COMPETENCE IN IVF WITH OLDER PATIENTS. Rie Matsunaga, M.A., Kana Isobe, B.A., Megumi Miura, M.A, Yuki Kobayashi, B.A., Minako Kamihata, B.A., Hiroshi Makino, Ph.D., Kurumi Iwaki, Ph.D., Tomoko Maeda, Ph.D, Toshitaka Horiuchi, Ph.D., Masanori Ochi, Ph.D. OCHI YUME CLINIC NAGOYA, Nagoya, Japan.

OBJECTIVE: Sperm DNA fragmentation can reduce the rate of embryo development and also increase the rate of miscarriage. Various methods have been developed to select and collect sperm with good motility. However, the DNA fragmentation index (DFI) of the collected sperm differs among these methods. The microfluidic sperm selection chamber (ZyMōt™; DxNow) is a selection kit designed to collect low DFI sperm. Although a few reports have suggested a relationship between embryo quality and euploidy rate (assessed by preimplantation testing for aneuploidy after intracytoplasmic sperm injection), there has been little investigation of the efficacy of microfluidic sperm selection (MSS) in IVF. We studied whether MSS can improve the success rate of embryo development in IVF.

DESIGN: The study was conducted between June 2019 and December 2019. Patients were divided into two groups according to the sperm processing method used: DGS (114 patients, 326 oocytes), and MSS (113 patients, 356 oocytes). For both groups, IVF was performed using selected sperm.

MATERIALS AND METHODS: We compared the rates of fertilization, blastulation, and available blastocysts (defined as those with Gardner Grade better than 4BC); we also compared the rates of available blastocyst cycle, defined as the rate of cycles that yielded at least one available blastocyst. IVF was performed using sperm selected by MSS; as a control, 4×10^4 sperm/ml was used for IVF in the DGS group.

RESULTS: The fertilization rates using 4×, 6×, and 8×104 sperm/ml in the MSS group were 44.8%, 55.3%, and 62.4%, respectively; by comparison, the rate in the DGS (control) group was 66.6%. Rates of oocyte fertilization using sperm selected by MSS were significantly lower at 4× and 6×104 sperm/ml than for the DGS control. However, the rate of fertilization improved with increasing sperm concentration in the MSS group and was comparable to DGS at the 8×104 sperm/ml concentration. Embryo development was compared for oocytes from women of different age ranges: under 34 years (A), 35–39 years (B), 40–42 years (C), and over 43 years (D). Blastulation rates did not differ between the DGS and MSS groups in A (76.9% vs. 71.7%), B (65.2% vs. 80.5%), C (70.0% vs. 53.6%), and D (35.3% vs. 62.5%). The rates of available blastocysts and the blastocyst cycle rates for MSS were comparable to DGS in A (49.1% vs. 53.8% and 81.3% vs. 83.3%, respectively), B (53.7% vs. 34.8% and 80.0% vs. 61.9%, respectively), and C (39.3% vs. 36.7% and 50.0% vs. 64.3%, respectively). These rates were significantly higher for MSS than DGS in D (33.3% vs. 5.9% and 53.8% vs. 9.1%, respectively).

CONCLUSIONS: The present study indicates that MSS might enable improvement in the rates of embryo development after IVF of oocytes from women with an advanced maternal age. The use of MSS for sperm