Data for each ART cycle was held on IDEAS version 6 Mellowood Medical and analysed using SPSS version 24.0 and STATA version 15.

Male partners were grouped into age ranges ≤35; 36 – 40; 41-44; 45-50; ≥51 years for analysis. Male age and female age <35 years was used as the reference groups for comparison.

Main results and the role of chance:

Median maternal and paternal ages were 36 years (IQR 33 – 39) and 38 years (IQR 35 – 42) respectively.

Significantly fewer men over 51 years met WHO semen analysis criteria (56/133, [42.1%, 95% CI 34.1 – 50.6]) compared to men under 51 years (2530/4138 [61.1%, 95% CI 60.0 – 62.6]) (p = 0.001).

2019/4833 (41.8%, 95% CI 40.4 – 43.2) of cycles resulted in clinical pregnancy. CPR declined with increasing maternal age ≤35 (1074/2102, 51.1% 95% CI 49.0 – 53.2), ≥40 (202/929, 21.7% 95% CI 19.2 – 24.5) (p = 0.001). CPR also declined with increasing paternal age; ≤35 (715/1433, 49.9% 95% CI 47.3 – 52.5), 36 – 40 (735/1731, 42.5% 95% CI 40.2 – 44.8), 41 – 45 (379/1076, 35.2% 95% CI 32.4 – 38.1), 46 – 50 (129/393, 32.8% 95% CI 28.4 – 37.6), ≥51years (61/200, 30.5% 95% CI 24.5 – 37.2). We performed multivariate logistic regression analysis with clinical pregnancy as dependent variable and maternal and paternal age class as independent variables. Maternal and paternal age were retained in the model. For all maternal age subgroups the probability of pregnancy decreased with paternal age over 51years (OR 0.655, 95% CI 0.477 – 0.927) (p = 0.001).

Limitations, reasons for caution:

The main limitation of this study is that it is retrospective and therefore vulnerable to confounding and bias. 80% of men ≥51years received ICSI treatment even though 42% had normal semen parameters. This may have confounded the results and reduced the perceived effect of increased paternal age.

Wider implications of the findings:

Paternal age over 50 significantly affects the chance of success of ART and there should be a public health message for men to not delay fatherhood. Alternative options for procuring semen for men over the age of 50 years may be discussed at the time of consultation.

Trial registration number:

not applicable

O-305 Factors influencing live birth outcomes of day 7 blastocysts following autologous single vitrified-warmed blastocyst transfer: A single-centre large cohort study

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Study question:

What factors influence live birth outcomes of day 7 blastocysts following single vitrified-warmed transfer (SVBT)?

Summary answer:

Live birth outcomes of day 7 blastocysts following SVBT are influenced by maternal age, time from insemination to blastulation, expansion time, and blastocyst diameter.

What is known already:

Preimplantation genetic testing has been promoted to prevent miscarriage after embryo transfer. Therefore, blastocyst culture has become standard for in vitro fertilisation (IVF), but it is unclear whether day 7 (d7) blastocysts should be cryopreserved and transferred. Clinical outcomes with d7-frozen blastocyst transfer (FBT) have been studied. However, as the usefulness of d7-blastocysts remains controversial, clinical outcomes of d7-FBT require further evaluation with a large cohort study. Investigation of factors influencing live birth (LB) after d7-FBT is also necessary to prioritize selection of blastocysts.

Study design, size, duration:

A retrospective cohort study of 49,044 autologous SVBTs (23,715 patients, mean age: 37.6±4.1) was conducted in a single centre between 2006 and 2015. Study 1: Factors influencing LB using d7-blastocysts following SVBT were investigated. Study 2: Cut-off values of factors influencing LB and criteria of d7-blastocysts were established and live birth rates (LBRs) for, d4-blastocysts (d4-SVBT), d5-blastocysts (d5-SVBT), d6-blastocysts (d6-SVBT) and d7-blastocysts (d7-SVBT) following SVBT were compared.

Participants/materials, setting, methods:

Blastocysts were vitrified using the Cryotop method according to criteria based on blastocyst diameter (Ueno et al., 2014). SVBT was performed in natural ovulatory cycles. Multivariable logistic regression (mLR) analysis was used to analyse the factors influencing LB. Multivariate receiver operating characteristic (ROC) curve analysis was used to establish cut-off values and criteria for d7-blastocysts. Chi-square tests were performed to compare LBR at >22 weeks of pregnancy among the groups.

Main results and the role of chance:

Study 1: mLR analysis to calculate adjusted odds ratios (aORs) included the following independent factors: age of females and males, number of previous IVF cycles, time from insemination to starting blastulation (tSB), expansion time (tExp: time from tSB to expanded blastocyst), and blastocyst diameter. mLR analysis revealed that age of females (aOR: 0.83, P < 0.05), tSB (aOR: 0.95, P < 0.05), tExp (aOR: 0.92, P < 0.05), and blastocyst diameter (aOR: 1.02, P < 0.05) were significantly correlated with LB in d7-SVBT. Study 2: ROC curve analysis determined cut-off values as follows: age of females < 39 years, tSB > 143 h post insemination, tExp: within 19 h, and blastocyst diameter > 210 μm (area under the curve: 0.76). The LBRs of d4-, d5-, d6- and d7-SVBT groups were 52.6% (n = 154), 40.1% (n = 23,484), 27.0% (n = 22,928), and 14.2% (n = 2,478), respectively. There were significant differences between the groups (P < 0.05). LBRs of d7-blastocysts that met the criteria (Adjusted-d7-SVBT group) were comparable to those of the d6-SVBT group (28.2% vs. 27.0%), but this rate was significantly lower compared to that for d4- and d5-SVBT groups (28.2% vs. 52.6% and 40.1%, P < 0.05).

Limitations, reasons for caution:

The present study did not include blastocyst morphology as an independent factor in the mLR analysis, because all d7-blastocysts analysed in this study had low-grade morphology. In addition, d7-blastocyst criteria may be influenced by clinical settings such as culture environment.

Wider implications of the findings:

Our results demonstrate that LBRs following d7-SVBT are comparable to those after d6-SVBT if d7-blastocysts fulfil strict criteria. Therefore, d7-blastocysts may have potential clinical usefulness for FBT.

Trial registration number:

None

O-306 The use of pronuclear transfer to overcome infertility disorders in mice

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Study question:

Can pronuclear transfer (PNT) overcome inferior embryonic development or reproductive ageing in a mouse model?

Summary answer:

The PNT technology is very efficient to restore embryonic developmental potential in infertility disorders such as reproductive ageing or embryo arrest.

What is known already:

Nuclear transfer such as PNT is being used to avoid the transmission of mitochondrial disorders. There is increasing interest to also use PNT for infertility disorders, however, scientific evidence in both animal and human models to support the use of PNT for infertility is currently lacking. It is important to reveal which infertility indications could benefit from this novel technology.

Study design, size, duration:

We used a reproductively-aged model (B6D2F1 mice) with age ranging from 6-8-weeks (control), 13-months (aged) to 16-months (very-aged); corresponding to women of <30, ~36 and ~45-year-old respectively. Secondly, another mouse strain (NZB mice, 6-8w) showing two-cell block was used. Finally, cytoplasmic transfer (CT) was performed by injection of a limited amount of

young B6D2 cytoplasm in both reproductively-aged and embryo-arrest models. We evaluated embryonic development in reconstituted PNT (n = 572) and CT (n=365) embryos.

Participants/materials, setting, methods:

Ovarian reserve was assessed by histological analysis in reproductively-aged mice. The Mitochondrial membrane potential ($\Delta\Psi m$) was measured by JC-1 staining in MII oocytes. The spindle-chromosomal morphology was examined by confocal analysis. PNT was performed by transferring pronuclei from fertilized oocytes (after ICSI) to enucleated counterpart zygotes between aged/very-aged and young mice, or between NZB/OlaHsd (embryo-arrest) and B6D2F1 (non-arrest control) mice.

Main results and the role of chance:

In comparison to the young mice, the ovarian reserve in aged/very-aged females was severely diminished, reflected by a lower number of ovarian follicles and lower ovulation rate ($P<0.001$). The average $\Delta\Psi m$ in aged/very-aged mouse oocytes was significantly reduced ($P<0.001$) compared to young mice. Moreover, the rate of abnormal spindle-chromosome configuration in MII oocytes of aged/very-aged group was significantly higher ($P<0.05$) than young mice. Following ICSI, oocytes from aged/very-aged mice showed significantly lower fertilization (60.7% and 45.3%) and blastocyst formation rates (51.4% and 38.5%) than the ICSI control with young mouse oocytes (FR = 89.7%, blastocyst 87.3%) ($P<0.001$). After PNT from aged/very-aged to young mice, the blastocyst formation rates were significantly improved (74.6% and 69.2%, respectively).

Similarly, as model of embryo arrest, most (61.8%) of *in vivo* zygotes of NZB/OlaHsd strain displayed two-cell block during *in vitro* culture, with a significantly decreased blastocyst rate compared to B6D2F1 strain (13.5% vs. 90.7%, respectively) ($P<0.001$). When transferring PN from embryo-arrested (NZB/OlaHsd) to non-arrested (B6D2F1) zygotes, most of reconstructed zygotes developed beyond two-cell stage, with significantly increased blastocyst rates (89.7%) ($P<0.001$). The application of CT did not overcome inferior embryonic development in both aged/very-aged and embryo-arrested mice ($P>0.05$).

Limitations, reasons for caution:

Considering the differences between animal models and women regarding various biological processes, validation of PNT in infertility patients to explore the reliability of this technique is still required.

Wider implications of the findings:

This is the first study in mice to determine whether PNT could overcome certain female infertility indications such as advanced maternal age or embryonic developmental arrest. Our data support that PNT, refreshing the oocyte or zygote cytoplasm, may represent a novel reproductive strategy to increase embryonic developmental potential.

Trial registration number:

NA

O-307 Impact of trophectoderm grade on infant physiological characteristics and gender after single frozen blastocyst transfers: an analysis of 1109 singletons after 3822 frozen blastocyst transfers

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Study question:

Does trophectoderm (TE) morphology grade affect infants' physiological characteristics and gender ratio after frozen blastocyst transfer?

Summary answer:

TE morphology grade was uncorrelated with birth weight, height or congenital abnormality in infants. High TE grade was significantly associated with gender ratio towards male.

What is known already:

Gardner's scoring criteria is often used to evaluate blastocyst quality. A strong correlation between blastocyst morphology grade and clinical outcome has been reported by many studies. However, the correlations between TE grade and physiological characteristics and gender ratio of infants have not been fully understood.

Study design, size, duration:

This retrospective study was conducted at Kyono ART Clinic in Japan from 2012 to 2017. This study includes a total of 1109 singletons born after 3822 single frozen blastocyst transfer in 2166 patients.

Participants/materials, setting, methods:

TE morphology was graded according to Gardner's scoring system and divided into the three grades (Grades A, B, and C). Grade A includes 638 cycles, 447 patients, and 254 children; Grade B, 1731 cycles, 944 patients, and 526 children; and Grade C, 1453 cycles, 775 patients and 329 children. The correlations between TE grade and clinical outcomes (pregnancy rate, miscarriage rate and ongoing pregnancy rate), physiological characteristics, and gender ratio were evaluated.

Main results and the role of chance:

Average maternal age in Grade C was significantly higher than in Grades A and B (35.5±3.1 vs. 34.8±3.2 and 35.1±3.2, $p<0.01$). Pregnancy rates in Grades A, B, and C were 60.7%, 50.5%, and 36.9%, respectively; Grade A was significantly higher than Grade C ($p<0.01$). Ongoing pregnancy rates in Grades A, B, and C were 54.1%, 45.5%, and 30.6%, respectively; Grade A was significantly higher than Grade C ($p<0.01$). Miscarriage rates in Grades A, B, and C were 12.1%, 11.5%, and 10.7%, respectively (N.S: not significant). Average gestational age (weeks) in Grades A, B, and C were 38.8±1.8, 38.7±2.3, and 38.4±2.4, respectively (N.S). Average height (cm) and weight (g) in Grades A, B, and C were 49.3±2.4, 49.0±3.7, and 49.0±3.2 (N.S), and 3,066±0.4, 3,047±0.5, and 3,040±0.5, respectively (N.S). Premature birth rates and low birth weight rates in Grades A, B, and C were 5.5% (n=14), 8.4% (n=44) and 7.9% (n=26) (N.S), and 6.3% (n=16), 9.3% (n=49), and 8.5% (n=28), respectively (N.S). Congenital abnormality rates in Grades A, B, and C were 2.8%, 2.9%, and 1.5% (N.S). Gender ratios (male:female) in Grades A, B, and C were 1.92:1, 1.26:1, and 0.94:1, respectively; Grade A was significantly higher than Grade C ($p<0.01$).

Limitations, reasons for caution:

In this study, we did not assess the correlation between inner cell mass and infants' physiological characteristics and gender ratio. Since male embryos grow faster than female embryos, high TE grade male embryos might be selected as transferred blastocysts in our study.

Wider implications of the findings:

It was particularly noteworthy that high grade TE clearly skews gender ratio towards male. Blastocyst TE grade is responsible for pregnancy rate. However, miscarriage rate, infants' physiological characteristics and congenital abnormality are not affected by TE grade.

Trial registration number:

None.

SELECTED ORAL COMMUNICATIONS
SESSION 79: NOVEL INSIGHTS IN PCOS
Wednesday 26 June 2019 Strauss 1+2 14:00 - 15:30

O-308 Association of childhood adiposity with irregular menstruation and polycystic ovary syndrome in adulthood: the Childhood Determinants of Adult Health Study and the Bogalusa Heart Study

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