Assessing the impact of semen quality on embryo development in an egg donation model

Lusine Aghajanova, M.D., Ph.D.,[a,b] Chia-Ning Kao, M.S.,[a] Marcelle Cedars, M.D.,[a] and Nam Tran, M.D., Ph.D.[a]

[a] Division of Reproductive Endocrinology and Infertility, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, and [b] Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Stanford School of Medicine, Sunnyvale, California

Objective: To investigate if any of the World Health Organization semen parameters and/or male age are associated with embryo development.
Design: Retrospective chart review between January 2008 and May 2015.
Setting: Academic fertility practice.
Patients: Anonymous egg donors aged $\leq$30 years.
Interventions: Chart review.
Main Outcome Measures: Sperm parameters were evaluated on a continuum and were dichotomized to determine if low values (strict morphology $<$ 4%, concentration $< 15 \times 10^6$, low motility $<$ 40%) or older age ($>$50 years) are associated with embryo morphology. Repeated linear regression measures to determine the associations and multivariate testing to determine independent effects for each predictor were performed.
Results: Three hundred eighty-four donors with 574 egg donation cycles were identified, and 205 subjects with 275 cycles were included in the final analysis. The mean donor age was 25.31 $\pm$ 2.81 years, with a mean antral follicle count of 28.09 $\pm$ 10.5. The mean male age was 43.25 $\pm$ 6.65 years. The mean World Health Organization semen parameters at fertilization were $55.8 \times 10^6 \pm 44.3 \times 10^6$/mL concentration, 44.8% $\pm$ 20.2% motility, and 6.9% $\pm$ 5.3% strict morphology. Neither male age nor sperm morphology was associated with embryo morphology. A low total motile count was significantly associated with a higher cell number in day-3 embryos and a 1.56-times higher chance of poor day-3 cell symmetry. There was no statistically significant difference in blastocyst formation, clinical pregnancy, or live-birth rates.
Conclusions: Although statistically significant, the effect of the low total motile count on day-3 cell number and cell symmetry are likely clinically insignificant. Male age, race, or poor sperm morphology were not associated with a poor cycle outcome or impaired embryo development. The use of intracytoplasmic sperm injection likely alleviates the negative effect of diminished semen quality on treatment outcome. (Fertil Steril Rep® 2021;2:22–9. ©2020 by American Society for Reproductive Medicine.)
Key words: Semen quality, embryo development, blastocyst, pregnancy outcome, male age, total motile count

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Embryo quality is one of the most important and established factors determining the success of in vitro fertilization (IVF)—an embryo transfer program (1–3). Oocyte quality, a key factor in female fertility, has a crucial role in fertilization and subsequent embryo development (4–7). The quality of the oocytes is determined mainly by nuclear content, mitochondrial function, and cytoplasmic maturity, all of which depend on age, causes of infertility, and microenvironment provided by the ovary and preovulatory follicle that may modify translation, which in turn may depend on types of ovarian stimulation and cause of infertility (8–10).

Although several studies have indicated a close relationship between oocyte and embryo qualities, the contribution of spermatozoa to early embryo development has been less clear. It was shown a few years ago that fertilization rate, embryo quality, and pregnancy rates are inversely associated with a high number of immature spermatozoa and aneuploidy rates (11, 12). The fertilization rates and embryo quality decreased as sperm DNA fragmentation or protamine

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Correspondence: Lusine Aghajanova, M.D., Ph.D., Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Stanford University School of Medicine, 1195 West Fremont Avenue, Sunnyvale, California 94087 (E-mail: aghajano@stanford.edu).

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concentration increased with age or infertility (13, 14). The same group showed that increased sperm DNA damage adversely affects embryo quality at all stages of development, resulting in reduced implantation rates (IRs) and pregnancy outcomes (15). Several meta-analyses were able to demonstrate that high sperm DNA fragmentation negatively affects clinical pregnancy rates (CPRs) in assisted reproductive technologies (ART) cycles and is associated with an increased miscarriage rate (16–18). However, another meta-analysis and the American Society for Reproductive Medicine practice guidelines do not currently recommend routine sperm DNA integrity testing in patients undergoing IVF (19, 20), and this testing is not offered in fertility clinics on a routine basis. Importantly, a recent report showed no effect of semen parameters on IVF or intracytoplasmic sperm injection (ICSI) treatment and obstetrical outcomes in cycles with vitrified frozen donor eggs, such as IR, CPR, live-birth rate (LBR), low-birth-weight and preterm deliveries (21).

The effect of paternal age on ART outcome has been addressed repeatedly over the years, and overall, the data are mostly indicative of paternal age having no significant effect on treatment outcome. This was recently confirmed by Begueria et al. (22), who showed no difference in reproductive outcomes (biochemical pregnancy rate, miscarriage rate, CPR, ongoing pregnancy rate, and LBR) among different male age groups in egg donation cycles. Additionally, Capelouto et al. (21), similarly, found no difference in IVF cycle outcomes in 949 frozen donor egg-recipient cycles when controlled for potential confounders. Likewise, the age of sperm donors $\leq$45 years old had no effect on LBR and miscarriage rate in ART treatment (23). Some studies have reported that an increased paternal age leads to an increased risk of single-gene mutations and some congenital malformations, including trisomy 21, Apert syndrome, achondroplasia, schizophrenia, Marfan syndrome, retinoblastoma, multiple endocrine neoplasia type 2, autism, and bipolar disorder. However, the risk is still low and has not been confirmed by other studies (24–26). Of note, no significant effect of paternal age on imprinting has been demonstrated thus far.

On the other hand, although it is well established that semen volume, sperm motility, and sperm morphology decrease with increasing male age, data concerning sperm concentration are conflicting (24, 27). A recent study has shown that for every 5 years of male age, sperm volume decreases, concentration increases, and sperm motility decreases (22). Few studies have analyzed the effect of male age on embryo morphology. Frattarelli et al. (27) showed that in an oocyte donor model, male age >50 years significantly affects pregnancy outcomes and blastocyst formation rates; however, the initial embryo morphology through cleavage stage is not affected. Using a model of oocyte donation cycles, in which eggs from 1 donor were split between 2 recipients or sperm sources, Salumets et al. (28) showed that the only observed effect of sperm was the positive association of strict sperm morphology with a blastomere cleavage rate. This study, however, did not report the sperm age, and ICSI cycles were not included. A case-control study using sibling donor oocytes demonstrated no significant effect of complete teratospermia on fertilization rate, pregnancy rate, and pregnancy outcomes in ICSI cycles (29).

Thus, based on the available literature, we recognized the gap remaining in our understanding of a potential correlation between the basic semen parameters, routinely assessed in any fertility clinic worldwide, and embryo quality and thus, treatment outcome.

Therefore, in the present study we aimed to investigate if any of the World Health Organization semen parameters and/or male age were associated with embryo development in ART cycles using an oocyte donation model where the egg quality was normalized to assess the isolated impact of sperm on embryo quality. To increase the significance and power of our study, we included repeated oocyte donors using different sources of semen.

MATERIALS AND METHODS

This study was performed under the approval of the University of California San Francisco institutional review board. A retrospective chart review was performed on all oocyte donors who presented to the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, from January 2008 through May 2015.

The inclusion criteria were as follows: donor age $\leq$30 years for anonymous donors and <32 years for known donors; fresh donor egg cycles only; embryo transfer performed; use of ejaculated partner sperm or donor sperm; antagonist or long lupron ovarian stimulation protocols; and complete semen parameter data, including total motile count (TMC) and sperm morphology. All the donors were screened according to the Food and Drug Administration guidelines. The exclusion criteria were as follows: surgical sperm retrieval; female donor age >30 years for anonymous donors and >32 years for known donors; frozen donor eggs; cycles that did not result in egg retrieval or embryo transfer and cancelled cycles; cycles with missing key data; or cycles in which the female recipient had a known uterine factor. Due to the anonymity of the sperm donors, their age and race data were not available. No genetic testing before implantation was performed on the embryos included in the study. The best-quality embryo was transferred first. The embryo quality was determined using the grading by Gardner's criteria (30, 31). Supernumerary embryos were frozen by the vitrification method for future use.

All the sperm samples were analyzed by a certified andrologist using standard laboratory procedures according to the World Health Organization guidelines (2010): volume > 1.5 mL, concentration > 15 $\times$ 10^6/mL, progressive motility > 40%, strict morphology > 4%. For the frozen sperm samples, semen parameters before the freeze were obtained.

Our primary outcome was embryo morphology on day 3 and days 5–6 (blastocyst stage). Of note, although all the embryos were intended to be cultured until the blastocyst stage, the embryo quality was checked on day 3, per clinic policy. The secondary outcomes were fertilization rate (number of fertilized eggs per total number of eggs), 2 pronuclei (2PN)

formation rate (number of normally fertilized eggs (2PN) per number of fertilized eggs), blastocyst conversion rate, IR (number of gestational sacs per transfer), CPR (presence of gestational sac per transfer), and LBR (occurrence of live birth per transfer). Data retrieval was performed with random cross-sampling of the data as quality control.

Statistical Analysis

The study's purpose was to investigate the relationship between sperm characteristics, specifically TMC and morphology, with the previously listed outcomes. Sperm TMC and morphology were grouped into normal and abnormal categories. For TMC, normal was defined as $\geq 10 \times 10^6$ and abnormal as $<10 \times 10^6$. A morphology of $\geq$4% was defined as normal and <4% as abnormal. To control potential confounding effects, all models were controlled for sperm age, IVF/ICSI, fresh vs. frozen sperm, stimulation protocol, follicle-stimulating hormone dose, and peak estradiol level. In addition, all the models included a nested within-subject effect to account for repeated measures. For continuous outcomes, an analysis of covariance model with a nested within-subject effect was used. For binary outcomes, a logistic regression model with a nested within-subject effect was used. Summary statistics were included as appropriate. All tests was performed at a 0.05 level of significance. SAS Windows 32-bit v9.4 was used for all statistical analyses.

RESULTS

Demographics

The basic demographic characteristics of the egg donors and male subjects are presented in Table 1. The semen samples were grouped based on their TMC and morphology into the following groups: abnormal TMC/abnormal morphology (Abn TMC/abn morph), abnormal TMC/normal morphology (Abn TMC/nl morph), normal TMC/abnormal morphology (Nl TMC/abn morph), and normal TMC/normal morphology (Nl TMC/nl morph).

The initial number of subjects meeting the inclusion criteria identified through a database was 384, with 574 egg donation cycles. After excluding the cancelled cycles (n = 40), cycles where the embryos were frozen at 2PN stage (n = 2) or where no fertilization occurred (n = 1), cycles using surgically retrieved sperm (n = 7), and cycles with missing clinical information (n = 249), a total of 205 subjects with 275 cycles were included in the final analysis (Fig. 1). One hundred sixty subjects (78.05%) undergwent only 1 oocyte donation cycle, whereas 45 subjects underwent $\geq$2 egg donation cycles (28 subjects underwent 2 cycles, 13 underwent 3 cycles, 1 underwent 4 cycles, 2 underwent 5 cycles, and 1 donated 6 times). Only ejaculated sperm was used. All multiple pregnancies were twin gestations.

There was no statistically significant difference in the egg donor characteristics, including donor age, baseline antral follicle count, infertility diagnosis/reason to use donor egg, type of stimulation protocol, gonadotropin dose used for stimulation, peak estradiol levels, or type of trigger, between the groups. There were no differences in the male age or race among the groups (Table 1).

Effect of Semen Parameters on Fertilization Rate and 2PN Formation Rate

The total number of eggs retrieved, number of mature eggs, fertilization rate, 2PN formation rate, and blastocyst conversion rate with regard to the semen parameters are presented in Table 2. There was no statistically significant difference in the total number of follicles, number of eggs retrieved, number of mature eggs, number of fertilized eggs, number of normally fertilized eggs (2PN), and blastocyst conversion rate among all 4 groups based on semen characteristics such as TMC and sperm morphology (Table 3). There was no association found between male age and any of the parameters above.

Effect of Semen Parameters on Embryo Quality

The effects of specific male partner characteristics on embryo morphology are presented in Tables 2 and 3. There was no association between male age and embryo morphology (data not shown). No significant association was found between any semen parameter (volume, concentration, motility [TMC], or morphology) on a continuum with embryo morphology on day 3 or days 5–6. However, low TMC was significantly associated with a higher chance of having day-3 embryos with a higher cell number (predicted difference 0.32 [95% confidence interval 0.01, 0.64], P=.04) and 1.56 times more likely to have poor day-3 cell symmetry (odds ratio 1.56 [95% confidence interval 1.11, 2.21], P=.01, Table 3). Nonetheless, this has not been associated with any significant difference in blastocyst conversion rate, good-quality blastocyst conversion rate, and quality of blastocysts themselves based on inner cell mass and trophectoderm grading.

Effect of Semen Parameters on Cycle and Pregnancy Outcome

Overall, no significant effect was observed on IR or pregnancy rate in the cycles that resulted in an embryo transfer (Table 3). Subsequently, no significant differences were observed in the miscarriage rate, CPR, or LBRs with regard to TMC and sperm morphology (Table 3). When we repeated the analysis with the TMC values at $<5 \times 10^6$ and $<2 \times 10^6$ and morphology values at <2% and <1% to account for the effect of extreme values, we were not able to detect any significant differences in the pregnancy outcome measures after adjusting for confounders; however, the numbers were very small at these extreme values (data not shown).

DISCUSSION

To the best of our knowledge, this is the first study analyzing the possible impact of semen parameters on embryo morphology at the cleavage and blastocyst stages using a donor oocyte model in detail. In addition, we analyzed the potential effect of semen parameters and male age on IVF cycle outcomes and pregnancy outcomes.

TABLE 1

Oocyte donor demographics and cycle characteristics, as well as male or sperm donor demographics and semen parameters (n = 275).

OOCYTE DONORS	**Overall n = 275**	**Abn TMC/abn morph n = 37**	**Abn TMC/nl morph n = 14**	**Nl TMC/abn morph n = 84**	**Nl TMC/nl morph n = 140**
Age, mean ± SD	25.31 ± 2.81	26.22 ± 2.48	26 ± 2.51	25.23 ± 2.95	25.04 ± 2.93
Baseline AFC, mean ± SD	28.09 ± 10.5	21.1 ±7.16	20.07 ± 8.84	19.73 ±7.41	35.79 ± 15.83
FSH dose, mean ± SD	2273.71 ± 794.95	2182.5 ± 692	2475 ± 1121.24	2249.09 ± 797.48	2291.06 ±784.3
Peak estradiol level, mean ± SD	3499.59 ± 1422.85	3583.75 ± 1601.95	3337.79 ± 1449.96	3580.08 ± 1596.27	3445.45 ± 1263.92
Number of follicles, mean ± SD	26.95 ± 11.49	26.97 ± 12.51	26 ± 8.25	26.33 ± 11.35	27.42 ± 11.66
Race, n (%)					
Caucasian	54 (19.4)	6 (16.2)	4 (28.6)	23 (27.4)	22 (15.7)
Black	2 (0.7)	0	1 (7.1)	0	1 (0.7)
Asian	39 (14.2)	5 (13.5)	2 (14.3)	7 (8.3)	25 (17.9)
Hispanic	4 (1.4)	2 (5.4)	0	0	2 (1.4)
Unknown	176 (64.1)	24 (64.9)	7 (50)	54 (64.3)	90 (64.3)
Recipient diagnosis, n %					
Age-related DOR	267 (97.1)	36 (97.3)	14 (100)	83 (98.8)	134 (95.7)
POI	7 (2.5)	1 (2.7)	0	1 (1.2)	5 (3.6)
Turner's syndrome	1 (0.4)	0	0	0	1 (0.7)
Stimulation protocol, n (%)					
Long luteal	201 (73.1)	30 (81.1)	9 (64.3)	66 (78.6)	96 (68.6)
Antagonist	74 (26.9)	7 (18.9)	5 (35.7)	18 (21.4)	44 (31.4)
Trigger type, n (%)					
HCG	247 (91.1)	31 (86.5)	13 (92.9)	79 (9)	126 (90)
LH agonist ± HCG	24 (8.9)	5 (13.5)	1 (7.1)	5 (6)	14 (10)
MALE/SPERM DONOR	**Overall, n = 275**	**Abn TMC/abn morph n = 37**	**Abn TMC/nl morph n = 14**	**Nl TMC/abn morph n = 84**	**Nl TMC/nl morph n = 140**
Age, mean ± SD	43.25 ±6.65	45.35 ±7.81	51.57 ±8.1	43.32 ±5.74	41.81 ±5.92
Race, n (%)					
Caucasian	119 (43.3)	17 (46)	8 (57.2)	36 (42.8)	58 (41.4)
Black	1 (0.4)	0	0	0	1 (0.7)
Asian	36 (13.1)	3 (8.1)	1 (7.1)	13 (15.5)	19 (13.6)
Hispanic	8 (2.9)	2 (5.4)	0	2 (2.4)	4 (2.9)
Unknown	111 (40.3)	15 (40.5)	5 (35.7)	33 (39.3)	58 (41.4)
IVF or ICSI, %					
IVF	51 (18.5)	0	0	6 (7.1)	45 (32.2)
ICSI	182 (66.2)	36 (97.3)	13 (92.9)	68 (80.9)	65 (46.4)
IVF/ICSI split	42 (15.3)	1 (2.7)	1 (7.1)	10 (12)	30 (21.4)

Note: No significant differences were observed when grouping by semen parameters (< .05). Continuous variables are presented as mean ± SD; categorical variables are presented as n (%). Age and race information is not available for anonymous donors. HCG = human chorionic gonadotropin; LH = luteinizing hormone; AFC = antral follicle count; FSH = follicle-stimulating hormone; DOR = diminished ovarian reserve; POI = primary ovarian insufficiency; TMC = total motile count; morph = morphology; 2PN = 2 pronuclei (normal fertilization).

Abn/abn TMC/morph: Both TMC and morphology of sperm are abnormal (TMC $< 10 \times 10^6$; morphology < 4%).

Abn/nl TMC/morph: TMC abnormal, morphology normal (TMC $< 10 \times 10^6$; morphology > 4%).

Nl/abn TMC/morph: TMC normal, morphology abnormal (TMC $> 10 \times 10^6$; morphology < 4%).

Nl/nl TMC/morph: Both TMC and morphology are normal (TMC $> 10 \times 10^6$; morphology > 4%).

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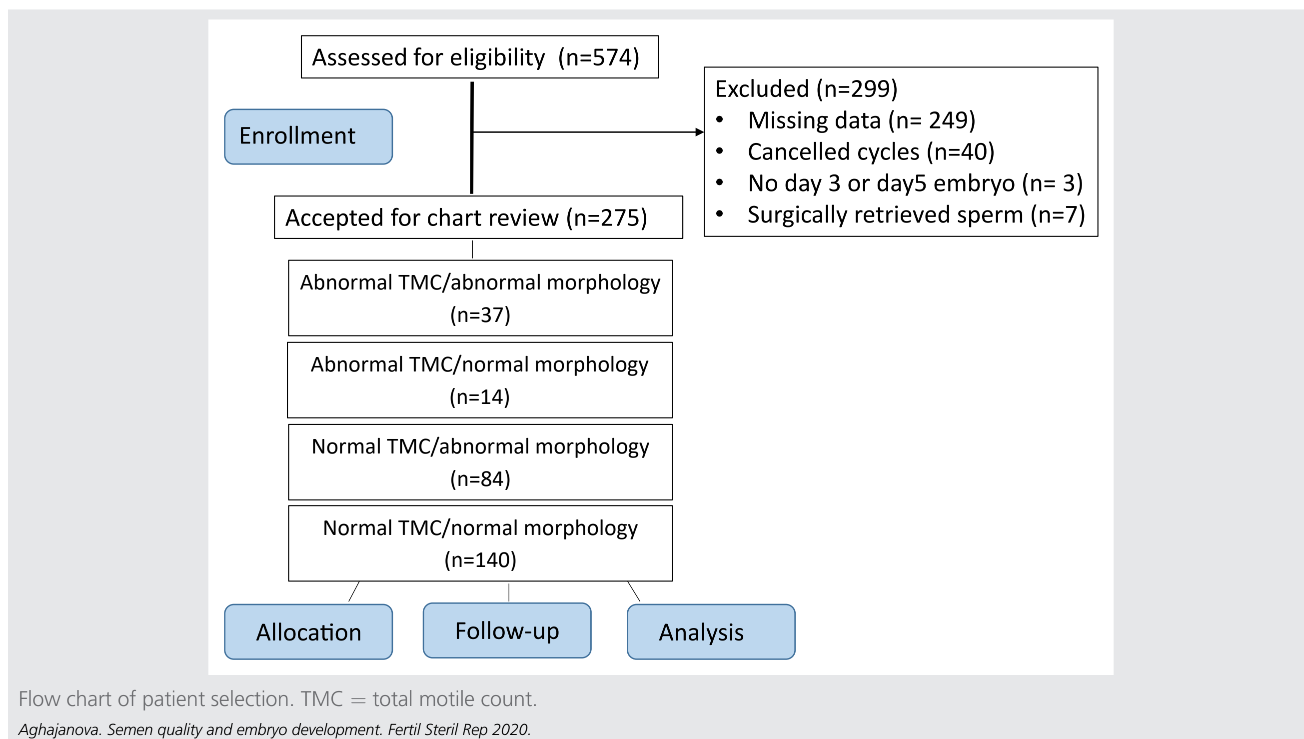
FIGURE 1



Flow chart of patient selection. TMC = total motile count.

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Most studies to date have focused on the correlation between sperm DNA fragmentation, oxidative stress, and hyaluronan-binding ability and IVF outcome (32–36). However, these tests are not performed routinely in fertility clinics around the world; therefore, the value of the data may be limited in general practice. In contrast, we performed a comprehensive correlation analysis between the commonly analyzed semen parameters and embryo morphology. We believe that this will provide valuable information to any IVF clinicfor daily practice. We used TMC as a single composite comparison because recent data has shown that it has a superior predictive value for treatment outcome in ICSI cycles compared to different World Health Organization 2010 cutoff values in a semen analysis and correlates well with the formation of high-quality embryos and pregnancy outcome (37).

In our study, we did not find any effect of paternal age on treatment outcomes, which is in line with previous reports (21, 22). A recent meta-analysis demonstrated no association of advanced paternal age with adverse outcomes in oocyte donation model, including fertilization, cleavage, implantation, pregnancy, miscarriage, and LBRs (38). Similarly, the ongoing pregnancy rate at 8 weeks in the first IVF/ICSI cycles was not affected by paternal age (39). This suggests that when ICSI is implemented for poor sperm quality, it can overcome the low reproductive potential of not only abnormal but also older sperm. In our study, according to the common guidelines, most of the cases with low TMC and/or abnormal morphology used ICSI.

We found that poor TMC is associated with an increased number of day-3 embryos with more blastomeres and poor symmetry. However, this did not translate into a poorer day-5 embryo quality or lower pregnancy rates. Pregnancy outcomes, such as CPR, miscarriage rate, or LBR, were unaffected. Therefore, the clinical significance of these statistically significant data is minimal. A recent study by Capelouto et al. (21) has also demonstrated that poor semen parameters have no detrimental effect on IRs, CPRs, and LBRs when ICSI is used in frozen oocyte donor cycles. Moreover, they showed that abnormal semen parameters have no effect on preterm birth rates and rate of low-birth-weight infants (21).

In summary, the main goal of this study was to assess the potential effect of abnormal semen parameters on embryo morphology and subsequently correlate this with cycle outcomes. An assessment of embryo aneuploidy was outside of the scope of the current study and is not routinely used in our clinic in donor egg cycles. There have been previous data showing that severe male factors can be associated with an increased aneuploidy risk, which is potentially related to an underlying cause of male infertility rather than the ICSI procedure (40, 41). On the other hand, a high DNA fragmentation index was not associated with an increased aneuploidy risk or pregnancy rates and pregnancy loss (42). Analysis of a large number of IVF/ICSI cycles, including those using surgically retrieved sperm, showed that a severe male factor can affect fertilization rate and embryo development; however, no correlation was observed between male factor and embryo euploidy rate, with similar miscarriage rate and LBRs (43).

TABLE 2

Cycle and embryo characteristics, overall and by semen parameters, n = 275.

	Overall, n = 275	Abn TMC/abn morph n = 37	Abn TMC/nl morph n = 14	Nl TMC/abn morph n = 84	Nl TMC/nl morph n = 140
Number of eggs retrieved, mean ± SD	22.5 ± 10.6	22.05 ± 12.46	22.14 ± 9.21	21.4 ± 9.85	23.31 ± 10.67
Number of MII eggs[a], (n) mean ± SD	(222) 15.91 ± 8.95	(36) 18.03 ± 10.9	(14) 17.14 ± 8.74	(79) 16.13 ± 8.79	(93) 14.71 ± 8.22
Number of fertilized eggs, mean ± SD	15.33 ± 8.6	14.89 ± 10.07	15.71 ± 7.3	14.62 ± 7.71	15.84 ± 8.86
Number of 2PN embryos, mean ± SD	14.19 ± 8.14	14.16 ± 9.93	14.64 ± 7.01	13.75 ± 7.39	14.41 ± 8.22
Fertilization rate, mean ± SD	0.68 ± 0.18	0.68 ± 0.17	0.73 ± 0.16	0.69 ± 0.19	0.68 ± 0.18
2PN rate, mean ± SD	0.93 ± 0.1	0.94 ± 0.08	0.94 ± 0.08	0.94 ± 0.11	0.91 ± 0.1
Blastocyst conversion rate, mean ± SD	0.81 ± 0.22	0.74 ± 0.21	0.84 ± 0.13	0.83 ± 0.18	0.8 ± 0.25
Day-3 embryos, (n) mean ± SD	(3760) 7.62 ± 2.12	(512) 7.91 ± 2.08	(205) 8.02 ± 2.03	(1081) 7.58 ± 2.13	(1962) 7.52 ± 2.13
Cell number, mean ± SD	7.62 ± 2.12	7.91 ± 2.08	8.021 ± 2.03	7.58 ± 2.13	7.52 ± 2.13
Severe fragmentation[b], n (%)	1031 (27.7)	148 (29.0)	65 (31.7)	307 (28.5)	511 (26.0)
Poor symmetry, n (%)	559 (15)	96 (18.9)	30 (14.6)	135 (12.6)	298 (15.4)
Day 5 embryos					
Arrested, morula, or early blast, n (%)	1233 (53.1)	168 (55.5)	89 (56.0)	376 (55.1)	600 (51.0)
Poor ICM, n (%)	197 (22.1)	35 (27.0)	6 (16.2)	60 (23.7)	96 (20.4)
Poor TE, n (%)	316 (32.0)	47 (33.1)	23 (48.0)	91 (32.7)	155 (29.8)
Presence of gestational sac fresh ET + first FET, n (%)	241 (88.3)	32 (86.5)	11 (78.6)	76 (90.5)	122 (88.4)
Miscarriage, n (%)	43 (16.2)	8 (21.6)	2 (16.7)	10 (12.1)	23 (17.3)
Live birth, n (%)	129 (52.9)	19 (54.3)	7 (63.7)	43 (55.1)	60 (50.0)
FET pregnancy, n (%)	61 (65.6)	6 (46.2)	3 (60.0)	22 (71.0)	30 (68.2)

TMC = total motile count; morph = morphology; MII = mature eggs; 2PN = two pronuclei (normal fertilization); ICM = inner cell mass; TE = tropectoderm; ET = embryo transfer; FET = frozen embryo transfer.
Abn/abn TMC/morph: Both TMC and morphology of sperm are abnormal (TMC $< 10 \times 10^6$; morphology < 4%).
Abn/nl TMC/morph: TMC abnormal, morphology normal (TMC $< 10 \times 10^6$; morphology > 4%).
Nl/abn TMC/morph: TMC normal, morphology abnormal (TMC $> 10 \times 10^6$; morphology < 4%).
Nl/nl TMC/morph: Both TMC and morphology are normal (TMC $> 10 \times 10^6$; morphology > 4%).
[a] Data available for ICSI cycles only
[b] Severe fragmentation is defined as >25%

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TABLE 3

Statistical analysis of overall cycle outcome in donor oocyte cycles based on semen parameters.

Cycle parameters	Sperm TMC abnormal vs. normal		Sperm morphology abnormal vs. normal	
	[a]Predicted difference (95% CI)	P value	[a]Predicted difference (95% CI)	P value
D3 cell number	0.32 (0.01, 0.64)	.04*	0.03 (−0.27, 0.33)	.85
Fertilization rate	0 (−0.05, 0.06)	.87	0 (−0.04, 0.05)	.87
2PN formation rate	−0.02 (−0.04, 0.01)	.27	0 (−0.02, 0.03)	.86
Blastocyst conversion rate—good quality	−0.06 (−0.14, 0.02)	.16	−0.06 (−0.13, 0.01)	.10
Blastocyst conversion rate —all	−0.07 (−0.15, 0.02)	.11	−0.01 (−0.07, 0.06)	.87
	[b]Odds ratio (95% CI)	P value	[b]Odds ratio (95% CI)	P value
D3 fragmentation	1.07 (0.71, 1.63)	.75	1.01 (0.74, 1.37)	.97
D3 cell symmetry	1.56 (1.11, 2.21)	.01*	0.97 (0.71, 1.3)	.82
D5 blastocyst development	1.02 (0.68, 1.52)	.92	1.21 (0.88, 1.66)	.24
D5 ICM	1.03 (0.59, 1.79)	.92	1.27 (0.76, 2.14)	.36
D5 TE	1.25 (0.74, 2.11)	.40	1.07 (0.68, 1.69)	.77
Gestational sac	1.42 (0.57, 3.52)	.45	0.58 (0.26, 1.30)	.18
Miscarriage rate	1.73 (0.71, 4.22)	.23	0.60 (0.29, 1.24)	.17
CPR after FET	2.51 (0.77, 8.19)	.13	1.16 (0.41, 3.34)	.78
Live-birth rate	0.88 (0.42, 1.81)	.72	0.70 (0.4, 1.24)	.23

Note: Predicted differences/odds ratio generated by comparing abnormal versus normal sperm parameters.
TMC = total motile count; CI = confidence interval; D3 = day 3; D5 = day 5; ICM = inner cell mass; TE = trophectoderm; CPR = clinical pregnancy rate; FET = frozen embryo transfer; IVF = in vitro fertilization; ICSI = intracytoplasmic sperm injection; FSH = follicle-stimulating hormone.
[a] Analysis of covariance model controlling for sperm age, IVF/ICSI usage, stimulation protocol, FSH dosage, and peak estradiol level. Within-patient effects were accounted for when appropriate.
[b] Logistic regression model controlling for sperm age, IVF/ICSI usage, stimulation protocol, FSH dosage and peak estradiol level. Within-patient effects were accounted for when appropriate.
* Statistical significance at the.05 level of significance.

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These data are so far reassuring, in that, abnormal male parameters do not correlate with abnormal pregnancy outcomes.

Strengths and limitations

The strengths of the current study include the relatively large number of donor egg cycles, including repeated donor cycles. We used TMC and sperm morphology as commonly used parameters of semen quality, which is done and can be done in any fertility laboratory around the world, regardless of resources, which makes the data usable for a larger audience. For the same reason, we excluded cycles with surgically retrieved sperm. We also did not include the cycles in which aneuploidy screening of the embryos was performed, especially because this is not a common practice in many clinics when using young donor oocytes and is not recommended by the American Society for Reproductive Medicine. The robust statistical analysis allowed for proper accounting of multiple cycles from repeat donors while controlling for potential confounders, such as sperm age, race, stimulation protocol, peak estradiol level, and others. The use of a donor oocyte model to control egg quality is a strength but also represents a limitation because more subtle effects of abnormal sperm quality may be more apparent in patients with poorer-quality oocytes, thus potentially making the current data not quite applicable to everyone in the general patient population with IVF.

In conclusion, we demonstrated that a commonly and widely used semen quality assessment, such as TMC, does not have a significant impact on embryo morphology at the blastocyst stage when using a fresh donor oocyte model. In addition, there is no significant effect on treatment outcomes, such as CPR, miscarriage rate, or LBR. We also did not find any significant effect of paternal age on IVF cycle outcome.

Although the donor oocyte model was purposefully used to normalize for egg quality and dissect out the sperm effect on the outcome, we realize that this is not an ideal model, and hence, generalization of the results to all patients with IVF should be made with caution. Nevertheless, we are hopeful that this information will provide an additional valuable data point to fertility specialists worldwide when counseling couples on treatment planning and benefits of ICSI.

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