Optimization of IVF pregnancy outcomes with donor spermatozoa

Jeff G. Wang · Nataki C. Douglas · Robert Prosser ·
Daniel Kort · Janet M. Choi · Mark V. Sauer

Received: 15 June 2008 / Accepted: 30 December 2008 / Published online: 28 January 2009
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Abstract

Purpose To identify risk factors for suboptimal IVF outcomes using insemination with donor spermatozoa and to define a lower threshold that may signal a conversion to fertilization by ICSI rather than insemination.

Method Retrospective, age-matched, case-control study of women undergoing non-donor oocyte IVF cycles using either freshly ejaculated ($N=138$) or cryopreserved donor spermatozoa ($N=69$). Associations between method of fertilization, semen sample parameters, and pregnancy rates were analyzed.

Results In vitro fertilization of oocytes with donor spermatozoa by insemination results in equivalent fertilization and pregnancy rates compared to those of freshly ejaculated spermatozoa from men with normal semen analyses when the post-processing motility is greater than or equal to 88%. IVF by insemination with donor spermatozoa when the post-processing motility is less than 88% is associated with a 5-fold reduction in pregnancy rates when compared to those of donor spermatozoa above this motility threshold. When the

post-processing donor spermatozoa motility is low, fertilization by ICSI is associated with significantly higher pregnancy rates compared to those of insemination.

Conclusion While ICSI does not need to be categorically instituted when using donor spermatozoa in IVF, patients should be counseled that conversion from insemination to ICSI may be recommended based on low post-processing motility.

Keywords Donor sperm · Fertilization · ICSI · Insemination · IVF · Pregnancy

Introduction

Assisted reproductive technology (ART) using cryopreserved donor spermatozoa is a widely available treatment for couples with severe male infertility (azoospermia) or for patients without male partners desiring pregnancy. While donor spermatozoa are commonly utilized for intrauterine insemination, concomitant female factors such as tubal disease or diminished ovarian reserve may require that donor spermatozoa be used for in vitro fertilization (IVF). In this setting, there is a paucity of information on whether intracytoplasmic sperm injection (ICSI) of cryopreserved donor spermatozoa can increase fertilization or pregnancy rates when compared to traditional insemination. As a result, when using donor spermatozoa, a variety of approaches to practice exist, with some centers performing insemination while others recommending ICSI.

The existing literature suggests that the cryopreservation methods used for the storage of donor spermatozoa do not significantly compromise pregnancy rates when used to inseminate oocytes for IVF(1–4). Although both the initial

Capsule In vitro fertilization of oocytes with donor spermatozoa by insemination results in equivalent fertilization and pregnancy rates compared to those of freshly ejaculated spermatozoa from men with normal semen analyses when the post-processing motility is greater than or equal to 88%. Below this threshold, pregnancy rates are low, and ICSI should be considered.

J. G. Wang (✉) · N. C. Douglas · R. Prosser · D. Kort ·
J. M. Choi · M. V. Sauer
Department of Obstetrics and Gynecology,
Division of Reproductive Endocrinology and Infertility,
College of Physicians and Surgeons, Columbia University,
1790 Broadway, 2nd Floor,
New York, NY 10019, USA
e-mail: jw781@columbia.edu

and post-processing concentration and motility of donor spermatozoa are generally lower than those of freshly ejaculated spermatozoa, it is believed that the impact on pregnancy rates is negligible. Nonetheless, the concentration and motility of donor spermatozoa can vary widely upon thawing. At this time, there are no known parameters to identify those at risk of poor treatment outcomes. Thus, when a mild to moderately abnormal donor specimen is encountered post-thaw, the decision to convert from insemination to ICSI remains relatively subjective.

In this study, we retrospectively compared the fertilization rates and pregnancy outcomes of IVF cycles that used donor spermatozoa for oocyte insemination against rates obtained during routine IVF in which freshly ejaculated spermatozoa from men without male factor infertility was used. Our aims were to identify predictors of poor outcomes with donor spermatozoa and to define a lower threshold that may signal a conversion to fertilization by ICSI rather than insemination. Lastly, we attempted to verify the efficacy of ICSI by comparing the outcomes of those IVF cycles identified to be at risk for poor outcomes using insemination to those of cycles in which ICSI was utilized because of similar risks factors.

Materials and methods

During the time period between January 1, 2006 and December 31, 2007, all cases of fresh non-donor oocyte IVF cycles using commercially purchased donor spermatozoa for traditional insemination or ICSI were retrospectively identified. All donor semen were obtained from sperm banks and prepared using standard cryopreservation techniques intended for intra-cervical insemination (ICI). Clinical indications included male partners with non-obstructive azoospermia, same sex couples, and single women without male partners desiring pregnancy.

IVF cycle information for all cases and controls were jointly stored in a clinical database chronologically sorted by cycle start dates. For each case of IVF using insemination with donor spermatozoa (Group A), the next two controls in the database (Group B) who matched the identified case by age were included in the analysis for comparison. Controls were selected from patients who underwent fresh non-donor oocyte IVF cycles with insemination of freshly ejaculated spermatozoa obtained from their male partners (Fig. 1). Semen analyses for all male partners were performed by the same andrology laboratory prior to the IVF cycle and showed concentrations greater

Fig. 1 Patient-group flow chart. Between 2006–2007, there were 111 fresh non-donor oocyte IVF cycles that used commercial donor spermatozoa. Of these cycles, fertilization occurred by routine insemination in 69 cycles (**Group A**) and by ICSI in 42 cycles. The age-matched control group consisted of 138 (2:1 ratio) cycles of fresh non-donor oocyte IVF during the same time period that used freshly ejaculated spermatozoa (**Group B**). Fertilization in the control group also occurred by insemination, and normal semen analyses were documented in the male partners prior to the treatment cycle. Post-processing motility of less than 88% was identified as a possible

predictor of poor pregnancy outcomes when using donor spermatozoa for insemination in IVF cycles. Group A was divided into those with post-processing motility of $\geq 88\%$ (**Group A1**) and those with $< 88\%$ (**Group A2**) for further analysis. Of the 42 cases of IVF using donor spermatozoa where insemination was converted to ICSI based on the recommendation of the andrologists, there were 36 cases where the post-processing motility was $< 88\%$ (**Group C**). The remaining six cases were excluded from the analysis because the post-processing spermatozoa motility was greater than or equal to 88% in each case

than 20 million spermatozoa per milliliter, motility greater than 50%, and Kruger morphology greater than 14%. Case-control matching by age and by cycle start date was intended to minimize the potential biases resulting from age-associated decline in oocyte quantity and quality and from unrecognized temporal variations in laboratory and culture conditions, respectively.

Additionally, all cases of IVF using donor spermatozoa where conversion from insemination to ICSI as a result of suboptimal post-thaw spermatozoa parameters were identified from the same study period (Fig. 1). Since no uniform criteria for poor quality donor specimen were objectively defined during this time, recommendations for conversion to ICSI in these cases were based on the clinical experience of the andrologists.

Standard protocols for controlled ovarian hyperstimulation (COH) with gonadotropins were used for all patients. Pituitary suppression was achieved either with two weeks of leuprolide acetate preceding COH or with a GnRH antagonist administered after five days of COH. Follicular monitoring was performed using serial transvaginal ultrasound and serum estradiol levels. 10,000 units of human chorionic gonadotropin (hCG) were administered when at least three follicles reached a diameter of eighteen millimeters or greater, and transvaginal ultrasound guided oocyte pick-up was performed 34–36 h later.

Freshly ejaculated as well as previously cryopreserved donor spermatozoa were routinely prepared by separation on a density gradient and/or by swim-up from a washed pellet. A standard concentration of 0.1×10^6 motile spermatozoa/ml was used to inseminate the oocytes. Fertilization results were verified within 16–18 h after insemination or microinjection. Embryos were cultured to either the cleavage or the blastocyst stage in proprietary culture medias for day three or day five embryo transfers, respectively. Clinical pregnancy was defined by the presence of a gestational sac on transvaginal ultrasound approximately four weeks after embryo transfer.

Patient age, stimulation, fertilization, and pregnancy outcomes, as well as initial and post-processing spermatozoa parameters were compared between IVF cycles using donor (Group A) and freshly ejaculated spermatozoa (Group B) for oocyte insemination. All continuous variables are summarized as medians with interquartile ranges and compared by the Wilcoxon signed-rank test. Dichotomous outcomes are expressed as percentages with standard deviations and compared using χ^2 or Fisher's exact test when appropriate.

To identify potential associations between spermatozoa quality and treatment outcomes, the initial and post-processing spermatozoa parameters for Groups A and B were collectively stratified and compared by pregnancy outcomes using the Wilcoxon signed-rank test. In addition,

multivariate logistic regression was performed to confirm the predictive value of these parameters controlling for potential confounders. Receiver operating characteristics (ROC) curve and cross tabulation were performed to further define the optimal discriminatory values for the statistically significant covariates.

Finally, the efficacy of ICSI in the setting of suboptimal donor spermatozoa parameters was evaluated by comparing the outcomes of the IVF cycles using donor spermatozoa insemination that were identified to be at the greatest risk for poor pregnancy outcomes to those of a similar patient group whose oocytes were fertilized by intracytoplasmic injection (ICSI) with donor spermatozoa (Group C).

Results

During the study period, there were 69 fresh IVF cycles in which non-donor oocytes were fertilized by insemination with donor spermatozoa (Group A). Using a two to one case-control ratio, 138 women matched by age and cycle start date who underwent fresh non-donor IVF cycles using freshly ejaculated spermatozoa from their partners (Group B) were selected for comparison (Fig. 1). There were no significant differences between the two groups in terms of age. In addition, the total number of oocytes and the number of mature oocytes retrieved were equivalent (Table 1).

The initial concentration ($p < 0.0001$), motility ($p < 0.0001$) and the total number of motile spermatozoa ($p < 0.0001$) were significantly greater in the freshly ejaculated semen compared to those of donor specimens. After processing by swim-up and/or density gradients, higher concentration ($p < 0.0001$), motility ($p < 0.0001$), and total motile spermatozoa count ($p < 0.0001$) were obtained from freshly ejaculated semen compared to those obtained for cryopreserved donor specimens.

Despite the significant differences in spermatozoa parameters, the rates of total and normal fertilization were equivalent between the two groups. IVF cycles using insemination with donor spermatozoa were associated with a significantly greater risk of having no suitable embryos for transfer compared to those cycles inseminated with freshly ejaculated spermatozoa ($18.8 \pm 4.7\%$ vs. $7.2 \pm 2.2\%$, $p < 0.028$). Nevertheless, the number of embryos transferred was equivalent and the pregnancy rates were similar between the two groups, whether adjusted by per retrieval or per embryo transfer. The likelihood of having day five blastocyst transfers was also equivalent.

In the univariate analysis combining donor spermatozoa (Group A) and freshly ejaculated partner sperm (Group B), cycles resulting in pregnancies were associated with higher initial total motile spermatozoa count ($p < 0.021$) and post-

Table 1 Patient characteristics, stimulation, fertilization, and pregnancy outcomes for cycles using partner versus donor Spermatozoa (median, interquartile range)

	(A)	(B)	
<i>Spermatozoa Source</i>	Donor	Freshly Ejaculated	
<i>Fertilization Method</i>	Insemination	Insemination	
	<i>N</i> = 69	<i>N</i> = 138	P-Value
Age	40 (38–42)	40 (37–42)	0.66
Percentage of cycles using GnRH Antagonist *	76.8±5.1	79.1±3.5	0.71
Number of oocytes retrieved	10 (6–15)	11 (7–16)	0.59
Number of mature oocytes	9 (6–14)	10 (6–15)	0.80
Spermatozoa parameters			
Initial concentration (million/ml)	38 (29–46)	50 (34–87)	0.0001
Initial motility (%)	44 (34–51)	60 (53–68)	0.0001
Initial total motile spermatozoa (million)	11 (8–16)	68 (41–101)	0.0001
Post-processing concentration (million/ml)	4 (3–7)	7 (5–10)	0.0001
Post-processing motility (%)	90 (85–93)	97 (94–100)	0.0001
Post-processing total motile spermatozoa (million)	1.0 (0.6–1.4)	4.6 (2.4–9.7)	0.0001
Fertilization rates			
Total (%)	86 (63–100)	86 (75–100)	0.94
Normal (%)	73 (50–83)	73 (57–83)	0.30
Outcomes			
Percentage of cycles without suitable embryos for transfer*	18.8±4.7	7.2±2.2	0.02
Percentage of cycles resulting in day 5 embryo transfers*	23.2±5.7	18.5±3.4	0.54
Number of embryos transferred	3 (2–4)	3 (3–4)	0.22
Pregnancy rate per retrieval (%)*	33.3±5.7	31.9±4.0	1.00
Pregnancy rate per embryo transfer (%)*	41.1±6.6	34.9±4.2	0.16

Summary statistics are expressed in median and interquartile range and compared using the Wilcoxon signed-ranked test unless otherwise specified, *Pearson χ^2 test

processing motility ($p<0.012$) compared to those of cycles that did not result in pregnancies (Table 2). None of the other spermatozoa parameters showed significant associations with pregnancy outcomes. In a multivariate logistic regression model predicting pregnancy outcomes (data not shown), these two covariates, initial total motile spermatozoa ($p<0.017$) and post processing motility ($p<0.030$), remained statistically significant after adjusting for potential confounders such as age, method of pituitary suppression, number of mature oocytes, donor versus partner spermatozoa, blastocyst transfer, and the number of embryos transferred.

Using ROC curves, the initial total motile spermatozoa count demonstrated a significant but low area under the curve (AUC) for predicting pregnancy outcomes (Fig. 2A: AUC=0.602, $p<0.017$). The discriminatory value of the initial total motile spermatozoa was limited to cycles inseminated with freshly ejaculated spermatozoa (Fig. 2B: AUC=0.643, $p<0.006$) and not statistically significant in cycles inseminated with donor spermatozoa (Fig. 2C: AUC=0.548, $p=NS$). In terms of the post-processing motility, the overall AUC combining all IVF cycles inseminated with either donor or partner spermatozoa was also significantly different from 0.5 (Fig. 2D: AUC=0.595, $p<0.025$) for predicting pregnancy outcomes. However, the

post-processing motility only had a significant discriminatory value in donor spermatozoa cycles (Fig. 2F: AUC=0.731, $p<0.002$) and not in IVF cycles inseminated with freshly ejaculated spermatozoa (Fig. 2E: AUC=0.578, $p=NS$). A threshold value of 88% in the post-processing donor

Table 2 Associations between Spermatozoa parameters and clinical pregnancy

	Not Pregnant	Pregnant	P-Value
Sperm Parameters (median, interquartile range)	<i>N</i> = 140	<i>N</i> = 67	
Initial concentration (million/ml)	42 (31–62)	47 (33–81)	.194
Initial motility (%)	56 (45–62)	58 (48–67)	.055
Initial total motile count (million)	40 (13–76)	53 (19–104)	.021
Post-processing concentration (million/ml)	6 (4–9)	6 (4–10)	.953
Post-processing motility (%)	94 (89–98)	96 (93–99)	.012
Post-processing total motile count (million)	2 (1–6)	3 (1–6)	.278

Summary statistics are expressed in median and interquartile range and compared using the Wilcoxon signed-ranked test unless otherwise specified

Fig. 2 Receiver Operating Characteristic Curves for Predicting Pregnancy Outcomes with Initial Total Motile Spermatozoa Count and Post-processing Motility. **(A)** Combining all IVF cycles using donor and partner spermatozoa for oocyte insemination, the initial total motile spermatozoa count demonstrated an area under the curve (AUC) of 0.602 for predicting pregnancy outcomes, significantly different from 0.5 ($p<0.017$). In the subgroup analyses, the discriminatory value was only significant in cycles using freshly ejaculated spermatozoa **(B)**, with an AUC=0.643 ($p<0.006$). The AUC in cycles using donor spermatozoa **(C)** was 0.548 ($p=$ NS). The post-processing motility also demonstrated significant discriminatory value (AUC= 0.595, $p<0.025$) for both groups combined **(D)**. However, the AUC of 0.578 was not significant in the freshly ejaculated spermatozoa subgroup **(E)**. For donor spermatozoa, post processing motility demonstrated a relatively high discriminatory value with an AUC of 0.731 ($p<0.002$). A threshold value of 88% in motility was associated with 80% sensitivity for positive pregnancy and 70% specificity for negative pregnancy

spermatozoa motility was associated with a sensitivity of 80% and a specificity of 70% for predicting positive and negative pregnancy outcomes, respectively (Fig. 2F).

When the 69 IVF cycles using insemination with donor spermatozoa were analyzed by the post processing spermatozoa motility, 45 cycles (Group A1) had motility greater than or equal to 88% while 24 cycles (Group A2) had motility less than the threshold value of 88% defined by the ROC curve (Table 3). The mean age and the number of

mature oocytes did not differ significantly between the two groups. The rates of normal fertilization were the same despite the difference in the post-processing motility. Although there were no significant differences in the number of embryos transferred, the pregnancy rate per retrieval was significantly lower when post processing donor spermatozoa with less than 88% motility were used for insemination compared to those of cycles inseminated with post-processing spermatozoa motility between 88–

Table 3 Comparison of fertilization and pregnancy outcomes by post-processing Spermatozoa motility

	(A1)	(A2)	
<i>Spermatozoa source</i>	Donor	Donor	
<i>Method of fertilization</i>	Insemination	Insemination	
<i>Post-processing semen motility</i>	≥88%	<88%	
	N= 45	N= 24	p-value
Age	40 (38–42)	41 (38–42)	0.98
Mature oocytes retrieved	10 (6–15)	10 (7–15)	0.85
Outcomes			
Normal fertilization rate (%)	75 (60–83)	64 (32–85)	0.177
Percentage of cycles without suitable embryos for transfer (%)*	15.5±5.5	25.0±9.0	0.251
Number of embryos transferred	3 (2–4)	3 (2–3)	0.510
Pregnancy rate per retrieval (%)*	46.6±7.5 (21/45)	8.3±5.8 (2/24)	0.001
Pregnancy rate per embryo transfer (%)*	55.2±8.2 (21/38)	11.1±7.6 (2/18)	0.002

Summary statistics are expressed in median and interquartile range and compared using the Wilcoxon signed-ranked test unless otherwise specified, *Fisher's exact test

100% (8.3±5.8% vs. 46.6±7.5%, $p<0.001$). The differences were still significant when pregnancy rates were adjusted by per embryo transfer (11.1±7.6% vs. 55.2±8.2%, $p<0.002$).

Of the 42 identified cases of IVF using donor spermatozoa where insemination was converted to ICSI based on the recommendation of the andrologists (Fig. 1), there were 36 cases where the post-processing motility was less than 88% (Group C). Compared to the 24 IVF cycles where the oocytes were inseminated with donor spermatozoa with motility less than 88% in the final preparation (Group A2),

pregnancy rates were significantly higher per retrieval ($p<0.001$) and per embryo transfer ($p<0.004$) in the ICSI group despite similar mean age, number of mature oocytes retrieved, rates of normal fertilization, and number of embryos transferred between the two groups (Table 4).

Discussion

Consistent with prior studies [1, 2], cryopreserved donor spermatozoa had lower initial concentration, motility, and

Table 4 Comparison of fertilization and pregnancy outcomes by methods of fertilization with low post-processing semen motility

	(A2)	(C)	
<i>Spermatozoa source</i>	Donor	Donor	
<i>Method of fertilization</i>	Insemination	ICSI	
<i>Post-processing semen motility</i>	<88%	<88%	
	N= 24	N= 36	p-value
Age	41 (38–42)	40 (35–42)	0.087
Mature oocytes retrieved	10 (7–15)	10 (5–17)	0.111
Outcomes			
Normal fertilization rate (%)	64 (32–85)	80 (64–89)	0.767
Percentage of cycles without suitable embryos for transfer (%)*	25.0±9.0	8.3±4.7	0.079
Number of embryos transferred	3 (2–3)	3 (2–4)	0.431
Pregnancy rate per retrieval*	8.3±5.8 (2/24)	47.2±8.4 (17/36)	0.001
Pregnancy rate per embryo transfer*	11.1±7.6 (2/18)	51.5±8.8 (17/33)	0.004

Summary statistics are expressed in median and interquartile range and compared using the Wilcoxon signed-ranked test unless otherwise specified, *Fisher's exact test

total motile count upon thawing when compared to those of freshly ejaculated semen samples from men with normal semen analyses. These disparities remained significant even after processing by separation on density gradients and/or by swim-up. However, the negative clinical impact of these lower donor spermatozoa parameters was not apparent in the general analyses.

Our study confirmed previously published results [5] that despite the lower concentration and motility, insemination of oocytes with donor spermatozoa in the setting of IVF does not result in lower total or normal fertilization rates compared to cycles using freshly ejaculated semen. Furthermore, there were no significant differences in the pregnancy rates observed comparing IVF cycles using cryopreserved donor to freshly ejaculated spermatozoa. These findings are also consistent with the results of prior studies [2, 5–7]. However, the negative findings must be interpreted with caution since this study did not have sufficient power to detect pregnancy rate differences less than 20% between cases and controls due to the limited number of IVF cycles using donor spermatozoa.

The negative findings from our own and other similar general statistical analyses [1–4] support the clinical dictum that *in vitro* fertilization by insemination is appropriate when using donor spermatozoa despite the well-recognized decreases in concentration and motility compared to those of freshly ejaculated spermatozoa. However, the categorical acceptance of this approach has precluded the recognition of signals indicating poor quality donor spermatozoa that may compromise clinical outcomes. To our knowledge, there have been no studies to date attempting to identify cryopreserved donor spermatozoa parameters capable of discriminating pregnancy outcomes.

The seemingly equivalent pregnancy outcomes between donor and partner spermatozoa despite widely disparate post-processing parameters suggest that lower quality donor spermatozoa either meet the minimal threshold for maintaining optimal outcome or the differences can be compensated for by adjustments in the processing methods or in the concentration of the inseminated spermatozoa. However, this analysis indicates that the initial total motile count and the post-processing motility of the spermatozoa may significantly impact pregnancy outcomes. The potential discriminatory value of these parameters was confirmed by the logistic regression model after controlling for potential confounders.

In the ROC curve analyses, initial total motile count had a significant but small area under the curve. In the subgroup analysis, discriminatory value of the initial total motile count was only significant in freshly ejaculated spermatozoa but not in cycles using donor spermatozoa. In contrast, post-processing motility had a significant discriminatory value in predicting pregnancy outcomes in cycles using

donor spermatozoa but not in cycles using freshly ejaculated spermatozoa. In the latter group, the median post-processing motility was 97% with only two percent of the cycles having motility below 88%. Due to this uniformly high post-processing motility in the freshly ejaculated spermatozoa, the parameter would not be expected to significantly influence pregnancy outcomes in this subgroup.

In IVF cycles using donor spermatozoa insemination, the ROC curve analysis suggested that a post-processing motility of 88% provided maximal discrimination of pregnancy outcomes. Motility values equal to or above this threshold value provided a sensitivity of 80% for positive pregnancy, and values below provided a specificity of 70% for negative pregnancy result. Indeed, the cross-tabulation results demonstrated that despite starting with equivalent numbers of mature oocytes and similar rates of normal fertilization, pregnancy rates were extremely low in the group inseminated with donor spermatozoa that had less than 88% motility compared to those with greater than or equal to 88%.

Cryopreservation leads to increases in chromatin instability and single-strand DNA fragmentation [8–10]. Although not investigated in the current analysis, the recent literature on sperm DNA fragmentation have consistently demonstrated that the degree of fragmentation strongly correlates with spermatozoa parameters such as concentration, motility, and morphology with correlation coefficients as high as 0.50 [11–15]. Hence it is possible that the post-processing spermatozoa motility may be an index of cryo-injury and DNA fragmentation [8].

Although post-processing motility less than 88% is associated with dramatically reduced pregnancy rates, the mechanism does not appear to be associated with a reduction in fertilization rates or in the number of available embryos for transfer. Interestingly, this observation is highly consistent with findings from studies analyzing sperm DNA fragmentation and IVF outcomes. The majority of those studies demonstrated high sperm DNA fragmentation does not preclude fertilization but negatively impacts subsequent embryo development and reduces pregnancy rates [12, 13, 15–17]. The initial steps of embryonic development from fertilization up to the 6–8 cell cleavage stage occur essentially independent of the embryonic/paternal genome and are predominately under the influence of maternal transcripts packaged into the oocytes at the time of ovulation [18]. Thus the deleterious effects of abnormal paternal gene expressions on embryonic development would not be apparent prior to embryo transfers and likely inhibit subsequent embryonic development *in utero* leading to the reduced pregnancy rates.

Whether the abnormalities associated with post-processing motility of less than 88% in donor spermatozoa can be compensated by ICSI could not be adequately analyzed in

this study because it was not a uniformly accepted criterion for conversion from routine insemination to ICSI at our center during the study period. However, the limited comparisons between all cases of conversions to ICSI with post-processing motility less than 88% and insemination with donor spermatozoa with similarly low post processing motility suggest that ICSI may provide significant benefits in improving pregnancy outcomes. Again, the mechanism does not seem to be directly related to an increase in the rate of normal fertilization or in the number of available embryos for transfer. A prospective study using the criterion established by this analysis is necessary to confirm the potential benefit of ICSI.

As with all retrospective analyses, our study was limited by potential confounders and biases despite adequate matching of baseline characteristics and the use of multiple regression models to confirm the results of the univariate analyses. In particular, information on factors that may influence fertilization and pregnancy outcomes such as sperm morphology [19–21] and total progressive motile sperm count [22, 23] was not available in this study. In addition, the sample size was limited by the small number of donor spermatozoa IVF cycles available for analysis. Despite these limitations, the large magnitude of the association between low post-processing motility and pregnancy outcomes found in this study warrants further attention and confirmation in larger prospective randomized studies.

In summary, our study confirmed that outcomes using donor spermatozoa for oocyte insemination in the setting of IVF generally did not differ from that of freshly ejaculated spermatozoa. However, further analyses identified post-processing motility of less than 88% in donor spermatozoa as a potential risk factor for poor outcomes. Converting from routine insemination to ICSI in these cases appears to significantly improve outcomes. In our study population, 56% of the donor spermatozoa had motility below this threshold value on final processing. Hence, while ICSI does not need to be categorically instituted when using donor spermatozoa in IVF, patients must be counseled in advance regarding the relatively high likelihood of conversion to ICSI based on the post-processing motility value.

Conflict of interest There are no conflicts of interest to declare for any of the authors.

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