Sperm DNA fragmentation is correlated with poor embryo development, lower implantation rate, and higher miscarriage rate in reproductive cycles of non–male factor infertility

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Objective: To study the implications of sperm DNA fragmentation (SDF) in intracytoplasmic sperm injection cycles for non–male factor infertility.
Design: Prospective cohort study.
Setting: Private university-affiliated IVF center.
Patient(s): Data from 475 cycles performed from June 2016 to June 2017.
Intervention(s): Cycles were divided according to SDF rate into two groups: <30% SDF (n = 433) and ≥30% SDF (n = 42). Laboratory and clinical outcomes were compared between groups by generalized linear models adjusted for potential confounders.
Main Outcome Measure(s): Embryo quality and miscarriage rates.
Result(s): Fertilization rate was similar between groups (≥30% SDF, 85.28% ± 1.06% vs. <30% SDF, 90.68% ± 3.61%). Significantly lower rates of normal cleavage speed (≥30% SDF, 61.12% ± 4.21% vs. <30% SDF, 72.53% ± 1.24%), high-quality embryos at day 3 (≥30% SDF, 23.07% ± 5.56% vs. <30% SDF, 36.41% ± 1.53%), blastocyst formation (≥30% SDF, 39.09% ± 2.73% vs. <30% SDF, 58.83% ± 7.59%), blastocyst quality (≥30% SDF, 11.97% ± 1.22% vs. <30% SDF, 30.09% ± 2.39%), and implantation (33.24% ± 1.66% vs. <30% SDF, 46.40% ± 4.61%) were observed in cycles with higher SDF, despite similar pregnancy rates (≥30% SDF, 30.40% vs. <30% SDF, 32.40%). A 2.5-fold miscarriage rate was observed in cycles with an SDF above the established cutoff (≥30% SDF, 42.8% vs. <30% SDF, 16.8%).
Conclusion(s): Higher SDF is correlated with poor embryo development, lower implantation rate, and higher miscarriage rate in non–male factor infertility intracytoplasmic sperm injection cycles. Since defects in sperm may be hidden, the SDF test can bring additional information to the sperm quality evaluation of men with unknown infertility history. (Fertil Steril® 2019;112:483–90. ©2019 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Sperm chromatin dispersion, sperm DNA fragmentation, ICSI, semen analysis, non–male factor infertility

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Several studies have demonstrated a trend toward a reduction in semen quality in the last decades, with implications for reproductive outcomes (1–4). Male factor infertility, defined by the alteration of at least one of the standard semen parameters recognized by the World Health Organization (WHO) (5), for example, sperm concentration, motility, and morphology, is estimated to contribute in 40%–50% of infertility cases (6–9).

Nevertheless, standard semen parameters provide a crude prediction of the male factor fertility potential and its implications on reproductive outcomes (10–12), since nearly 15% of infertile men have semen parameters within normal reference ranges (5). It has been suggested that there must exist subcellular or nuclear factors that are not identified in conventional semen analysis, which may contribute to male factor infertility (5).

Therefore, new methodologies were developed to improve semen analysis at a functional level. Sperm DNA fragmentation (SDF) is a measure of chromatin integrity damage that is induced by processes such as apoptosis, enzymatically induced DNA breaks, radical oxidants species, or gonadotoxic treatments (13). The value of SDF testing in predicting reproductive outcomes is considered to be related to the extent and type of DNA damage as well as to the inherent sperm DNA repair ability of the oocyte (13). It is known that the ability of the oocyte to repair the fertilizing sperm DNA damage depends on its cytoplasmic and genomic quality, which are negatively affected by poor ovarian reserve (14) and increasing maternal age (15–17).

The goal for the present study was to study the influence of SDF on the outcomes of intracytoplasmic sperm injection (ICSI) cycles with female factor infertility.

MATERIALS AND METHODS

Experimental Design, Patients, and Inclusion and Exclusion Criteria

This prospective cohort study included data from 475 ICSI cycles performed from June 2016 to June 2017 in a private university-affiliated IVF center. The inclusion criteria were as follows: couples with primary infertility undergoing their first ICSI cycle as a result of non–male factor infertility indications, which exclusively had fresh ET at day 5. The distribution of female factor infertility is shown in Table 1.

TABLE 1

Distribution of female factor infertility included in the analysis.

Female factor infertility	Percentage of cycles
Ovarian	50.7 (241/475)
Tubal	15.1 (72/475)
Endometriosis	10.9 (52/475)
Polycystic ovarian syndrome	7.9 (37/475)
Mixed	6.3 (30/475)
Tuboperitoneal	5.9 (28/475)
Uterine	3.2 (15/475)

Borges. Sperm DNA fragmentation and ICSI outcomes. Fertil Steril 2019.

The exclusion criteria were as follows: presence of any altered seminal parameter according to the cutoff values established (5), history of male factor infertility, any alteration detected during male partner workup, paternal smoking habit, previous conventional IVF cycle, ICSI cycle with vitrified/thawed or donated oocytes, surgical sperm retrieval, cryopreserved sperm, vitrified/thawed ET, or preimplantation genetic tests. Couples with a history of pregnancy loss were also excluded from the analysis.

Cycles were divided according to SDF rate into two groups: low fragmentation ($\leq$30% SDF, n = 433) and high fragmentation (>30% SDF, n = 42) (18–21). Laboratory and clinical outcomes were compared between groups.

All patients signed a written informed consent form. The study was approved by the local Institutional Review Board.

Male Partner Workup

Hormone profile and karyotyping were requested for every patient. Male partners underwent testis physical examination, which was performed by the same urologist. The testis size and consistency, presence and consistency of the vasa deferentia, consistency of the epididymis, and the presence of varicoceles were evaluated during the examination. Any detected alteration during the exam caused the exclusion of the couple from the study. Additionally, patients were asked about smoking habits and medicine intake. None of the patients were taking any medications to improve semen parameters or reduce SDF before or during the study period.

Semen Analysis and Preparation

Semen samples were collected in the laboratory by masturbation. After liquefaction for 30 minutes, semen samples were evaluated for sperm count, motility, and morphology. Sperm count and motility assessment were performed by following the instructions of the counting chamber manufacturer (Leja slide, Gynotec Malden). The volume of the ejaculate was determined by aspirating the liquefied sample into a graduated disposable pipette. The sperm concentration is expressed as 10^6 spermatozoa/mL and total sperm count is expressed as 10^6 spermatozoa. Sperm motility was assessed in 100 random spermatozoa by characterizing them as progressive motility, nonprogressive motility, and immotile. The motility was expressed as a percentage. Sperm morphology was evaluated on air-dried smears, fixed, and stained using the quick-stain technique (Diff-Quick; Quick-Panoptic). A total of 200 sperm cells were characterized as morphologically normal or abnormal, and the final morphology was expressed as a percentage. Total motile sperm count was calculated by multiplying total sperm count by progressive motility divided by 100.

Sperm samples were prepared using a two-layered density gradient centrifugation technique (50% and 90% Isolate, Irvine Scientific) before ICSI.

SDF

SDF was measured using a sperm chromatin dispersion (SCD) test (Halosperm, Halotech), which is a fast method based on a

controlled DNA denaturation and protein depletion to determine DNA fragmentation in sperm cells (22). A total of 200 cells were examined by one highly trained technician to avoid interobserver variability. Results were expressed as percentage of cells with DNA fragmentation.

Controlled Ovarian Stimulation

Controlled ovarian stimulation was achieved by the administration of daily doses of recombinant FSH (Gonal-F, Serono) beginning on day 3 of the cycle. Pituitary suppression was performed using GnRH antagonist (Cetrotide; Merck KGaA) beginning when at least one follicle $\geq$14 mm was visualized. Follicular growth was monitored using the transvaginal ultrasound examination beginning on day 4 of gonadotropin administration. When three or more follicles attained a mean diameter of $\geq$17 mm and adequate serum E_2 levels were observed, recombinant hCG (Ovidrel, Merck KGaA) was administered to trigger final follicular maturation. Oocyte retrieval was performed 35 hours later.

Oocyte Preparation

Retrieved oocytes were maintained in culture media (Global for fertilization, LifeGlobal) supplemented with 10% protein (LGPS, LifeGlobal) and covered with paraffin oil (Paraffin oil P.G., LifeGlobal) for 4 hours before cumulus cell removal. The surrounding cumulus cells were removed after exposure to a HEPES-buffered medium containing hyaluronidase (80 IU/mL, LifeGlobal). The remaining cumulus cells were then mechanically removed by gently pipetting with a hand-drawn Pasteur pipette (Humagen Fertility Diagnostics). Oocytes were maintained in culture for 1–3 hours before ICSI.

Oocyte morphology and maturation stage were assessed using an inverted Nikon Diaphot microscope with a Hoffmann modulation contrast system under 400× magnification (Eclipse TE 300 microscope, Nikon), just before sperm injection (5–7 hours after retrieval). Oocytes that had released the first polar body were considered mature (metaphase II stage) and were submitted to ICSI.

ICSI

ICSI was performed according to Palermo et al. (23) by a highly trained IVF laboratory team. Sperm selection was analyzed at 400× magnification using an inverted Nikon Eclipse TE 300 microscope. The injection was performed in a microinjection dish prepared with 4 μL droplets of buffered medium (Global w/HEPES, LifeGlobal) and covered with paraffin oil on a heated stage at 37.0°C $\pm$ 0.5°C on an inverted microscope. Fertilization was confirmed by the presence of two pronuclei and the extrusion of the second polar body 16–18 hours after ICSI. Embryos were maintained in a 50 μL drop of culture medium (Global) with 10% protein supplement and covered with paraffin oil in a humidified atmosphere under 6% CO_2 at 37°C for 5 days.

Embryo Quality and ET

Embryos were morphologically evaluated on days 3 and 5 of development using an inverted Nikon Diaphot microscope with a Hoffmann modulation contrast system (Eclipse TE 300 microscope) under 400× magnification.

Cleavage-stage morphology on day 3 was evaluated according to the Istanbul consensus (24). The following parameters were recorded: the number of blastomeres, the percentage of fragmentation, the variation in blastomeric symmetry, the presence of multinucleation, and the defects in the zona pellucida and cytoplasm. High-quality cleavage-stage embryos were defined as those with all of the following characteristics: 7−10 cells on day 3, <10% fragmentation, symmetric blastomeres, the absence of multinucleation, colorless cytoplasm with moderate granulation and no inclusions, the absence of perivitelline space granularity, and the absence of zona pellucida dimorphisms. Embryos lacking any of these characteristics were considered to be of low quality.

Normal cleavage speed rate was defined as the number of embryos with 7–10 cells at day 3 divided by the total number of embryos at day 3 in each cycle.

The blastocyst rate was defined as the number of embryos that reached blastocyst stage at day 5 divided by the number of two pronuclei embryos in each cycle.

Blastocyst morphology on day 5 was evaluated according to Gardner and Schoolcraft (25). The following parameters were recorded: degree of blastocoel expansion, trophectoderm quality and cell number, and inner cell mass quality and cell number. Blastocoel expansion was classified as 1, early blastocyst; 2, blastocyst; 3, full blastocyst; 4, expanded blastocyst; 5, hatching blastocyst; and 6, hatched blastocyst. Trophectoderm quality was defined as A, many cells forming a cohesive epithelium; B, few cells forming a loose epithelium; and C, very few large cells. Inner cell mass cells were classified as A, tightly packed with many cells; B, loosely grouped with several cells; and C, very few cells and disorganized. Blastocyst quality rate was determined by the number of top scoring blastocysts ($\geq$3AA) divided by the total number of blastocysts.

On day 5, one to two embryos were transferred per patient, using a soft catheter with transabdominal ultrasound guidance.

Clinical Follow-up

A serum β-hCG pregnancy test was performed 10 days after ET. All women with a positive test (serum β-hCG >40 mIU/mL) received a transvaginal ultrasound scan after 2 weeks. Clinical pregnancy was diagnosed when fetal heartbeat was detected. Implantation rate was calculated as the number of gestational sacs divided by the number of embryos transferred. Pregnancy rates were calculated per ET. Miscarriage was defined as a pregnancy loss before 20 weeks.

Data Analysis and Statistics

The sample size calculation using G*Power 3.1.7 (Franz Faul, Universität Kiel) suggested that 416 cycles would be enough

to demonstrate a 20% effect with 80% power and 5% significance level (α) considering as the primary outcome the high-quality embryo rate. Data are expressed as the mean ± SD for continuous variables, while percentages are used for categorical variables. The analysis was performed using SPSS Statistics 21 (IBM).

The analyses were performed in two different manners. In the first analysis, the DNA fragmentation index (DFI) was treated as a categorical variable, and to assess the association of SDF groups (≤30% SDF and >30% SDF) on ICSI outcomes, generalized linear models followed by Bonferroni post hoc were used. In the second analysis, DFI was treated as a continuous variable, and its influence on ICSI outcomes was investigated using generalized linear models. For both analyses, laboratory outcomes (fertilization rate, normal cleavage speed rate, high-quality embryos on day 3 rate, blastocyst rate, and blastocyst quality rate) were adjusted for maternal age, maternal body mass index (BMI), total FSH dose, number of retrieved oocytes, and paternal age. Clinical outcomes (implantation rate, pregnancy rate, and miscarriage rate) were adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, paternal age, number of transferred embryos, and endometrial thickness. Finally, a multivariable regression analysis using general linear models was performed to investigate whether SDF is an independent predictor of ICSI outcomes.

RESULTS

The descriptions of patients' demographics and controlled ovarian stimulation outcomes for the categorical DFI are shown in Table 2. All variables were equally distributed among the groups. No influences of continuous SDF on patient's demographics and controlled ovarian stimulation outcomes were observed (Supplemental Table 1).

The SDF <30% group presented a mean SDF of 17.48% ± 8.70%, while the ≥30% group mean was 37.67% ± 6.39%. Cycles with SDF ≥30% presented higher paternal age (P=.009), longer abstinence interval (P=.002), higher seminal volume (P=.001), higher total sperm count (P=.003), but lower total (P<.001) and progressive (P<.001) motility (Table 3). Similarly, there was a positive correlation between continuous SDF and paternal age (P<.001), abstinence interval (P=.001), seminal volume (P=.018), and total sperm count (P=.011) and an inverse correlation between continuous SDF and total motility (P<.001) and progressive motility (P<.001; Supplemental Table 2). No influence of continuous SDF was observed on laboratory and clinical parameters (Supplemental Table 3). Cycles from the SDF ≥30% group showed significant lower rates of normal cleavage speed (P=.010), high-quality embryos at day 3 (P=.021), blastocyst development (P=.016), blastocyst quality (P<.001), and implantation (P<.001), compared with cycles from the SDF <30% group, despite similar pregnancy rates (risk ratio, 0.773, confidence interval, 0.434–1.379; P=.383). A significantly higher miscarriage rate was observed in cycles with SDF above the cutoff (P=.018; Table 4).

The results from the multivariable analysis are shown in Supplemental Table 4. There was no significant association between SDF and ICS outcomes.

Female factor infertility did not influence laboratory and clinical outcomes (Supplemental Table 5).

DISCUSSION

Conventional semen analysis is essential for male factor infertility evaluation; however, it is not sensitive enough to detect subtle sperm defects that may interfere with patient fertility. Our evidence suggests that SDF above 30% is a

TABLE 3

Descriptive analysis of seminal parameters according to SDF groups.

Parameter	<30% SDF (n = 433)	≥30% SDF (n = 42)	*P* value
Paternal age, y	38.68 ± 5.65	41.19 ± 6.35	.009
Ejaculatory abstinence, d	3.92 ± 2.42	5.51 ± 5.46	.002
Seminal volume, mL	2.94 ± 0.50	3.79 ± 1.09	.001
Seminal concentration, $\times 10^6$/mL	77.70 ± 29.83	81.09 ± 33.23	.677
Total sperm count, $\times 10^6$	214.58 ± 72.95	303.71 ± 78.80	.003
Total sperm motility, %	63.45 ± 12.75	55.52 ± 17.55	<.001
Progressive sperm motility, %	54.90 ± 14.27	46.50 ± 16.77	<.001
Total motile sperm count	121.11 ± 98.24	146.89 ± 139.09	.120
SDF, %	17.48 ± 8.70	37.67 ± 6.39	<.001

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TABLE 2

Descriptive analysis of patient demographics and controlled ovarian stimulation outcomes according to SDF groups.

Variable	<30% SDF (n = 433)	≥30% SDF (n = 42)	*P* value
Maternal age, y	37.40 ± 4.51	38.66 ± 4.58	.068
Maternal BMI, kg/m^2	24.48 ± 3.90	25.26 ± 5.26	.249
Total FSH administered, IU	2,596.67 ± 705.00	2,806.94 ± 596.94	.083
Estradiol level at hCG trigger day, pg/mL	1,429.11 ± 1,100.01	1,770.36 ± 1,498.24	.089
No. of follicles	13.71 ± 11.31	13.04 ± 12.24	.719
No. of retrieved oocytes	9.51 ± 8.25	9.82 ± 8.37	.173
No. of metaphase II oocytes	6.99 ± 6.32	7.26 ± 6.52	.208

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TABLE 4

Effect of SDF on laboratory and clinical outcomes.

Variable	< 30% SDF (n = 433)	≥30% SDF (n = 42)	*P* value
Laboratory outcomes[a]			
Fertilization rate	90.10 ± 3.50	85.67 ± 1.03	.226
Normal cleavage speed rate	72.16 ± 1.30	61.56 ± 4.40	.010
High-quality embryos at day 3 rate	36.47 ± 1.51	23.89 ± 5.51	.021
Blastocyst rate	56.25 ± 2.01	39.01 ± 1.40	.016
Blastocyst quality rate	30.54 ± 2.27	11.32 ± 7.72	< .001
Clinical outcomes[b]			
Implantation rate	46.09 ± 0.55	33.21 ± 1.96	< .001
Chemical pregnancy rate	34.99	33.11	.940
Clinical pregnancy rate	32.42	30.33	.774
Miscarriage rate	17.8	39.9	.018

[a] Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, and paternal age.
[b] Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, paternal age, number of transferred embryos, endometrial thickness.

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contributing factor for poor embryo development and higher miscarriage rates in female factor infertility ICSI cycles.

SDF is an independent measure of sperm quality that may have better diagnostic and prognostic capabilities than standard sperm parameters (18, 26). Nonetheless, the impact of abnormal SDF depends on the combined effects of the extent of DNA or chromatin damage in the spermatozoa and the capacity of the oocyte to repair that damage (13).

The spermatozoa chromatin has a unique structure acquired during spermiogenesis, in which most histones are displaced by protamines (27). Packaging of sperm chromatin is a fundamental step for both biophysical and developmental functions, protecting genetic integrity and setting the appropriate genes to be expressed in the early embryonic development (28). Many chromatin structural problems can arise during sperm formation, including DNA strands breakage, nicks, and deletions (18, 26).

SDF measurement can be made by two types of assays: those that directly measure the extent of DNA fragmentation with the use of probes and dyes and those that measure the susceptibility of DNA to denaturation, which is higher in fragmented DNA (29). The SCD test, also known as the Halo test, belongs to the second type of assays and was the method used for SDF evaluation in the present study. The SCD is a simple, fast, and low-cost SDF test that uses an indirect technique based on the concept that sperm with fragmented DNA do not produce the characteristic halo of dispersed DNA loops that are observed in sperm with nonfragmented DNA after controlled acid denaturation and depletion of nuclear proteins (30). The amount of sperm with nondispersed chromatin is directly proportional to the double-strand DNA damage (31). Considering that the SCD test measures the presence of damaged and nondamaged DNA in sperm, reported indirect SDF rates reflect the integrity of the genetic material of the gametes (30). An SCD threshold of ≥ 30% has been associated with poor reproductive outcomes (19–21). In this study we reaffirmed that 30% SDF is correlated with ICSI outcomes.

During in vivo reproduction, the natural selection process ensures that only spermatozoa with normal genomic material fertilize an oocyte. However, ICSI bypasses this selection process, leading to the possibility that abnormal spermatozoa could be selected (32). One may argue that DNA damage should affect the entire sperm population to affect ICSI outcomes or, if that is not the case, that a non DNA-damaged sperm could still be selected. However, the chance of selecting a spermatozoon with fragmented DNA increases as a function of damaged spermatozoa proportion, and the spermatozoa not showing injured DNA in the same ejaculate can possibly contain the same kind of damage, albeit to a lesser degree, but to an extent that significantly reduces paternal genome competence (18).

Although we cannot determine whether the oocytes from the selected cycles were capable of DNA repairing or the real extension of individual spermatozoon DNA damage, given the mean maternal age of 38 years, we hypothesized that the oocytes from these older women were less likely to repair sperm DNA damage, resulting in a low blastocyst development rate and high early pregnancy loss rate. One could argue that female age could have biased the results, since the difference between the SDF groups for that variable almost reached statistical significance; however, all the statistical analyses were controlled for female age, and thereafter, the differences observed between SDF groups are independent of maternal age.

This study corroborates previous studies of our group, which suggest that sperm damage effect depends on oocyte quality (32–35). In addition, a negative effect of SDF has been observed in cycles with only female factor infertility indications (36).

Since the paternal genome is activated between four and eight cell embryo stages, high DNA damage load is presumed to have no effect on the fertilization and manifests itself in the later stages of embryonic development, reflected, for example, in a failure to obtain blastocysts (37, 38). This assumption has been corroborated by our results, in which no significant effect on fertilization rate was observed; however, day 3 embryo quality and cleavage speed rates as well as day 5 blastocyst and quality rates were lower in

cycles with higher SDF. Negative correlation between SDF with embryo quality and blastocyst development had been reported when DNA damage was assessed also by TUNEL and sperm chromatin structure assay methods (37, 39, 40).

Defects in the male genetic status have been shown to lead to postimplantation failure (37, 41, 42). The presence of unrepaired DNA damage above a critical threshold has been postulated to explain the block in embryo development observed after embryo implantation (18, 40, 41). In fact, we observed that cycles with higher SDF presented a lower implantation rate and a 2.5-fold increase in miscarriage rate, which indicates that embryos derived from oocytes fertilized by highly damaged spermatozoa may have a compromised implantation leading to increased chance of miscarriage.

Moreover, SDF assessment may reveal a hidden abnormality of sperm DNA in infertile men classified as idiopathic based on apparently normal standard sperm parameters and may be a tool for evaluation of semen samples before their use in assisted reproductive techniques (43). Sperm DNA above the cutoff represented 10% of our non–male factor infertility cases; therefore SDF assessment among this subgroup of patients could, at least partly, explain ICSI outcomes. These result are in accordance with Bungum et al. (44) who estimates that up to 40% of all cases of unexplained infertility can be related to increased amount of DNA damage.

It has been suggested that some cases of sperm DNA damage are potentially curable by lifestyle modifications, dietary supplements, antioxidants, and varicocele repair (45–47). Routine application of the SDF assay could help to decide on the suitable therapeutics in these men and may be a valuable supplement, adding independent information about the gamete status of the male partner (44, 48, 49).

Despite the importance of the results here presented, we are aware of the limitations of this study. In addition to the small study population, SDF was not an independent predictor of any ICSI outcome, but a contributing factor when the covariates were introduced into the model, which does not implicate causality but correlation only. Another limitation was the SDF technique employed, which has a higher interobserver and interexam variability in comparison with the sperm chromatin structure assay gold standard; however, as we have already discussed, the SCD test is less costly, can be used in reproduction centers with limitations of space and staff, and, therefore, are more applicable on a daily basis. It is important to highlight that SCD measures of the present study were performed by a highly trained technician.

In conclusion, higher SDF can lead to poor embryo development, lower implantation rate, and higher miscarriage rate in non–male factor infertility ICSI cycles. Since defects in sperm may be hidden, the SDF test can bring additional information to the sperm quality evaluation of men with an unknown history of infertility.

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La fragmentación de ADN espermática está correlacionada con un peor desarrollo embrionario, menor tasa de implantación y mayor tasa de aborto espontáneo en ciclos de reproducción asistida sin indicación de factor masculino

Objetivo: estudiar las implicaciones de la fragmentación del ADN espermático (SDF) en los ciclos de inyección intracitoplasmática de espermatozoides sin indicación de factor masculino.

Diseño: estudio de cohorte prospectivo.

Lugar: Centro de FIV privado asociado a universidad.

Paciente(s): Datos de 475 ciclos realizados desde Junio de 2016 hasta Junio de 2017.

Intervención(es): Los ciclos fueron divididos acorde a la tasa de SDF en dos grupos: <30% SDF (n ¼ 433) y R30% SDF (n ¼ 42). Los resultados clínicos y los del laboratorio se compararon entre los grupos mediante modelos lineales generalizados y ajustados para posibles factores de confusión.

Principales medidas de resultado(s): Calidad embrionaria y tasas de aborto.

Resultado(s): La tasa de fecundación fue similar entre los grupos (>30% SDF, 85.28% ±1.06%vs. <30% SDF, 90.68% ± 3.61%). Tasas significativamente más bajas de velocidad de división celular (>30% SDF, 61.12% ± 4.21% vs. <30% SDF, 72.53% ± 1.24%), embriones de alta calidad en día 3 (>30% SDF, 23.07% ± 5.56% vs. <30% SDF, 36.41% ± 1.53%), formación de blastocistos (>30% SDF, 39.09% ± 2.73% vs. <30% SDF, 58.83% _ 7.59%), calidad de los blastocistos(>30% SDF, 11.97% _ 1.22% vs. <30% SDF, 30.09% ± 2.39%), e implantación (>30% SDF 33.24% ± 1.66% vs. <30% SDF, 46.40% ± 4.61%) fueron observadas en ciclos con nivels más altos de SDF, a pesar de tener tasas de embarazo similares (R30% SDF, 30.40% vs. <30% SDF, 32.40%). Se observó una tasa de aborto espontáneo de 2,5 veces más altas en ciclos con un SDF por encima del límite establecido (>30% SDF, 42.8% vs. <30% SDF, 16.8%).

Conclusión(es): Niveles más altos de SDF están correlacionados con un peor desarrollo embrionario, menor tasa de implantación, y una tasa más alta de aborto en ciclos de inyección intracitoplasmática sin indicación por factor masculino. Como los defectos en los espermatozoides pueden estar ocultos, la prueba SDF puede brindar información adicional a la evaluación de la calidad de los espermatozoides de hombres con un historial de infertilidad desconocido.