RESULTS: Including our unpublished data, a total of 31 studies were included. The included studies generally scored 6 or more on the Newcastle-Ottawa Quality Assessment Scale. The primary meta-analysis of 26 studies comprising 8173 couples showed a significantly higher miscarriage rate in the high DFI group than in the low DFI group [RR=1.76(1.31,2.37), P=0.002<0.01]. The meta-analysis of 8 studies comprising 17631 embryos revealed a significantly lower good quality embryo rate [RR=0.64(0.61, 0.67), P<0.00001]. The meta-analysis 13 studies comprising 3496 couples showed that the high DFI group had a significantly lower clinical pregnancy rate than the low DFI group [RR=0.77(0.69, 0.85), P<0.0001].

CONCLUSIONS: With such a large number of samples supported, we can safely conclude that high DFI does adversely affect ART outcome, although the mechanism involved remains to be determined. More well-designed studies exploring the association between DFI and ART outcome are desired, and a standard threshold of DNA damage needs to be established for various DNA assays in routine clinical use.

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MICROFLUIDIC SORTING SELECTS SPERM FOR CLINICAL USE WITH REDUCED DNA DAMAGE COMPARED TO DENSITY GRADIENT CENTRIFUGATION IN SPLIT SEMEN SAMPLES. M. Quinn,[a] T. Chinnasamy,[b] M. Miansarigavzan,[b] L. Jalalian,[a] M. Cedars,[a] U. Demirci,[b] M. Rosen.[a] [a]University of California, San Francisco, San Francisco, CA; [b]Stanford University, Palo Alto, CA.

OBJECTIVE: An increased DNA fragmentation index (DFI) has been associated with lower fertilization rates, impaired embryo progression, and decreased pregnancy rates. Standard semen processing by centrifugation may induce reactive oxygen species and DNA damage in sperm. Microfluidic-based sperm sorting allows for the selection of highly motile, morphologically normal sperm from an unprocessed specimen. We aim to determine if microfluidic sorting improves the selection of sperm with lower DFI over standard density gradient centrifugation in split semen samples.

DESIGN: Controlled laboratory study

MATERIALS AND METHODS: Discarded samples were collected following routine semen analysis performed as part of an infertility workup. For each sample, an aliquot of unprocessed semen was set aside and the remainder split for processing by clinic standard density gradient centrifugation and sorting by the microfluidic chip. Processed sperm was spread over a glass slide and fixed with a methanol and acetic acid mixture. The presence of fragmented DNA was established by TUNEL assay. Fluorescence microscopy was performed by providers blinded to method of sample processing. DFI was calculated as the number of cells with fragmented DNA divided by the total number of cells counted on a slide. Samples were divided into DFI quartiles based on DFI in the unprocessed sample. Statistical analysis was performed by Wilcoxon Signed-Rank test of paired samples. For summary descriptive statistics, median values with interquartile range (IQR: 25th-75th percentile) were calculated.

RESULTS: A total of 62 split semen samples were analyzed. Among unprocessed samples, median (IQR) sperm concentration was 76.5 million per mL (49-108), motility 51.5% (45-57), and morphology 6.5% normal (4-10). In paired analyses of all samples, those processed by the microfluidic chip demonstrated significantly decreased DFI compared to centrifuged and unprocessed samples. When limiting to samples with the highest quartile DFI, those processed by microfluidics again demonstrated a significantly decreased DFI compared to centrifuged and unprocessed samples, while centrifuged samples had a lower DFI than unprocessed samples.

	Highest quartile DFI n=16	Overall n=62
Unprocessed DFI	7.03% (5.89-8.90)[ac]	2.41% (1.23-4.55)[ad]
Density gradient centrifuge DFI	4.06% (1.31-7.83)[b]	2.02% (0.81-6.40)[a]
Microfluidic chip DFI	0.86% (0-2.56)	0.39% (0-1.29)

DFI=DNA Fragmentation Index %
All values median (IQR)
Wilcoxon Signed-Rank test for paired samples
[a]p<0.001 for comparison with microfluidic chip
[b]p=0.003 for comparison with microfluidic chip
[c]p=0.044 for comparison with centrifuge
[d]p=0.695 for comparison with centrifuge

CONCLUSIONS: Microfluidic sorting of unprocessed semen allows for the selection of clinically usable sperm with lower DNA fragmentation than standard processing. An investigation of microfluidic sperm sorting and clinical outcomes in assisted reproduction is warranted.

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SEMEN PARAMETERS AND INTRAUTERINE INSEMINATION (IUI) PERFORMANCE CHARACTERISTICS: RELATION TO LIVE-BIRTH RATE IN OVARIAN STIMULATION (OS)-IUI TREATMENTS IN A MULTICENTER TRIAL. K. R. Hansen,[a] R. M. Coward,[b] J. Trussell,[c] S. Chen,[d] R. A. Wild,[e] for the Reproductive Medicine Network[f]. [a]Obstetrics and Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [b]Urology, University of North Carolina, Chapel Hill, NC; [c]Upstate University Hospital, Syracuse, NY; [d]College of Public Health, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [e]Ob/Gyn, OUHSC, Oklahoma City, OK; [f]NICHD, NIH, Rockville, MD.

OBJECTIVE: To determine if semen parameters and IUI performance characteristics were associated with the outcome of live-birth following up to four cycles of OS with Letrozole, Clomiphene Citrate (CC), or gonadotropins plus IUI in couples with unexplained or mild male factor infertility.

DESIGN: Secondary analyses of a prospective, randomized, multicenter clinical trial investigating pregnancy, live-birth, and multiple pregnancy rates following OS-IUI treatments.

MATERIALS AND METHODS: This secondary analysis included all 900 couples undergoing 2314 OS-IUI cycles as part of The Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) clinical trial. Briefly, this trial enrolled women at 12 sites, age 18-40 with at least one patent fallopian tube and regular menses who underwent OS-IUI with Letrozole, CC or gonadotropins for up to four treatment cycles. Male partners were required to have a semen analysis with at least 5 million total motile sperm in the ejaculate. Generalized estimating equations, accounting for multiple cycle attempts within a given couple, were used to adjust for the association of IUI performance characteristics with the outcome of live-birth. A p-value of < 0.05 was considered statistically significant.

RESULTS: In unadjusted analyses, pre-prep sperm concentration ($p = 0.011$) and motility ($p = 0.003$), catheter type ($p = 0.024$), and multiple IUI attempts ($p = 0.015$) were significantly related to the outcome of live-birth. However, after adjustment for age, treatment group, pretreatment AMH level, cycle attempt, BMI, number of follicles $\geq$ 18 mm on the day of HCG trigger, and duration of infertility, only pre-prep sperm concentration (AOR 1.004 per million/ml; 95% CI 1.001, 1.007; $p = 0.01$), and motility (AOR 1.012 per 1% increase; 95% CI 1.002, 1.023; $p = 0.02$), were associated with greater odds of live-birth. Catheter type, ultrasound guidance, perceived difficult IUI, post-prep total motile count, multiple IUI attempts, sperm prep type (wash vs. density gradient), and the timing of IUI relative to HCG trigger (0-44 hours), were not significantly related to live-birth.

CONCLUSIONS: Pre-prep sperm concentration and motility demonstrated a modest association with live-birth in OS-IUI cycles in the AMIGOS trial. IUI performance characteristics, including post-prep total motile count, sperm prep type, and the timing of IUI relative to the HCG trigger, were not significantly related to live-birth rate.

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USING AN IN-HOME SEMEN TESTING SYSTEM TO EVALUATE TOTAL SPERM COUNT AND TIME TO CONCEPTION: A PILOT STUDY. G. Sommer,[a] A. Wesselink,[b] T. Trinidad,[a] U. Schaff,[a] M. Eisenberg,[c] E. E. Hatch,[b] L. A. Wise.[b] [a]Sandstone Diagnostics, Livermore, CA; [b]Epidemiology, Boston University School of Public Health, Boston, MA; [c]Urology, Stanford University, Stanford, CA.