HIGH SPERM DNA FRAGMENTATION INDEX NEGATIVELY IMPACTS EMBRYO MORPHOKINETICS, BUT NOT EMBRYO MORPHOLOGY AND DEVELOPMENT RATES: THE IMPORTANCE OF TIME-LAPSE IMAGING SYSTEM

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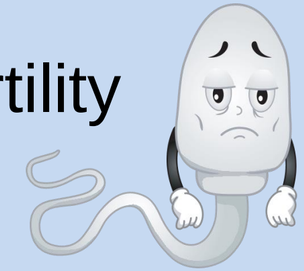
INTRODUCTION

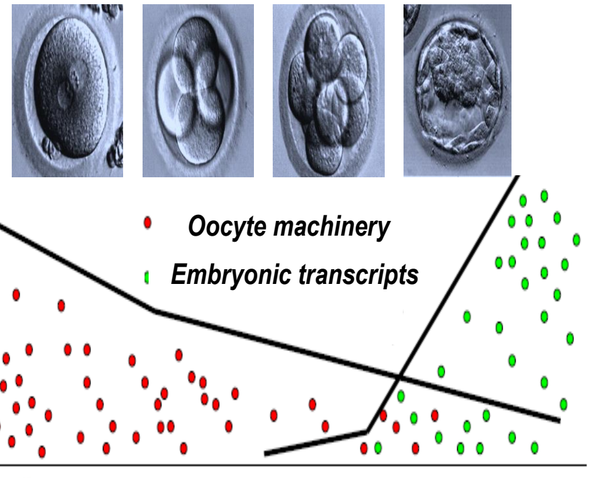
Sperm DNA fragmentation (SDF)

Male infertility



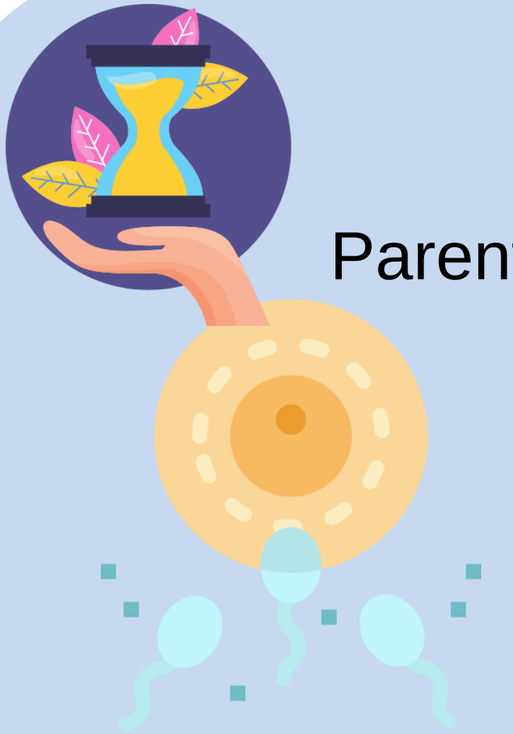
Reproductive outcomes

Pregnancy loss



Genetic diseases in the offspring

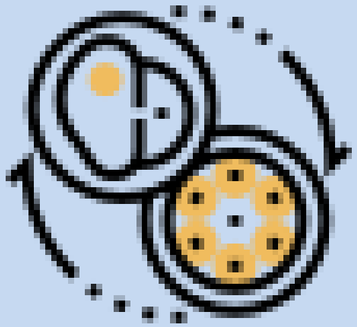
INTRODUCTION



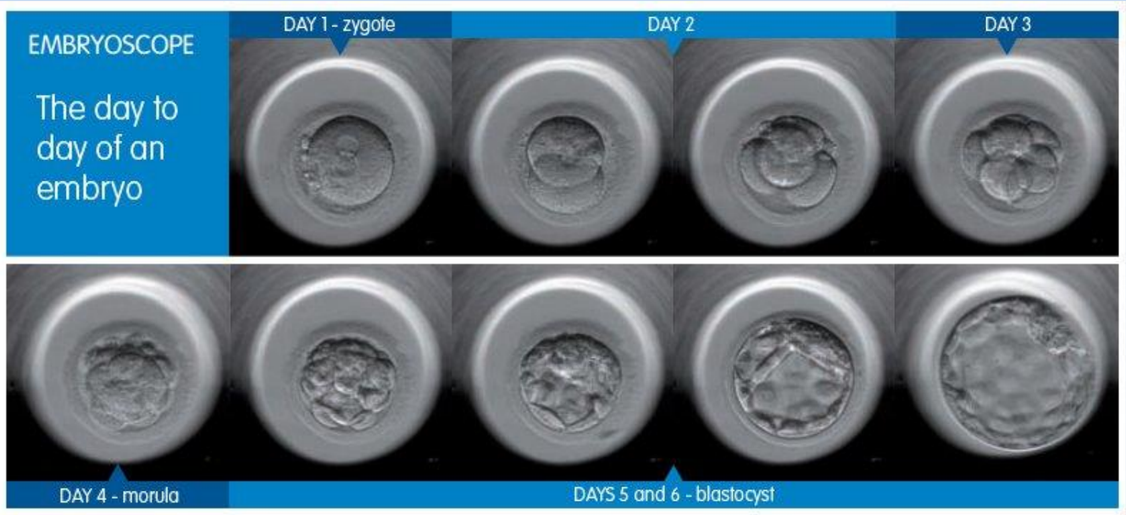
Parental age

COS

Culture media



Intrinsic embryonic quality



Time-lapse imaging (TLI)

INTRODUCTION

Hypothesis

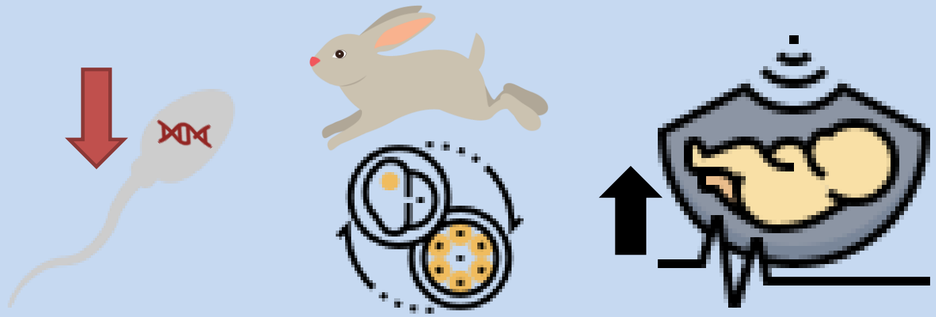
DNA fragmentation may interfere with speed and pattern of cell divisions

INTRODUCTION

Reprod Biol. 2015 Jun;15(2):94-100. doi: 10.1016/j.repbio.2015.03.003. Epub 2015 Apr 2.

The effect of sperm DNA fragmentation on the dynamics of the embryonic development in intracytoplasmatic sperm injection

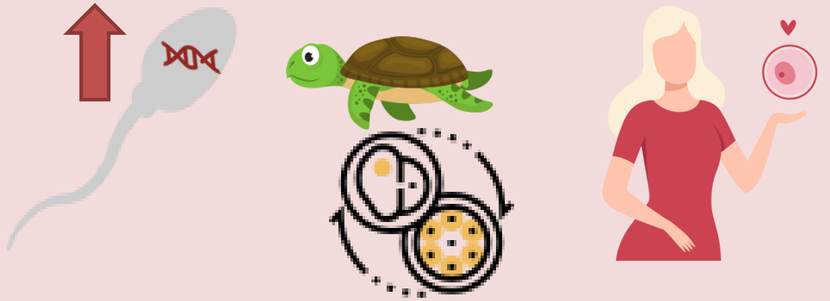
Artur Wdowiak [1], Szymon Bakalczuk [2], Grzegorz Bakalczuk [3]



Andrology. 2018 Sep;6(5):697-706. doi: 10.1111/andr.12551. Epub 2018 Sep 26.

High sperm DNA fragmentation delays human embryo kinetics when oocytes from young and healthy donors are microinjected

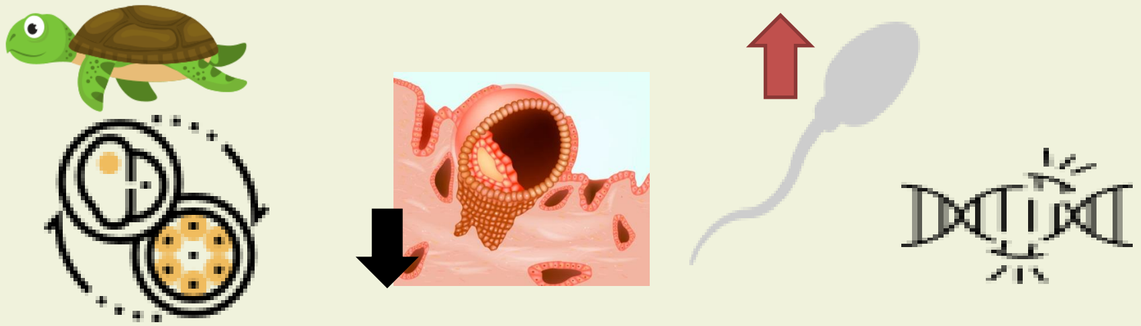
M Esbert [1], A Pacheco [2], S R Soares [3], D Amorós [1], M Florensa [1], A Ballesteros [1], M Meseguer [4]



Observational Study Fertil Steril. 2019 Apr;111(4):699-707.e1.
doi: 10.1016/j.fertnstert.2018.11.035. Epub 2019 Feb 28.

Double-stranded sperm DNA damage is a cause of delay in embryo development and can impair implantation rates

Aida Casanovas [1], Jordi Ribas-Maynou [2], Sandra Lara-Cerrillo [2], Ana Raquel Jimenez-Macedo [1], Olga Hortal [1], Jordi Benet [3], Joan Carrera [1], Agustín García-Peiró [4]

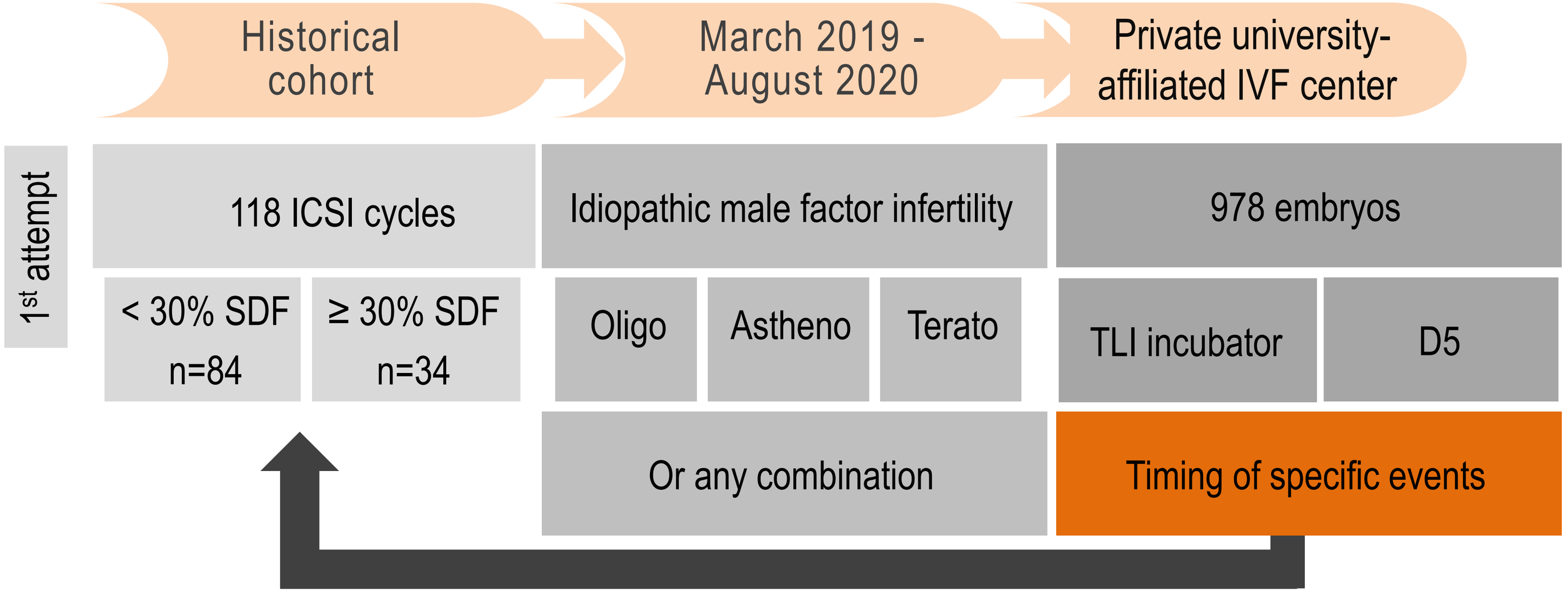


OBJECTIVE

To investigate if TLI can identify morphokinetic events impacted by high DFI, irrespective of conventional morphological embryo assessment and development rate

MATERIAL AND METHODS

Study desing



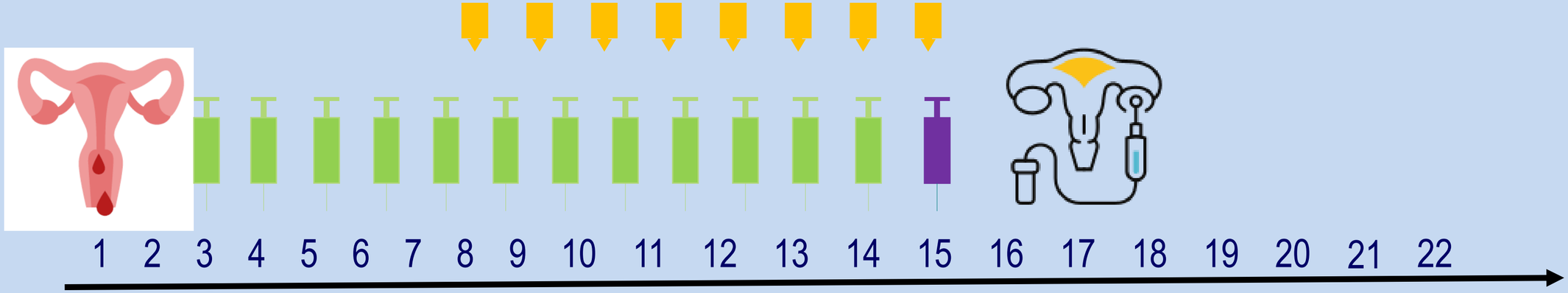
FERTILITY MEDICAL GROUP

MATERIAL AND METHODS

Controlled ovarian stimulation

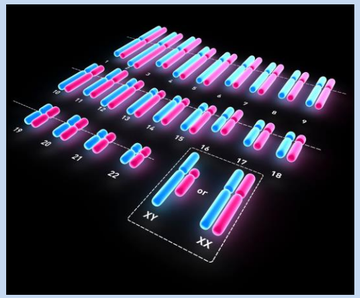
- GnRH Antagonist
- Recombinant FSH
- Recombinant hCG

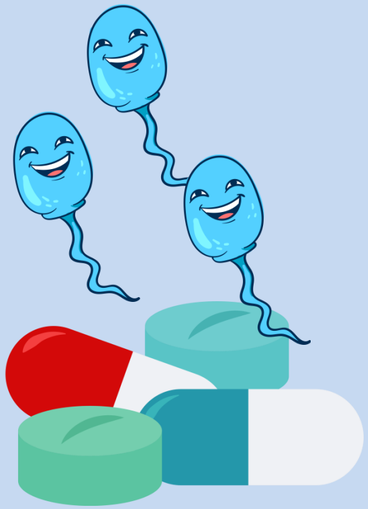
E2

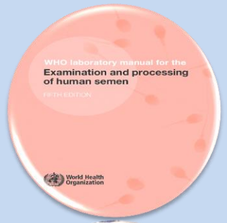


MATERIAL AND METHODS

Male partner workup

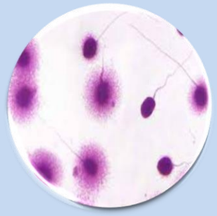






WHO guidelines

2-layered density gradient centrifugation



Sperm chromatin dispersion (SCD) test

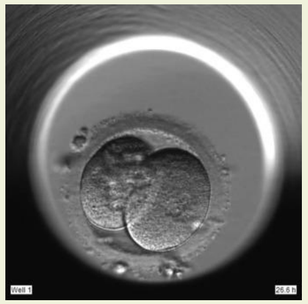
MATERIAL AND METHODS

Embryo culture

Until day 5

11 focal planes

Every 10 minutes



Multinucleation

Abnormal cleavage patterns

One or two embryos transferred

FERTILITY MEDICAL GROUP

MATERIAL AND METHODS

Data analysis and statistics

Post hoc power analysis

GPower 3.1

α 5%

527 blastocysts

Effect tB

Superior to 80%

IBM SPSS Statistics

GzLM

Bonferroni post hoc

Timing of specific events

Independent: DFI groups

Dependent: kinetic markers

Covariates: maternal and paternal ages, retrieved oocytes, EA

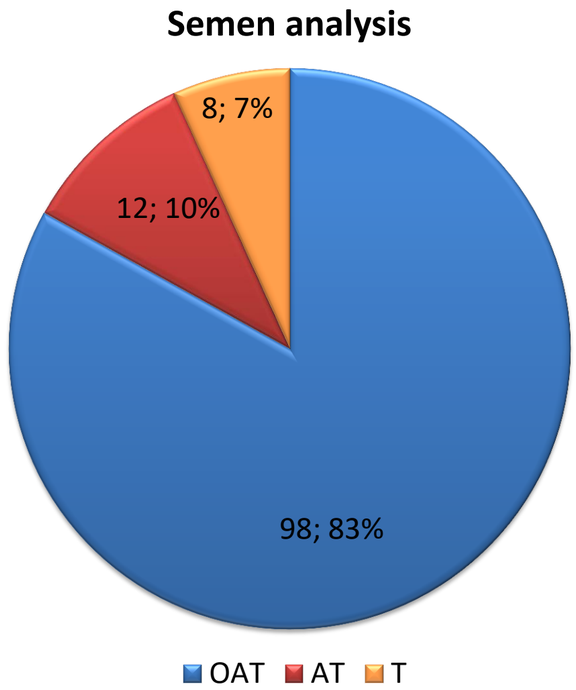
Mean ± SD

OR with 95% CI

p-values (5%)

FERTILITY MEDICAL GROUP

RESULTS



Variable	<30% DFI (n=84)	≥30% DFI (n=34)	p-value
Semen analysis			
Male age (years)	39.7 ± 5.0	38.8 ± 6.6	0.457
Ejaculatory abstinence length (days)	2.4 ± 0.9	2.6 ± 0.6	0.092
Sperm DFI (%)	18.2	42.8	<0.001
Semen volume (mL)	3.0 ± 2.9	2.6 ± 0.9	0.430
Sperm concentration ($x10^6$/mL)	8.9 ± 12.7	9.1 ± 11.1	0.961
Sperm count ($x10^6$)	34.3 ± 87.9	24.7 ± 31.3	0.416
Sperm motility (%)	38.0	36.3	0.600
Progressive sperm motility (%)	31.3	31.2	0.960
Sperm morphology (%)	1.7	1.7	0.906

FERTILITY MEDICAL GROUP

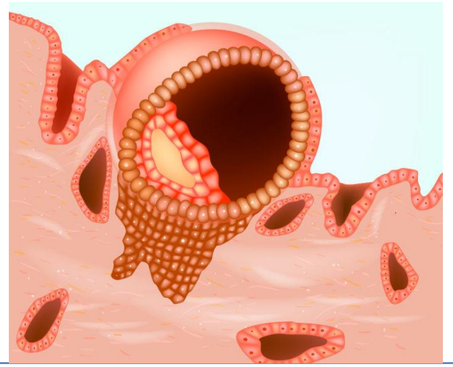
RESULTS

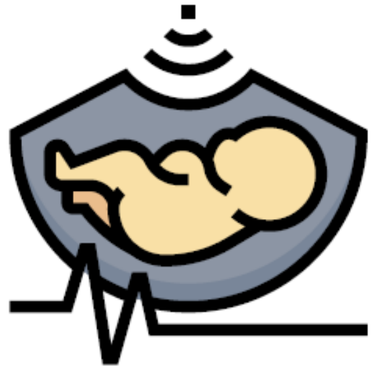
Variable	<30% DFI (n=84)	≥30% DFI (n=34)	p-value
Female age (years)	35.9 ± 4.2	36.9 ± 1.9	0.078
Female BMI (kg/m²)	24.0 ± 3.3	24.6 ± 4.8	0.466

RESULTS

Morphokinetic data (hours)	<30% DFI (n=592)	≥30% DFI (n=386)	p-value
tPNa	6.1 ± 0.2	6.8 ± 0.2	0.030
tPNf	23.0 ± 0.3	24.2 ± 0.3	0.009

RESULTS



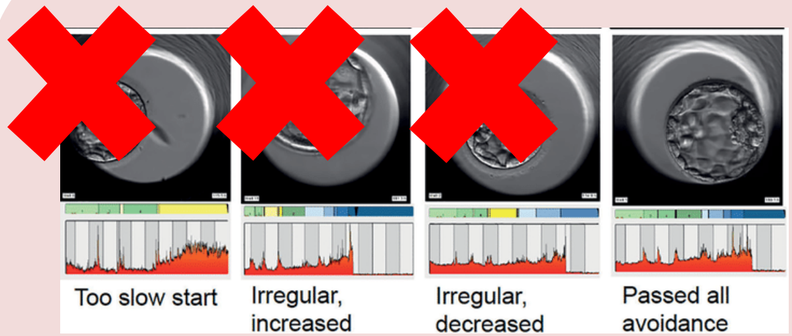


Variable	<30% DFI (n=84)	≥30% DFI (n=34)	p-value
Clinical outcomes			
Transferred embryos (n)	1.5 ± 0.5	1.5 ± 0.5	0.775
Implantation rate (%)	25.6	25.0	0.922
Pregnancy rate (%)	40/70 (57.1)	14/25 (56.0)	0.921
Miscarriage rate (%)	7/40 (17.5)	3/14 (21.4)	0.708

WIDER IMPLICATIONS OF THE FINDINGS

The findings presented here highlight the importance of TLI in the presence of high sperm DFI.

Variable	<30% DFI	≥30% DFI
Blastocyst development (%)	53.1	55.1
High-quality blastocyst rate (%)	87.9	86.2



Clinical outcomes (%)	<30% DFI	≥30% DFI
Implantation rate	25.6	25.0
Pregnancy rate	57.1	56.0
Miscarriage rate	17.5	21.4

Hum Reprod. 2011 Oct;26(10):2658-71. doi: 10.1093/humrep/der256. Epub 2011 Aug 9.

The use of morphokinetics as a predictor of embryo implantation

Marcos Meseguer [1], Javier Herrero, Alberto Tejera, Karen Marie Hilligsøe, Niels Birger Ramsing, Jose Remohí

CONCLUSION

Embryo morphokinetic parameters are negatively impacted by high sperm DFI, resulting in delayed cell cleavage and blastulation, whereas conventional morphological embryo assessment and blastocyst development rate are not related to DNA integrity

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