SPERM DNA FRAGMENTATION INDEX: IMPLICATIONS FOR MALE INFERTILITY AND ASSISTED REPRODUCTIVE TECHNOLOGY OUTCOMES

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CONFLICT OF INTEREST DISCLOSURE

- I have nothing to disclose

INTRODUCTION

- Approximately one in six will experience infertility at some point during their lifetime, and it is estimated that factors related to the male partner are attributable to 50% of infertility cases.

- While sperm DNA damage is broadly defined as any defect in sperm chromatin structure, sperm DNA fragmentation (SDF) relates specifically to the single- or double-stranded breaks (SSBs or DSBs) within DNA strands.

World Health Organization 2021

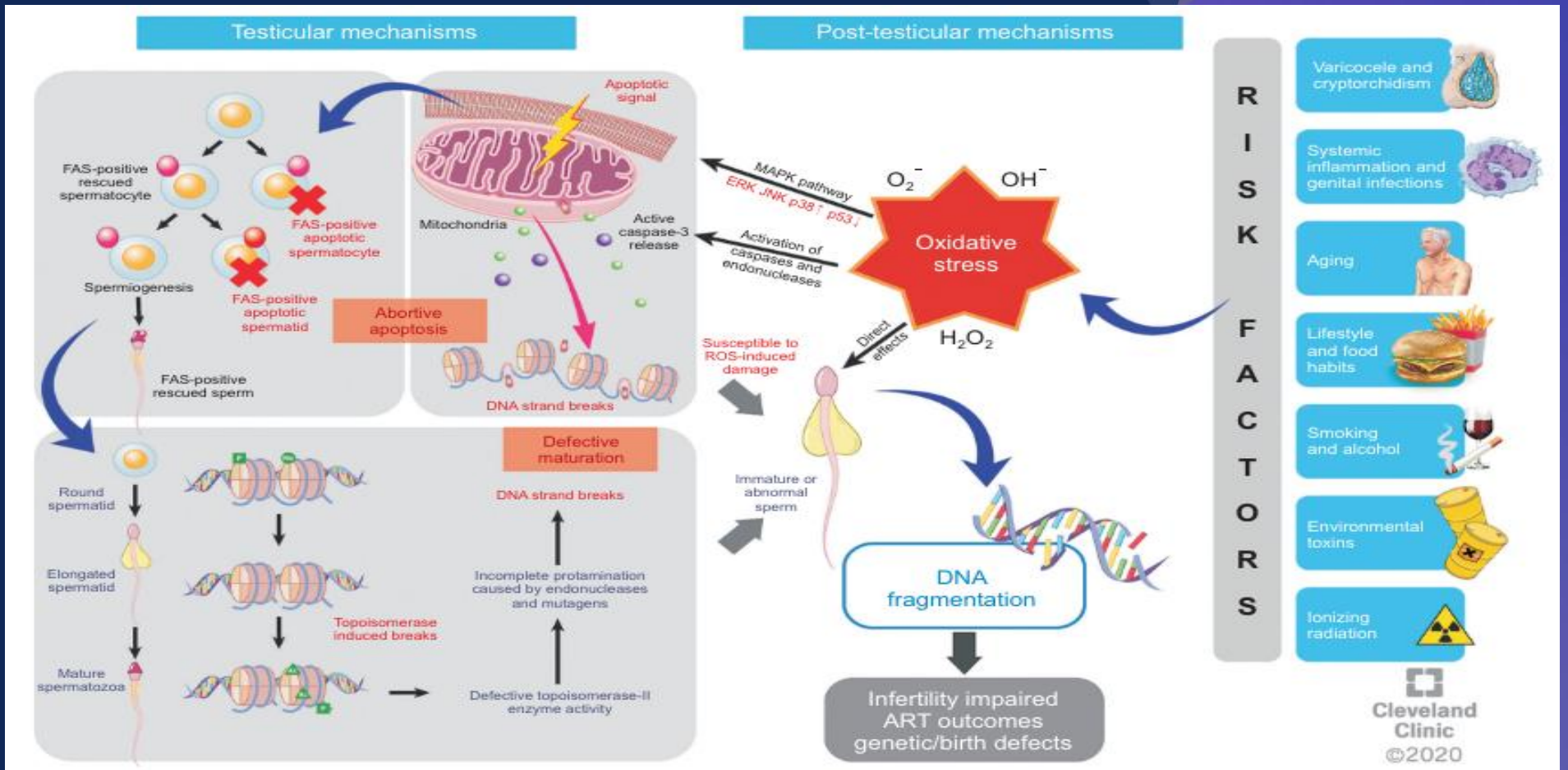

Fig. 2. Overview of the origins of sperm DNA fragmentation (SDF). SDF result from underlying mechanisms such as defective maturation, abortive apoptosis, and oxidative stress. Moreover, clinical (age, infection, cancer, hormonal imbalances, obesity, diabetes) and environmental (heat exposure, environmental toxins, radiation, smoking, drug abuse, diet) risk factors lead to SDF. MAPK: mitogen-activated protein kinase, ERK: extracellular signal-regulated kinase, JNK: c-JUN N-terminal kinase, ROS: reactive oxygen species, ART: assisted reproductive techniques.

Agarwal et al. World J Mens Health 2020

Marinaro and Schlegel. Int J Mol Sci 2023

STANDARD SEMEN ANALYSIS LIMITATIONS

- Significant intra-individual biological variability
- Poor standardization in semen analyses between laboratories
- Not providing any information on the chromatin status

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ORIGINAL ARTICLE

ANDROLOGIA WILEY

Normal sperm parameters per se do not reliably account for fertility: A case–control study in the real-life setting

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TABLE 1 Semen characteristics among the whole cohort according to fertility status [no. (%)] (no. = 2,040)

	Fertile	Infertile
Normal sperm parameters	42 (40.8)	235 (12.1)
Isolated teratozoospermia	37 (35.9)	185 (9.6)
Isolated oligozoospermia	0 (0.0)	64 (3.3)
Isolated asthenozoospermia	1 (1.0)	205 (10.6)
2 sperm abnormalities	18 (17.5)	461 (23.8)
OAT	5 (4.9)	375 (19.4)
Azoospermia	0 (0.0)	412 (21.3)

Abbreviation: OAT, oligoasthenoteratozoospermia.

ASSOCIATION WITH CONVENTIONAL SEMEN PARAMETERS

Table 2. Correlations among semen, clinical parameters, and DFI.

Semen Parameters	Sperm DFI	
	p-Value	Correlation (r)
Concentration (10^6/mL)	0.001	0.953
Total sperm number (10^6/Ejaculate)	0.019	0.345
Normal morphology (%)	−0.074	**0.0001**
Head defects (%)	0.009	0.645
Midpiece defects (%)	−0.057	**0.004**
Tail defects (%)	0.096	**<0.0001**
Total motility (%)	−0.248	**<0.0001**
Progressive motility (%)	−0.257	**<0.0001**
Motility Grade A (%)	−0.254	**<0.0001**
Motility Grade B (%)	0.032	0.106
Motility Grade C (%)	0.055	**0.005**
Motility Grade D (%)	0.253	**<0.0001**
Age	0.088	**<0.0001**
Abstinence time (Days)	0.076	**0.0001**
Volume (ml)	0.063	**0.001**
PH	−0.066	**0.001**
Viscosity	−0.025	0.214

Chua et al. J Pers Med 2023

Table 2. Correlations Between DFI and Sperm Parameters in Fertile and Infertile Men*

Semen Parameters	DFI	
	Fertile Group	Infertile Group
Sperm concentration	-0.23 (.21)	-0.29 (.12)
Progressive motility	-0.02 (.91)	-0.05 (.80)
Normal morphology	-0.06 (.74)	-0.15 (.44)

* Values are correlation coefficient (*P*). DFI indicates DNA Fragmentation Index.

Khalili et al. Urol J 2006

Study or Subgroup	Fertile men Mean	SD	Total	Infertile men Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Zini 2001	13.3	2.5	7	27.6	2.5	33	2.7%	-5.61 [-7.14, -4.08]	2001
Saleh 2002	15.5	8.44	16	29.5	48.58	71	3.6%	-0.31 [-0.86, 0.23]	2002
Saleh 2003	16	9.38	16	23.5	19.66	23	3.6%	-0.45 [-1.10, 0.20]	2003
Khalili 2006	37.7	19.6	30	46.1	16.7	30	3.7%	-0.46 [-0.97, 0.06]	2006
de Paula 2006	5.47	2.73	30	8.6	3.63	47	3.7%	-0.94 [-1.42, -0.45]	2006
Plastira 2007	6.2	1.8	49	30	7.1	61	3.5%	-4.36 [-5.05, -3.66]	2007
Nicopoullos 2008	8.4	5.6	28	22.8	14.6	56	3.7%	-1.15 [-1.64, -0.66]	2008
Winkle 2009	7.21	5.62	27	21.12	17.71	70	3.7%	-0.90 [-1.36, -0.44]	2009
Mehdi 2009	9.19	6.84	30	21.37	17.26	30	3.7%	-0.92 [-1.45, -0.38]	2009
Brahem 2011b	10.14	3.77	30	32.54	10.61	70	3.6%	-2.43 [-2.98, -1.88]	2011
Brahem 2011a	10.37	4.39	16	27.66	15.84	79	3.6%	-1.17 [-1.74, -0.61]	2011
Venkatesh 2011	26.67	8.16	50	35.37	43.27	100	3.8%	-0.24 [-0.58, 0.10]	2011
Mangiarini 2013	8.4	1.56	18	11.45	2.31	14	3.4%	-1.55 [-2.35, -0.74]	2013
Alkhayal 2013	8	6	15	17	10	102	3.6%	-0.93 [-1.49, -0.38]	2013
Chenio 2014	16.8	19.63	31	30.5	27.54	77	3.7%	-0.53 [-0.96, -0.11]	2014
Evgeni 2015b	14.5	58.44	184	35	67.25	485	3.8%	-0.32 [-0.49, -0.14]	2015
Evgeni 2015a	23.85	22.84	78	33.5	88.64	539	3.8%	-0.12 [-0.35, 0.12]	2015
Garolla 2015	13.2	5.3	61	29.2	8.9	100	3.7%	-2.06 [-2.45, -1.67]	2015
Muratori 2015	31.35	38.48	86	44.35	107.65	348	3.8%	-0.13 [-0.37, 0.10]	2015
Ni 2016	12.02	7.94	25	16.86	5.83	15	3.6%	-0.66 [-1.31, 0.00]	2016
Bareh 2016	9.4	2.7	31	36.8	2.7	26	2.2%	-10.01 [-11.98, -8.03]	2016
Malić Vončina 2016	37	128	51	44	204	85	3.8%	-0.04 [-0.39, 0.31]	2016
Liu 2016	15.1	3.2	50	30.4	5.4	50	3.6%	-3.42 [-4.04, -2.80]	2016
Wiweko 2017	20	13	36	30.45	17.08	78	3.7%	-0.65 [-1.06, -0.25]	2017
Dorostghoal 2017	15.12	26.48	105	21.12	59.42	112	3.8%	-0.13 [-0.40, 0.14]	2017
Atig 2017	12.23	4.73	50	28.88	5.87	40	3.6%	-3.13 [-3.76, -2.51]	2017
Zandieh 2017	25.71	3.37	30	40.36	3.58	28	3.3%	-4.16 [-5.10, -3.22]	2017
Carlini 2017	12.8	5.3	114	37.5	4.7	114	3.7%	-4.91 [-5.44, -4.39]	2017
Total (95% CI)			1294			2883	100.0%	-1.67 [-2.12, -1.21]	

Heterogeneity: Tau² = 1.39; Chi² = 865.17, df = 27 (P < 0.00001); I² = 97%

Test for overall effect: Z = 7.21 (P < 0.00001)

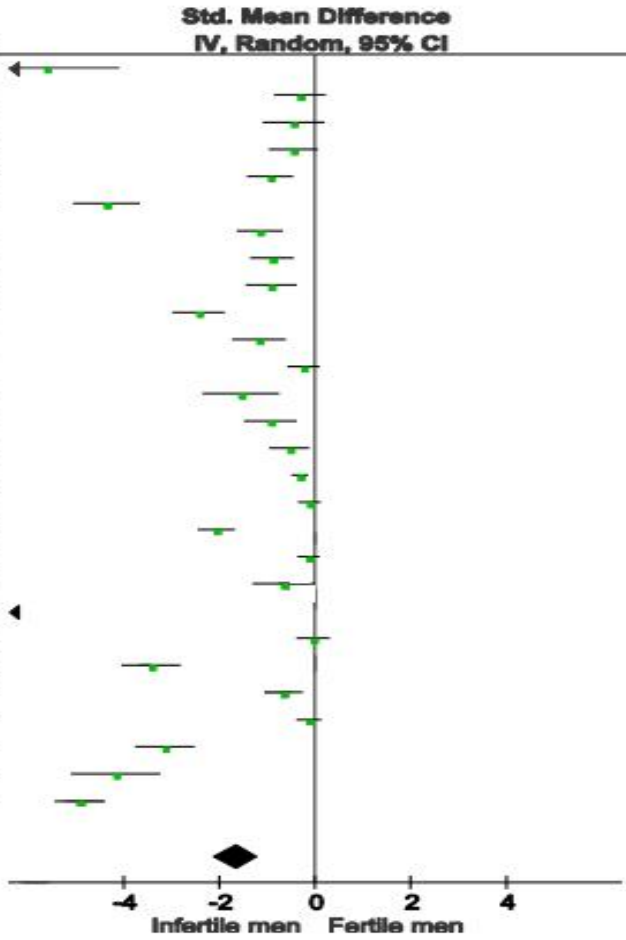

Figure 2 – Forest plot comparing sDF in fertile with infertile men (Meta-analysis 1).

Santi et al. Reprod Biomed Online 2018

DFI TESTS

Table 1. Summary of the four currently recommended assays for measuring sperm DNA fragmentation. TUNEL: terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end labeling; SCSA: sperm chromatin structure assay; SDF: sperm DNA fragmentation.

Assay	Technique	Advantages	Disadvantages
TUNEL	Fluorescent-marked deoxynucleotides incorporated in sites of breaks and detected by microscopy or flow cytometry	• Sensitive • Reliable • Minimal interrater variability	• Expensive • Requires specialized equipment and training
SCSA	Depends of different fluorescence of acridine orange dye if bound to intact or denatured DNA (at sites of breaks)	• Standardized protocol • Reproducible • Can examine a large number of cells	• Expensive • Requires specialized equipment and training
SCD	Acid denaturation followed by dispersion of fragmented DNA	• Simple equipment • Commercial kits available	• High interobserver variability
Comet	Electrophoresis detecting migration of DNA fragments	• Sensitive • Reproducible • Can be performed with very low sperm counts	• Interobserver variability • Requires experienced observer • Variable protocols

Farkouh et al. Arab J Urol 2023

TABLE 1 Characteristics of sperm DNA fragmentation assays

Test	Acronym	Principle	Specimen requirements	Thresholds[a]			Can be done in surgically retrieved specimens (e.g. testicular spermatozoa)?
				Male infertility diagnosis	IUI (likelihood of pregnancy and/or miscarriage)	IVF/ICSI (likelihood of pregnancy and/ or miscarriage)	
Terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labelling	TUNEL	The assay relies on a terminal deoxynucleotidyl transferase (TdTA) enzyme for the 'direct' labelling of 3′ free ends of DNA. The sites of breaks can be identified with the aid of optical fluorescence microscopy or flow cytometry. The TUNEL test essentially assays the protamine toroid linker DNA as the relatively large TdTA molecule might not penetrate the highly compacted protamine toroid. Protocol modifications have been introduced to increase its sensitivity, including DNA decompaction using dithiothreitol (DTT)	Whole ejaculate, $2.0–2.5 \times 10^6$ spermatozoa for flow cytometry. 10,000 cells/ events are counted. With microscopy, a total of 500 spermatozoa are assessed.	>17% by flow cytometry[1]	No thresholds defined for neat semen; >12% for post-wash specimen using fluorescence microscopy[2]	No clear thresholds using flow cytometry established. >36% using fluorescence microscopy[3,4]	Yes, using fluorescence microscopy only.[5]

Esteves et al. Andrologia 2020

Test	Acronym	Principle	Specimen requirements	Thresholds[a]			Can be done in surgically retrieved specimens (e.g. testicular spermatozoa)?
				Male infertility diagnosis	IUI (likelihood of pregnancy and/or miscarriage)	IVF/ICSI (likelihood of pregnancy and/or miscarriage)	
Sperm Chromatin Structure Assay	SCSA	The assay is based on acid denaturation of the DNA at the sites of existing single- or double-strand breaks. Acridine orange (AO) is used for staining; the dye penetrates the sperm chromatin and intercalates into double-stranded DNA (intact DNA), which fluoresces green when exposed to blue laser light. In contrast, AO attachment to single-strand DNA creates a complex that produces a metachromatic shift to red fluorescence. The red fluorescence represents DNA strands that originate from the sites of single- or double-strand breaks. The fluorescence patterns emitted by spermatozoa are captured using a flow cytometer, and the ratio of red to total (green + red) fluorescence intensity is used to calculate the percentage of spermatozoa with DNA fragmentation (DFI; DNA fragmentation index).	>0.5 million sperm/ml raw semen for direct measurement. If <0.5 million/ml, specimens should be concentrated by centrifugation and resuspended. Specimens are shipped to the reference laboratory as ~0.2 ml frozen raw semen aliquot in boxed dry ice or LN2 dry shipper.	>20%–25%[6] (DFI) >20%–25% (HDS)	>25%[7-9] (DFI) >25% (HDS)	>30%–35%[7-9] (DFI) >25% (HDS)	Yes, if sufficient number of spermatozoa.

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Test	Acronym	Principle	Specimen requirements	Thresholds[a]			Can be done in surgically retrieved specimens (e.g. testicular spermatozoa)?
				Male infertility diagnosis	IUI (likelihood of pregnancy and/or miscarriage)	IVF/ICSI (likelihood of pregnancy and/ or miscarriage)	
Sperm Chromatin Dispersion	SCD	The assay relies on the principle that spermatozoa with DNA fragmentation fail to produce the characteristic halo of dispersed DNA loops that are observed in spermatozoa with nonfragmented DNA, following acid denaturation and removal of nuclear proteins. Sperm suspensions are embedded in agarose gel on slides and treated with an acid denaturation solution (HCl) to generate restricted single-strand DNA motifs at the sites of existing single- or double-strand breaks. The denaturation is stopped, and spermatozoa are exposed to a lysing solution based on DTT, sodium dodecyl sulphate, and NaCl to remove the sperm membrane and nuclear proteins. Then, slides are stained with DAPI (4′,6-diamidino-2-phenylindole) or Diff-Quik, and spermatozoa with nondispersed and dispersed chromatin loops are identified by fluorescence or bright-field microscopy examination,respectively, to calculate the percentage of sperm with DNA fragmentation. The halos correspond to relaxed DNA loops attached to the residual nuclear structure as seen in spermatozoa with low or no SDF. By contrast, spermatozoa with very small or no halos correspond to those exhibiting SDF as confirmed by DNA breakage detection-fluorescence in situ hybridisation, a procedure in which the restricted single-stranded DNA motifs generated from DNA breaks can be detected and quantified.	The test can be performed in a single to several hundred spermatozoa, both in fresh and frozen-thawed specimens. The recommended sperm concentration is 1–3 million per ml, but it can be performed using less concentrated samples.	In general, thresholds ranging from >16% to 30% are used for male infertility diagnosis, with 20% considered the value that best discriminates infertile from fertile men.[6] Using sperm donors and patients attending an infertility clinic, a threshold of >16% was found to best discriminate both cohorts with an AUC of 0.874, specificity of 85% and specificity of 75%.[10]	20%[11]	Using oocyte donor cycles to control for female factors, a 25% threshold discriminates between clinical pregnancy and no pregnancy, with an AUC of 0.711.[12]	Yes. The SCD test can be used on PESA, MESA, TESA or TESE obtained spermatozoa as well as low concentrated samples derived from IMSI, PICSI, MACS or microfluidics. In TESA/TESE specimens, somatic cells and spermatozoa can be distinguished using a dual combination of fluorochromes with DNA and protein specificity.[13]

Esteves et al. Andrologia 2020

Test	Acronym	Principle	Specimen requirements	Thresholds[a]			Can be done in surgically retrieved specimens (e.g. testicular spermatozoa)?
				Male infertility diagnosis	IUI (likelihood of pregnancy and/or miscarriage)	IVF/ICSI (likelihood of pregnancy and/or miscarriage)	
Single-cell gel electrophoresis assay	Comet	The assay relies on DNA decompaction and protein depletion coupled to single-cell electrophoresis in agarose microgel. Removal of protamines and histones creates a nucleoid-like structure containing supercoiled loops of DNA. Alkaline or neutral pH conditions allow the uncoil of double-stranded DNA, which under electrophoresis results in migration of fragments of single- and double-stranded DNA towards the anode, thus forming a comet tail that can be observed under fluorescence microscopy. The relative fluorescence in the tail compared with its head reflects the level of SDF; spermatozoa with increased fluorescence intensity in the comet tails have high levels of chromatin damage. Additional quantitative parameters can be used to increase the test's precision, such as nucleus diameter, olive tail movement and comet length. The alkaline Comet assay detects global SDF, i.e., both single- and double-stranded DNA breaks, as well as alkali-labile sites, whereas the neutral Comet assay detects double-stranded DNA breaks only. Alternatively, the two-tailed Comet assay can be used to assess and differentiate the type of break in the same spermatozoon. The assay firstly applies neutral lysis and electrophoresis to detect double-strand breaks, and then, by turning the slide 90° and applying alkaline lysis and electrophoresis, single-strand breaks are detected. The Comet assay provides three parameters: (i) ACS: average SDF across 100 individual spermatozoa; (ii) HCS: the proportion of spermatozoa with high DNA damage; (iii) LCS: the proportion of spermatozoa with low DNA damage.	A minimum of 100 µl volume of neat semen containing a minimum of 5,000 spermatozoa.	>26% (ACS)[14,15] <74% (LCS) >4% (HCS) AUC of these parameters = 0.909–0.936[14,15]	>26% (ACS)[15] <70% (LCS) >2% (HCS) AUC of these parameters = 0.883–0.969[15]	>27% (ACS)[14,15] <68% >10%	Yes; the Comet assay can be used on PESA, MESA, TESA or TESE obtained spermatozoa as well as low concentrated samples derived from IMSI, PICSI, MACS or microfluidics.

Esteves et al. Andrologia 2020

Table 2. Cut-off values with sensitivity and specificity for each assay

Technique	Number	Area[a)]	Cut-off value (%)	Sensitivity	Specificity
TUNEL	95	0.901	22.08	0.754	0.942
SCSA	100	0.790	19.90	0.594	0.872
SCD	100	0.871	24.74	0.734	0.920
Oxisperm	90	0.504	35.38	0.991	0.322
Neutral Comet	100	0.511	36.37	0.996	0.319
Alkaline Comet	100	0.977	48.47	0.840	0.918

TUNEL, terminal deoxynucleotidyl transferase dUTP nick end labelling; SCSA, sperm chromatin structure assay; SCD, sperm chromatin dispersion.
[a)]Area under the receiver operating characteristic curve.

- Strong and significant correlations were observed between:
  - SCD test and SCSA ($r = 0.70$, $p < 0.001$),
  - SCD test and the TUNEL assay ($r = 0.68$, $p < 0.001$),
  - SCSA and the TUNEL assay ($r = 0.77$, $p < 0.001$).

Javed et al. Clin Exp Reprod Med 2019

INDICATIONS

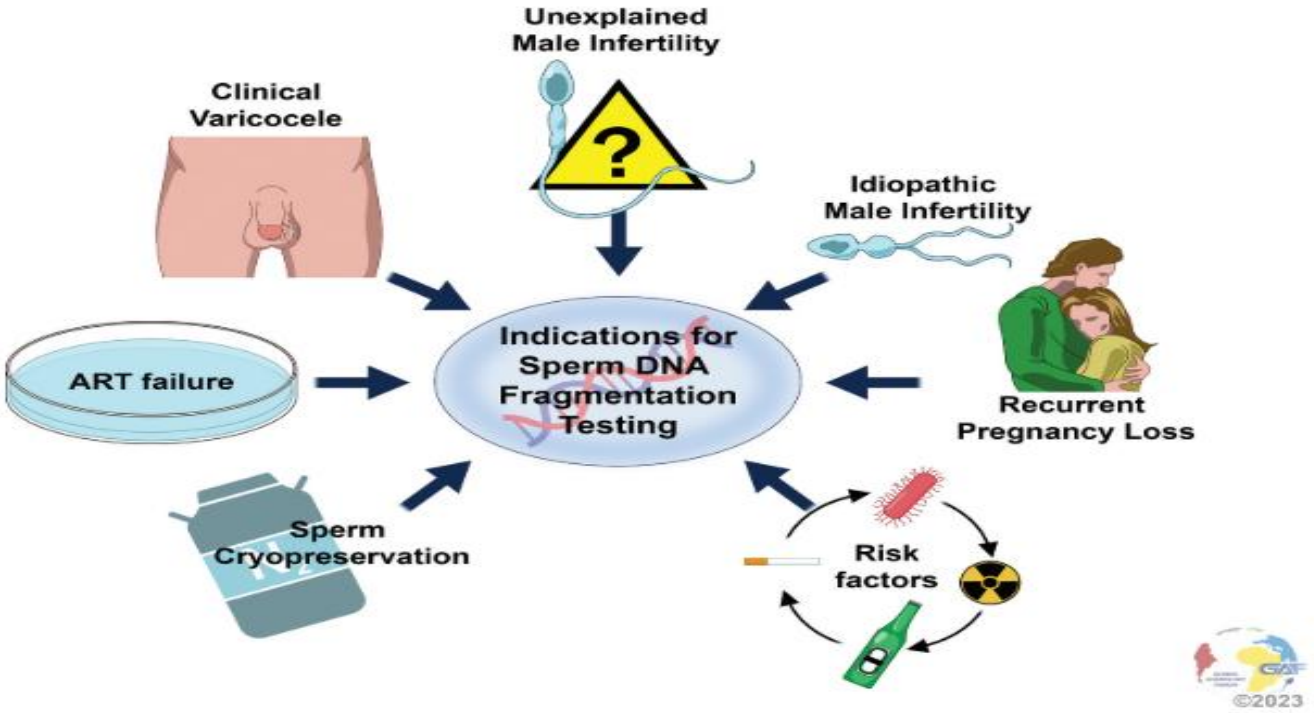

Figure 1. Indications for sperm DNA fragmentation testing. Reproduced from Agarwal A, et al. Controversy and consensus on indications for sperm DNA fragmentation testing in male infertility: a Global survey, Current guidelines, and expert recommendations. World J Mens Health. 2023 Jul;41(3):575–602 with permission, Global Andrology Forum ©2023. All rights reserved. ART: assisted reproductive technologies.

Farkouh et al. Arab J Urol 2023

Table 1 Associated factors and effect of high SDF on ART outcomes.

Factors contributing to increased SDF	Impact of high SDF on ART outcomes
Idiopathic or unexplained infertility • High degree SDF despite having normal semen parameters [13] **Advanced male age** • Positive correlation with age [71] • %DFI higher in men aged ≥40 years [72] **Varicocele** • Positive association exists between varicocele and SDF [73] • High SDF in both fertile and infertile men with varicocele **Chemo/radiotherapy** • Impaired spermatogenesis and fertility [74] • Radiotherapy increased SDF and chemotherapy lowered SDF [75] • Radioiodine therapy for thyroid cancer increased DFI [76] **Testicular trauma/severe infection** • Oxidative stress positive correlated with SDF [77] • High SDF even in low levels of leucocytospermia [78] **Male obesity** • Poor spermatogenesis [79] and associated with high SDF [80] **Occupational exposure** • High SDF in workers exposed to pesticides and ionising radiations • Bisphenol-A exposure leads to high SDF [81] **Patient life style** • Smoking has negative impact on sperm DNA integrity [82] • Excessive alcohol consumption increases SDF [83]	**Natural pregnancy** • Very low conception rates [84] **IUI** • Low pregnancy rate (odds ratio 9.9) [85] • Pregnancy loss with SDF >12% [86] and DFI >27% [87] **IVF/ICSI** • Negatively correlated with SDF • Fair to poor predictive value of different SDF assays for prediction of pregnancy [88] **Fertilisation rate and embryo quality** • SDF ≥22.3% had significantly lower fertilisation rates with ICSI [89] • Negative impact on reduced cleavage [90]and blastulation rate [91] decreased blastocyst development [92] **Live-birth rate** • Negative association with live-birth rate after IVF [93] • Increased live-birth rate with low SDF [94] • High miscarriage rates and recurrent spontaneous abortion after IVF and ICSI [95]

Selvam and Agarwal Arab J Urol 2018

Table 1 Characteristics of meta-analyses investigating the association between sperm DNA fragmentation and pregnancy outcomes in assisted reproductive technology cycles

Study	ART	*n*	(*n*)	Fertilization rate	Embryo development	Implantation rate	Pregnancy rate	Live birth rate
Collins et al[83]	IVF	–	1,107	NA	NA	NA	DOR = 1.53 [0.77; 3.02]	NA
	ICSI	–	549	NA	NA	NA	DOR = 1.12 [0.59; 2.15], $p = 0,41$	NA
	IVF + ICSI	–	505	NA	NA	NA	DOR = 1.91 [0.79; 4.57]	NA
Evenson and Wixon[78]	IVF	838	–	NA	NA	NA	OR = 2.0 [1.02; 2.84], $p = 0.03$	
	ICSI and/or IVF	212	–	NA	NA	NA	OR = 1.6 [0.92; 2.94], $p = 0.06$	NA
Li et al[79]	IVF	–	816	RR = 0.79 [0.54; 1.16], $p = 0.23$	NA	NA	RR = 0.68 [0.54; 0.85], $p = 0.006$	NA
	ICSI	–	201	RR = 1.03 [0.55; 1.04], $p = 0.09$	NA	NA	RR = 0.75 [0.55; 1.04], $p = 0.09$	NA
Zini et al[43]	IVF	1,805	–	NA	NA	NA	OR = 0.70 [1.30–2.23], $p \leq 0.05$	NA
	ICSI	1,171	–	NA	NA	NA	OR = 1.15 [0.90; 1.55], $p = 0.65$	NA
Zhao et al[72]	IVF	–	1,680	NA	NA	NA	OR = 0.66 [0.48; 0.90], $p = 0.008$	NA
	ICSI	–	1,422	NA	NA	NA	OR = 0.94 [0.70; 1.25], $p = 0.65$	NA
Osman et al[80]	IVF	706	–	NA	NA	NA	NA	RR = 1.27 [1.05; 1.52], $p = 0.0001$
	ICSI	552	–	NA	NA	NA	NA	RR = 1.11 [1.00; 1.23], $p = 0.04$
Deng et al[73]	IVF	[a]	[a]	NA	RR = 0.57 [0.54; 0.60], $p < 0.01$	NA	RR = 0.77 [0.59–1.00], $p < 0.05$	RR = 0.84 [0.67; 1.06], $p = 0.15$
	ICSI	[a]	[a]	NA	NA	NA	RR = 0.75 [0.44; 1.27], $p > 0.05$	NA
	IVF + ICSI	[a]	[a]	NA	RR = 0.93 [0.87; 1.01], $p = 0.01$	NA	NA	0.95 [0.72; 1.26], $p = 0.74$
Ribas-Maynou et al[37]	IVF	[b]	–	NA	NA	RR = 0.68 [0.52;0.89], $p < 0.01$	RR = 0.72 [0.55; 0.95], $p = 0.02$	RR = 0.48 [0.22; 1.02], $p = 0.06$
	ICSI	[b]	–	NA	NA	RR = 0.79 [0.60;1.04], $p = 0.09$	RR = 0.89 [0.78; 1.02], $p = 0.09$	RR = 0.92 [0.67; 1.27], $p = 0.62$
Simon et al[81]	IVF	3,734	–	NA	NA	NA	OR = 1.65 [1.34–2.04], $p < 0.0001$	NA
	ICSI	2,282	–	NA	NA	NA	OR = 1.31 [1.08–1.59], $p = 0.0068$	NA
	IVF + ICSI	2,052	–	NA	NA	NA	OR = 2.37 [1.89–2.97], $p < 0.0001$	NA
Simon et al[69]	IVF	–	9,363	NA	NA	NA	OR = 1.15 [1.05; 1.27), $p = 0.0033$	NA
	ICSI	–	3,260	NA	NA	NA	OR = 0.89 [0.80; 0.99), $p = 0.0254$	NA
	IVF + ICSI	–	2,121	NA	NA	NA	OR = 2.00 [1.66; 2.41], $p < 0.0001$	NA

Abbreviations: DOR, log diagnostic odds ratio; *n*, number of included cycles; (*n*), number of included patients; NA, data not available; OR, odds ratio; RR, risk ratio.

[a]Several meta-analysis performed using different studies for each outcome: the meta-analysis for embryo development included 17,879 embryos, the meta-analysis for pregnancy rate included 6,771 cycles, and the meta-analysis for live birth rate included 1,785 patients.

[b]Several meta-analysis performed using different studies for each outcome: the meta-analysis for implantation rate included 4,055 and 3,405 patients for IVF and ICSI studies, respectively; the meta-analysis for pregnancy rate included 3,711 and 5,467 patients for IVF and ICSI studies, respectively; and the meta-analysis for live birth rate included 1,634 and 3,017 patients for IVF and ICSI studies, respectively.

Nielsen et al. Semin Reprod Med 2023

CONCLUSIONS

- Ultimately, while there is growing evidence related to SDF and its impact on fertility, it remains a controversial topic. More RCTs are needed.

- Need for comprehensive guidelines.

- Collaboration between reproductive specialists and reproductive endocrinologists to recognize the role of sperm in reproductive failure and clinicians can more easily select an optimal treatment plan for the couple.

از معلّم جان روشن یافتیم
از پدر گر قالب تن یافتیم
از معلم جان روشن یافتیم