

Analysis of Sperm DNA Fragmentation Clinical applications

Sperm DNA Fragmentation

Sperm DNA Fragmentation (SDF) is an important additional piece of information about seminal quality. An SDF value that exceeds a threshold value of 30% suggests sub-par sperm quality (Evenson et al., 2002). The SDF value confers clinicians the power to make **informed** decisions in their daily practice and take action based on **quantitative** results.

What is the use of assessing SDF?

1. To distinguish which couples are suitable for treatment by IUI.
2. To assess the quality of semen samples or donors for suitability.
3. To assess the efficacy of medical interventions or treatment of infectious diseases.
4. To provide answers to cases of unexplained infertility, ART failure or repeated abortions.

What *clinical actions* should be followed based on SDF?

1. To distinguish which couples are suitable for treatment by IUI:

High SDF values have been shown to reduce the efficacy of intra-uterine insemination (IUI) from 16% to 4% (Bungum et al., 2004) or lower (Duran et al., 2002). In contrast, the same SDF values do not seem to affect the outcome of in vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI) techniques –the best results being obtained in ICSI (Benchaib et al., 2007, Bungum et al., 2004)–. This is probably due to the fact that there is a selection process involved during these techniques, in which the best spermatozoon and fertilized embryo are chosen before implantation thus reducing the impact of low sperm quality.

When facing an SDF above the 30% threshold, it is therefore recommended that clinicians avoid unnecessary IUI cycles and proceed directly to IVF or ICSI.

How does one choose spermatozoa with low SDF values for use in IVF or ICSI?:

Numerous techniques have been suggested in order to select sperm cells with intact DNA. These include:

- a. The use of polarization microscopy to select cells with highest birefringence in the sperm head (Gianaroli et al., 2008a, Gianaroli et al., 2008b).
- b. The use of high magnification microscopy for intracytoplasmic morphologically selected sperm injection (IMSI) (Tarozzi et al., 2007, Bartoov et al., 2003, Hazout et al., 2006).
- c. The use of Hyaluronic Acid (HA) selects spermatozoa with low DNA fragmentation (Parmegiani et al., 2009).

2. To assess the quality of semen samples or donors for suitability:

Traditional WHO and Kruger criteria for the assessment of semen quality present several limitations:

- a. Traditional parameters are based on subjective observations and are prone to variability (Keel, 1990).
- b. A cut-off based on traditional parameters creates overlap between fertile and infertile populations and is thus of little predictive value (Aziz and Agarwal, 2008).
- c. A traditional analysis does not take into account the diverse array of biological properties of a spermatozoon –the most important of which being its ability to transmit an intact genome for the initiation of a viable pregnancy (Fernández et al., 2005)–.
- d. Traditional parameters do not provide a diagnosis of the cause of male infertility (Agarwal and Allamaneni, 2005, Nallella et al., 2006).

A call has therefore been made by the international community to look beyond these criteria to improve seminal analysis (Aziz and Agarwal, 2008).

In light of the available technology, SDF analysis provides the obvious answer for clinicians to assess in a rigorous manner the quality of semen samples from a donors or patients undergoing ART.

3. To assess the efficacy of medical interventions or treatment of infectious diseases:

A. Varicocele:

Infertile men with varicocele show a high proportion of sperm cells with intense nuclear DNA damage levels (Enciso et al., 2006). Varicocelectomy interventions have been demonstrated to significantly reduce SDF levels (Werthman et al., 2008). Studies are currently in progress showing that SDF levels decrease only transiently following varicocelectomy (Suresh et al. personal communication).

Measurement of SDF values following varicocelectomy provide a much more quantifiable parameter than morphology in order to assess the efficacy of such an intervention. Measuring SDF allows the clinician to follow the progress of his patient and select the best semen sample from different time intervals following varicocelectomy for ART.

B. *Chlamydia trachomatis* and *Mycoplasma* infections:

The percentage of spermatozoa with fragmented DNA is significantly higher in patients with *Chlamydia trachomatis* and *Mycoplasma* infections (Gallegos et al., 2008). Antibiotic therapy in these patients was demonstrated to significantly reduce SDF levels(Gallegos et al., 2008).

As opposed to other seminal parameters that are unaffected by these genitourinary tract infections, measurement of SDF levels allows clinicians to check the efficacy of antibiotic treatments and select the best semen samples for ART following treatment.

4. To provide answers to cases of unexplained infertility, ART failure or repeated abortions:

High SDF levels have been shown to influence fertilization rate (Muriel et al., 2006a, Muriel et al., 2006b) and embryo quality (Velez de la Calle et al., 2008), leading to repeated pregnancy loss(Carrell et al., 2003) and low ART outcome (Henkel et al., 2004, Sakkas et al., 2004, Virro et al., 2004). Failures may therefore be due to poor sperm DNA quality.

When facing an SDF value exceeding 30%, a clinician should consider factors that may influence sperm DNA fragmentation such as: medications, toxic compounds, fever, smoking, drugs, infectious diseases, varicocele, age and long abstinence. Importantly, high SDF values have been shown to be reversible using 1 g vitamin C and 1 g vitamin E daily for 2 months (Akmal et al., 2006, Greco et al., 2005) or Menevit (antioxidant) –one capsule per day for three months before ART (Tremellen et al., 2007)–.

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