Commentary

Measure of sperm DNA fragmentation (SDF): how, why and when?

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Sperm DNA fragmentation (SDF) is a frequent topic of discussion in the field of reproductive technologies and three main questions remain unanswered: (I) which of the many assays available is the "best" test to measure SDF? (II) can a measure of SDF be useful for patient's diagnosis, prognosis and permit to adopt the best therapy for the patient? and (III) if deemed relevant, for which indication a measure of SDF should be encouraged?

In this issue of *Translational Andrology and Urology (TAU)*, Agarwal and colleagues (1) provide a detailed and comprehensive review of the techniques available to assess the extent of DNA alterations (fragmentation and compaction) in sperm and list the pros and cons of each technique. Unfortunately, the existing techniques—described in the paper by Agarwal *et al.*—that can be used to directly or indirectly measure DNA fragmentation are poorly reproducible in to different extent: (I) acridine orange (AO) staining; (II) aniline blue (AB) staining; (III) chromomycin A3 (CMA3) staining; (IV) toluidine blue (TB) staining; (V) terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assessed by flow cytometry; (VI) sperm chromatin structure assay (SCSA) by flow cytometry; (VII) sperm chromatin dispersion (SCD) (or halo test) and (VIII) single cell gel electrophoresis (SCGE) assay. Fluorescent assays which can be automated by flow cytometry are the most reproducible and thus the most promising techniques but few reproductive laboratories are equipped with these relatively expensive devices.

With its current imperfection, SDF assays should only be proposed to certain patients. In their manuscript, Agarwal and colleagues (1) describe three clinical scenarios describing situations, which may benefit most from SDF testing. The first clinical indication is the presence of varicocele. It is believed that varicoceles increase the average scrotal temperature and hence oxidative stress. For low grades varicoceles, surgery could thus be proposed only to patients with a high SDF, who are most likely to benefit from the procedure. In their second group the authors aggregate several indications including patients presenting with either unexplained infertility, recurrent pregnancy loss or intrauterine insemination failure. What is common between these three indications is that semen parameters might be normal and therefore SDF assay may provide a better diagnostic potential to these otherwise often idiopathic infertilities. This has been recently confirmed by Carlini *et al.* [2017] (2) who reported a significant positive correlation between pregnancy losses and elevated levels of SDF. Thirdly, SDF measurement can be interesting to evaluate the deleterious effects of various risk factors such as obesity, pollutant exposure or cigarette smoking. For these indications SDF measurements could highlight that lifestyle changes should be undertaken before initiating *in vitro* fertilization or other assisted reproductive technologies.

In conclusion although not perfect and not ready to be used systematically in routine settings, a measurement of SDF comes as an interesting and relevant test for a variety of situations where the classic measurement of sperm parameters included in spermograms and spermocytograms

might not be sufficient to obtain a relevant diagnostic and prognostic.

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Footnote

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