Commentary

Clinical use of sperm DNA fragmentation analysis results, a practical example of how to deal with too much information from the literature in reproductive medicine

Nicolás Garrido[1], Rocío Rivera[2], Satur Luján[2,3]

[1]IVI Foundation, Valencia, Spain; [2]Andrology Laboratory and Sperm Bank, Instituto Universitario IVI, Valencia, Spain; [3]Department of Urology, Hospital Universitari i Politècnic La Fe, Valencia, Spain

Correspondence to: Dr. Nicolas Garrido. IVI Foundation, Parc Científic Universitat de València C Catedrático Agustín Escardino nº 9 Edificio 3, 46980 Paterna, Spain. Email: nicolas.garrido@ivi.es.

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Although a huge amount of information regarding the origin, causes, and impact on reproductive implications of DNA fragmentation in spermatozoa has been raised in the last decades (1), the way to deal with it from the practical and clinical perspective remains unclear.

Research on this topic has been favored by the easiness to gather biological samples to be analyzed, the insignificant annoyance or disturbance for the patients, the wide availability and relatively low cost of the tests to measure sperm DNA strand breaks together with the potential interest generated from the pioneering works linking DNA fragmentation in sperm to reproductive results.

Paradoxically, this originated, instead of a bulk of evidences leading to straightforward clinical recommendations and behavior, a significant background noise and confusion about when to ask for these tests, how to deal and manage the results, how to inform the patients and what recommendations, either medical treatments for patients or laboratory techniques for sperm selection are needed to be applied in order to improve sperm quality, to (theoretically) enhance reproductive results.

Hypothetically speaking, having damaged DNA in sperm could lead to worse reproductive results or mid-long term health problems in offspring, given that this is the way genetic information is delivered to the next generation. Fortunately, the evidence available so far may relax these assertions.

First, the ability of the oocyte to repair, at least to some extent, DNA damage (2). This means that samples with low to moderate damage, combined with good quality oocyte may exert no effect on reproductive outcomes.

Second, the fact that only a small percentage of sperm DNA encodes biologically relevant data (3), and sperm DNA fragmentation (SDF) tests are still not able to point where the break is located, or if there are expected pathological consequences conditioned by the location of detected breaks.

Moreover, using DNA fragmentation as a predictive tool is likely to be a mistake. Probably, no sperm diagnostic tool could ever be developed, since measuring any marker in sperm will hardly predict the results of combining sperm with oocytes and then endometrial receptivity, and also, as it has been previously suggested, sperm quality seems to be multifactorial given the number of molecular factors related with sperm function.

Concerning assisted reproductive technology (ART), also there is an existing limitation regarding the fact that any sperm analyzed this way, can't be used with reproductive purposes.

At most, the measurement of a degree of similarity with previously successful samples employed as a model, and ideally, the development of treatments or techniques to improve sperm selection is aimed. This could be useful to establish recommendations about what to do regarding SDF results aiming to provide our patients the best counseling possible and improve their reproductive chances (4).

Also, different origins and causes of DNA fragmentation in sperm have been described, each of them requiring a different approach in order to be prevented, avoided, solved, or considered when designing reproductive counseling or interventions to improve results.

This may include a myriad of interventions, including lifestyle changes, medical, surgical or nutraceutical treatments, changes in lab protocols or advanced sperm selection techniques.

In a time of personalized and individualized medicine escaping for "one fits all" solutions, identifying the population where tests need to be applied, being able to forecast expected results, helping in the decision-taking process, as well as the most appropriate therapeutic options in a case by case manner is crucial.

Clinical varicocele, unexplained infertility or repeated ART failures, recurrent pregnancy losses and the harming effects of lifestyle factors on reproductive outcomes are very frequent scenarios to be faced by male infertility specialists, or even gynecologists from practices not having these professionals, that can be helped by the proper sperm evaluation, and correct interpretation of the literature, followed by expert's recommendations in a cost-benefit approach (5).

On their work, Agarwal and colleagues performed a brilliant exercise of condensing the evidences available, considering their quality and providing with useful insights and counsels about all the previous pitfalls related to SDF analysis in a relevant piece of literature, whose contents can easily be applied by the clinicians as the reference manual lacking so far.

Furthermore, the rationale for the origin of DNA fragmentation in each case, and the most convenient way to proceed depending on the evidences available are discussed, and the clinical results of the interventions to improve reproductive outcomes.

This useful piece of literature will undoubtedly be a reference for the clinicians for years, until more detailed information is available on the topic.

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Footnote

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