Commentary

A guide to sperm DNA fragmentation testing

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A conundrum exists in the field of male infertility as in many other areas of medical study. It is described by the adage that advises one to not order a test or exam if you don't know what to do with the results. The urologists' conundrum is: how to use the information we have learned about abnormalities in sperm chromatin, specifically DNA fragmentation, in our daily practice. How to measure it, what are the qualitative and quantitative norms, what are the effects (on fertilization and pregnancy both natural and assisted) of deviations from these norms, is it treatable or just manageable with some sort of work-around? These are some of the questions the urologist/male fertility specialist must consider when he or she is requested to consult on a man referred for "evaluation of an abnormal sperm DNA fragmentation test". These tests are relatively easy to obtain and at least one has been standardized and commercially available for a number of years. The article on "Clinical utility of sperm DNA fragmentation testing" addresses these issues (1).

The reader is led on a well-organized journey into the field of the clinical utility of DNA fragmentation testing. The introduction concisely tells us the detrimental effects of sperm DNA fragmentation (SDF) as well as the multifactorial etiologies so far known. The next section is an excellent description of eight of the most well-published tests of SDF, including an illustrative table summarizing the principle upon which they are based, and their strengths and weaknesses. They accurately point out the obstacles that exist in methodology, precision, variability in lab or clinical conditions, and general lack of standardization which prevent, at the current time, widespread adaptation of this test as a more accurate indicator of male fertility status than semen analysis. Nevertheless, in the next section they present some carefully chosen and well-explained clinical scenarios where the use of SDF measurement may have clinical utility in patient management.

The clinical scenarios presented included varicocele, unexplained infertility, recurrent (natural) pregnancy loss, recurrent intrauterine insemination (IUI) failure, *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) failures, and lifestyle risk factors. In each instance, after a detailed discussion of the rationale involved, a clinical recommendation is made. Another excellent table accompanying the text in this section summarizes the most pertinent evidence forming the rationale upon which the recommendations are based. The simplest and perhaps most useful recommendation (based on frequency of occurrence) involves varicoceles where, in essence, SDF testing is recommended in cases where a varicocele is present and normal or near normal semen parameters exist. In this case, based on the best evidence available, the presence of abnormal levels of SDF would be an indication for surgical intervention. The least convincing recommendation for SDF testing is in the area of lifestyle risk factors which include age, obesity, smoking and environmental or occupational exposures. In these instances, the recommendation suggests that SDF "can help reinforce the importance of lifestyle modification, predict fertility, and monitor the patient's response to intervention".

One of the weaknesses inherent to the use of a clinical scenario to illustrate a point is that it may not apply to a slightly different scenario, i.e., the recommendation may have limited utility. The recommendations related to assisted reproductive technology (ART) are individually

relevant, but when taken together, may be at odds with each other or confusing to some extent when trying to develop a treatment plan. For example: high SDF rates are associated with recurrent spontaneous abortions (RSA) as well as lower pregnancy rates with IUI. The recommendation is that SDF testing be done when there is RSA and suggests that IVF or ICSI may serve the couple better suggesting that IUI be avoided if SDF is high. A separate section on IVF/ICSI points out an apparent detrimental effect of high SDF on conventional IVF but not ICSI pregnancy rates. More importantly, however, is the discussion of the significantly increased rate of pregnancy loss after IVF and ICSI in couples where the SDF is high. The recommendation of this section is that SDF can be a useful prognostic tool and the carefully worded advice that several studies have shown a benefit in the use of testicular sperm rather that ejaculated sperm. It seems that the rationale for the use of testicular sperm was as sensible and well-supported as many of the recommendations made elsewhere and given the lack of any other "simple" work-around to the problem could have been more strongly worded.

As is common, a paper of this sort, even though intended as a guideline, brings new questions. What is the clinical utility of SDF testing in the situation of severe oligozoospermia when the most likely treatment for the couple will be ICSI and the only currently available commercial test, sperm chromatin structure assay (SCSA), may not be reliable at very low sperm concentrations? Should we assume the worst and go directly to testicular sperm rather than ejaculated sperm? Is it reasonable and/or cost effective for an andrology lab to perform its own SDF testing?

This article, "*Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios*", is intended to be a clinical guideline that deals with a real-life problem in the clinical management of the infertile male. Even considering the minor criticisms made above, the authors are to be commended for producing a product that achieves a good balance between being encyclopedic and concisely to the point while maintaining its orientation toward clinical utility. The tables were extremely useful in their summaries of the text details. Any time a group of experts in a given field is convened to produce a guideline such as this, a grand opportunity for experts' bias arises. It is to their credit that there is very little evidence of bias in this informative and well-constructed paper.

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Footnote

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References

1. Agarwal A, Majzoub A, Esteves SC, et al. Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios. Transl Androl Urol 2016;5:935-50.

