

Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios

We are fortunate to live in a time when large strides have been made in the field of reproductive health and its testing, including sperm DNA fragmentation (SDF) testing. The goal of such tests should allow better evaluation, treatment and counseling in the majority of men with male factor infertility including varicoceles in selected situations.

Despite the belief that traditional semen analysis (SA) is the cornerstone of the male infertility evaluation, it is no surprise that it is suboptimal in providing a full assessment of sperm quality. The inadequacy of the SA in providing more specific information on sperm quality and fertilization capability makes the case for specialized tests such as SDF testing that may improve the diagnostic evaluation of infertile men when the SA fails to identify the etiology of infertility. Generally, SDF testing should be reserved for circumstances where results would clearly help to direct treatment. Numerous studies have negatively linked SDF to infertility as well as spontaneous recurrent miscarriages. Particularly, an elevated SDF may affect fertility by hindering fertilization, early embryo development, implantation, and subsequent pregnancy.

This text is unique in its consideration and recommendation for the indications of SDF testing. Drawing on the experience of international experts in the field, this review is designed to provide a summary of state-of-the-art developments of SDF testing and to provide a useful reference for practicing urologists and reproductive specialists in identifying the most appropriate clinical scenarios in which SDF testing could be of greatest value.

Currently, there seems to be insufficient evidence to support the routine use of SDF in male factor evaluation, nevertheless the importance of SDF testing has been acknowledged in the latest American Urological Association (AUA) and European Association of Urology (EAU) guidelines on male infertility. Specific indications for SDF testing which may allow clinicians to better select varicocelectomy candidates include (I) men with clinical varicocele and borderline to normal semen parameters; (II) men with grade 2/3 varicocele with normal conventional semen parameters; and (III) men with grade 1 varicocele with borderline/abnormal conventional semen parameters. Additional indications for SDF testing are couples with history of recurrent assisted reproductive therapy (ART) failure that can be useful prognostic information on subsequent ART cycles. Several studies have shown some benefit in using testicular sperm rather than ejaculated sperm in men with oligozoospermia, high SDF and recurrent *in vitro* fertilization (IVF) failure. Moreover, infertile men with evidence of exposure to pollutants or those found to have a modifiable lifestyle risk factors (e.g., cessation of cigarette smoking, antioxidant therapy), during evaluation should be offered SDF testing if traditional SA is unrevealing.

Finally, specific and current indications of SDF testing in evaluating men with infertility are reviewed in depth. It is intended to be clear, concise, and clinically-based to allow the reader to obtain rapid answers to this challenging medical and infertility scenarios. Special emphasis is placed on diagnostic and treatment algorithms to aid in standardizing evaluations and management of these patients. The text is designed for urologists, reproductive endocrinologist, fertility specialist, and allied health providers who have the privilege of assisting men with infertility. There is now fair evidence indicating that SDF testing is a useful diagnostic tool in male infertility evaluation and may contribute to enhance clinical decision making and treatment selection in certain situations. We hope this comprehensive review stimulates your interest in this issue as we partner to assist these patients toward a fulfilling post-infertility life.

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