Editorial

The missing piece in management of infertile couple—clinical andrology

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Dr. Kovac, in his commentary (1), highlighted the often more complicated real-world practice than the clinical scenarios discussed in the practice recommendations by Agarwal *et al.* (2). The author further commented by providing an excellent example: the choice between varicocele repair or testicular sperm retrieval in a patient with failed *in vitro* fertilization (IVF), high sperm DNA fragmentation (SDF), and grade 3 varicocele. We would like to elaborate on some of the points by Dr. Kovacs such as: (I) the role of practice guidelines; (II) the process of management decision; and (III) the overuse of ART in treating male infertility.

Fertility specialists are now equipped with a variety of clinical practice guidelines from various professional societies (3-5). These documents help clinicians in efficiently handling the ever expanding medical knowledge and evolving practice. The guidelines are of utmost importance in discouraging potentially harmful and ineffective interventions (6). However, it is equally important to realize that the multiple coexisting male and female factors in the human reproductive system cannot be completely covered by any kind of guideline. The decision to a particular investigation, e.g., SDF testing, should be an individualized one for a particular couple (7). Guidelines should not defer the delivery of better care to our patients, as long as the principles are abided to. By putting up the current best evidence in clinical utilization of SDF testing, the practice recommendations by Agarwal *et al.* (2) aims at illustrating the principles behind SDF testing rather than limiting the use of the test to certain clinical scenarios. Clinicians may start incorporating SDF testing in their practice in areas with more solid evidence as suggested by the practice recommendations including: varicocele, unexplained infertility, recurrent pregnancy loss, recurrent failures with assisted reproductive technologies (ART), and lifestyle risk factors. We anticipate wider clinical application of SDF tests outside the practice recommendations supported by evolving evidence from various studies together with experience and confidence among clinicians. The comprehensive review of different testing methodologies in the practice recommendations should also help clinicians in interpreting test results and selecting the most appropriate test for their patients.

The case scenario proposed by Dr. Kovac needs further discussion to illustrate the complex process of treatment decision. There are certainly diverging opinions among fertility specialists when they encounter a patient with high SDF undergoing IVF who has grade 3 varicocele and testicular atrophy on physical examination (1). The case serves a valid example in demonstrating the limitation of clinical practice guidelines. Both the options of varicocele repair and future conception with ejaculated sperm, and testicular sperm extraction +/– varicocele repair and fresh ART cycle seem rational. Each option has pros and cons as discussed by the author (1). Indeed, clinical practice

guidelines often do not give a clear-cut answer in the real-world practice. The management decision depends on multiple factors including male and female age, conventional semen parameters, and testicular volume. And, after all, it is the mutual understanding between the clinician and couple after thorough discussion of management options. Family planning, preference of natural conception over ART or vice versa, and financial issues are just a few among the long list of socioeconomic factors which are also involved in the process of decision. There is no absolute right or wrong about a clinical management decision. Communication between clinician and infertile couple is the basis of individualized care in reproductive medicine. The art of communication in medicine forms another pillar in addition to the scientific evidence. It is also of note that management options are usually not mutually exclusive, e.g., patients can still pursue ART with testicular sperm in case varicocelectomy failed to improve SDF and result in pregnancy.

The case scenario also reflects the often-encountered situation in the current practice: a patient is referred to male infertility specialist only after ART despite the presence of clinical varicocele and testicular atrophy. The remarkable evolution of ART has significantly changed the outlook of male infertility evaluation and management (8). The "success" of ICSI in bypassing severe male factors (9) hinders the development of clinical andrology over the last decades. In contrast to the tremendous advancement in ART (10), semen analysis remains the mainstay of male fertility evaluation. It is the high time to recognize: (I) the drawback of using conventional semen parameter in male fertility evaluation (11); and (II) the live birth rate by ICSI as the treatment of male factor infertility is no more than 30% (12). We believe that comprehensive evaluation of male partner and correction of male factors are essential in improving the outcome. If the patient having a clinical varicocele and testicular atrophy and high SDF is assessed by a male fertility specialist early, varicocelectomy is probably the more preferable treatment option over ART as supported by the predictive value of SDF on ART outcomes (7). The primary role of a male fertility specialist should be restoring the fertility potential and maximizing the chance of natural conception as far as possible. This approach empowers the couple with autonomy in family planning as their fertile counterpart. It also minimizes the risk of ART, particularly for the female partner, and its associated financial burden.

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Footnote

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References

1. Kovac JR. Practical considerations for DNA fragmentation testing in the management of male fertility. Transl Androl Urol 2017;6:S479-80.
2. 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.
3. Jungwirth A, Diemer T, Dohle GR, et al. EAU Guidelines of Male Infertility; 2015. Available online: http://uroweb.org/wp-content/uploads/17-Male-Infertility_LR1.pdf
4. Practice Committee of American Society for Reproductive Medicine. Diagnostic evaluation of the infertile male: a committee opinion. Fertil Steril 2015;103:e18-25.
5. Jarow J, Sigman M, Kolettis PN, et al. Optimal Evaluation of the Infertile Male. Available online: https://www.auanet.org/education/guidelines/male-infertility-d.cfm
6. Esteves SC, Chan P. A systematic review of recent clinical practice guidelines and best practice statements for the evaluation of the infertile male. Int Urol Nephrol 2015;47:1441-56.
7. Agarwal A, Cho CL, Esteves SC. Should we evaluate and treat sperm DNA fragmentation? Curr Opin Obstet Gynecol 2016;28:164-71.
8. Schlegel PN, Girardi SK. Clinical review 87: in vitro fertilization for male factor infertility. J Clin Endocrinol Metab 1997;82:709-16.
9. Oehninger S, Veeck L, Lanzendorf S, et al. Intracytoplasmic sperm injection: achievement of high pregnancy rates in couples with severe male infertility is dependent primarily upon female and not male factors. Fertil Steril 1995;64:977-81.
10. Merchant R, Gandhi G, Allahbadia GN. In vitro fertilization/intracytoplasmic sperm injection for male infertility. Indian J Urol 2011;27:121-32.

11. Esteves SC, Zini A, Aziz N, et al. Critical appraisal of World Organization's new reference values for human semen characteristics and effect on diagnosis and treatment of subfertile men. Urology 2012;79:16-22.
12. Neri QV, Tanaka N, Wang A, et al. Intracytoplasmic sperm injection. Accomplishments and qualms. Minerva Ginecologica 2004;56:189-96.

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