

# Integrating surgical and clinical andrology is essential to improve the quality of care delivered to infertile couples

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Drs. Yovich and Keane's commentary (1) about the recently published clinical practice guidelines for sperm DNA fragmentation (SDF) testing based on clinical scenarios (2) is an excellent piece of writing. The authors commence by acknowledging the importance of male infertility evaluation and integration of clinical and laboratory andrology in the modern workup of infertile couples. However, they pointed out that current practice values the male factor only if semen analysis is severely abnormal in contrast to the usual comprehensive female infertility evaluation. Given the success of ICSI, male infertility is indeed often neglected. This factor is aggravated by the limitations of semen analysis, to which we concurred and discussed elsewhere (3-6). To illustrate their point, Yovich and Keane discussed the often debated issue of varicocele and male infertility. Despite overwhelming evidence confirming the adverse effect of varicocele on several sperm markers and the benefit of varicolectomy in selected men (7-12), only recently—and after more than 150 years since the first publication about varicocele—the Cochrane review confirmed that there might be a benefit to performing varicolectomy in subfertile men (13). Regrettably, many subfertile men could have benefitted from treatment; the benefit of performing varicocele repair using microsurgery techniques has been advocated for a long time by eminent urological microsurgeons (14-16). Along these lines, Dr. Yovich himself contributed significantly to the evolution of laboratory and clinical andrology in his distinguished career in reproductive

medicine for over 35 years (17). His seminal works on human sperm function in the 90's had a tremendous impact on clinical practice and set the path for future research (18-22).

Drs. Yovich and Keane go on by suggesting ways to integrate clinical andrology as an essential element in evaluation of infertile couple. A comprehensive male evaluation including sperm function testing, such as SDF, ultrasound, use of microsurgical techniques for varicocele repair, and incorporation of clinical and surgical andrology are amongst their proposals. Additionally, the authors shared their experience in Australia, where the lack of urologists dedicated to male infertility represents a significant shortcoming to improved clinical care. To overcome this fact that seems to plague many countries alike, the authors propose the integration of both reproductive endocrinology and andrology within the scope of reproductive medicine fellowship programs. Obviously, this proposition needs to be analyzed in the perspective of each country due to the existence of plain boundaries limiting the practice of gynecologists and urologists. But if successful, urologists may become an integral part of reproductive care rather than serving as mere technicians performing sperm retrievals. Lastly, Yovich and Keane stressed the importance of quality management to fertility centers willing to improve their quality of care for both male and female, an element that we also feel to be essential as discussed elsewhere (23).

Yovich and Keane overall supported the use of SDF

testing in all clinical scenarios presented by Agarwal *et al.* (2). However, they have reservations to bypassing the epididymis as this organ is necessary for sperm maturation. The authors' preference is to search for debris-free micro-epididymal sperm aspiration (MESA) samples containing motile spermatozoa in preference to testicular sperm extraction (TESE). We, in contrast, advocate the use of testicular sperm in preference over ejaculated and testicular sperm in men with high SDF in semen undergoing ART, provided all measures to reduce DNA damage have been attained (2). The reason is that SDF rates in testicular sperm are significantly lower than both testicular sperm and epididymal sperm (24) [(reviewed by Esteves *et al.* (25)]. With regards to epididymal sperm, in particular, Steele *et al.*, using the Comet assay, showed that DNA integrity was higher ( $83.0\% \pm 1.2\%$ ) in testicular specimens of men with obstructive azoospermia than in proximal epididymal counterparts ( $75.4\% \pm 2.3\%$ ;  $P < 0.05$ ) (26). Their results were corroborated by Suganuma *et al.*, who used an experimental mice model to demonstrate that the passage of sperm through the epididymis was associated with a loss of sperm DNA integrity and fertilizing capacity (27). The results of these studies and others (28) indicate that SDF may be triggered during sperm transport through the epididymis as a result of excessive oxidative stress. Therefore, the use of testicular sperm for ICSI in preference over epididymal and ejaculated sperm becomes attractive as the probability of selecting spermatozoa free of DNA damage can be increased (25).

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## Footnote

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

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