We read with interest the commentary by Drs. Basar and Kahraman (1). The authors provide a comprehensive review of sperm DNA fragmentation (SDF) from etiologies and assisted reproduction outcomes to treatment strategies. We wish to further elaborate the discussion on the use of SDF testing in managing varicocele.

Varicoceles can be found in 35–50% and up to 69–81% of men with primary infertility and secondary infertility, respectively (2,3). It is considered the most commonly identifiable and surgically correctable male infertility factor. However, controversies continue to plague the studies designed to answer the clinical question related to the effect of varicocele repair on improvement in semen parameters and pregnancy rates. Results from systematic review and meta-analyses were divided and have led to more confusion (4-6). These conflicting results are the main contributing factor to the vague and inconsistent guidelines on the diagnosis and treatment of varicoceles from various professional societies including the American Society for Reproductive Medicine (ASRM) (7), American Urological Association (AUA) (8) and European Urological Association (EAU) (9). Although most professional society guidelines agree on varicocele repair in patients with clinical varicocele and impaired semen parameters, however, they fail to settle the debate of varicocele treatment.

Despite the fact that repair of subclinical varicocele is generally not recommended by guidelines and meta-analyses, there are reports suggesting potential role of treatment for subclinical varicocele (10). The possible benefit of simultaneous repair of subclinical varicocele with a contralateral clinical varicocele has also been recognized (11,12). On the other hand, repair of clinical varicocele does not necessarily lead to desirable outcome. Recent data support an association between grade of clinical varicocele and improvement in semen parameters after repair. Several studies consistently reported a significant difference in semen parameter outcomes after repair of high- vs. low-grade varicocele. The total motile sperm count after varicocelectomy improved by 128% in men with grade 3 varicoceles compared with a mere 21% and 27% in men with grade 2 and 1 varicoceles respectively (13). Takahara et al. also demonstrated the relationship between clinical grading of varicocele and post-varicocelectomy increase in sperm density. There was an improvement in sperm density of 38 (±36) × 10^6/mL for large varicocele compared to 3 (±18) × 10^6/mL improvement in small varicocele (14). As a result, the dichotomous classification of clinical and subclinical varicocele in decisions to proceed with surgical repair may be flawed. Similarly, the use of abnormal semen parameters in treatment decision may not be ideal. The revised lower reference limits for semen analyses by the World Health Organization (WHO) in 2010 (15) re-categorized previously abnormal men as normal and may leave this
group of men untreated (16,17). Therefore, supplementary
diagnostic tools including sperm function tests are needed
in refining the assessment of varicocele patients.

The association between SDF and varicocele, and the
effect of varicocelectomy on SDF provide proof in supporting
the potential role of SDF testing to better identify surgery
candidates (18). The use of SDF testing is further supported
by an understanding of the pathophysiological relationship
among varicocele, oxidative stress and SDF (19). Drs. Basar
and Kahraman pointed out that impaired seminal parameters
regardless of varicocele grade already fulfill the indication
to operate according to the current international guidelines,
which is correct (1). However, we wish to point out the
shortcoming of the current guidelines. The use of physical
examination finding and conventional semen parameters in
treatment decision of varicocele patients is far from perfect.
Indeed, based on the current best evidence, Agarwal et al.
did not recommend the routine use of SDF testing in all
patients with varicocele but highlighted the value of the
test in patients with high grade varicocele with normal
semen parameters and low grade varicocele with borderline/
abnormal semen parameters (20). We believe that the
additional information on sperm function offered by SDF
testing will allow selection of a subset of patients who have
compromised sperm function and yet normal conventional
semen parameters.

The more widespread use of SDF testing in patients
with varicocele and incorporation of the test into various
professional society guidelines require more supporting
evidence in the literature. However, the shortcoming of
the current practice should not be overlooked. We believe
that SDF testing is an important tool in completing the
assessment of infertile men. The practice recommendations
proposed by Agarwal et al. is only the first step forward to
bridge the gap between research and clinical practice in
promoting SDF testing. There is a long way to go before
we can fully unmask the mysteries of varicocele. We hope
the practice recommendations will serve as a valuable
reference to researchers and clinicians alike and a stimulus
to provoke further discussion. Better understanding of
male infertility and refinement of SDF testing would not
be possible without the broad support of fertility specialists
from around the world.

Acknowledgements

None.

Footnote

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

References

1. Basar MM, Kahraman S. Clinical utility of sperm DNA
 fragmentation testing: practice recommendations based on
2. Gorelick JL, Goldstein M. Loss of infertility in men with
3. Witt MA, Lipshultz L. Varicocele: a progressive or static
4. Evers JL, Collins JA, Vandekerckhove P. Surgery or
embolisation for varicocele in subfertile men. Cochrance
varicocele in subfertile men: The Cochrane review—a
the value of varicocelectomy as a treatment for male
subfertility with a new metaanalysis. Fertil Steril
7. Practice Committee of the American Society for
Reproductive Medicine. Diagnostic evaluation of
the infertile male: a committee opinion. Fertil Steril
2015;103:e18-25.
evaluation of the infertile male: best practice statement
reviewed and validity confirmed 2011. Available online:
https://www.auanet.org/education/guidelines/male-
infertility-d.cfm
org/guideline/male-infertility/#5
the role of subclinical varicocele in infertile men with
impaired semen quality: a prospective study. Urology
2015;85:826-30.
worthwhile to operate on subclinical right varicocele in
patients with grade II-III varicocele in the left testicle? J
12. Elbendary MA, Elhadry AM. Right subclinical varicocele:
how to manage in infertile patients with clinical left


Cite this article as: Cho CL, Agarwal A, Majzoub A, Esteves SC. It is high time for clinical application of sperm DNA fragmentation testing. Transl Androl Urol 2017;6(Suppl 4):S577-S579. doi: 10.21037/tau.2017.06.16