Effect of microsurgical varicocelectomy on sperm DNA integrity and association with reproductive outcomes of IVF/ICSI

Hudson Pierce,[1] Phil V Bach, MD,[1] Ryan Flannigan, MD[1], Vanessa Dudley[1] , Marc Goldstein, MD[1]

New York-Presbyterian Hospital/Weill Cornell Medicine, New York, NY

Background

- Varicocele is present in 15-20% of the general male population, with an increased prevalence of up to 40% in infertile men[1].
- Men with clinical varicocele have been shown to have elevated levels of sperm DNA fragmentation (DFI), which is associated with adverse reproductive outcomes[2,3].

Research Objectives

- Examine the effect of microsurgical subinguinal varicocele repair (VR) on sperm DFI assessed by TUNEL assay and/or sperm chromatin structure assay (SCSA)
- Correlate these data with pregnancy rates and live birth outcomes via IVF/ICSI

Methods

- Retrospective review of 78 men who underwent microsurgical subinguinal VR by a single surgeon for male factor infertility and had pre and postoperative measurements of sperm DFI.
- Sperm DFI was assessed by TUNEL and/or SCSA assay and compared with IVF/ICSI outcomes.
- Comparisons assessed with t-test and McNemar's test.

Results

Effect of microsurgical varicocelectomy on sperm DNA integrity

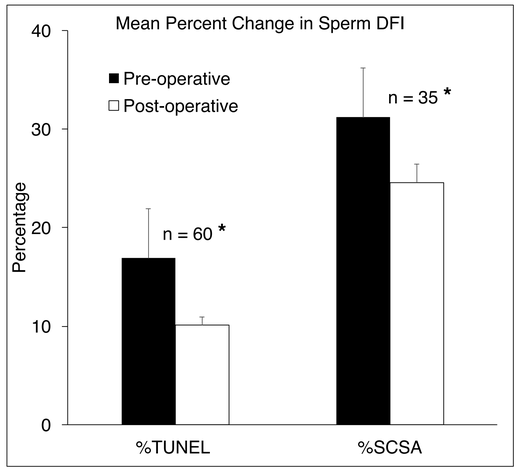

Figure 1. Mean TUNEL (p<0.001) and SCSA (p=0.009) values both decreased significantly following varicocele repair.

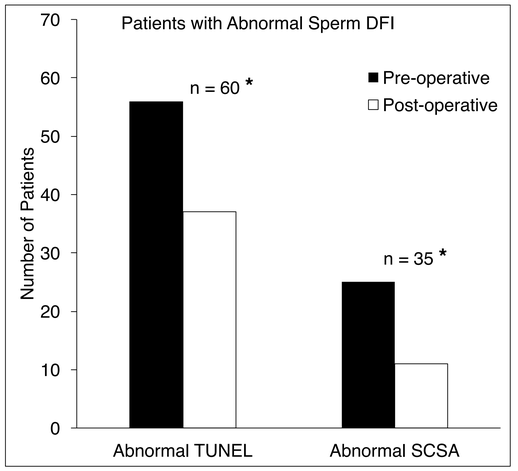

Figure 2. Number of patients with an abnormal TUNEL or SCSA assay (defined as >7% TUNEL-positive sperm or >30%, respectively) decreased following varicocele repair (p<0.001).

Comparison of sperm DFI changes following VR between pregnant and non-pregnant groups (all receiving postoperative IVF)

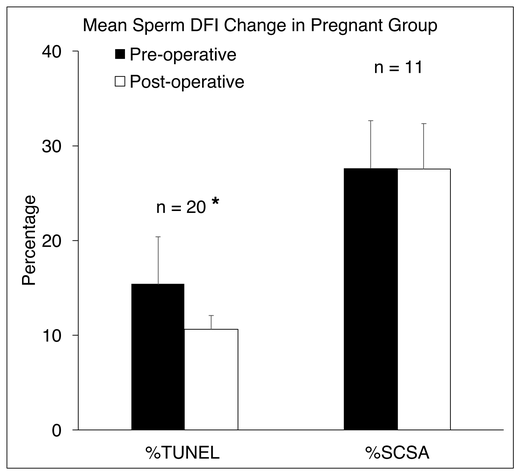

Figure 3. Of couples that achieved pregnancy, the mean decrease in TUNEL was significant (p=0.019), while decreases in SCSA were not (p=0.98).

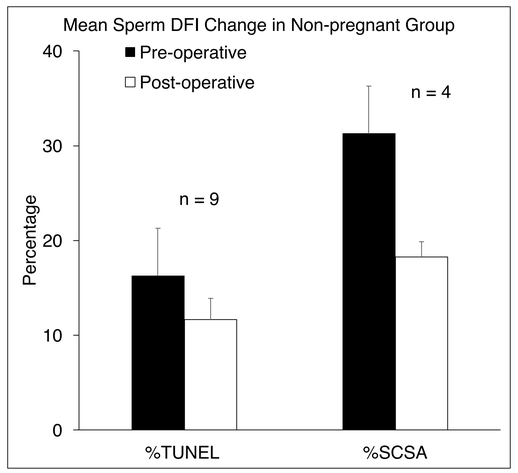

Figure 4. Changes in TUNEL/SCSA among couples who did not achieve pregnancy via IVF were not significant (p=0.21 and 0.28, respectively).

Postoperative pregnancy outcomes

- Of the 78 men, 35 couples received postoperative IVF at this institution.
- Pregnancy rate was 71% (25/35) and live birth rate 40% (14/35)
  - Total IVF cycles: 73
  - Failed cycles: 35/73
  - Total pregnancies: 38/73
- 11 couples conceived naturally postop, with a live birth rate of 9/11. 32 men were lost to follow-up.
- Pregnancy rates were improved in men whose DFI moved from abnormal to normal postop (defined as <7% for TUNEL and <30% for SCSA)

Conclusions

- Treatment of varicocele using microsurgical subinguinal VR technique significantly improves sperm DFI as measured by TUNEL and SCSA.
- Improvements in TUNEL following VR are associated with improved pregnancy outcomes using IVF/ICSI.
- There is evidence suggesting elevated sperm DFI results in less successful pregnancy outcomes[3]. The present study suggests that lowering sperm DFI via VR may result in improved reproductive outcomes.

References

1. Naughton, C. K., Nangia, A. K., & Agarwal, A. (2001). Varicocele and male infertility: Part II: Pathophysiology of varicoceles in male infertility. *Human reproduction update*, *7*(5), 473-481.
2. Saleh, R. A., Agarwal, A., Sharma, R. K., Said, T. M., Sikka, S. C., & Thomas, A. J. (2003). Evaluation of nuclear DNA damage in spermatozoa from infertile men with varicocele. *Fertility and sterility*, *80*(6), 1431-1436.
3. Larson-Cook, K. L., Brannian, J. D., Hansen, K. A., Kasperson, K. M., Aamold, E. T., & Evenson, D. P. (2003). Relationship between the outcomes of assisted reproductive techniques and sperm DNA fragmentation as measured by the sperm chromatin structure assay. *Fertility and sterility*, *80*(4), 895-902.