



Impact of Varicocele Repair on the Sperm DNA Fragmentation in Infertile Men, and Reproductive Outcome

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Abstract

Oxidative stress and related sperm DNA damage have been identified as significant causes of male infertility in men with varicocele because are usually elevated, in both abnormal and normal parameters by current World Health Organization. The current study was designed to determine the role of varicocele repair as a means of relieving SDF and improving fertility. Semen samples from 40 patients with clinical varicocele and control group were examined. Varicocele sperm samples were classified as normal or abnormal, according to World Health Organization guidelines and Sperm DNA fragmentation evaluated pre- and post- varicocele repair. The results of the study confirmed the effectiveness of varicocelectomy as a means of both reduced sperm DNA fragmentation and improved semen quality and fertility, suggesting that varicocele repair should be offered as a part of treatment options for male partners of infertile couples.

Keywords: Varicocele treatment; male infertility; sperm DNA fragmentation; oxidative stress; varicocele repair

Introduction

Varicocele is considered one of the major causes of male infertility, found in approximately 15-20% of the general male population, a prevalence in adolescents and with frequency ranging between 41% in men with primary infertility and 80% in those with secondary infertility. This anatomical anomaly, which appears as a dilatation of the pampiniform plexus overlying and surrounding the testicle, is probably one of the most common causes of poor sperm production and alteration of seminal parameters [1-3]. However, the pathogenetic mechanisms through which varicocele induces testicular dysfunction with consequent alteration of spermatogenesis have not yet been fully clarified [4]. Among the defects involved in this process, the most reproducible and probable would seem to be venous stasis with consequent testicular hypoxia and increase in temperature inside the testicle

itself. But it is hypothesized that several factors could be involved, including oxidative stress, and it is precisely the latter that is considered one of the central pathogenetic mediators of infertility associated with varicocele [5].

Several studies in the literature on infertile patients with a clinical diagnosis of varicocele have identified oxidative stress as one of the major causes of sperm dysfunction with a negative impact on the sperm membrane, compromising its motility and ability to interact effectively with the oocyte membrane. Furthermore, it has been widely demonstrated that it alters the integrity of sperm DNA, the latter being considered fundamental in determining normal fertilization and embryonic development in spontaneous and assisted conceptions [6,7]. On the basis of these evidences, it would follow that the role of surgical correction of varicocele could

be that of re-establishing a state of normal fertility by reducing the oxidative activity at the seminal level. However, this role still remains quite controversial among the various authors in the literature [8-11]. The aim of our study was to evaluate the effect of surgical correction of varicocele on semen quality and sperm DNA fragmentation in adult male subjects of infertile couples, as well as the pregnancy rate.

Materials and Methods

60 couples were included in the study (females aged between 25-36 years, males between 27-45 years) referred to our service for tests aimed to diagnose the causes of infertility. The male partners, investigated from an andrological point of view, presented clinical signs of varicocele, confirmed by ultrasound and scrotal color Doppler flow velocimetry ultrasound. They were also investigated from a seminological point of view with a complete examination of the seminal fluid (WHO 2010) and study of the fragmentation of sperm DNA through the use of the Halosperm test (SCD method) expressed in % DFI (DNA Fragmentation Index) [12]. In the group of patients studied, 40 of them underwent varicocele surgery, while the remaining 20 only performed controls after three months. Evaluations of seminal parameters were performed with the following criteria: 1) at the time of diagnosis of varicocele, for all patients included in the study; 2) three months after surgery for the 40 patients undergoing varicocele surgery; 3) three months after diagnosis for the 20 patients who did not undergo surgery (control group). The seminal parameters had also compared each other and correlated to the patient's age, the degree of varicocele, the effectiveness of the intervention and controls with therapy

alone (without intervention). Finally, both in the group of subjects undergoing surgery and in the control group, the spontaneous pregnancy rate or from PMA was evaluated in the 1-year follow-up.

Results

Patients with slightly altered seminal parameters benefited more from the varicocele correction surgery, restoring normal values (they returned to the WHO 2010 5th percentile) already three months after the surgery itself. The intervention led to an improvement in total motility and above all in progressive, which went from an average of 14% to an average of 20%, while remaining slightly below the parameters at the 5th percentile of the WHO 2010. The sperm DNA fragmentation index was significantly reduced for the most of the patient's undergoing surgery, going from an average value of 27% to a post-operative average value of 19%. In the most critically ill patients (i.e., with all the seminal parameters altered), the operation was resolved only for the fragmentation of the sperm DNA (the % DFI was reduced by 15%). The patients who did not undergo surgery (control group) did not show significant changes in seminal parameters after three months and the DFI was also unchanged, passing from a value of 22% to 21%. Pregnancy rate was also observed in the one-year follow-up, in approximately 18% of patients undergoing varicocele surgery:

- a) "SPONTANEOUS" in 7.5% of cases.
- b) with PMA II level in 6.5% of cases.
- c) with IUI in 2.5% of cases.

In the control group, spontaneous pregnancy rate was observed in the one-year follow-up, only in 5% of patients.

Data Collection

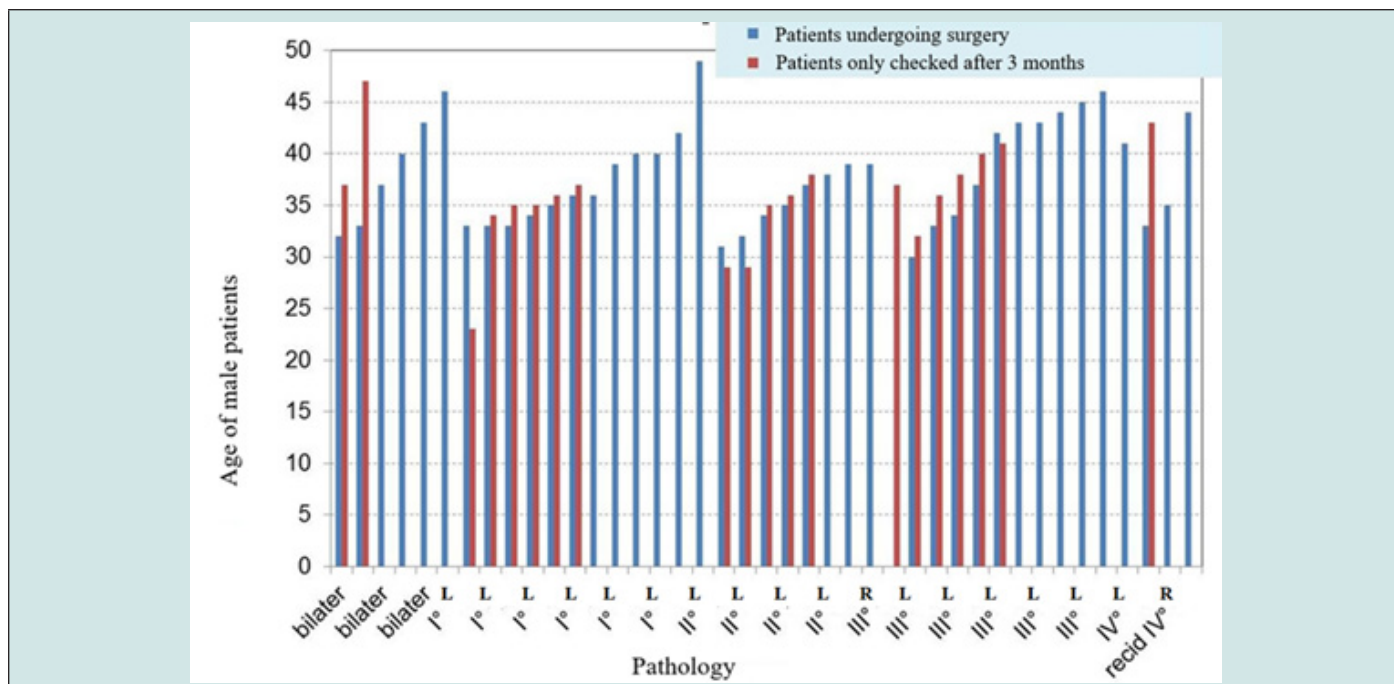


Figure 1

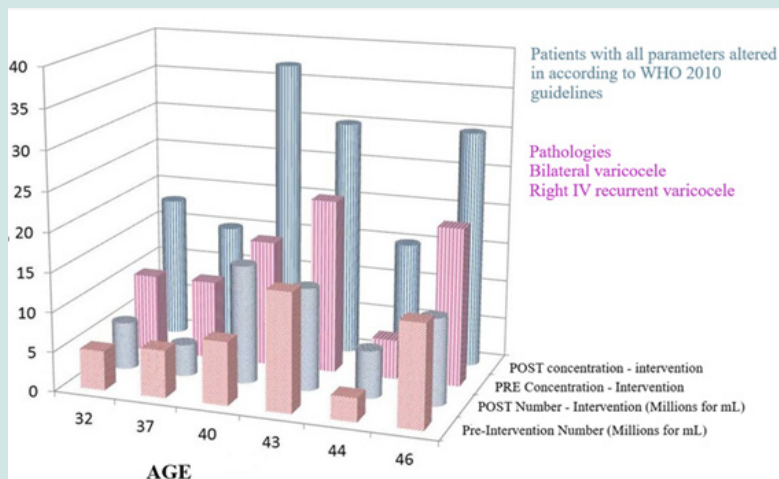


Figure 2

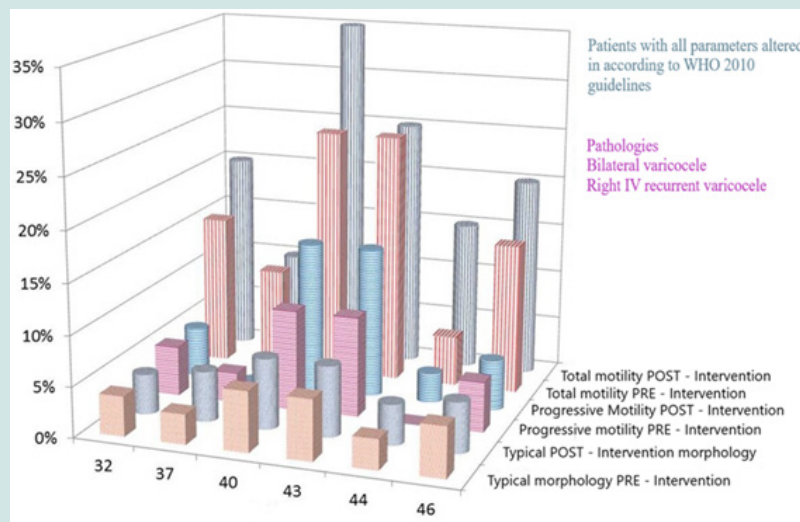


Figure 3

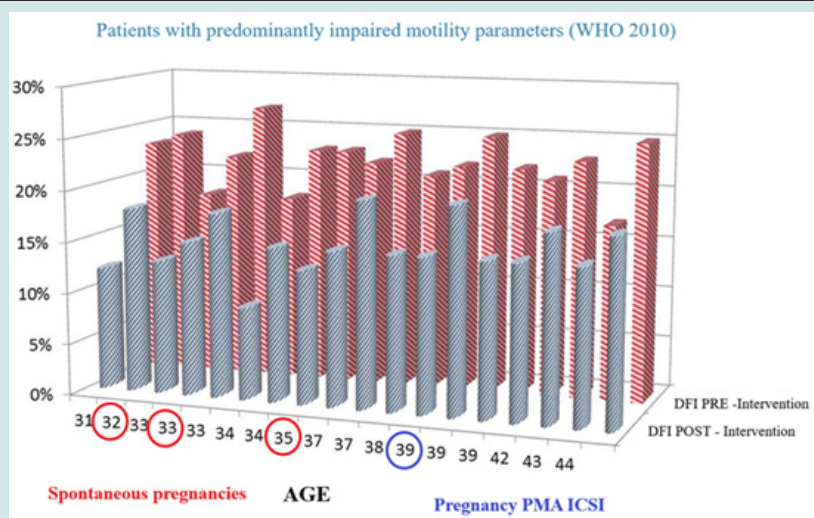


Figure 4

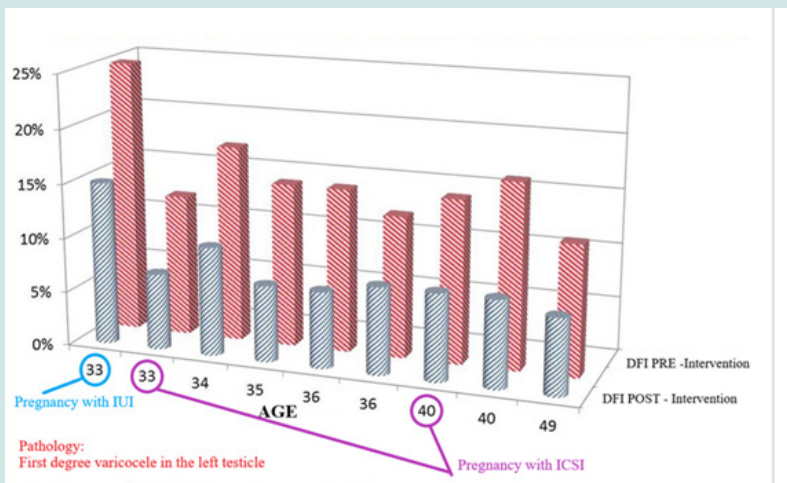


Figure 5
Figures 4&5: Out-Come Reproductive After Correction of Varicocele.

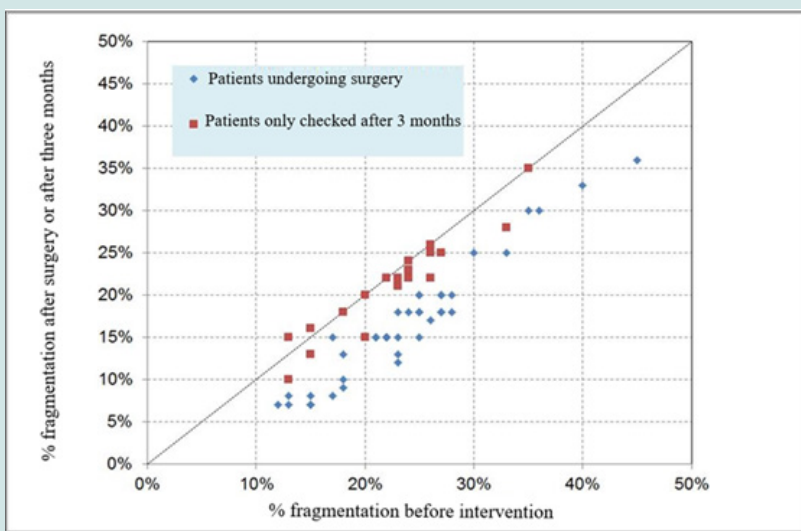


Figure 6

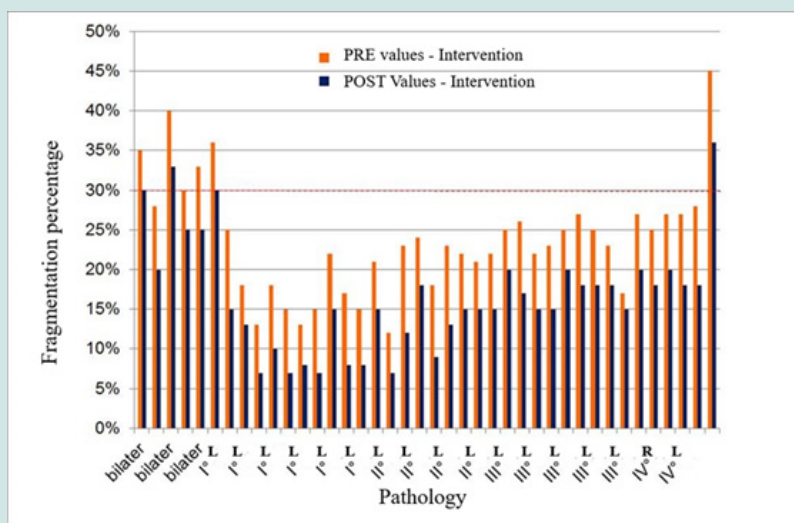


Figure 7
Figures 6&7: Evaluation DFI (%) in the Samples Studied.

Conclusions

Our data agree with what was claimed by the various authors on the effectiveness of surgical varicocele correction in restoring natural fertility and improving outcomes in PMA [10,11-13]. Our study showed that, after the operation, there was a significant improvement in seminal parameters, especially in patients with mild forms of varicocele [13,14]. But, the most relevant data, arose from the significant reduction of sperm DNA fragmentation which occurred in all patients undergoing surgery, even the most critical ones (with severely altered semen parameters) [15-17]. Therefore, our data increasingly support the hypothesis that varicocele correction surgery may be the best semen remediation approach since it has a remarkable action in reducing sperm DNA damage and improving the fertilizing capacity of the sperm, not only in natural fertility but above all, for the purposes of PMA, where the quality of the sperm is crucial, depending fundamentally on the integrity of its DNA.

References

- Kursh ED (1987) What is the incidence of varicocele in a fertile population? *Fertil Steril* 48(3): 510-511.
- Molina J, Castilla JA, Castano JL, Fontes J, Mendoza N, et al. (2001) Chromatin status in human ejaculated spermatozoa from infertile patients and relationship to seminal parameters. *Hum Reprod* 16(3): 534-539.
- (1992) The influence of varicocele on parameters of infertility in a large group of men presenting to infertility clinic. *World Health Organization. Fertil Steril* 57(6): 1289-1293.
- Hauser R, Paz G, Botchan A, Yogev L, Yavetz H (2001) Varicocele and male infertility: effect on sperm function. *Hum Reprod Update* 7(5): 482-485.
- Pasqualotto FF, Sharma RK, Nelson DR, Thomas AJ, Agarwal A (2000) Relationship between oxidative stress, semen characteristics, and Irvine clinical diagnosis in men undergoing infertility investigation. *Fertil Steril* 73(3): 459-464.
- Irvine DS, Twigg JP, Gordon EL, Fulton N, Milne PA, et al. (2006) DNA integrity in human spermatozoa: relationships with semen quality. *J Androl* 21(1): 33-44.
- Smit M, Romijn JC, Wildhagen MF, Veldhoven JLM, Weber RFA, et al. (2010) Decreased sperm DNA fragmentation after surgical varicolectomy is associated with increased pregnancy rate. *J Urol* 183(1): 270-274.
- Okeke L, Ikuero O, Chiekwe I, Etukakpan B, Shittu O, et al. (2007) Is varicolectomy indicated in subfertile men with clinical varicoceles who have asthenospermia or teratospermia and normal sperm density? *Int J Urol* 14(8): 729-732.
- Esteves SC, Roque M, Agarwal A (2016) Outcome of assisted reproductive technology in men with treated and untreated varicocele: systematic review and meta-analysis. *Asian J Androl* 18: 254-258.
- Zini A, Blumenfeld A, Libman J, Willis J (2005) Beneficial effect of microsurgical subinguinal varicolectomy on human sperm DNA integrity. *Hum Reprod* 20(4): 1018-1021.
- Wang YJ, Zhang RQ, Lin YJ, Zhang RG, Zhang WL (2012) Relationship between varicocele and sperm DNA damage and the effect of varicocele repair: a meta-analysis. *Reprod Biomed Online* 25(3): 307-314.
- Fernández JL, Muriel L, Goyanes V, Segrelles E, Gosálvez J, et al. (2005) Simple determination of sperm DNA fragmentation with an improved sperm chromatin dispersion (SCD) test. *Fertil Steril* 84(4): 833-842.
- Esteves SC, Chan P (2015) A systematic review of clinical practice guidelines and best practice statements for the evaluation of the infertile male. *Int Urol Nephrol* 47(9): 1441-1456.
- Tisco BC, Esteves SC, Cocuzza MS (2016) Summary evidence on the effects of varicocele treatment to improve natural fertility in subfertile men. *Asian J Androl* 18: 239-245.
- Esteves SC, Santi D, Simoni M (2020) An update on clinical and surgical interventions to reduce sperm DNA fragmentation in infertile men. *Andrology* 8(1): 53-81.
- Qiu D, Shi Q, Pan L (2021) Efficacy of varicolectomy for sperm DNA integrity improvement: a meta-analysis. *Andrologia* 53(1): e13885.
- Wang SL, Bedrick BS, Kohn TP (2021) What is the role of varicolectomy in infertile men with clinical varicoceles and elevated sperm DNA fragmentation? *Fertil Steril* 116(3): 657-658.



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