

Evaluation of the Effects of Surgical Varicocelectomy on the Seminal Fluid Parameters in Patients with Clinical and Subclinical Varicocele

Ibrahim J. Hammadi*
Ghassan Th. Saeed**
Read How. Abed Tawney***

MB ChB MSc. ART
MB ChB MSc. PhD
MB ChB, FICMs (Radiology)

Abstract:

Background: Varicoceles defined as abnormally dilated testicular veins (pampiniform plexus) of in the scrotum and it is found in approximately 15% of the general population and associated with adverse effects on the seminal fluid and fertility. According to size of that blood vessels; the varicocele is divided into clinical that are discovered in physical examination and subclinical that are only discovered by Doppler examination. It is well known that clinical varicocele affect the seminal fluid and always treated surgically as a part of treatment of infertility or because of pain or cosmetic purpose but the controversy is about the cases of subclinical varicocele and the indication of surgery and its outcome.

Objective: To assess the effects of varicocelectomy on the seminal fluid parameters of patients with clinical and subclinical varicoceles.

Patients and method: 80 infertile patients with varicocele included in this study 50 had clinical and 30 had subclinical diagnosed by Doppler study. Two seminal analyses were done from the patients, one before and the other 3 to 6 months after varicocelectomy.

Results: a significant improvement in the sperms count was found after the operation in both clinical and subclinical varicocele but the sperm motility percentage seems to be not affected in patients with subclinical varicocele unlike the clinical cases that showed a significant improvement after varicocelectomy. There was a non-significant decrease in the percentage of sperms with abnormal morphology in both cases.

Conclusion: varicocelectomy is indicated and had good outcome on the seminal fluid parameters in cases of clinical varicocele while in cases of subclinical varicocele it should be recommended only in patients with low sperm count and assisted reproductive technique must be suggested in cases of poor motility or high percentage of abnormal sperms.

Key words: varicoceles, varicocelectomy, seminal fluid parameters.

Fac Med Baghdad
2015; Vol.57, No.1
Received: Dec.,2014
Accepted: Feb.,2015

Introduction:

Varicocele is the most common surgically correctable cause of the male infertility and found in 30% of infertile males (1). Infertility nowadays is one of the main public health problems and affects about 15% of the couples of reproductive age (2). The male causes are blamed in 40% - 50% of infertility cases (3).

Varicocele found in about 19% to 41% of males with primary infertility and about 45% to 81% in males with secondary infertility (4)

Varicocele is defined as an abnormal dilatation and tortuosity of veins of the pampiniform plexus that drain the testis. It located within the spermatic cord and can be either palpated on physical examination and called clinical varicocele or discovered on Doppler ultrasound and named as subclinical varicocele. Varicoceles always detected after puberty and its prevalence is about 11-15% among healthy adult men (5).

*Corresponding Author: AL-Yarmuok Teaching Hospital/Infertility Center Ibrahim hamdi988@yahoo.com

**Dept. of physiology. Baghdad Medical College/y.

***AL-Mustanserria Medical College /Department Of Radiology.

Various mechanisms have been suggested for male infertility associated with varicocele. The etiology remains to be proved, but proposed mechanisms include hypoxia and stasis, testicular venous hypertension, increased testicular temperature, increased levels of spermatic vein catecholamine, increased oxidative stress, decreased antioxidant activity of seminal plasma, or increase percentage of sperms with DNA fragmentation and apoptosis (6-8) However, the exact cause is still unknown.

Varicocele is classified into:

Grade I: small, palpable with Valsalva maneuver only.

Grade II: moderate, palpable with patient standing.

Grade III: large, visible through scrotal skin, and palpable with patient standing.

While Subclinical varicocele only determined by ultrasound examination to detect spermatic veins diameter (larger than 2.5mm considered being varicocele) (1).

Previous studies have shown that seminal fluid abnormalities included the sperm count, motility, and morphology in varicocele patients improve after surgical correction. Marmar

and Kim (9), found that subinguinal microsurgical technic in 466 patients gave pregnancy rate was 35.6% after one year of the operation and another group of 272 clinical varicocele patients showed a significant improvement in sperm count and sperm motility after varicocelectomy (10).

Varicocele treatment for infertility is not indicated in patients with either normal semen quality or a subclinical varicocele as state by the Practice Committee of the American Society for Reproductive Medicine (11). Cina and his team (12) could not find any significant associations between venous diameter and retrograde flow (measured by Doppler ultrasound) and semen fluid parameters among healthy men with normal semen analyses while Caşkurlu and his coworkers (13) examined 100 infertile patients without clinical varicocele, 100 infertile patients with clinical varicocele, and 50 fertile men without clinical varicocele, and state that measured venous diameters should not be used as diagnostic criteria for subclinical varicocele because the highest mean diameters of the veins did not differ significantly across the studied groups.

As it is well known that despite technological advances, the cause of male infertility is unknown in 25% of cases. These cases categorized as “infertility of unknown origin” and classified into idiopathic male infertility and unexplained male infertility according to semen quality. In idiopathic male infertility the men have an unexplained reduction of semen quality. In contrast, in cases of unexplained male infertility there are normal sperm parameters (normospermia) (14).

Because the methods of assisted reproductive techniques are expensive and poor in Iraq, the subclinical varicocele sometimes is the only founded abnormality so, in this study, we tried to find the impact of varicocelectomy on the seminal

fluid parameters of infertile males with subclinical varicocele and study its significance as a treatment of male infertility.

Patients and Methods:

This study was done from the period of March 2012 to October 2013. 80 infertile patients were included; 50 suffering from clinical of different grades and 30 with subclinical varicocele diagnosed by Doppler ultrasound studies, who presented to Al- Yarmuok teaching Hospitals seeking advice for infertility treatments.

All the patients subjected to full history, clinical examination, semen analysis, color Doppler ultrasonography (scrotal). Patients with recurrent varicocele, azoospermic (zero sperms in ejaculate) or have cause of infertility other than varicocele were excluded from the study and who were treated by other approaches such as high ligation, laparoscopic, or subinguinal microscopic surgery also excluded to avoid its effect on the results .

Color Doppler ultrasound examination was performed using a Toshiba SSA-140A color Doppler ultrasound scanner (Tokyo Japan) with the subjects in supine position; abdomen and chest were elevated to about 158dgree. Examination was performed at the level of the inguinal canal and just over the superior-lateral edge of the testis or posterior-lateral edge in large varicoceles. The maximum venous diameters in the testicular veins were measured both during rest and Valsalva maneuver (maximal abdominal strain against a closed epiglottis just after a deep inspiration) using a 7.5 MHz linear array transducer. Veins that are larger than 2.5 mm in diameter at rest were considered to be a varicocele.

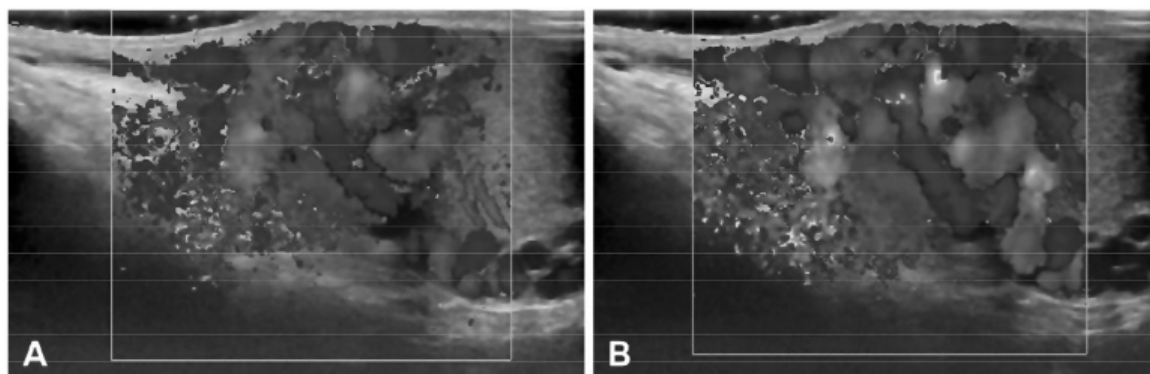


Figure 1: Varicocele with enlarged veins (A) whose calibers increase during the Valsalva maneuver (B)

The semen analyses were performed according to the WHO guidelines (2). Semen samples were obtained by masturbation after at least 3days of abstinence. Samples were collected into sterile containers and allowed to liquefy at 37°C for 30 min, and then analyzed for the sperm concentration, percent motility and morphology.

Semen analysis was done for all patients and Semen parameters

were evaluated one before the operations and the second semen analysis was done about 3-6 months after varicocelectomy.

In both groups, varicocelectomy was done using inguinal approach for all patients.

The follow-up period was between 3 to 6 months. During the follow-up period, we focused on surgical complications, varicocele recurrence, and spontaneous pregnancy.

Patients with any surgical complication or recurrence were excluded.

The patients were informed that further investigations will be done on their samples for academic purposes and the sample will be discarded using heat after finishing the experience, all the patient's information for this study remained confidential. All statistical analyses were performed with Statistical Package for the Social Sciences (SPSS), version 16.0. Multivariate analysis was performed using grade of varicocele and seminal fluid parameters. One-way analysis of variance and student's test were used to compare the preoperative and postoperative TMCs among the two groups. Probability (P) values < 0.05 were considered in terms of seminal parameters.

Results:

The improvement in sperm count was found to be highly significant (P < 0.5) in both groups but the difference in the percentage of normal sperm morphology was not significantly increased in both groups.

Regarding sperm motility, a significant improvement in the sperm motility quality was observed after varicocelectomy in patients having clinical varicocele while a non-significant change in the motility state of the sperms of subclinical varicocele patients.

The incidence of spontaneous pregnancy in the follow up period (3 to 6 months) was 6 of 50 (12%) in the patients of clinical varicocele while 2 of 30 (6.7%) in case of subclinical varicocele.

Table 1: The results of seminal fluid parameters in patients with clinical and subclinical varicocele before and after varicocelectomy.

Sperm parameters	groups	Values before operation	Values after operation	p-values
Sperm count (million per ml)	clinical	42.62 ± 23.78	50.76 ± 17.95	<0.05
	subclinical	40.4 ± 14.7	62.7 ± 13.6	<0.05
Percentage of motile sperms	clinical	62.4 ± 13.2	65.6 ± 9.9	<0.05
	subclinical	64.75 ± 23.85	61.85 ± 21.07	NS
Percent of sperm with normal morphology	clinical	59.75 ± 19.45	56.35 ± 17.51	NS
	subclinical	39.2 ± 22.4	42.6 ± 16.9	NS

Abbreviation: NS, Non-significant.* Data are given as mean ± SD.

Discussion

In this study varicocelectomy had favorable results in patients with clinical and subclinical varicocele by a significant increase of sperm counts. It is well known that varicocele affect the sperm producing cells in different ways and the primary proposed hypotheses involved were hyperthermia, venous pressure, hormonal imbalance, toxic substances, and reactive oxygen radicals, being implicated in the pathophysiology (15) and varicocelectomy cause an improvement in sperm count and motility in the clinical varicocele cases (16-18) and this was in harmony with our findings.

The significant improvement in sperm quality after the operation of subclinical varicocele seen in our results was found to be in agreement with the findings of pierik et al (19) regarding the sperm count part and disagree with their found regarding the sperm motility as they noticed significant improvements in postoperative sperm quality (density, motility) of studied patients with clinical and subclinical varicocele and showed that surgical operation had the same positive results regardless

of the type of the disease. In contrast, our results were found to be in total disagreement with the results of Unal et al (20), Yamamoto et al (21) and Jarow and his team (22) that found negative results after performing varicocelectomy on patients with subclinical varicocele. And also with Sharlip and his team (23) who found that the subclinical varicocele causes no harmful effects on the seminal fluid and varicocelectomy is not indicated in patients having none clinically noticed scrotal veins.

Regarding the sperm motility, a significant increase in the percentage of active motile sperms was found after the operation on clinical cases while a non-significant change was found in the subclinical patients.

As said above, varicocelectomy cause an improvement in the seminal quality of the clinical varicocele and Jarow and his team (22) concluded that there is a direct relationship between the size of varicocele and their adverse effects on seminal fluid parameters. They found also that not all the patients of varicocele (clinical and subclinical) had improved after the

operation and a significant improvement in sperm quality was found in 67% of clinical varicocele while only founded in 41% of subclinical cases. They concluded that varicocelectomy should not suggest as infertility treatment in subclinical cases. In the present study, there was a non-significant change in the percentage of sperms of normal morphology in both clinical and subclinical cases and this theme was in harmony with the conclusions of Okeke and his team (24) who found that there was no improvement in sperm morphology after the operation and that the varicocelectomy is not indicated in teratospermia. Also with Maciejko and his coworkers (25) who proposed that neither asthenospermia nor teratozoospermia showed improvement which was true in our results in the subclinical varicocele cases.

The seminal fluid analysis of varicocele patient may show oligospermia, azospermia, or normal count but defective functionally due to their adverse effects, Baazeem and his coworkers (26) concluded that in addition to improving sperm parameters (count and total and progressive motility), Varicocelectomy reduces sperm DNA damage and seminal oxidative stress, and improves sperm ultramorphology. While Mancini and his team (27) found that surgical treatment does not seem to modify absolute values of Total Antioxidant Capacity of the seminal fluid that cause bad effects on sperm function and DNA integrity. In contrast, Cayan and his coworkers (28) found that varicocelectomy promotes Sertoli and Leydig cell function with a significant increase in serum free testosterone level that resulted in a significant improvement in sperm concentration and motility. Garcia-Peiró and coworkers had used sperm DNA determination test and found that clinical and subclinical varicoceles have a similar negative effect on sperm DNA integrity in infertile patients and that varicocelectomy improves sperm DNA quality in clinical but not in subclinical varicocele patients (29). And this was in agreement with the findings of the present study that showed that the percentage of abnormal sperm morphology was much higher in subclinical cases and it is known that the DNA integrity is directly correlated with good morphology and the simple selection of morphologically normal shape motile spermatozoa really can eliminate most of the apoptotic spermatozoa and exclude them from a possible normal fertilizing process during intrauterine insemination (IUI) and In-vitro fertilization (IVF) (30).

And also a significant increase of serum inhibin B hormone level which has been proposed as a major indicator for Sertoli cell function and spermatogenesis was found by Ozden's team (31) with no statistically significant difference between the mean serum follicle-stimulating hormone, luteinizing hormone, prolactin and testosterone levels of the patients before and after the treatment.

Diegidio and his team (32) found after a period of follow up of about 6 months post varicocelectomy that the incidence of

spontaneous conception was about 34% unlike the present study that showed that incidences were much lower in both groups.

We can conclude that poor morphology observed in varicocele patients might not be only because of the presence of varicoceles. Thus, varicocelectomy is not indicated in those patients.

According to our results and evidence of previous studies, it may be therefore recommended that varicocelectomy had a good outcome in cases of clinical varicocele patients as a part of infertility treatment when there were accepted ranges of normal sperm morphology. While suggested if there was only low sperm count in subclinical cases as it cause no improvements in motility and morphology states.

Normospermic subfertile men with clinical or subclinical varicoceles and patients with poor sperm morphology should be subjected to assisted reproductive techniques rather than surgical varicocelectomy.

Authors Contributions:

Ibrahim Jasim Hammadi: Work designer

Ghassan Thabet Saeed: Final approval of the work

Read How. Abed Tawney: Data analyzer

References:

1. Dubin I, Amelor RD. Etiological factors in 1294 consecutive cases of male infertility *Fertil.Steril* 1973; 22:469.
2. World Health Organization. *Laboratory manual for the examination of human semen and sperm-cervical mucus interaction*. 5th Ed. New York USA: Cambridge University Press; 2010.
3. Speroff L, Glass RH, Kase NG. *Clinical Gynecologic Endocrinology and Infertility*. 6th Ed. Baltimore USA: Lippincott Williams & Wilkins; 1999. *Infertility*; pp. 201–246.
4. Kibar Y, Seckin B, and Erduran D: *The effects of subinguinal varicocelectomy on Kruger morphology and semen parameters*. *J Urol* 168: 1071–1074, 2002.
5. Kumar Rajeev, Shah Rupin. *Varicocele and male infertility: current status*. *J Obstet Gynecol India Vol. 55, No. 6: November/December 2005 P: 505-516*.
6. Jarow JP, *Effects of varicocele on male fertility*, *Hum Reprod Update*, 2001; 7(1):59–64.
7. Naughton C, Nangia A, Agarwal A. *Pathophysiology of varicoceles in male infertility*. *Hum Reprod Update* 2002; 7:473– 81/ (IVSL high wire).
8. Witt MA, Lipshultz LI, *Varicocele: a progressive or static lesion?* *Urology*, 1993; 42(5):541–3.
9. Marmar JL, Kim Y. *Subinguinal microsurgical varicocelectomy: A technical critique and statistical analysis of semen and pregnancy data*. *J Urol* 1994; 152:1127-32.

10. Jungwirth A, Gogus C, Hauser G et al. Clinical outcome of microsurgical subinguinal varicocelectomy in infertile men. *Andrologia* 2001; 33:71-4.
11. Male Infertility Best Practice Policy Committee of the American Urological Association; Practice Committee of the American Society for Reproductive Medicine. Report on optimal evaluation of the infertile male. *Fertil Steril* 2006; 86: S202-9.
12. Cina A, Minnetti M, Pirronti T, Vittoria Spampinato M, Canadè A, Oliva G, et al. Sonographic quantitative evaluation of scrotal veins in healthy subjects: normative values and implications for the diagnosis of varicocele. *Eur Urol* 2006; 50: 345-50.
13. Caşkurlu T, Taşçi AI, Resim S, Sahinkanat T, Ekerbiçer H. Reliability of venous diameter in the diagnosis of subclinical varicocele. *Urol Int* 2003; 71: 83-6.
14. Sabanegh EJ, Agarwal A. Male infertility. In: Campbell MF, Walsh PC, Wein AJ, editors. *Campbell-Walsh urology*. 10th ed. Philadelphia: Saunders Elsevier; 2012. pp. 616-647.
15. Ricardo M., Sandro C. E. A Critical Appraisal on the Role of Varicocele in Male Infertility. *Advances in Urology* 2012(2012), Article ID 597495.
16. Schlesinger M. H. Wilets I. F. Nagler H. M. Treatment outcome after varicocelectomy: a critical analysis, *Urologic Clinics of North America*. 1994; 21: 517 – 529.
17. Diegidio P, Jhaveri J. K., Ghannam, S. Pinkhasov R., Shabsgh R, Fisch H. Review of current varicocelectomy techniques and their outcomes. *BJU International* 2011; 108: 1157 – 1172.
18. Chen S. S., Huang W. J. Differences in biochemical markers and body mass index between patients with and without varicocele. *Journal of the Chinese Medical Association* 2010; 73: 194 – 198.
19. Pierik FH, Vreeburg TJ, Stijnen T, van Rooijen JH, et al. Improvement of sperm count and motility after ligation of varicoceles detected with colour Doppler ultrasonography. *Int J Androl*. 1998 Oct; 21(5):256-60.
20. Unal D, Yeni E, Verit A, et al. Clomiphene citrate versus varicocelectomy in treatment of subclinical varicocele: a prospective randomized study. *Int J Urol* 2001; 8:227-30.
21. Yamamoto M, Hibi H, Hirata Y et al. Effect of varicocelectomy on sperm parameters and pregnancy rate in patients with subclinical varicocele: a randomized prospective controlled study. *J Urol*. 1996; 155: 1636-8.
22. Jarow JP, Ogle SR, Eskew LA. Seminal improvement following repair of ultrasound detected subclinical varicoceles. *J Urol*. 1996 Apr; 155 (4):1287-90.
23. Sharlip ID, Jarow JP, Belker AM et al. Best practice policies for male infertility. *Fertil Steril* 2002;77: 873-82.
24. Okeke L, Ikuerowo O, Chiekwe I, et al, Is varicocelectomy indicated in subfertile men with clinical varicoceles who have asthenospermia or teratospermia and normal sperm density? *International Journal of Urology*, vol. 14, no. 8, pp. 729-732, 2007.
25. Maciejko A., Kim P., Jang T., et al. "Isolated teratospermia: is varicocelectomy indicated?" *Journal of Urology*, vol. 173, supplement 4, p. 369, 2005.
26. Baazeem A, Belzile E, Ciampi A, et al, Varicocele and male factor treatment: a new meta-analysis and review of the role of varicocele repair. *Eur Urol*. 2011 Oct; 60(4):796-808.
27. Mancini A, Meucci E, Milard D, et al, Seminal antioxidant capacity pre and postoperative varicocele. *J Androl*. 2004 Jan-Feb; 25 (1):44-9.
28. Cayan S, Kadioglu A, Orhan I, et al, The effect of microsurgical varicocelectomy on serum follicle stimulating hormone, testosterone and free testosterone levels in infertile men with varicocele. *BJU Int*. 1999 Dec; 84 (9):1046-9.
29. García-Peiró A, Ribas-Maynou J, Oliver-Bonet M, Navarro J, Checa A, Nikolaou A, et al, Multiple Determinations of Sperm DNA Fragmentation Show That Varicocelectomy Is Not Indicated for Infertile Patients with Subclinical Varicocele, *Biomed Res Int*. 2014; 181396.
30. Shen, H.M, Dai, J., Chia, S.E., Lim, A., and Ong. C.N.: Detection of apoptotic alterations in sperm in subfertile patients and their correlations with sperm quality. *Human Reproduction*, 2002; 17(5): 1266-1273.
31. Ozden C, Ozdal OL, Bulut S, et al, Effect of varicocelectomy on serum inhibin B levels in infertile patients with varicocele. *Scand J Urol Nephrol*. 2008; 42 (5):441-3.
32. Diegidio P, Jhaveri J. K., Ghannam, S. Pinkhasov R., Shabsgh R, Fisch H., " Review of current varicocelectomy techniques and their outcomes", *BJU International* 2011; 108: 1157 – 1172.