

Varicocele and Fertility: Relationship Between Testicular Volume and Seminal Parameters Before and After Treatment

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ABSTRACT: Varicocele is a condition of varicosity and tortuosity of the pampiniform plexus that is often associated with a reduction in the volume of the affected testicle. Today there is much debate about how much the varicocele actually damages the reproductive system and the mechanism through which this occurs. Furthermore, it has not yet clearly been established if treatment is truly useful to restore testicular function. The goal of this study was to evaluate changes in the volume of the affected testis after treatment and to examine any correlations between volume and seminal parameters. We evaluated 43 patients with left idiopathic varicocele with ultrasound scan of the testis before and after surgery; testicular volume was obtained using the ellipsoid formula. We also examined semen parameters before and at an average time of 1 year after the procedure, using the WHO indications. We performed 2 statistical analyses, comparing changes in testicular volume before and after surgery, and volume with

seminal parameters. Statistical analysis shows a significant increase of testicular volume after varicocele treatment ($P < .05$). Furthermore, the total number of spermatozoa and fast progressive spermatozoa rates significantly increased after surgery (respectively $P < .05$ and $P < .01$) (Figure 1). The Spearman correlation coefficient shows a good relationship between testicular volume and total number of spermatozoa ($r = .445$; $P = .01$). Our data point to the possibility that the affected testicle could benefit in terms of trophism and function after varicocele treatment. Ultrasound scan at follow-up permits assessment of not only the presence of recurrence, but it is also useful for evaluating trophism.

Key words: Ultrasound, testicular volume, infertility, surgical treatment, Tauber procedure.

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Varicocele is a condition of varicosity and tortuosity of the pampiniform plexus that is often associated with a reduction in the volume of the affected testicle. The rate of clinical varicocele ranges from 9% to 23%, but this increases to 40% in infertile patients; nevertheless, there is currently much debate about how much the varicocele actually damages the reproductive system and the mechanism through which this occurs (Onozawa et al, 2002; Segenreich et al, 1997).

Furthermore, it has not yet clearly been established if treatment is truly useful to restore testicular function. Though the role of treatment in prepubertal and pubertal subjects has now been commonly accepted (particularly when varicocele is associated with testicular hypotrophy), there is a large disagreement in the most recent literature regarding its usefulness in adult subjects (Schlesinger et al, 1994; World Health Organization, 1992; Evers and Collins, 2003).

Therefore, the goal of this study was to evaluate changes in testicular volume before and after surgical

treatment in patients with idiopathic varicocele, and to examine any correlations between volume and seminal parameters.

Materials and Methods

Between January 2003 and November 2004 we evaluated 43 patients with left idiopathic varicocele (mean age: 26 years; range: 17–40 years): all patients were assessed preoperatively via physical examination and scrotal color Doppler imaging for classification purposes and with ultrasound scan in B-mode to obtain testicular volume, which was calculated using the ellipsoid formula (volume = $4/3\pi a \cdot b \cdot c$ where a, b, and c are the semiaxes of the ellipsoid).

Ultrasound scan was performed with a 7.5-MHz convex probe in supine and orthostatic position. The ultrasound scan was repeated at the 1-year follow-up to permit the testicle to resume normal function after surgery.

The technician (L.M.) was blinded with respect to the subjects, with a significant overlap of volume measurements.

We also examined seminal parameters (with 2 semen analyses) before and at an average time of 1 year after the procedure (WHO guidelines). All semen samples were collected by masturbation after a period of 3–5 days of abstinence.

All patients underwent open surgery or antegrade sclerotherapy (Tauber procedure) for hypofertility or testicular hypotrophy: 22 patients underwent open varicocelectomy with

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inguinal approach, while the Tauber procedure was performed on 21 patients.

We performed a statistical analysis comparing testicular volume before and after surgery, subsequently comparing these results with seminal data, which were likewise evaluated pre- and postoperatively. The relationship with age of the subject with respect to volume or semen analysis completed the statistical analysis.

Wilcoxon signed rank tests for paired data and Spearman rank correlation were used to analyze nonparametric data. The level of statistical significance was set at $P < .05$. All calculations were carried out with SPSS release 13.0 (SPSS Inc, Chicago, Ill).

The study was approved by our local ethics committee, and all patients gave written informed consent.

Results

Of the 43 patients examined in this study, 6 presented grade I left varicocele, 16 grade II, and 21 grade III. Only 2 patients were affected by bilateral varicocele.

In terms of seminal parameters, 18 patients had oligoasthenospermia, 20 had asthenospermia, and 5 had normal values; treatment was nevertheless performed on the latter 5 because they were young (less than 23 years old) with Grade III varicocele and concomitant testicular hypotrophy.

In terms of volume of the left testis, more than 60% were smaller than the contralateral testis with a median value of 13.2 cm³ (range: 4.2–23.7 cm³); right testicular volumes were normal, and only 2 patients showed hypotrophy (one of the 2 subjects had bilateral varicocele).

Detailed results are shown in the Table.

Statistical analysis shows a significant increase of testicular volume after varicocele treatment ($P < .05$). Furthermore, the total number of spermatozoa and fast progressive spermatozoa rates significantly increased after surgery (respectively $P < .05$ and $P < .01$) (Figure).

The Spearman correlation coefficient shows a good relationship between testicular volume and total number of spermatozoa ($r = .445$; $P = .01$).

There is no statistical correlation between age and testicular volume or seminal parameters before and after treatment.

All patients completed this study, and we had 3 recurrent varicoceles at follow-up.

Discussion

Varicocele is a pathological condition present in a noteworthy percentage of the male population, and the incidence of this disease increases within infertile patient groups.

Many reports have demonstrated the correlations between varicocele and infertility, and the literature published over the past 40 years has shown that both sperm parameters and pregnancy rates improve in varicocele patients after treatment (Segenreich et al, 1997; Schlesinger et al, 1994).

With regard to prepubertal and pubertal subjects, there are no parameters that can predict loss of fertility in adulthood; nevertheless, the most recent data in the literature seem to favor treatment instead of wait-and-see.

Varicocele is often accompanied by testicular growth arrest and reduced volume (Sayfan et al, 1997; Aragona et al, 1994; Haans et al, 1991): reduced testicular volume means fewer tubules and thus also a lower number of germ cells (Lipshultz and Corriere, 1977).

It has also been demonstrated that there is clearly an increase in testicular size in adolescent subjects following surgical repair as a resumed growth of the testicle (Okuyama et al, 1988; Laven et al, 1992; Yamamoto et al, 1995; Paduch and Niedzieski, 1997).

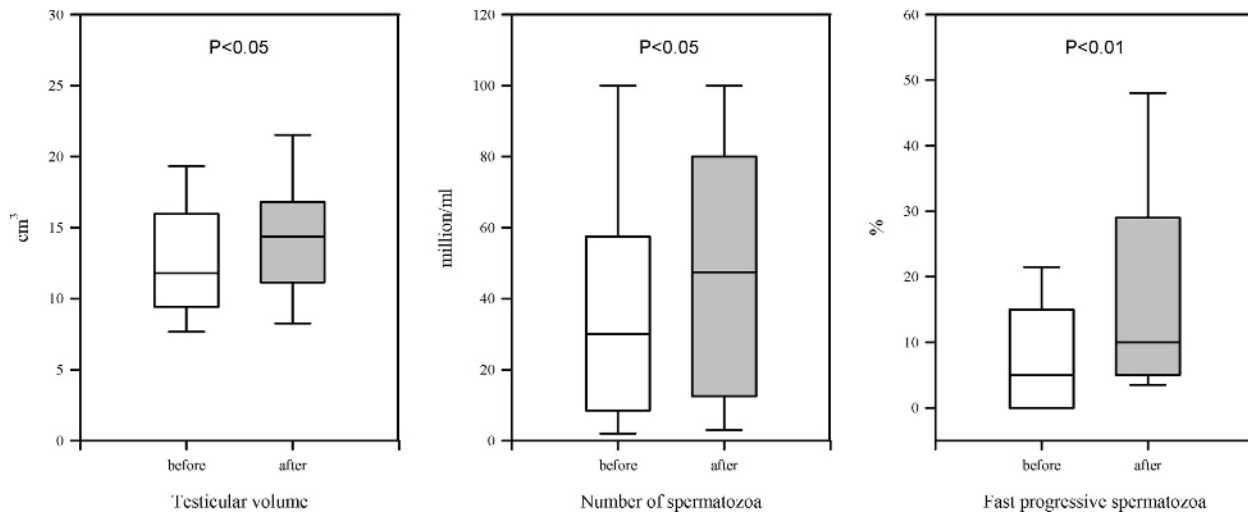
Unquestionably, the problem is more widely debated with regard to adult subjects, as the theory that correction of varicocele means improved fertility has not been universally accepted.

The wide variability of the data reported in the literature is mainly due to the lack of randomized long-term studies and to the evaluation of different parameters, such as semen parameters or pregnancy rate. Furthermore, the larger part of current literature does not value testicular volume or testicular growth but only fertility improvements.

Based on these assumptions, there are two different and diametrically opposed clinical-scientific fronts. The first supports the treatment of varicocele, underlying the importance of performing more epidemiological studies

Pre and post-treatment values of testicular volume and main seminal parameters expressed as mean \pm SD and range

	Pretreatment	Posttreatment
Testicular volume (cm ³)	13.4 \pm 4.4 (range: 4.27–23.79)	14.0 \pm 4.5 (range: 4.40–24.98)
Number of spermatozoa (million/ml)	38.2 \pm 33.4 (range: 2–80)	48.0 \pm 33.8 (range: 3–80)
Fast progressive spermatozoa (%)	9.11 \pm 11.2 (range: 5–45)	18.9 \pm 19.8 (range: 5–60)



Box and whiskers plots of pre- and postoperative testicular volume, number of spermatozoa, and percentage of fast progressive spermatozoa. The middle box covers the middle 50% of data, between the lower and upper quartiles; the "whiskers" extend out to the 10th and 90th percentiles, while the central line is at the median.

and of doing an early diagnosis of this pathology; it assigns a primary role of treatment of varicocele in patients with clinical varicocele and primary infertility, or to prevent secondary infertility, extending indications also to subclinical varicocele. These authors consider postoperative improvements in seminal parameters and testicular trophism as real and positive factors in terms of fertility (The Male Infertility Best Practice Policy Committee of the American Urological Association and The Practice Committee of the American Society for Reproductive Medicine, 2004; Zini et al, 1997).

The second group of authors is against varicocele treatment and focuses on contributing to some of the biofunctional properties, present or residual in certain varicocele patients, that do not improve after surgical repair. Moreover, most of these authors consider pregnancy rates alone as the final effective result (World Health Organization, 1992; Evers and Collins, 2003).

Based on our results, and in accordance with the first group of authors, it seems clear that in most cases surgery or sclerotherapy improved trophism in affected testis: in adult subjects, the increase of a mean of about 1 cm³ in the size of the testicle at the 1-year follow-up simply confirms the undeniable utility of these treatments.

Moreover, it can clearly be noted that an increase in testicular volume and trophism corresponds to an increase of approximately 50% in the number of spermatozoa produced, with a doubled fast progressive spermatozoa rate.

About treatment choice we report here our data recently published in the *Journal of Andrology* (Zucchi et al, 2005) showing differences in terms of earlier

improvement in seminal parameters, with regard to sperm motility, in the patients who underwent antegrade sclerotherapy (Tauber procedure).

From this standpoint, the possibility of treating varicocele represents a big advantage even in cases requiring fertilization in vitro embryo transfer or intra cytoplasmic sperm injection procedures, as it gives these subjects the possibility of obtaining a better semen quality.

Lastly, we must consider that the ultrasound scan allows us to monitor the affected testis, adequately providing indirect information on functional recovery. Nevertheless, it is advisable that follow-up ultrasound imaging be performed at the same specialized center using the same instrument. Likewise, it is essential to conduct a detailed measurement of all testicular diameters, calculating testicular volume and also examining the parenchymal aspect in order to get a truly complete picture of testicular trophism.

Conclusions

Despite the lack of consensus in the latest literature regarding the usefulness of treating varicocele, in light of these data the possibility that the affected testicle can benefit in terms of trophism and function must certainly be taken into consideration. The improvement in trophism is reflected in the improvement in seminal parameters, which is helpful not only in relation to physiological fertility but also in subjects who opt for FIVET or ICSI procedures.

Lastly, ultrasound imaging performed during the follow-up of treated patients not only makes it possible

to monitor the presence of recurrent varicocele, but is also extremely helpful for evaluating trophism and testicular function.

References

- Aragona F, Ragazzi R, Pozzan GB, De Caro R, Munari PF, Milani C, Glazel GP. Correlation of testicular volume, histology and LHRH test in adolescents with idiopathic varicocele. *Eur Urol*. 1994;26:61–66.
- Evers JL, Collins JA. Assessment of efficacy of varicocele repair for male subfertility: a systematic review. *Lancet*. 2003;361:1838–1839.
- Haans LC, Laven JS, Mali WP, te Velde ER, Wensing CJ. Testis volumes, semen quality and hormonal patterns in adolescents with and without a varicocele. *Fertil Steril*. 1991;56:731–736.
- Laven JS, Haans LC, Mali WP, te Velde ER, Wensing CJ, Eimers JM. Effects of varicocele treatment in adolescents: a randomized study. *Fertil Steril*. 1992;58:756–762.
- Lipshultz LI, Corriere JN Jr. Progressive testicular atrophy in the varicocele patient. *J Urol*. 1977;117:175–176.
- The Male Infertility Best Practice Policy Committee of the American Urological Association and The Practice Committee of the American Society for Reproductive Medicine. Report on varicocele and infertility. *Fertil Steril*. 2004;82:142–145.
- Okuyama A, Nakamura M, Namiki M, Takeyama M, Utsunomiya M, Fujioka H, Itatani H, Matsuda M, Matsumoto K, Sonoda T. Surgical repair of varicocele at puberty: preventive treatment for fertility improvement. *J Urol*. 1988;139:562–564.
- Onozawa M, Endo F, Suetomi T, Takeshima H, Akaza H. Clinical study of varicocele: statistical analysis and the results of long term follow-up. *Int J Urol*. 2002;9:455–461.
- Paduch DA, Niedzieski J. Repair versus observation in adolescent varicocele: a prospective study. *J Urol*. 1997;158:1128–1132.
- Sayfan J, Siplovich L, Koltun L, Benyamin N. Varicocele treatment in pubertal boys prevents testicular growth arrest. *J Urol*. 1997;157:1456–1457.
- Schlesinger MH, Wilets IF, Nagler HM. Treatment outcome after varicocelectomy. A critical analysis. *Urol Clin N Am*. 1994;21:517–529.
- Segenreich E, Israilov SR, Shmueli J, Niv E, Servadio C. Correlation between semen parameters and retrograde flow into the pampiniform plexus before and after varicocelectomy. *Eur Urol*. 1997;32:310–314.
- World Health Organization. The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics. *Fertil Steril*. 1992;57:1289–1293.
- Yamamoto M, Hibi H, Katsuno S, Miyake K. Effects of varicocelectomy on testis volume and semen parameters in adolescents: a randomized prospective study. *Nagoya J Med Sci*. 1995;58:127–132.
- Zini A, Buckspan M, Berardinucci D, Jarvi K. The influence of clinical and subclinical varicocele on testicular volume. *Fertil Steril*. 1997;68:671–674.
- Zucchi A, Mearini L, Mearini E, Costantini E, Bini V, Porena M. Treatment of varicocele: randomized prospective study on open surgery versus Tauber antegrade sclerotherapy. *J Androl*. 2005;26:328–332.