



# Efficacy of spermatic vein ligation in patients affected by high grade left varicocele

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## ABSTRACT

**Purpose:** To study the effect of high grade varicocele treatment in infertile patients.

**Materials and Methods:** Seventy-five patients were selected by the following criteria: infertility persisting for more than 1 year; abnormal semen parameters; no other infertility-related disease; no obvious causes of infertility in the subject's partner; basal eco-color Doppler ultrasound demonstrating continuous reflux in the spermatic vein. All patients considered for the study had at least a six months period from the diagnosis to the surgery due to waiting list, choice of the patient or time needed to complete diagnostic evaluation of the couple. The surgical procedure was performed through an inguinal approach. All enrolled patients were counseled to have unprotected intercourse during the ovulation period in order to maximize the probability of pregnancy within the 6-month preoperative period. The achievement of pregnancy and semen parameters were recorded during the preoperative and postoperative period.

**Results:** Two of the seventy-five patients were excluded because of persistent varicocele after surgery. The preoperative pregnancy rate was 1.3% (1 couple). The postoperative pregnancy rate was 42.5%. The stratification of pregnancies by semester showed a significantly higher rate in the first postoperative period ( $p = 0.0012$ ). Mean time to conception was 13.5 months. Mean preoperative sperm count was  $17.6 \times 10^6/\text{mL}$  compared to  $19.7 \times 10^6/\text{mL}$  in the postoperative period ( $p < 0.0001$ ). Mean percentage of progressive sperm motility was 13.7%, compared to 17.6% in the postoperative period ( $p < 0.0001$ ). Mean percentage of normal sperm morphology was 7.6%, compared to 15.2% postoperatively ( $p < 0.0001$ ).

**Conclusion:** Surgical treatment of high grade varicocele proved to effectively treat associated infertility by improving seminal parameters and pregnancy rate in our patient cohort.

## ARTICLE INFO

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## INTRODUCTION

Varicocele is a common scrotal condition characterized by the elongation and enlargement of the network of veins leaving the testis that join to form the testicular vein.

The incidence is reported to be as high as 20-24% in the adult male population (1) with a higher prevalence in the left side. The condition is more common in men in infertile marriages, in which it affects 25-40% of men with abnormal semen analysis (2,3).

The exact association between reduced male fertility and varicocele is not known because prospective randomized studies on varicocele treatment in adults have given conflicting results (4-8). The largest study indicated a benefit (8,9), whereas meta-analysis of most of the prospective randomized trials did not (10). However, in previous studies, selection criteria based on the clinical and ultrasonographic grade of varicocele did not take into consideration a homogeneous population. It would be probable that a lower grade of varicocele does not affect fertility as well as the quality of seminal parameters, and a significant bias might exist.

For this reason, our intent was to study a series of infertile patients with high grade varicocele before and after surgical treatment. Our aim was to obtain reliable results from a homogeneous and selected patient population.

## MATERIALS AND METHODS

From January 2006 to February 2011, we studied 75 patients with high grade left varicocele who presented with infertility. Patients were selected by the following criteria: (a) infertility persisting for more than 1 year despite regular, unprotected intercourse; (b) abnormal semen parameters as assessed by World Health Organization (WHO) guidelines 2010; (c) no other infertility-related disease; and (d) no obvious causes of infertility in the subject's partner.

All men underwent a standard diagnostic infertility evaluation (physical examination, blood tests, including hormonal dosages and testing for Y deletion and chromosomal defects when needed according to seminal and clinical features, color Doppler ultrasound of the scrotum). The examination was performed after the patient stood for various minutes in a warm room; the scrotum was inspected and palpated in the upright position. In all cases, an ultrasound with color-Doppler study was performed using a linear 7.5 MHz probe both in supine and upright position. According to this method, varicocele was graduated as follows: 1st grade, reflux was visible only under Valsalva maneuver; 2nd grade, venous reflux was intermittent under basal conditions; 3rd grade, basal continuous reflux was demonstrated (11,12).

Infertility was defined, according to the WHO, as the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year (13).

At least two preoperative semen analyses were obtained by masturbation after 3 days of abstinence from sexual activity, and the average value was considered.

All possible causes of male infertility were ruled out, including history of maldescended testis, infections, general diseases, or chronic medication. The partner was studied in all cases to rule out any cause of infertility (such as anovulation, endometriosis, tubal blockage, etc.)

All patients considered for the study had periods between 6 and 9 months (mean: 7.2 months, SD 0.8) from the diagnosis to the surgery due to waiting list, choice of the patient or time needed to complete diagnostic evaluation of the couple.

All the enrolled patients fulfilled the study inclusion criteria and were counseled to have unprotected intercourse during the ovulation period in order to maximize the probability of getting pregnant during the 6 months before intervention, when the patient was on the surgical waiting list.

The patients underwent spermatic vein ligation through an inguinal approach with optical magnification performed by a single-surgeon. Optical magnification using frontal loops (3x) was utilized to spare the spermatic artery and lymphatic ducts.

The achievement of pregnancy and semen parameters were recorded during the preoperative and postoperative period. Postoperative semen analyses were obtained 6 months after surgery.

Categorical data were examined by the chi-square test; continuous variables were tested by t-test assuming  $p < 0.05$  as significant. The results were elaborated using the statistical program SigmaStat™ for Windows® V2.03.

## RESULTS

All 75 patients had 3rd grade left varicocele. Two patients were excluded because of basal continuous reflux after surgery. The patients' mean age was 33.2 years (range 23-48

years). The mean study follow-up time was 32.4 months (range 24-47 months). The mean age of the partners was 28.5 years (range 23-39 years). No patient reported previous episodes of cryptorchidism, hydrocele, or testicular trauma, nor had they undergone surgery of the urogenital tract. No other causes of infertility were found.

The mean infertility period was 23 months (SD ± 8.4, range 12-39 months).

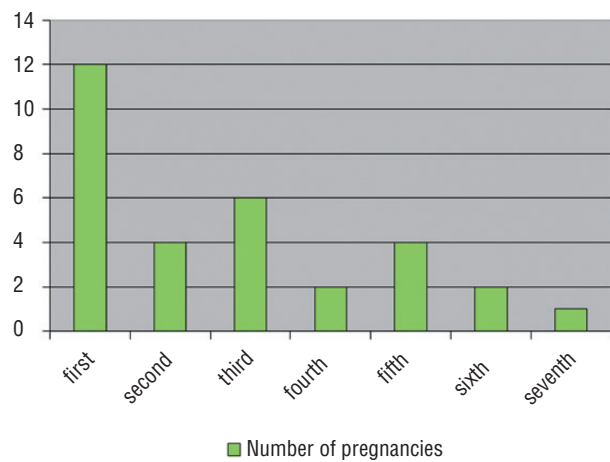
During the 6-9 months preoperative period while patients were on the surgery waiting list, pregnancy was achieved in 1 couple (1.3%).

The mean preoperative sperm count was  $17.6 \times 10^6$ /mL compared to  $19.7 \times 10^6$ /mL in the postoperative period ( $p < 0.0001$ ). The mean preoperative percentage of progressive sperm motility was 13.7% compared to 17.6% in the postoperative period ( $p < 0.0001$ ). The mean preoperative percentage of normal sperm morphology was 7.6% compared to 15.2% in the postoperative period ( $p < 0.0001$ ) (Table-1).

During the first 6-month postoperative period, 12 couples got pregnant (16.5%). A comparison of the pregnancies occurring in the preoperative period to the occurrence during the first postoperative semester showed a significant difference ( $p < 0.0001$ ). In the following months, 19 more pregnancies occurred. The stratification of pregnancies by semester showed a significantly higher rate during the first postoperative period ( $p = 0.0012$ ) (Figure-1). The mean time to conception was 13.5 months.

The persistence rate of varicocele was 2.6%, and no minor or major postoperative complications were registered. All patients were discharged within 24 hours.

**Figure 1 - Postoperative pregnancies stratified by semester.**



## DISCUSSION

The main point of discussion is the clear benefit for the rate of pregnancy when varicocele is treated in infertile patients if other causes of male infertility, as well as obvious causes of female infertility, are ruled out. However, this point is debated by the scientific literature because even prospective randomized controlled trials of varicocele treatment in adults have given conflicting results. Studies on this topic are divided into those that conclude there is no influence on infertility by treatment of varicocele (6,7,14,15) and those that find a real benefit on semen parameters and pregnancy rate (8,9).

However, the heterogeneous inclusion criteria, the small number of analyzed patients, and, in some cases, the high percentage of varicocele

**Table 1 - Pregnancies and sperm characteristics before and after operation.**

	Pre-op semester	1st post-op semester	p
Pregnancies	1 (1.3%)	12 (16.5%)	< 0.0001
Mean sperm count	$17.6 \times 10^6$ /mL	$19.7 \times 10^6$ /mL	< 0.0001
Mean percentage of progressive sperm motility	13.7%	17,6%	< 0.0001
Mean percentage of normal sperm morphology	7.6%	15.2%	< 0.0001

persistence after treatment do not allow to draw any final conclusion based on the evidence. We agree that the meta-analytic interpretation of these data does not provide information based on evidence that is useful in improving clinical practice (16). In particular, the high rate of patients who dropped out and/or were lost to follow-up calls into question the propriety of randomized studies comprised of an untreated arm that may appear unethical in such patients. In this regard, our method might be closer to real clinical practice than randomized clinical trials that have a higher percentage of randomization refusal. In our study, the same patients are their own controls because seminal parameters and pregnancy rate are measured before and after surgical treatment for varicocele in the same population.

Our positive results for pregnancy rate and improved seminal parameters may be explained by our selection criteria. Only 3rd grade varicocele according to color Doppler classification was taken into consideration differently from previous randomized studies that usually consider clinical classifications, which are known to have low sensitivity (3).

Another bias present in previous studies is the different treatment used to correct the venous reflux and, in some cases, the high persistence rate of varicocele. In our series, treatment was the same in all patients and consisted in the microsurgical inguinal ligation that, in our hands, had a lower persistence rate (2.6%).

Our study was prospective but not randomized, and this is the main limitation. We do not know if the simple counseling done during the waiting list months could be a treatment comparable to surgical treatment of varicocele. To answer this question, we should have considered a randomized non-operated group of patients treated by counseling alone. However, data on efficacy of counseling alone with no surgical procedures in infertile couples with associated varicocele are lacking therefore we are not able to assess if counseling alone might increase pregnancy rate in this selected group of patients.

In the absence of any significant data on counseling efficacy we think it is unethical not to treat patients strongly motivated to have children.

## CONCLUSIONS

The surgical treatment of high grade varicocele effectively treats infertility, improving seminal parameters and pregnancy rate. Increased improvement occurs early after treatment. A microsurgical inguinal approach seems to be a good treatment because the incidence of persistence is acceptable.

Study limitations: We did not have a control group for comparison with our treatment data. We agree that a control would be ideal to provide high level evidence of treatment benefits, but is ethically questionable to exclude a well-defined patient group from a recommended therapy.

## CONFLICT OF INTEREST

None declared.

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