Assessment of Time-dependent Changes in Semen Parameters in Infertile Men After Microsurgical Varicocelectomy

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OBJECTIVE To characterize the changes in seminogram findings in infertile men after varicocelectomy.

METHODS This study included 71 consecutive infertile men who underwent microsurgical low ligation varicocelectomy and received 3 semen analyses, 1 before microsurgical varicocelectomy and again at 3 and 12 months after. Total motile sperm count (TMSC) was calculated using the following formula: [volume (mL) × concentration (millions/mL) × motility (%)].

RESULTS Despite the lack of significant changes in the proportion of sperm with abnormal morphology, sperm concentration, motility, and TMSC in the 71 patients were significantly higher at 3 and 12 months after varicocelectomy than before surgery. However, no further improvement in these parameters at 12 months after varicocelectomy was noted compared with those at 3 months. Furthermore, when the included men were divided into 3 groups according to preoperative TMSC as <3 million, 3-9 million, and >9 million, TMSCs at 3 months after varicocelectomy in all 3 groups were significantly higher than those before varicocelectomy; however, TMSCs at 12 months after surgery in all groups were similar to those at 3 months.

CONCLUSION The level of improvement in semen parameters at 3 months after varicocelectomy may be stable at 12 months after surgery, irrespective of baseline values of TMSC. Therefore, varicocelectomy could be offered as a therapeutic option for infertile men, even for couples with an older woman, because its efficacy is evaluable at 3 months after surgery, and assisted reproductive technology could be immediately applied to ineffective cases. UROLOGY 86: 48–51, 2015. © 2015 Elsevier Inc.

Varicocele is the most frequently identifiable and treatable cause of male infertility, found in ~15% of the general adult male population and in up to 40% of infertile men.[1] Although impaired spermatogenesis induced by excess heat due to varicocele is the commonly proposed mechanism, the exact pathophysiology of male infertility caused by varicocele has not been completely clarified[2]; thus, the optimal treatment for men with varicocele remains controversial in the field of clinical andrology.

To date, a number of studies have described approaches to performing a varicocele repair, including embolization, open surgical ligation, and laparoscopic repair.[3] Of these, the microsurgical approach to low ligation varicocelectomy has become popular because it enables the identification of small spermatic veins and better differentiation of the testicular artery and lymphatics, resulting in a marked decrease in the incidence of complications and recurrence after surgery.[4] However, no difference in fertility rates has been reported among any of the techniques used to repair varicocels.[5]

Despite ongoing debate concerning the effect of varicocele repair on fertility rates, that semen parameters, including sperm concentration, motility, and morphology, can improve after the repair of varicoceles has been well documented.[6] In fact, 2 recent meta-analyses showed that surgical varicocelectomy improved semen parameters in infertile men with a palpable varicocele.[7,8] We also reported improved sperm quality and fertility potential, even in men with severe oligozoospermia who were treated with microsurgical varicocelectomy.[9] Furthermore, varicocelectomy has been shown to improve additional parameters that reflect sperm quality that could not be captured by standard semen testing such as sperm deoxyribonucleic acid fragmentation.[10]

From the practical viewpoint, assessing the interval required for varicocele repair to improve semen parameters is important. The American Society for Reproductive Medicine Practice Committee proposed in 2008 that patients wait at least 1 year to evaluate the effect of varicocele repair on the changes in semen parameters and the need to move to other assisted reproductive

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techniques (ARTs)[11]; however, this committee modified the report in 2014 as follows: time to improvement is typically 3 to 6 months, which corresponds to 1 to 2 spermatogenic cycles.[12]

In fact, Al Bakri et al[13] assessed the proper duration needed for the improvement of sperm parameters after varicocelectomy. The findings indicated that sperm parameters improved by 3 months after surgery and subsequently did not further improve. The study, however, included patients who received embolization, inguinal, or subinguinal microsurgical repair, and derived the findings from the data on semen testing within 6 months after varicocele repair. Considering these findings, we evaluated the changes in semen parameters in 71 consecutive infertile men who underwent microsurgical varicocelectomy using the subinguinal approach and received semen analyses before and at 3 and 12 months after surgery to characterize the time-dependent changes in semen parameters after microsurgical varicocelectomy.

METHODS

This study was conducted as a prospective observational study and included 71 consecutive patients who fulfilled the following criteria: no gynecologic problems in the wife of each patient, a palpable varicocele was diagnosed and confirmed by Doppler scrotal ultrasound, no findings on semen analyses showing azoospermia, microsurgical low ligation varicocelectomy was performed as the initial treatment for subfertility at our institution between 2000 and 2013, and semen analyses were conducted within 1 month before and at 3 and 12 months after surgery. Written informed consent for participating in this study was obtained from each patient before varicocelectomy. The study design was approved by the Research Ethics Committee of our institution.

Semen specimens were analyzed before surgery and then at 3 and 12 months after surgery according to guidelines in the World Health Organization laboratory manual. Specimens collected by masturbation after a 3-day period of sexual abstinence were analyzed within 1 hour of collection to measure the volume of ejaculate, sperm count, motility rate, and morphology using a Makler chamber. Total motile sperm count (TMSC) was calculated using the following formula: [volume (mL) × concentration (millions/mL) × motility (%)]. In addition, an endocrine evaluation consisting of measurement of serum follicle-stimulating hormone, luteinizing hormone, and testosterone levels in a blood sample was performed, and varicocele was graded by physical examination in a warm room using the World Health Organization diagnostic classification.[14] In this series, microsurgical varicocelectomy was performed using the subinguinal approach, as previously described.[15]

Statistical analyses were performed using Statview 5.0 software (Abacus Concepts Inc., Berkeley, CA), and P values of $<.05$ were considered significant. Comparison of semen parameters between different time points was performed by a paired 2-tailed t test.

RESULTS

Table 1 summarizes the baseline characteristics of the 71 patients included in this study. Table 2 presents the findings of semen analyses performed before and at 3 and 12 months after varicocelectomy. Semen volume and the proportion of sperm with abnormal morphology did not differ significantly among the 3 time points. Sperm concentrations and motilities were significantly increased by 3 and 12 months after surgery compared with those before surgery; however, no significant change was noted in sperm concentrations or motilities between 3 and 12 months after surgery. TMSCs were also significantly elevated at 3 and 12 months after surgery compared with before surgery, but the difference in TMSCs between 3 and 12 months after surgery was not significant. Furthermore, TMSCs were increased in 51 men (71.8%) at 3 months and in 54 men (76.1%) at 12 months after surgery compared with those before surgery. Although 9 patients (12.7%) showed an elevation of TMSCs from the baseline values at 12 months but not 3 months after surgery, the difference in TMSCs between before and 12 months after surgery in these 9 patients was not significant.

Table 1. Baseline patient characteristics

Parameters*	Patients (n = 71)
Age (y)	34.1 ± 5.3 (24-47)
Laterality of varicocele	
Unilateral	21 (29.6)
Bilateral	50 (70.4)
Grade of varicocele	
Right	
I	11 (50.0)
II	10 (45.5)
III	1 (0.5)
Left	
I	6 (8.6)
II	25 (35.7)
III	39 (55.7)
Semen volume (mL)	3.3 ± 1.6 (0.5-9.0)
Sperm concentration (million/mL)	11.3 ± 12.0 (0.2-60.4)
Sperm motility (%)	31.2 ± 17.4 (0-80.2)
Sperm with abnormal morphology (%)	54.3 ± 17.2 (6.2-96.3)
Total motile sperm count (million)	10.9 ± 14.8 (0-87.8)
Follicle-stimulating hormone (IU/L)	7.5 ± 5.9 (1.8-37.8)
Luteinizing hormone (IU/L)	4.7 ± 3.4 (1.3-22.5)
Testosterone (ng/mL)	5.5 ± 2.2 (1.9-11.6)

* Continuous variables are expressed as mean ± standard deviation (range) and categoric variables as number (%).

We then divided the 71 patients into 3 groups according to the baseline TMSC value: <3 million (n = 24), 3-9 million (n = 22), and >9 million (n = 25). As reported in Table 3, the TMSC in each group exhibited time-dependent changes similar to that in the overall population; that is, in all 3 groups, despite the lack of significant differences between 3 and 12 months after surgery, TMSCs at 3 and 12 months after surgery were significantly greater than before surgery.

Follow-up data >24 months were available in 35 of the 71 patients. Of these 35 patients, ART was applied to 24