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Impact of Inguinal Varicocele Ligation on Testicular Volume, Sperm Parameters, and Pregnancy Rates

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ABSTRACT

INTRODUCTION: The purpose of this prospective investigation was to study the impact of inguinal varicocele ligation on testicular volume, sperm parameters, and pregnancy rates before and after varicocelectomy.

METHODS: Participants were an experimental group of 50 infertile men with a mean age of 29.6 years (range, 23-36 years) and a comparison group of 50 age-matched, healthy fertile men. All infertile men had a clinical left grade 2 or grade 3 varicocele. Each participant received the same baseline tests of clinical examination, semen analysis, and scrotal ultrasonography. Tests were repeated 3 and 6 months after inguinal varicocele repair for patients in the experimental group. Outcome measures were semen parameters, testicular volumes, percentage of volume difference between the right and left testicles, and pregnancy rates. The *t* test was used to compare the baseline measures of the 2 groups. A Freidman repeated measures analysis of variance was performed to compare the results of the experimental group at baseline and at 3 months and 6 months after surgery. Comparison group baseline data were also compared with the experimental group data at 6 months.

RESULTS: Participants in the experimental group had significantly lower baseline mean sperm concentration and sperm motility and higher mean testicular volume differences than the participants in the comparison group (all with $P < .0001$); there was no significant group difference in baseline mean semen volume. Varicocele ligation resulted in significantly increased mean sperm concentration and motility and significantly decreased mean testicular volumes 3 months and 6 months after surgery (all with $P < .0001$). There was no significant change in semen volume. Sperm concentration and sperm motility reached near-normal levels following surgery, but patients continued to have significantly larger mean testicular volume differences than those of the comparison group. Mean right and left testicular volume difference was significantly correlated with mean sperm motility 6 months postoperatively (Pearson $r = -0.365$; $P = .009$), but not significantly correlated with sperm concentration or semen volume. The partners of 24 patients (48%) were pregnant 6 months postoperatively.

CONCLUSION: Varicocele ligation improves ipsilateral testicular volume loss, semen profile, and pregnancy rates.

KEYWORDS: Varicocele; Pregnancy rates; Semen parameters; Testicular volume

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Abbreviations and Acronyms

TV, testicular volume
WHO, World Health Organization

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original study

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INTRODUCTION

A varicocele is a common cause of male infertility [1,2]. It is present in approximately 15% of healthy men in the general population and approximately 35% of men who present for infertility evaluation [3-5]. Between 45% and 81% of men with secondary infertility have a varicocele that is detected during their clinical evaluation [6].

Varicoceles are associated with smaller ipsilateral testes in both adolescents and adults [7]. Studies in adults have demonstrated increased testicular size after varicocele repair, as measured with conventional methods of calipers or orchidometry [8-11]. Scrotal ultrasonography is generally considered the most accurate way to measure testicular volume [12-14].

There is a controversy regarding the association between testicular volume increase after repair of a varicocele in adults and improvement in postoperative semen parameters. If such a correlation exists, improvement in testicular volume after varicocele repair could be considered one of the prognostic factors of good fertility outcome. The purpose of the present prospective investigation was to study the impact of inguinal varicocele ligation on testicular volume, sperm parameters, and pregnancy rates before and after varicocelectomy.

METHODS

This prospective study was performed from January 2008 to June 2009. The protocol was approved by an ethics committee at the authors' institution. All patients provided informed consent.

Participants

Experimental group. A total of 50 male patients with primary infertility were included in the experimental group. *Primary infertility* was defined as patients who had never achieved pregnancy after 1 year of unprotected vaginal intercourse, when female causes of infertility were excluded. In addition to infertility, the patients had symptoms of scrotal pain and swelling. Their mean age was 29.6 years (SD = 3.7; range, 23-36 years). All patients had a clinical left varicocele that was rated according to the Dubin-Amelar system [3] as grade 2 (moderate - nonvisible and palpable with standing position; n = 23) or grade 3 (large - visible on gross inspection; n = 27).

Exclusion criteria were: (1) major endocrine or sexual abnormalities, (2) previous intervention for varicocele, (3) history of cryptorchidism, testicular trauma, or previous scrotal surgery, (3) azospermia. Female infertility factors were excluded by gynecologic evaluation of the female partners. The female partners ranged in age from 20 to 29 years.

Comparison group. The comparison group consisted of 50 age-matched, healthy volunteers. None of these participants had a varicocele. Fertility was confirmed by history of at least 1 offspring.

Procedures

Clinical examination. All participants in the experimental and comparison groups received the same clinical examination. The examination consisted of a thorough sexual, developmental, medical, and social history and general and local physical assessments. Local examination focused on the diagnosis and grade of the varicocele, evaluation of the testis (size, texture, and sensation), and detection of any associated scrotal lesions. Patients were examined in a warm room in the standing and supine positions. While standing, patients were asked to perform the Valsalva maneuver to assess reversal of venous flow. All varicoceles emptied when the patients were supine.

Semen analysis. All participants had 2 or more preoperative semen analyses. This test was repeated 3 months and 6 months postoperatively for patients in the experimental group. Semen was collected by masturbation after 72 hours of sexual abstinence. The results were evaluated according to the WHO laboratory manual [15]. Normal sperm values are: (1) sperm count ≥ 20 million per mL; (2) sperm motility ≥ 50% with forward progression or ≥ 25% with rapid progression within 60 minutes of ejaculation; (3) sperm morphology ≥ 30% with normal forms.

Duplex scan. All participants had baseline duplex scans of the scrotal contents and pampiniform plexus. Scans were also performed 3 months and 6 months postoperatively for men in the experimental group. The scans were evaluated by different radiologists who were blind to the study. Scrotal ultrasound was performed with a 5-10 MHz high-frequency linear-array transducer. The examination started with all participants in the supine position to evaluate the varicocele (presence, site, size, and presence of reflux), testes (size and texture), epididymis (size and echopattern), and tunica (presence of hydrocele). The participant was then examined in the standing position. A Valsalva maneuver was used to evaluate the size of the varicocele and any associated reflux. The testes were examined in at least 2 planes, along the long and transverse axes. The size and echogenicity of each testis and the epididymis were compared with those on the opposite side. Color Doppler and pulsed Doppler parameters were optimized to display low-flow velocities, to demonstrate blood flow in the testes and surrounding scrotal structures. The structures within the scrotal sac were examined to detect extratesticular masses or other

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abnormalities. A varicocele was diagnosed in the presence of: (1) 2 or more tortuous dilated veins with a width > 3 mm, (2) reflux flow persisting for more than 1 second, based on Doppler color change, and (3) increased retrograde flow in the pampiniform plexus before or during a valsalva maneuver when the patient was in the supine or standing position.

Testicular volume. Testicular length, width, and height were measured, excluding the epididymis. The largest measurement obtained for each testicular dimension was used for the volume calculation and statistical analysis. Ultrasonographic testicular volume (TV) was calculated using the formula: TV = length × width × height × 0.71. The percentage difference of TV between the right and left testes was calculated as: (Right TV – left TV) × 100 / right TV.

Surgery. All participants in the experimental group had classic inguinal varicocele ligation.

Data Analysis

A *t* test was used to compare the baseline measures of the 2 groups. Continuous variables were expressed in means and standard deviations (SD); categorical variables were expressed in frequencies. Results of the baseline history and clinical examination, semen analysis, and scrotal ultrasound for the participants in the comparison group were compared with those of the patients in the experimental group at baseline and 6 months after surgery by using a *t* test. A nonparametric repeated measures analysis of variance (Freidman test) was performed to compare the results of the experimental group at baseline and at 3 months and 6 months after surgery. A probability < .05 was considered statistically significant. Statistical analyses were conducted using SPSS-12 (IBM Corp; Somers, NY).

RESULTS

Outcome Measures

Table 1 contains the baseline measures of sperm concentration, sperm motility, and sperm volume and right versus left testicular volume differences for participants in both groups, with the probability of significant differences. Sperm concentration and motility were higher than the WHO criteria for a normal semen analysis in the comparison group; both baseline variables were lower than the WHO criteria for the experimental group. Mean semen volume was normal for patients in both groups, according to the WHO criteria. There were statistically significant group differences in mean sperm concentration, motility, right and left testicular volume difference, and right and left percent of testicular volume difference (all with $P < .0001$). The participants in the experimental group had lower mean sperm concentration and sperm motility and higher mean testicular volume differences than the participants in the comparison group. There was no significant group difference in mean semen volume ($P = .268$).

Table 2 contains the outcomes of sperm concentration, sperm motility, and sperm volume and right versus left testicular volume differences at baseline and at 3 months and 6 months after surgery for participants in the experimental group, with the probability of significant differences. Results of the repeated measures Freidman test revealed that there was a significant difference in mean sperm concentration, sperm motility, testicular volume difference, and percent of testicular volume difference 3 months and 6 months postoperatively when compared with baseline (all with $P < .001$). Mean sperm concentration and sperm motility increased significantly from baseline; mean testicular volume measures decreased

Table 1. Baseline Measures of Sperm Concentration, Sperm Motility, and Sperm Volume and Right Versus Left Testicular Volume Differences for Participants in Both Groups; Probability of Significant Differences (N = 100).
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Baseline Measure	Comparison Group (n = 50)		Experimental Group (n = 50)		*P*
	Mean	SD	Mean	SD	
Sperm concentration (sperm/mL)	91,060,000	16,555,916	9,628,000	5,204,395	<.0001
Sperm motility (%)	63.5	13.6	29.5	21.1	<.0001
Semen volume (mL)	3.46	0.9	3.85	2.2	.268
Testicular volume difference (cc)	0.27	0.26	2.74	1.2	<.0001
Testicular volume difference (%)	1.9	1.9	18.68	7.6	<.0001

Table 2. Sperm Concentration, Sperm Motility, and Sperm Volume and Right Versus Left Testicular Volume Differences at Baseline and 3 and 6 Months After Surgery for Patients With Varicoceles; Probability of Significant Differences (n = 50). doi: 10.3834/uij.1944-5784.2011.02.02t2

Outcome Measure	Baseline		3-Months After Surgery		6-Months After Surgery		*P*
	Mean	SD	Mean	SD	Mean	SD	
Sperm concentration (sperm/mL)	9,628,000	5,204,395	35,000,000	21,302,521	84,640,000	52,276,252	<.0001
Sperm motility (%)	29.5	21.1	51.2	13.8	59.7	8.4	<.0001
Semen volume (mL)	3.85	2.2	3.27	1.2	3.76	1.1	.653
Testicular volume difference (cc)	2.74	1.2	1.17	0.5	0.84	0.8	<.0001
Testicular volume difference (%)	18.68	7.6	7.88	3.1	4.86	3.9	<.0001

significantly from baseline. There was no significant change in semen volume 3 months and 6 months after surgery when compared with semen volume before intervention ($P = .653$).

Table 3 contains the outcomes of sperm concentration, sperm motility, and sperm volume and right versus left testicular volume differences at baseline (comparison group) and at 6 months after surgery (experimental group), with the probability of significant group differences. There were no significant group differences in mean sperm concentration, sperm motility, and sperm volume ($P = .418$, $P = .119$, $P = .196$, respectively). This result suggests that these parameters reached near-normal levels following surgery for patients in the experimental group. There was a significant difference in mean testicular volume and the percent of testicular volume difference ($P < .001$). The participants in the experimental group continued to have larger mean testicular volume differences than those of the comparison group.

Using a Pearson 2-tailed test, we found a significant correlation between mean right and left testicular volume difference and mean sperm motility 6 months postoperatively ($r = -0.365$; $P = .009$). There was no significant correlation between mean testicular volume difference and sperm concentration ($r = -0.203$; $P = .158$) and mean testicular volume difference and semen volume 6 months postoperatively ($r = 0.024$; $P = .869$).

Pregnancy Outcome

Out of the 50 participants in the experimental group, the female partners of 24 patients (48%) were pregnant 6 months

Table 3. Sperm Concentration, Sperm Motility, and Sperm Volume and Right Versus Left Testicular Volume Differences at Baseline (Comparison Group) and 6 Months After Surgery (Experimental Group); Probability of Significant Differences (N = 100). doi: 10.3834/uij.1944-5784.2011.02.02t3

Variable	Comparison Group Baseline (n = 50)		Experimental Group 6 Months After Surgery (n = 50)		*P*
	Mean	SD	Mean	SD	
Sperm concentration (sperm/mL)	91,060,000	16,555,916	9,628,000	5,204,395	<.0001
Sperm motility (%)	63.5	13.6	29.5	21.1	<.0001
Semen volume (mL)	3.46	0.9	3.85	2.2	.268
Testicular volume difference (cc)	0.27	0.26	2.74	1.2	<.0001
Testicular volume difference (%)	1.9	1.9	18.68	7.6	<.0001

postoperatively. Pregnancy was achieved naturally without any assisted reproduction techniques.

DISCUSSION

Sakamoto and colleagues [16] noted that varicocele repair in adults with a clinical left varicocele increased left testicular volume and improved semen profiles. Among 44 men, 21 underwent microsurgical subinguinal varicocelectomy, 17 had laparoscopic varicocelectomy, and 6 had retrograde percutaneous sclerotherapy. The mean right testicular volume was larger than the mean left testicular volume both before and after varicocele repair for all 44 patients. The mean left and total testicular volumes increased significantly after repair of the varicocele, but the right testicular volume showed no significant increase. The mean (SD) increase in volume after repair was 0.9 (3.4) mL in the right testes, 1.5 (2.7) mL in the left testes, and 2.4 (5.2) mL in total testicular volume. Mean sperm density, motility percentage, total sperm count, and total motile sperm count improved significantly after varicocele repair. These results are consistent with those from our study, in which sperm count and motility showed significant increase 3 and 6 months postoperatively when compared with baseline and a comparison group of fertile men without varicocele. Sakamoto et al [16] concluded that testicular volume increase was associated with improvement in semen parameters such as sperm density and motility. Similar results were also found by Zucchi and colleagues [17]. These results are in contrast with previous reports showing an increase in both right and left testicular volumes following varicocele repair.

We hypothesize that the outcome differences from some studies of varicocelectomy may be due to the way that testicular volume was measured. Sakamoto et al [16], Zucchi et al [17] and the authors of the present study calculated testicular volume with a formula that is based on ultrasound measurements. We believe that the formula (length × width × height × 0.71) is more accurate than actual testicular volumes obtained from orchidectomy specimens or by a caliper or orchidometer.

Kibar et al [18] compared semen parameters before and after varicocelectomy. They found that surgical correction of varicocele was associated with significant improvement in sperm density and sperm motility. Their results showed a significant improvement in sperm concentration 3 months postoperatively and further sharp improvement 6 months postoperatively. The preoperative mean sperm concentration of 22.1 (4.2) million per mL (range 6 million to 68 million) increased to 38.3 (6.1) million per mL at postoperative month 6. The Wilcoxon signed rank test showed that sperm concentration improved significantly after varicocelectomy (P = .0002). The mean sperm motility increased from 23.2% (.2%) to 45.1% (1.9%) at postoperative month 6 (P = .0001). However, the preoperative mean semen volume of 2.8 (0.2) mL did not significantly differ from the postoperative value of 2.6 (0.3) mL. These findings are all consistent with those from our study; we also found significant improvements in sperm density and motility and an insignificant difference in semen volume 3 and 6 months after varicocelectomy. The 6-month follow-up period between repair and subsequent ultrasound and semen analysis in both of these studies is short; longer follow-up of improvement in testicular volume and semen quality could be more informative. Nonetheless, because human spermatogenesis is completed in 74 days, these follow-up intervals for ultrasound and semen analysis would appear sufficient for assessing changes in spermatogenesis and testicular volume after varicocele repair.

Regarding the pregnancy outcome after varicocelectomy, Pasqualotto and colleagues [11] found that varicocelectomy improved pregnancy outcome in patients with maturation arrest. In their study, 60 patients underwent varicocelectomy and had a testicular histology diagnosis of germ-cell aplasia (group 1; n = 28) or maturation arrest (group 2; n = 32). The mean volume of the right and left testicle was smaller for patients in group 1 than group 2. In addition, the mean sperm concentration before treatment was lower in group 1 than group 2. The mean volume of the left and right testicle increased in group 1 after the intervention. The mean postoperative sperm concentration and motility in group 2 showed no increase; the mean sperm concentration in group 1 increased. The pregnancy rate was higher in group 2 (14/26, 53.8%) than in group 1. This pregnancy outcome was a little higher than that obtained in our study (48% at 6 months postoperatively), probably because Pasqualotto et al had a longer follow-up period of 27 months.

CONCLUSIONS

Varicocele decreases testicular volume on the ipsilateral side. Right and left testicular volume difference and percent of testicular volume difference showed marked improvement from baseline to 3 months and 6 months after varicocelectomy, although the mean volume remained higher than that of men without a varicocele. Varicocele repair also significantly improved semen concentration and motility and led to a 48% pregnancy rate 6 months postoperatively. Improvement in testicular volume after varicocele repair may be a prognostic indicator of good fertility outcome.

Conflict of Interest: none declared.

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