Infertility

Efficacy of Bilateral and Left Varicocelectomy in Infertile Men With Left Clinical and Right Subclinical Varicoceles: A Comparative Study

Yi Qun Zheng, Xin Gao, Zhi Jian Li, Yuan Long Yu, Zhi Gang Zhang, and Wei Li

OBJECTIVES
To determine whether it is necessary to perform bilateral varicocelectomy (BV) in infertile men with left clinical and right subclinical varicoceles by comparing the outcomes of BV with those of left varicocelectomy (LV) in these patients.

METHODS
A total of 104 infertile men with left clinical and right subclinical varicoceles were randomly divided into 2 groups: BV (n = 51) and LV (n = 53). Both BV and LV were performed using a retroperitoneal approach with ligation of the dilated internal spermatic veins. The sperm concentration, sperm motility, normal morphology, serum testosterone level, bilateral testicular volume, and spontaneous pregnancy rate were measured pre- and postoperatively. Statistical analysis was performed using analysis of variance and the \( \chi^2 \) test, with significance determined by \( P < .05 \).

RESULTS
The patients in the 2 groups had comparable preoperative age, partner age, sperm concentration, sperm motility, normal morphology, left varicocele grade, serum testosterone level, and bilateral testicular volume (\( P > .05 \)). Both BV and LV resulted in significant increases in sperm concentration, sperm motility, and normal morphology (\( P < .05 \)). No significant changes in serum testosterone level or bilateral testicular volume were observed after varicocelectomy in the 2 groups (\( P > .05 \)). No significant differences were found in the postoperative sperm concentration, sperm motility, normal morphology, bilateral testicular volume, serum testosterone level, and spontaneous pregnancy rate between the 2 groups (\( P > .05 \)).

CONCLUSIONS
These findings suggest that no benefit is realized with BV compared with LV in infertile men with left clinical and right subclinical varicoceles. UROLOGY 73: 1236 –1240, 2009. © 2009 Elsevier Inc.

Varicocele is the most common identifiable etiologic factor in male infertility, and varicocelectomy has a beneficial effect on male fertility and pregnancy outcomes.\(^1\)\(^-\)\(^3\) More recently, the results of clinical research have demonstrated that most left clinical varicoceles are usually accompanied by right small or subclinical varicoceles detected by color Doppler ultrasoundography or radiologic examination.\(^4\)\(^,\)\(^5\) Nevertheless, no consensus has yet been reached on whether the benefit of BV is superior to that of LV in patients with left clinical and right subclinical varicoceles. Grasso et al.\(^6\) found no significant difference between the effect of BV and that of LV in patients with bilateral varicoceles (grade 2-3 on the left side and grade 1 on the right) with regard to the improvement of the seminal parameters. Scherr and Goldstein,\(^7\) however, found that BV resulted in significantly greater improvement of the seminal parameters than did LV in patients with grade 2-3 left varicoceles and grade 1 right varicoceles, and even a small untreated palpable right varicocele continued to have detrimental effect on bilateral testicular function. However, whether it is necessary to perform BV in infertile men with left clinical and right subclinical varicoceles is a topic that has rarely been investigated. To the best of our knowledge, although Pasqualotto et al.\(^8\) noted that BV should be performed in the patients with left clinical and right subclinical varicoceles in 2005, no such detailed studies were available before we began the present study. In light of the heterogeneity of humans, we considered it indispensable to perform more studies of this topic.

In the present study, to determine whether it is necessary to perform BV in infertile men with left clinical...
and right subclinical varicoceles, we compared the preoperative and postoperative sperm concentration (× 10⁶/mL), sperm motility (%), normal morphology (%), serum testosterone level (ng/dl), bilateral testicular volume (mL), and spontaneous pregnancy rate (%) in the BV group with those in the LV group.

MATERIAL AND METHODS

We performed this prospective study on 104 infertile men (defined as the inability to achieve conception after a 12-month period of regular sexual intercourse with a partner without an identifiable cause of infertility) with left clinical and right subclinical varicoceles and abnormal seminal parameters at 2 urology departments. These patients were randomly distributed to the BV group (n = 51) and LV group (n = 53), and underwent either LV or BV during a 4-year period (from March 2002 to March 2006). Our institutional review board approved this study, and each patient provided written informed consent. Each patient underwent a thorough medical and reproductive history evaluation to rule out aspects that might be related to male primary infertility; female factor infertility was ruled out by thorough gynecologic examinations.

In the present study, clinical varicoceles were graded according to the criteria of Dubin and Amer: grade 1, palpable venous distension only during a Valsalva maneuver; grade 2, palpable intrascrotal venous distension without a Valsalva maneuver but not visible; and grade 3, the distended venous plexus bulges visibly through the scrotal skin and is easily palpable without a Valsalva maneuver. Subclinical varicoceles were detected using a color Doppler flow imaging system and 7.5-MHz linear array transducer (ALOKA SSD2000, Tokyo, Japan). The diagnostic criteria of a subclinical varicocele include that the spermatic veins are impalpable on a careful physical examination during a Valsalva maneuver, with reversal of blood flow in spermatic veins but not visible; and grade 3, the distended venous plexus bulges visibly through the scrotal skin and is easily palpable without a Valsalva maneuver. Subclinical varicoceles were detected using a color Doppler flow imaging system and 7.5-MHz linear array transducer (ALOKA SSD2000, Tokyo, Japan). The diagnostic criteria of a subclinical varicocele include that the spermatic veins are impalpable on a careful physical examination during a Valsalva maneuver, with reversal of blood flow in spermatic veins but not visible; and grade 3, the distended venous plexus bulges visibly through the scrotal skin and is easily palpable without a Valsalva maneuver. Subclinical varicoceles were detected using a color Doppler flow imaging system and 7.5-MHz linear array transducer (ALOKA SSD2000, Tokyo, Japan).

Table 1. Preoperative characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LV (n = 53)</th>
<th>BV (n = 51)</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>31.8 ± 1.57*</td>
<td>32.2 ± 1.49</td>
</tr>
<tr>
<td>Partners’ age (y)</td>
<td>29.1 ± 1.65*</td>
<td>30.4 ± 1.57</td>
</tr>
<tr>
<td>Left varicocele grade (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.8 (2/53)*</td>
<td>3.9 (2/51)</td>
</tr>
<tr>
<td>2</td>
<td>35.8 (19/53)*</td>
<td>35.3 (18/51)</td>
</tr>
<tr>
<td>3</td>
<td>60.4 (32/53)*</td>
<td>60.8 (31/51)</td>
</tr>
<tr>
<td>Testosterone level (ng/dl)</td>
<td>598.6 ± 157.3*</td>
<td>614.7 ± 159.4*</td>
</tr>
<tr>
<td>Seminal parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sperm concentration (× 10⁶/mL)</td>
<td>7.6 ± 2.3*</td>
<td>7.1 ± 2.1</td>
</tr>
<tr>
<td>Sperm motility (%)</td>
<td>29.5 ± 10.1*</td>
<td>30.3 ± 11.3</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>16.6 ± 7.9*</td>
<td>18.2 ± 7.1</td>
</tr>
<tr>
<td>Testicular volume (cm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>12.4 ± 3.9*</td>
<td>12.1 ± 4.2</td>
</tr>
<tr>
<td>Right</td>
<td>18.6 ± 5.4*</td>
<td>17.9 ± 5.7*</td>
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</table>

LV = left varicocelectomy; BV = bilateral varicocelectomy. * P < .05 compared with BV group; using χ² test for left varicocele grade and analysis of variance for rest of variables, with significance determined at P < .05.

Medical Electronic Systems, Caesarea Industrial Park, Israel). The achievement of spontaneous pregnancy, which refers to pregnancy without assisted reproductive technology in which ≥1 gestational sac is present within the uterus as detected by ultrasonography, was recorded within a 24-month follow-up period. The serum specimen of each patient was obtained between 8:00 and 10:00 AM both preoperatively and 12 months after varicocelectomy, and the serum testosterone level was detected using radioimmunoassay.

All measurement data are presented as the mean ± SD. The statistical analysis included analysis of variance for the measurement data and the χ² test for the other data. A P < .05 was considered statistically significant.

RESULTS

The preoperative general characteristics of the patients in 2 groups are listed in Table 1. No statistically significant differences were observed in terms of age, partner age, sperm concentration, sperm motility, normal morphology, serum testosterone level, left varicocele grade, or bilateral testicular volume between the 2 groups (P > .05; Table 1).

Both LV and BV resulted in significant increases in sperm concentration, sperm motility, and normal morphology (P < .05); however, neither BV nor LV resulted in significant changes in serum the testosterone level or bilateral testicular volume (P > .05; Table 2).

No significant differences were found in the postoperative sperm concentration, sperm motility, normal morphology, serum testosterone level, bilateral testicular volume, or spontaneous pregnancy rate in BV group compared with those in the LV group (P > .05; Table 2).
prove the seminal parameters in infertile men with.

A recent meta-analysis indicated that varicocelectomy can significantly improve the seminal parameters in infertile men with palpable varicoceles and abnormal seminal parameters.1 The presence of a varicocele negatively affects certain parameters in the semen analysis, namely sperm concentration, motility, and morphology.17 A recent meta-analysis indicated that varicocelectomy can significantly improve the seminal parameters in infertile men with palpable varicoceles and abnormal seminal parameters.1 Even repair of subclinical varicoceles can significantly improve the semen quality.5,18,19 In the present study, we found that both BV and LV resulted in significant increases in sperm concentration, sperm motility, and normal morphology, but no significant differences were found in the postoperative sperm concentration, sperm motility, and normal morphology between the 2 groups. This indicated that repair of right subclinical varicocele did not significantly improve the semen quality. Jarow et al.10 also found that the improvement in semen quality after subclinical varicocelectomy was significantly less than that of clinical varicocele repair and suggested that subclinical varicocelectomy is of questionable benefit. In a study similar to ours, Pasqualotto et al.8 found that LV induced a slight increase in the sperm concentration and BV induced a significant increase in the sperm concentration, but no significant change in sperm motility was observed after either LV or BV. Ishikawa and Fujisawa20 reported that no relationship was found between the varicocele grade and improvement in the seminal parameters after varicocelectomy.

COMMENT

Although varicoceles have long been considered to occur mainly on the left side, investigators have recently observed that most left clinical varicoceles are usually accompanied by right-sided small or subclinical varicoceles.5,12,13 This finding has given rise to an argument as to whether the repair of an accompanying small or subclinical right varicocele is necessary. Some investigators have recommended that patients with left larger and right smaller varicoceles undergo bilateral repair.7,8 Martínez-Chamorro et al.14 and Demirbaş et al.15 even advocated diagnosing and treating intratesticular varicocele. In contrast, Jarow et al.10 and Yamamoto et al.16 found little evidence that repair of subclinical varicoceles had a positive effect on male fertility and, therefore, limited value in using scrotal ultrasonography for the detection of varicoceles in subfertile men.

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Abundant evidence has demonstrated that varicoceles have been associated with ipsilateral testicular growth retardation in adolescents and testicular atrophy in adults, and so-called catch-up growth has consistently appeared in affected testes after varicocele repair.8,21,22 However, our results signify that left clinical varicocele caused ipsilateral testicular atrophy that was not observed in the right testis with subclinical varicocele, and no significant change in the bilateral testicular volume was observed 12 months after either LV or BV. Sakamoto et al.23 also found that left clinical varicocele was associated with relative ipsilateral testicular hypotrophy in infertile patients; however, a subclinical varicocele was not important in determining the difference between the right and left testicular volumes.

The effect of varicocele on the serum testosterone level in humans is controversial. Andò et al.24 found that the serum testosterone level significantly decreased in patients with varicoceles and that the duration of varicocele influenced testicular hormone secretion. However, Canales et al.25 did not find a relationship between the presence of varicocele and changes in the serum testosterone level. This might have been because the testosterone level in the peripheral blood is extremely low and changes dramatically with the irregular annual and daily rhythms. Spermatogenesis is an androgen-dependent process that optimally occurs with very high intratesticular testosterone levels, and the intratesticular testosterone level could more exactly reflect the status of testicular hormone secretion.26 However, it is difficult to detect intratesticular testosterone levels in humans, because surgical invasion for experimental purposes is forbidden by the ethical concerns of human research. To reduce the influence of annual and daily rhythms on the serum testosterone level as far as possible, we took serum from each patient during the same period of 8:00-10:00 AM. Neither a preoperative abnormality in the serum testosterone level nor a significant change in the serum testosterone level after varicocelectomy was observed in our study.

Table 2. Comparison of seminal parameters and other outcome measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>LV Group (n = 53)</th>
<th>Preoperative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>Seminal parameter</td>
<td></td>
<td></td>
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<td>Testicular volume (mL)</td>
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<td>12.4 ± 3.9†</td>
<td>12.1 ± 4.2†</td>
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</tr>
<tr>
<td>Right</td>
<td>18.6 ± 5.4†</td>
<td>17.9 ± 5.7†</td>
<td></td>
</tr>
<tr>
<td>Spontaneous pregnancy rate (%)</td>
<td>0 (20/53)†</td>
<td>0 (20/53)†</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

* P < .05, intragroup comparison.
† P > .05, comparison of postoperative data between both groups, using χ² test for spontaneous pregnancy rate and analysis of variance for other variables, with significance set at P < .05.
It has been widely accepted that varicoceles result in deleterious effects on testicular function and male fertility. However, the treatment of varicoceles to achieve pregnancy in infertile partners remains controversial, and all investigations to date have been subject to criticism.\(^\text{27}\)

The reported spontaneous pregnancy rate after varicocelectomy has varied from 5.3% to 66.7%.\(^\text{8,28}\) Our results showed an increase in the spontaneous pregnancy rate after both BV (39.2%, 20/51) and LV (37.7%, 20/53) but no significant difference between them.

In addition, we observed some distinctive changes after LV and BV. At 3 months after LV, the reversal of blood flow in the internal spermatic veins and dilated spermatic veins could not be detected ultrasonographically on the right during the Valsalva maneuver. However, the diameter of the right spermatic veins increased slightly from 3.13 ± 0.11 mm to 3.97 ± 0.16 mm at 3 months after BV, and the reversal of blood flow in the internal spermatic veins and dilation of the spermatic veins had vanished ≤6 months after BV. We believe these physiopathologic changes might be related to the pathophysiology of varicocele. Varicocele is a disorder characterized by dilation of the pampiniform plexus secondary to an increased intravenous pressure from the left renal vein that can be transmitted to the left spermatic veins. Also, the presence of communicating branches between the 2 gonadal veins can cause an increase in contralateral pressure, with the development of a milder varicocele on the right side as well.\(^\text{29}\) We supposed that LV eliminated the transmission of the increased intravenous pressure from the left renal vein to the left and right testicular pampiniform plexus, and thus, not only the left clinical varicocele, but also the secondary right subclinical varicocele, would be cured. In contrast, because the internal spermatic veins are the main testicular venous drainage,\(^\text{30}\) ligation of the right internal spermatic veins might lead to testicular venostasis due to vascular compromise.

Patients with varicocele vary in age, duration and grade of varicocele, preoperative seminal parameters, lifestyle, work environment, and other health-related issues. Thus, it is impossible to arrive at a true conclusion on this topic through several studies, and it is possible that more controversies will be addressed by future investigators. We advocated performing multicenter and large sample studies on this topic.

**CONCLUSIONS**

In the present study, we did not found statistically significant differences between the efficacy of BV and LV in infertile men with left clinical and right subclinical varicoceles. Therefore, we suggest that it is not necessary to emphasize the necessity of BV for these patients. Because of the heterogeneity of humans, we believe ongoing studies are needed to provide more information on this topic.

**References**


