

Available online at www.sciencedirect.com

# **ScienceDirect**

journal homepage: www.elsevier.com/locate/ajur





CrossMark

# Does varicocele grade predict the postoperative changes of semen parameters following left inguinal micro-varicocelectomy?

Hongzhen Wang, Xueke Wang\*, Dingjun Fu, Hua Zhu, Ming-kuen Lai

Division of Urology, Department of Surgery, Chang Gung Hospital, Xiamen, Fujian, China

Received 3 April 2015; received in revised form 29 April 2015; accepted 6 July 2015 Available online 13 July 2015

Varicocele; Grade; Microsurgery; Infertility; Inguinal Microsurgery; Infertility; Inguinal Mathematical and the properative of semen parameters following left inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectory. Methods: The study included 44 patients undergoing left microsurgical inguinal varicocelector		
	Varicocele; Grade; Microsurgery; Infertility;	Methods: This study included 44 patients undergoing left microsurgical inguinal varicocelectomy. Internal spermatic veins were classified as large (4 mm or more in diameter), medium (2–4 mm), or small (2 mm or less). Changes in sperm activity, morphology and count were estimated perioperatively. The introperative findings and semen parameters were compared between varicocele groups of grades 2 and 3. Results: Both sperm motility and count improved significantly postoperatively (from (31.9 ± 16.3)% to (47.3 ± 15.5)%, from (28.1 ± 28.1) × 10 <sup>6</sup> /mL to (52.1 ± 74.2) × 10 <sup>6</sup> /mL). In varicoceles with grade 2 and 3, significant differences were found in the number of large veins (0.4 ± 0.6 vs. 1.2 ± 0.7, $p < 0.001$ ) and ultrasonographic maximum diameters of spermatic vein in supine and standing positions (2.3 ± 0.4 cm vs. 2.8 ± 0.6 cm, 3.1 ± 0.7 cm vs. $3.9 \pm 0.7$ cm, $p = 0.001$ and 0.001 respectively). However no difference of changes in sperm motility and count was detected ((16.3 ± 13.5)% vs. (14.4 ± 12.6)%, (30.5 ± 84.4) × 10 <sup>6</sup> /mL vs. (12.9 ± 20.6) × 10 <sup>6</sup> /mL respectively, $p = 0.65$ and 0.40 respectively). Conclusion: Preoperative varicocele grade might not predict postoperative semen changes regardless of possible existence of anatomic and ultrasonographic associations. © 2015 Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (http://

\* Corresponding author. *E-mail address:* wxk3639@adm.cgmh.com.cn (X. Wang). Peer review under responsibility of Shanghai Medical Association and SMMU.

http://dx.doi.org/10.1016/j.ajur.2015.07.002

2214-3882/© 2015 Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

#### 1. Introduction

Varicoceles are abnormally dilated pampiniform plexus in the scrotum which may cause impaired testicular function. They are more common on the left side. Varicoceles occupy 19%-41% of men with primary infertility and 45%-81% of men with secondary infertility [1,2]. Reports have shown that repair of varicocele might improve the male fertility status [3,4].

Clinically, varicocele grade is determined by physical examination. Relationship between preoperative grade and the postoperative response in semen quality is still controversial. Some reports showed that postoperative outcomes were significantly associated with the clinical grade of varicocele [5,6], while other result was completely different [7].

Therefore, to clarify the contradictions, we attempted to estimate the relationship between preoperative grades of varicoceles and postoperative improvement of semen parameters following microsurgical inguinal varicocelectomy in subfertile men.

#### 2. Patients and methods

A total of 46 adult men with left varicocele underwent microsurgical inguinal varicocelectomies in our clinic between May 2011 and February 2014. The protocol and informed consent were approved by the Institutional Review Board, and that all subjects gave informed consent. All patients presented with infertility at least 1 year of unprotected intercourse and had clinically palpable varicoceles. They all had impaired semen guality (at least one of the following semen parameters: sperm motility<50%, normal morphology < 20% or sperm count < 20  $\times$  10<sup>6</sup>/mL). Of these men, two patients with azoospermia were excluded. Forty-four men were followed up with physical examination and ultrasound to evaluate recurrence, hydrocele formation and testicular size for at least 6 months after the day of surgery. The mean age of the men undergoing primary varicocele repair was 27.7  $\pm$  5.6 years. The varicocele grade distribution of the left-side varicoceles units (n = 44) was as follows: one was grade 1, 59.1% grade 2 (26/44), and 38.6% grade 3 (17/44) varicoceles (Table 1).

Table 1Patientcharacteristicsofleftvaricocelectomy.	inguinal
Variable	n(%)
Total patients	44(100)
Patients with nutcracker syndrome	3(4.5)
Patients having external spermatic vein or veins	15(34.1)
Varicocelectomy indications	
Infertility	44(100)
Primary infertility	31(70.5)
Secondary infertility	13(29.5)
Grade	
1	1(2.3)
2	26(59.1)
3	17(38.6)

Varicocele was clinically diagnosed by physical palpation and classified as grade 1 (palpable only with the Valsalva maneuver), 2 (palpable without the Valsalva maneuver) or 3 (visible through scrotal skin). Diagnosis was confirmed by color Doppler ultrasound with room temperature between 21.5 and 23.5 °C. The maximum diameters of internal spermatic vein were measured and recorded at inguinal level in both supine and standing positions with the detection of vein reflux by color Doppler ultrasound. Patient who was found anteroposterior diameter ratio between the distended and narrowed portions of the left renal vein over 4.0 was diagnosed as nutcracker syndrome. Routine urine examinations were checked perioperatively to investigate proteinuria or hematuria. All semen samples were obtained pre-operatively and postoperatively by masturbation with as a sum of days of sexual abstinence (3-5 days) as possible. Multiple data from the semen analyses were averaged to allow comparison as a single parameter.

All of the microsurgical inguinal varicocelectomies were performed under general anesthesia by the same surgeon (X.K.W). A 2-3 cm incision was made over the inguinal canal. The external obligue fascia was sharply opened. The spermatic cord was dissected with a pusher and surrounded by a Penrose drain. The dissection plane was close to the internal inguinal ring. A Zeiss NC-4 operating microscope (Carl Zeiss, SIP: 6623502157) was used intraoperatively. The internal spermatic vessels were exposed under 10 imesmagnification. The vas deferens vasal veins and arteries were identified and preserved. A second Penrose was placed between the vas deferens and the internal spermatic structures. Internal spermatic artery or arteries were preserved. All veins including external spermatic vein were doubly ligated with clips or 4-0 silk ties and divided. Spermatic veins were flattened on a micro-ruler and classified as large (4 mm or more in diameter), medium (2-4 mm), or small (2 mm or less).

Changes in sperm motility, morphology and count were estimated perioperatively. Then clinical grades were compared with anatomic findings and semen parameters. The statistical analyses were performed using the two-sample paired *t* tests and Chi-square analyses using SPSS Statistic version 21.0 software (IBM, NY, USA). Values were presented as the mean  $\pm$  SD. Differences were considered significant if p < 0.05.

#### 3. Results

In the 44 patients, both sperm motility and count significantly improved postoperatively. The mean sperm motility increased from  $(31.9 \pm 16.3)\%$  (mean  $\pm$  SD) preoperatively to  $(47.3 \pm 15.5)\%$  postoperatively (p < 0.001, paired t test) and the mean sperm count increased from  $(28.1 \pm 28.1) \times 10^6$ /mL preoperatively to  $(52.1 \pm 74.2) \times 10^6$ /mL postoperatively (p = 0.02, paired t test). Although the mean normal morphology slightly improved from  $(23.9\% \pm 12.1)\%$  preoperatively to  $(26.6 \pm 9.3)\%$  postoperatively, there was no difference between them (p = 0.2, paired t test). Therefore, changes in motility and sperm count were both measured pre-operatively and postoperatively as parameters to evaluate the relationship between grades and outcomes.

Because no significant correlation between changes in sperm motility and count was found (Spearman correlation 0.029), the differences between different grades of varicoceles and the changes of two semen parameters were investigated separately. Therefore, we assessed differences in variables between grade 2 and 3 patients (n = 43) using independent t tests, including age, total ligated spermatic veins, large veins, medium veins, small veins, ultrasonographic maximum diameter of spermatic vein in both supine and standing positions, changes in motility and sperm count (Table 2).

Between varicoceles of grade 2 and 3, the data showed that the differences in the number of large veins, ultrasonographic maximum diameter of spermatic vein in supine and standing positions were significant ( $0.4 \pm 0.6$  vs.  $1.2 \pm 0.7$ ,  $2.3 \pm 0.4$  cm vs.  $2.8 \pm 0.6$  cm, and  $3.1 \pm 0.7$  cm vs.  $3.9 \pm 0.7$  cm respectively, p = 0.000, 0.001 and 0.001 respectively). No difference of changes in sperm motility and count postoperatively was found (16.3% vs. 14.4% and  $30.5 \times 10^6$ /mL vs.  $12.9 \times 10^6$ /mL respectively, p = 0.65 and 0.40 respectively). Although the number of medium veins in patients with grade 2 varicocele was higher than that in patients with grade 3 (1.6 vs. 1.0), there was no difference between them (p = 0.06). Furthermore, no statistical difference was detected in total number of veins with the varicocele grades, number of small veins and ages of patients.

In our study, three patients (3/44) (6.8%) were diagnosed as nutcracker syndrome and no proteinuria or hematuria was found. Two patients (2/44) (4.5%) were diagnosed with recurrence but none with testicular atrophy or hydrocele was found. External spermatic vein or veins were found in 15 patients (15/44, 34.1%).

#### 4. Discussion

Our study demonstrated the significant improvement in sperm motility and count after varicocelectomy (p < 0.001, p = 0.02 respectively). Although the exact mechanism how repair of varicocele would restore semen quality has not yet been satisfactorily explained, previous studies have reported an improvement in sperm quality postoperatively [3,4]. Our result showed the similar outcome. This result

implied a cause and effect relationship between impaired semen parameters and varicocele.

In present study, no significant difference in changes in motility and sperm count was found between varicoceles of grade 2 and 3 (p = 0.65, p = 0.40 alternatively), although the number of large veins, maximum diameter of spermatic vein in supine and standing positions were different (p = 0.000, 0.001 and 0.001 respectively). Steckel et al. [6] found that men with varicoceles of grade 3 presented greater relative improvement in sperm count than men with varicoceles of grade 2 and 1. On the contrary, Braedel et al. [7]. found less improvement in sperm count in men with grade 3 varicocele than men with smaller varicoceles. Our data showed that patients with varicocele of grade 2 had better recovery in sperm motility and count (16.3% vs. 14.4% and 30.5  $\times$  10<sup>6</sup>/mL vs. 12.9  $\times$  10<sup>6</sup>/mL). Our result was close to the Braedel's findings, but the differences in sperm motility and count were not significant. Therefore, our result was different from previous reports. Our findings suggested that the multiple factors might influence improvement of postoperative semen quality.

Microsurgical varicocelectomy can be performed either by a subinguinal or inguinal approach. Previous report showed that at subinguinal level, grade 3 varicoceles had an average of 1.0 large vein while grade 2 varicoceles had 0.5 large vein [8]. Our study firstly found that at inguinal level, grade 3 varicoceles had an average of 1.2 large vein while grade 2 varicoceles had 0.4 large vein. To our knowledge, such microsurgical description has not been accomplished before. With the same size definition for large vein, our result showed that the anatomic difference between large vein and grade 2, 3 may be similar at inguinal and subinguinal level. Therefore, if a patient presents with a grade 3 varicocele, we may find at least one large vein to be ligated in both approaches. As a complement, our result may be contributed to describe clearer and more complete anatomic association between varicocele grade and intraoperative veins findings at both levels. Furthermore, our study showed that the ultrasonographic maximum diameters of spermatic vein in supine and standing positions were significantly different between grade 2 and 3

Table 2 Differences between grade 2 and 3 patients.						
Variable	Total	Grade 3	Grade 2	p-Value		
Patients (n)	43	17	26	_		
Age (year)	$\textbf{27.7} \pm \textbf{5.6}$	$\textbf{26.8} \pm \textbf{6.7}$	$\textbf{28.3} \pm \textbf{4.7}$	0.38		
No. of total ligated veins	$\textbf{5.8} \pm \textbf{2.9}$	$\textbf{5.4} \pm \textbf{1.8}$	$\textbf{6.2} \pm \textbf{3.5}$	0.38		
Large (≥4 mm)	$\textbf{0.7} \pm \textbf{0.8}$	$\textbf{1.2} \pm \textbf{0.7}$	$\textbf{0.4} \pm \textbf{0.6}$	0.000		
Medium (>2 mm and <4 mm)	$1.4 \pm 1.1$	$\textbf{1.0} \pm \textbf{0.9}$	$1.6 \pm 1.1$	0.06		
Small (≤2 mm)	$\textbf{4.0} \pm \textbf{3.1}$	$\textbf{3.2} \pm \textbf{1.9}$	$\textbf{4.5} \pm \textbf{3.7}$	0.18		
Color Doppler ultrasound (cm)						
Supine	$\textbf{2.5} \pm \textbf{0.5}$	$\textbf{2.8} \pm \textbf{0.6}$	$\textbf{2.3} \pm \textbf{0.4}$	0.001		
Standing	$\textbf{3.4} \pm \textbf{0.8}$	$\textbf{3.9} \pm \textbf{0.7}$	$\textbf{3.1} \pm \textbf{0.7}$	0.001		
Changes of motility (%)	$\textbf{15.6} \pm \textbf{13.0}$	$\textbf{14.4} \pm \textbf{12.6}$	$\textbf{16.3} \pm \textbf{13.5}$	0.65		
Changes of sperm count ( $\times$ 10 <sup>6</sup> /mL)	$\textbf{24.0} \pm \textbf{66.2}$	$\textbf{12.9} \pm \textbf{20.6}$	$\textbf{30.5} \pm \textbf{84.4}$	0.40		

Data were presented as mean  $\pm$  SD. SD, standard deviation.

(2.3 cm vs. 2.8 cm, 3.1 cm vs. 3.9 cm respectively). This result might be helpful for ultrasonographic diagnosis of different varicocele grades.

The study has several limitations: first, we did not evaluate the effectiveness of microsurgical varicocelectomy on the spontaneous pregnancy rate. The influence of varicocelectomy on the semen parameters might not predict the improvement of spontaneous pregnancy rate completely. The second limitation is that the criteria for vein size definition are subjective, which were built on the distribution of vein sizes frequency in the varicocele grade groups. Therefore, results might be changed according to the different vein size definitions. The third limitation is that there was only one patient with grade 1 on the left side, difference among grade 1 and other grades could not be compared. The fourth limitation is that we chose the fourth edition of WHO laboratory manual as the criteria of semen parameters. Different standards of semen parameters might differ in the results. Histopathological analysis is needed to be included in further study. In the face of arteries with small size, the pulsation may be difficult to identify. Therefore, arterial ligation might indeed not have been recognized.

#### 5. Conclusion

Our study showed that preoperative varicocele grade might not predict postoperative semen outcomes, although the anatomic and ultrasonographic association might exist.

## **Conflicts of interest**

None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in manuscript.

### Acknowledgments

We thank Dr. Shian-Shiang Huang for providing support of surgical skills.

#### References

- Dubin L, Amelar RD. Varicocelectomy: 986 cases in a twelveyear study. Urology 1977;10:446.
- [2] Cocuzza M, Cocuzza MA, Bragais FMP, Agarwal A. The role of varicocele repair in the new era of assisted reproductive technology. Clinics 2008;63:395–404.
- [3] Zini A, Azhar R, Baazeem A, Gabriel MS. Effect of microsurgical varicocelectomy on human sperm chromatin and DNA integrity: a prospective trial. Int J Androl 2011;34:14–9.
- [4] Abdel-Meguid TA, Al-Sayyad A, Tayib A, Farsi HM. Dose varicocele repair improve male infertility? An evidence-based perspective from a randomized, controlled trial. Eur Urol 2011;59:455-61.
- [5] Al-Ali BM, Shamloul R, Pichler M, Augustin H, Pummer K. Clinical and laboratory profiles of a large cohort of patients with different grades of varicocele. Cent Eur J Urol 2013;66(1): 71-4.
- [6] Steckel J, Dicker AP, Goldstein M. Relationship between varicoceles size and response to varicocelectomy. J Urol 1993;149: 769–71.
- [7] Braedel HU, Steffens J, Ziegler M, Polsky MS, Platt ML. A possible ontogenetic etiology for idiopathic left varicocele. J Urol 1994;151:62–6.
- [8] Belani JS, Yan Y, Naughton CK. Does varicocele grade predict vein number and size at microsurgical subinguinal repair? Urology 2004;64:137–9.