Comparison between Microsurgical Subinguinal Varicocelectomy with and without Testicular Delivery for Infertile Men: Is Testicular Delivery an Unnecessary Procedure?

Yi Hou, Ying Zhang, Yun Zhang, Wei Huo, Hai Li*

Purpose: Controversy still exists as to whether testicular delivery during microsurgical subinguinal varicocelectomy (MSV) provides benefit to the patient or not. This study specifically compared the therapeutic effect of MSV with and without testicular delivery for the treatment of varicocele in a cohort of infertile men.

Materials and Methods: We conducted a prospective, randomized, controlled study to evaluate the therapeutic efficacy of MSV with and without testicular delivery for the treatment of varicocele in infertile men. A total of 100 patients were specifically recruited using strict inclusion criteria to undergo MSV with testicular delivery (group1, n = 50) or MSV without testicular delivery (group 2, n = 50). All patients were followed-up at 3, 6 and 12 months following surgery. Semen parameters, pregnancy and recurrence rates, and complications were monitored.

Results: Mean surgical time for group 1 was significantly longer than group 2 (90.50 ± 15.60 min vs. 84.30 ± 15.58 min; $P = .001$). Sperm count and motility were significantly improved at the 12-month follow-up appointment in both groups compared with pre-operative values, but were not significantly different at 3, 6, and 12 months when compared between the two treatment groups. The incidence of scrotal edema, and spermatic/testicular engorgement were higher in group 1 (both $P = .001$), although natural pregnancy rate was not significantly different between the two groups at the 12 month follow-up appointment (46% vs. 42%) ($P = .817$).

Conclusion: MSV with testicular delivery did not reduce the risk of recurrence and led to improved semen quality compared with MSV without testicular delivery. However, there was a higher risk of complication with this technique, which must be borne in mind when considering the clinical implications of our dataset.

Keywords: microsurgery; recurrence; treatment failure; varicocele; surgery; young adult; semen analysis; treatment outcome.

INTRODUCTION

The negative impact of varicocele upon spermatogenesis has been recognized for some time and manifests in 21%-41% of men presenting with primary infertility, and 75%-81% of men diagnosed with secondary infertility.[1,2] When untreated, this condition can lead to impaired spermatogenesis, poor Leydig cell function, and lead to reductions in testicular volume.[3] Compared to non-microscopic surgery, MSV permits clinicians to specifically identify the testicular artery and associated lymphatic system, thus minimizing the potential risk of arterial injury while also reducing the chances of complication and post-operative recurrence.[4]

The recurrence of varicocele is a major concern for urologists, and some studies report that the predominant factor underlying this problem are the gubernacular veins.[5,6] Testicular delivery during surgery allows the gubernacular veins to be ligated, which is likely to reduce the incidence of varicocele recurrence. However, this practice remains a controversial issue. Whether MSV with testicular delivery is a superior technique to that without testicular delivery is still unclear. To our best knowledge, only one study has directly compared these two methods in the published literature, and concluded that testicular delivery does not offer any beneficial effect.[7] However, this earlier study is s retrospective analysis without a randomized controlled study (RCT) design, and is therefore very limited in terms of evidence-based medical science. Up until now, there has been no RCT carried out in order to specifically compare the therapeutic outcome of the two types of microscopic varicocelectomy. In the present study, we prospectively evaluated and compared sperm count, motility, pregnancy and recurrence rates, and complication rates of MSV with and without testicular delivery in a cohort of infertile men using an RCT design.

MATERIALS AND METHODS

Study Participants

This prospective RCT was carried out in the China and Japan Union Hospital (Changchun, China), with appropriate institutional ethical approval. We enrolled a total of 100 infertile male patients diagnosed with varicocele who sought treatment in our center from April 2011 to August 2012. According to the date of hospital admission, patients were randomly divided into two groups: group 1 (MSV with testicular delivery, n = 50)

Department of Urology, China and Japan union hospital of Jilin University, 126 Xiantai Street, Changchun City, Jilin province, China.
*Correspondence: Department of Urology, China and Japan union hospital of Jilin University, 126 Xiantai Street, Changchun City, Jilin Province, China.
Tel: +88 604 3189876981. Fax: +88 604 3189876971. E-mail: muandkamu_2012@ aliyun.com.
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Table 1. Demographic and clinical characteristics of patients in each treatment group.

Variables	Group 1 (n = 50)	Group 2 (n = 50)	*P* Value
Age, years	27.94 ± 3.46	28.32 ± 3.89	.59
Age of spouse, years	26.12 ± 3.14	25.82 ± 2.27	.57
Grade of varicocele, no.			
I	6	7	.77
II	13	10	.48
III	31	33	.68
Serum hormone levels			
T (ng/mL)	6.24 ± 2.25	6.74 ± 2.17	.23
FSH (IU/L)	5.25 ± 0.94	5.08 ± 0.86	.39
PRL (mIU/L)	197.80 ± 65.93	202.43 ± 56.612	.67
Laterality, no. (%)			
Left	36/50 (72)	35/50 (70)	.83
Bilateral	14/50 (28)	15/50 (30)	.83

Abbreviations: T, testosterone; FSH, follicle stimulating hormone, PRL, prolactin.
Group 1 = Microsurgical subinguinal varicocelectomy with testicular delivery; Group 2 = Microsurgical subinguinal varicocelectomy without testicular delivery.

and group 2 (MSV without testicular delivery, n = 50). Allocation of patients into the two treatment groups was carried out according to the date of admission; if the date was an odd number, then the patients were allocated to group 1, otherwise patients were allocated to group 2.

Evaluations

Patient age and history of infertility was recorded, and semen was analyzed twice after 3-5 days of abstinence, at a minimum of 15-day intervals, in accordance with the latest World Health organization (WHO) guidelines for human semen analysis. The mean value of these 2 tests showed at least 1 abnormal parameter and serum follicle stimulating hormone (FSH), testosterone (T), and prolactin (PRL) were also measured prior to operation. Physical examination and color Doppler ultrasound were used to diagnose varicocele. The degree of varicocele was defined according to the established Dubine and Amelar's classification.[8] Testicular volume was also measured ultrasonographically using the formula: 0.71 × Length × Width × Height. Patients were selected for the RCT according to the following criteria: 1) if the diameter of the internal spermatic vein was greater than 3mm and/or presence of venous reflux without Valsalva maneuver; 2) if there was no history of urogenital abnormality or infection, trauma or surgery; 3) if sperm count was abnormal (< 20 × 10^6/mL) and/or motility was poor (< 50%); 4) if there was a negative mixed agglutination reaction for immunoglobulin (Ig) G and IgA; 5) if FSH level was normal; or 6) if gynecological assessment of the spouse was normal. Any patients who did not complete the follow-up period were excluded from the study. The study protocol, and the potential

Table 2. Operative data and post-operative complications in the two treatment groups.

Variables	Group 1 (n = 50)	Group 2 (n = 50)	*P* Value
Operation time (min)	90.50 ± 15.60	84.30 ± 15.58	.001
Postoperative hospital stay (day)	2.04 ± 0.49	2.01 ± 0.14	.77
Complications, no. (%)			
Hydrocele	0	0	-----
Recurrence	0	0	-----
Scrotal edema	24/50 (48.0)	7/50 (14.0)	.001
Wound infection	1/50 (0.2)	3/50 (0.6)	.31
Spermatic engorgement	22/50 (44.0)	6/50 (12.0)	.001
Testicular engorgement	14/50 (28.0)	4/50 (8.0)	.001
Orchitis and epididymitis	1/50 (2.0)	0	-----
Testicular hardness	1/50 (2.0)	0	-----

Group 1 = Microsurgical subinguinal varicocelectomy with testicular delivery; Group 2 = Microsurgical subinguinal varicocelectomy without testicular delivery.

Table 3. Comparison of sperm count and motility between preoperative and one year follow-up in study groups.

Variables	Preoperative	One Year Follow-up	*P* Value
Group 1 (n = 50)			
Motility	25.14 ± 10.38	39.34 ± 14.23	.001
Count	20.46 ± 5.79	27.99 ± 8.90	.001
Group 2 (n = 50)			
Motility	24.20 ± 9.91	40.59 ± 13.05	.001
Count	21.36 ± 6.48	29.54 ± 10.99	.001

Group 1 = Microsurgical subinguinal varicocelectomy with testicular delivery; Group 2 = Microsurgical subinguinal varicocelectomy without testicular delivery.

complications were explained to each patient in detail and all patients provided written informed consent prior to surgery. To ensure that the study was robust and consistent, all surgical procedures were performed by the same surgeon and all ultrasound tests were performed by the same Sonographer using the same instrument. This ensured consistency and therefore added rigor to the experimental design and analysis. A flow chart depicting this process is given in **Figure 1**. Given that this was a single-blinded RCT, only the patient group needed to be blinded.

Operative Technique

MSV with Testicular Delivery

Surgery was conducted under spinal or general anesthesia and began with a 2 cm traverse incision being made in the skin over the external inguinal ring in order to approach the spermatic cord. Following deepening of the incision, a Babcock clamp was used to grasp and deliver the spermatic cord, along with the testis, directly onto a rubber tissue. Surgical steps were carried out using a surgical microscope at 8×-15× magnification, focused upon the field of operation. External spermatic veins, and the gubernacular, trans-scrotal and collateral veins were ligated and divided following exposure. Once the spermatic fascia had been opened, we separated, ligated and divided the internal spermatic veins either with or without the assistance of color Doppler ultrasound. The isolated artery (or arteries) and associated lymphatic system were preserved.

MSV without Testicular Delivery

This procedure was similar to the one described above (MSV with testicular delivery), with the exception that, here, the testis was not delivered, and the gubernacular, trans-scrotal, and collateral veins, were not ligated.

The lengths of time taken for surgery, and the length of hospital stay following the operation, were recorded, as was the incidence of complications. Given that all of our patients received either spinal or general anesthesia, there was an absolute requirement for a 1-2 day post-operative stay in hospital. Operative times were determined for unilateral varicocele. If patients exhibited bilateral varicocele, then operative time was designated as one and half times that allocated for unilateral surgery. Patients were followed up, and examined physically and with ultrasound, at 3, 6 and 12 months post-operative periods. Semen parameters were evaluated by semen analysis, and pregnancy rate was determined following the 12 months follow-up appointment. Persistence or recurrence of varicocele was determined by the Valsalva maneuver. Testicular atrophy is defined as when there is a 20%, or greater, differential in volume between the two testicles.[9]

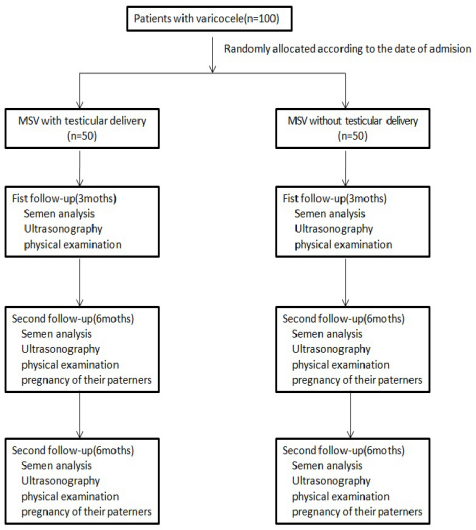
Statistical Analysis

Statistical analysis was performed on the basis of 'intention to treat'. All data are described herein as mean ± standard deviation (SD), and were analyzed using Sta-

Table 4. Postoperative semen quality and pregnancy outcome in the two study groups.

Variables	Group 1 (n = 50)	Group 2 (n = 50)	*P* Value
Sperm count (×10^6/mL)			
Preoperative	20.46 ± 5.79	21.36 ± 6.48	.39
3 months	23.5 ± 4.49	24.8 ± 5.88	.18
6 months	28.34 ± 9.48	26.91 ± 8.79	.27
12 months	27.99 ± 8.90	29.54 ± 10.99	.14
Sperm motility (%)			
Preoperative	25.14 ± 10.39	24. 20 ± 9.91	.58
3 months	31.99 ± 12.62	30.86 ± 11.85	.64
6 months	38.172 ± 13.55	37.21 ± 12.44	.69
12 months	39.34 ± 14.23	40.59 ± 13.05	.63
Spontaneous pregnancy, no. (%)	21/50 (42.1)	24/50 (44.7)	.817

Group 1 = Microsurgical subinguinal varicocelectomy with testicular delivery; Group 2 = Microsurgical subinguinal varicocelectomy without testicular delivery.



tistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 16.0. Raw data was tested for normality prior to analysis. Given that our data were normally distributed, they were subsequently compared using the unpaired Student's *t*-test or χ^2 test as appropriate. Differences in which $P < .05$ were considered statistically significant.

RESULTS

All 100 of our recruited patients completed the trial to the 12 months follow up, and therefore none were excluded. No significant differences were detected between the two treatment groups in terms of mean patient's age, age of spouse, laterality, grade of varicocele, or pre-operative hormonal levels (FSH, T and PRL) (**Table 1**). Mean operation time for group1 (with testicular delivery) was significantly longer than that of group 2 (90.50 ± 15.60 min vs. 84.30 ± 15.58 min, $P < .001$; **Table 2**). No significant differences were detected between the two groups in terms of post-operative hospital stay (2.04 ± 0.49 days vs. 2.01 ± 0.14 days) ($P > .05$; **Table 2**).

Compared to pre-operative values, sperm count and motility were significantly increased in both groups when measured at the 12 months follow-up appointment ($P < .001$; **Table 3**). Interestingly, sperm count and sperm motility were not significantly different between the two groups when measured at the 3, 6, and 12 months follow-up appointments ($P > .05$; **Table 4**). Natural pregnancy rate was not significantly different between the two groups when calculated at the 12 months follow-up appointment: 21/50 (42%) in group1 and 23/50 (46%) in group 2 ($P > .05$). Compared with group 1, a higher complication rate was observed in group 2 (Table 2), including the incidence of scrotal edema (24/50 vs. 7/50), spermatic cord edema (22/50 vs. 6/50), and testicular engorgement (14/50 vs. 4/50). One case of epididymitis, and one case of testicular hardness, were observed in group 1. There was no recorded recurrence of varicocele, or hydrocele, in either of the two groups.

DISCUSSION

Over recent years, several studies have recommended MSV as the standard method for treating varicocele in infertile men.[10,11] Evidence for the use of MSV in such patients includes lower recurrence and hydrocele rates, better improvement of spermatogenesis and higher spontaneous pregnancy rates.[11,12] Using this technique, it is possible to additionally ligate the gubernacular, trans-scrotal, and collateral veins, a practice believed to reduce the incidence of varicocele recurrence.[5,6] However, there appears to be confusion over whether MSV should involve testicular delivery or not, and this, therefore, remains a controversial issue. It is not yet clear whether MSV with testicular delivery is a superior technique to that without testicular delivery. Thus far, only one study has directly compared these two methods, and concluded that testicular delivery does not appear to offer any beneficial effect.[7] However, this earlier study is a retrospective study without a RCT design, and is therefore limited in terms of evidence-based fact. The present study was carried out to represent the first RCT, to specifically compare therapeutic outcome of the two different types of microscopic varicocelectomy. In the present study, we found no statistically significant difference in terms of varicocele reoccurrence when compared between patients receiving MSV with or without testicular delivery. This was in line with the data reported earlier by Ramasamy and Schlegel, who also observed equivalent post-operative outcomes with and without testicular delivery.[7] Interestingly, an earlier study, involving venography, reported that recurrence can be caused by the parallel, gubernacular, and trans-scrotal veins.[13] However, several studies involving MSV have reported a very low recurrence rate (0-2%) in patients where the veins thought to underlie recurrence were not ligated.[14,15] Indirectly, such studies demonstrated that testicular delivery might not be of use in helping to reduce the recurrence rate of varicocele following microsurgical varicocelectomy.

Although there was no difference in the recurrence rate of varicocele between the treatment groups in the present study, the complication rate in group 1 (with testicular delivery) was significantly higher than that for group 2 (without testicular delivery). Scrotal edema and testicular engorgement were observed in two patients from group 1. While these complications are highly likely to disappear gradually over a 2 months period following the operation, these complications would worry the patients and cause discomfort. Ramasamy and Schlegel[7] have previously stated that inflammatory changes in the scrotum are associated with the increased trauma and surgical time involved with testicular delivery. The precise mechanism(s) underlying the testicular engorgement observed in the present study remain unknown at this time. However, since the main difference between the two techniques used in the present study was that the gubernacular, trans-scrotal, and collateral veins were ligated during MSV with testicular delivery in one group, but not in the other group, strongly suggests that obstruction of blood drainage contributed to profuse small vein ligation, and thus represent the main pathological reason for testicular engorgement. One of our cases was particularly interesting; testicular hardness was found by palpation following engorgement but had disappeared by the time of the first follow up. Subsequent color Doppler ultrasound revealed normal blood flow in the testis but no improvement in sperm parame-

ters by the end of the follow up period. The underlying cause for this observation could not be determined as the patient refused to undergo testicular biopsy. Fibrosis of the testicular tissues secondary to engorgement is therefore our best assumption at this time. Our study, therefore indicates that excessive ligation of veins is not necessary, and supports the earlier observations of Will and colleagues[16] who claimed that some veins must be preserved so as to allow drainage of blood from the testis and thus prevent vascular engorgement.

Preservation of the testicular artery and associated lymphatic system is another vital advantage of microscopic varicocelectomy, although some urologists believe that it is impossible to ligate the internal spermatic artery without inducing testicular atrophy.[17] However, Abul-Fotouh and colleagues[12] reported a 2.5% incidence rate of atrophy using non-microsurgical methods. Penn and colleagues[17] further reported an incidence of 14% when the testicular artery was purposefully ligated during renal transplantation. Animal studies have also reported detrimental effects upon ipsilateral testicular blood flow and morphology following ligation of the spermatic artery.[18,19] Collectively, these results indicate that preservation of the testicular arteries plays an important role in preventing irreversible morbidity and improving spermatogenesis. Hydrocele formation, however, is caused by ligation of the lymphatic system, a hypothesis that was proven by the fact that protein concentration of the hydrocele fluid was consistent with that of the lymphatic fluid.[20] In the present study, we successfully preserved the lymphatic system, and at least one testicular artery, in all of our patients irrespective of treatment grouping, and did not observe testicular atrophy or post-operative hydrocele.

In summary, varicocelectomy leads to an improvement in key sperm parameters (sperm count, total and progressive motility), and reduces sperm DNA damage and seminal oxidative stress, while improving Leydig cell function and serum T levels.[21-23] While the MSV technique is advocated as the most effective treatment for varicocele in infertile men,[6,24] there has been some confusion over whether MSV should be carried out with or without testicular delivery. The present study represented the first RCT to address this controversial issue and concluded that MSV with testicular delivery confers no additional benefit to the patient than if the procedure was carried out without testicular delivery. We further found that sperm count and motility were significantly increased at post-operative follow up in both treatment groups compared to pre-operative values, although there was no significant difference between the two groups. There was no difference between the two groups in terms of spontaneous pregnancy rate, but complications were more likely in the group undergoing testicular delivery. Future research should expand these initial data by examining a larger cohort of patients over a longer follow-up period. In our current RCT all operations were performed by the same surgeon and all ultrasound tests were performed by the same sonographer using the same instrument. The purpose behind this strategy was to enhance consistency and increase the rigor of our experimental design and thus, analysis. However, it is conceivable that there may have been some potential bias, especially given our small sample size and short follow-up period. Together, these factors represent the main limitations of our study, and should be considered when interpreting the clinical implications of our data.

CONCLUSIONS

In conclusion, MSV with testicular delivery did not provide additional benefit to reducing the risk of reoccurrence, or to the improvement of semen quality, compared with MSV without testicular delivery. Indeed, MSV carried out with testicular delivery was appears to carry greater risk of complication.

CONFLICT OF INTEREST

None declared.

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