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*Original Article*

# Clinical effect of microscopic subinguinal varicocelectomy or bypass surgery on nutcracker phenomenon-associated varicocele

Wei Huang*, Yan Zhang*, Jun-Jie Cao, Min Cao, Xiao-Dong Jin

*Department of Urology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China. *Equal contributors.*

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**Abstract:** Objective: The goal of this study was to assess the effectiveness and safety of microscopic subinguinal varicocelectomy or bypass surgery on nutcracker phenomenon-associated varicocele. Methods: A total of 96 patients with varicocele were retrospectively analyzed in our institution between August 2015 and August 2017. In group 1, 35 patients were included with nutcracker phenomenon-associated varicocele underwent microscopic subinguinal varicocelectomy. In group 2, 30 patients were included with nutcracker phenomenon-associated varicocele underwent bypass surgery. In group 3, 31 patients were included with varicocele underwent microscopic subinguinal varicocelectomy. Results: There was no significant difference among the three groups in term of left testicular volume, left internal spermatic vein diameter, and semen parameters. After 6 months postoperative, the mean semen parameters were significantly improved substantially in all groups. However, no significant difference was observed in left testicular volume, left internal spermatic vein diameter, and reflux time after surgery among group 1, group 2, and group 3. The improvement of semen parameters showed no significant difference in patients with nutcracker phenomenon-associated varicocele that underwent microscopic subinguinal varicocelectomy compared with those that underwent bypass surgery. None of the patients reported serious adverse events. Conclusion: Outcomes of microscopic subinguinal varicocelectomy and bypass surgery are similar in term of surgical effect and safety for the management of nutcracker phenomenon-associated varicocele.

**Keywords:** Varicocele, varicocelectomy, microsurgery, nutcracker phenomenon

## Introduction

Varicocele has been considered as a common cause of male infertility because of its potential adverse effect on spermatogenesis, and the damage is progressive [1, 2]. Timely and effective treatment may reverse damage of varicocele to the spermatogenesis [3].

The nutcracker phenomenon, characterized as compression of the left renal vein (LRV) between the aorta and the superior mesenteric artery (SMA), was first described by El-Sadr and then named by de Schepper in 1972 [4, 5]. Symptoms like hematuria, chronic fatigue, orthostatic proteinuria, and flank pain could appear after LRV hypertension caused by LRV compression [6-8]. In general, treatment of nutcracker phenomenon is mainly based on the severity of its clinical symptoms [9]. Surgical therapy is recommended for patients with severe clinical symptoms, and invalid or aggravation after conservation treatment for 2 years [10]. For asymptomatic or mild to moderate symptomatic patients, conservative treatment is preferred [11].

One of the common clinical manifestations of nutcracker phenomenon is varicocele and it is impractical to consider conservative treatment for patients with nutcracker phenomenon of asymptomatic or mild to moderate symptomatic associated-varicocele. Therefore, treatment for nutcracker phenomenon associated-varicocele is still a challenge. On the one hand, surgery related to nutcracker phenomenon is associated with high operative risk, high cost, and severe complications. On the other hand,

the nutcracker phenomenon of mild to moderate symptomatic may disappear spontaneously along with the physical development [12]. According to the literature, Li et al. reported that bypass surgery (microscopic spermatic-inferior epigastric vein anastomosis) was a safe and efficient treatment for nutcracker phenomenon-associated varicocele [13]. But there are a few reports about the outcomes of microscopic subinguinal varicocelectomy (MV) compared to bypass surgery for nutcracker phenomenon-associated varicocele.

The aim of our study was to access the effect of MV or bypass surgery on nutcracker phenomenon-associated varicocele.

## Materials and methods

Between August 2015 and August 2017, 96 patients with varicocele from our institution were included in the study. In group 1, 35 patients were included with nutcracker phenomenon-associated varicocele underwent MV. In group 2, 30 patients were included with nutcracker phenomenon-associated varicocele underwent bypass surgery. In group 3, 31 patients were included with varicocele underwent MV. Ethical approval was obtained from the Human Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine. Patients provided written informed consent.

The diagnosis of varicocele depends on physical examination and scrotal ultrasound [14]. The nutcracker phenomenon was diagnosed by doppler ultrasonography of the LRV, which was made by an experienced radiologist. Doppler ultrasonography was made with the patient in a supine position. Peak velocity in the LRV were measured in the transverse plane at two points, one at the proximal portion of the LRV near the hilum, and the other at the LRV portion between the aorta and SMA. Then, the peak velocity ratio of aortomesenteric-to-proximal LRV was calculated and patients with a peak velocity ratio greater than 5 were defined as nutcracker phenomenon [6, 15].

### *Inclusion criteria*

All patients were clinical grade III varicocele on the left side. Patients with varicocele had impaired semen quality or male infertility or scrotum discomfort. Patients with nutcracker phenomenon-associated varicocele had no gross hematuria, no proteinuria, no impairment of renal function, no severe flank pain, and no aggravation after conservation treatment for 2 years. All patients included had no trauma, no infection, no tumors, or no history of urogenital abnormality.

### *MV*

After general anesthesia, patients with supine position, received a 3 cm oblique incision about 1 cm below the left external inguinal ring. The overlaying fascia was opened and exposed the spermatic cord, which was grasped with a Babcock clamp and delivered through the wound. The cord was surrounded with a large Penrose drain. Subsequently, all identifiable external spermatic veins were divided and ligated. The operating microscope was then brought into the field. After opening the spermatic fascia, the vas deferens and its vessels were identified and dissected free from the internal spermatic vascular system. All identifiable testicular arteries and lymphatics were counted and carefully preserved from internal spermatic vascular system. The internal spermatic veins were counted and separated, ligated with 5-0 silk ties, and divided.

### *Bypass surgery*

After general anesthesia, the patients were placed in the supine position. A 3 cm oblique incision was made parallel to the inguinal ligament at the level of left internal inguinal ring. In the inner side of internal inguinal ring, the largest inferior epigastric vein was identified and divided behind the transversus abdominis and transversalis fascia. Subsequently, the spermatic cord was exposed and delivered through the wound and the external spermatic veins were divided and ligated. An operating microscope was then positioned above the operating field. After opening the spermatic fascia, the vas deferens and its vessels were identified and dissected free from the internal spermatic vascular system. The testicular arteries and lymphatics were identified and preserved. The internal spermatic veins were ligated with 5-0 silk, and only the largest vein was preserved and divided for anastomosis with the inferior epigastric vein. The proximal part of the preserved internal spermatic vein, the one closer

**Table 1.** Baseline characteristics of group 1, group 2, and group 3

| | Group 1, n=35 | Group 2, n=30 | Group 3, n=31 | *P* Value |
|---|---|---|---|---|
| Age, years, mean (SD) | 22.6 (6.7) | 23.6 (1.8) | 28.4 (8.7) | 0.001 |
| BMI, mean (SD) | 19.2 (2.5) | 20.3 (1.9) | 22.9 (3.1) | <0.001 |
| Time of surgery (min), mean (SD) | 78.2 (12.6) | 155.3 (26.2) | 72.8 (17.4) | <0.001 |
| Serum hormone levels, mean (SD) | | | | |
| T (ng/dl) | 496.9 (108.1) | 507.2 (155.0) | 476.4 (111.1) | 0.621 |
| E2 (pg/ml) | 39.3 (8.2) | 40.0 (8.7) | 41.0 (9.2) | 0.731 |
| FSH (mIU/mL) | 4.7 (2.0) | 4.4 (1.9) | 4.4 (2.8) | 0.860 |
| LH (mIU/mL) | 4.6 (1.7) | 5.1 (2.0) | 4.4 (1.2) | 0.287 |
| PRL (ng/mL) | 19.3 (10.3) | 20.8 (9.8) | 16.7 (8.4) | 0.231 |
| Left testicular volume (ml), mean (SD) | 14.7 (4.7) | 14.3 (1.8) | 13.9 (3.1) | 0.619 |
| Left spermatic vein diameter (mm), mean (SD) | 3.0 (0.7) | 3.1 (0.6) | 2.8 (0.7) | 0.186 |
| Reflux time (s), mean (SD) | 4.0 (0.8) | 3.9 (0.8) | 2.9 (1.2) | <0.001 |
| Peak velocity ratio, mean (SD) | 9.7 (4.0) | 10.0 (4.9) | 3.7 (1.7) | <0.001 |
| Semen parameters, mean (SD) | | | | |
| Vitality (%) | 32.3 (13.5) | 39.2 (22.3) | 35.9 (17.7) | 0.313 |
| Progressive motility (%) | 27.5 (14.1) | 29.3 (17.8) | 34.9 (14.1) | 0.138 |
| Sperm concentration ($10^6$/ml) | 49.8 (28.9) | 59.6 (28.7) | 47.8 (22.9) | 0.192 |
| Total sperm number ($10^6$/ejaculate) | 153.5 (106.9) | 138.6 (79.0) | 160.9 (96.7) | 0.652 |

to the testis, and the distal part of the preserved inferior epigastric vein, the one farther away from the iliac vein, were ligated. The distal stump of the spermatic vein was anastomosed in an end-to-end fashion to the proximal stump of the inferior epigastric vein with 8-0 nylon.

*Follow up and outcomes*

Baseline characteristics including age at surgery, body mass index (BMI), time of surgery, serum hormone levels (Testosterone, T; Estrogen, E2; Follicle-Stimulating Hormone, FSH; Luteinizing hormone, LH; Prolactin, PRL), left testicular volume, left internal spermatic vein diameter, and the reflux time without the Valsalva maneuver, the peak velocity ratio of aortomesenteric-to-proximal LRV, and semen parameters (vitality, progressive motility, sperm concentration and total sperm number per ejaculate) were recorded. Postoperative outcomes including left testicular volume, left internal spermatic vein diameter, the reflux time without the Valsalva maneuver, and semen parameters were recorded. Postoperative complications were recorded. All patients were followed up to more than 6 months after surgery.

*Statistical analyses*

Statistical analyses were performed using SPSS version 16.0 software (IBM, Armonk, NY, USA). All variables were compared among groups with the use of the Pearson chi-square or Fisher exact test, Student t-test, the Wilcoxon rank sum test, respectively, for categorical outcomes, normally distributed continuous outcomes and nonnormally distributed continuous outcomes. A two-tailed $p$ value <0.05 was considered statistically significant.

## Results

In total, 96 patients were enrolled in the study. **Table 1** summarizes baseline characteristics of group 1, group 2, and group 3. There was a significant difference in age, BMI, and time of surgery among group 1, group 2, and group 3. The age at surgery of group 3 was significantly older than that of the other groups (p=0.001), which was consistent with the result of BMI (p<0.001). The mean time of surgery of group 1, group 2, and group 3 was 78.2 ± 12.6 min, 155.3 ± 26.2 min, and 72.8 ± 17.4 min, respectively (p<0.001). The operation time of bypass surgery was significantly longer than MV. There was a significant difference in the reflux time of the left internal spermatic vein without the Valsalva maneuver and the peak velocity ratio of aortomesenteric-to-proximal LRV among group 1, group 2, and group 3. Compared with the other two groups, group 3 had shorter reflux time and smaller peak velocity ratio. There was no significant difference among the three

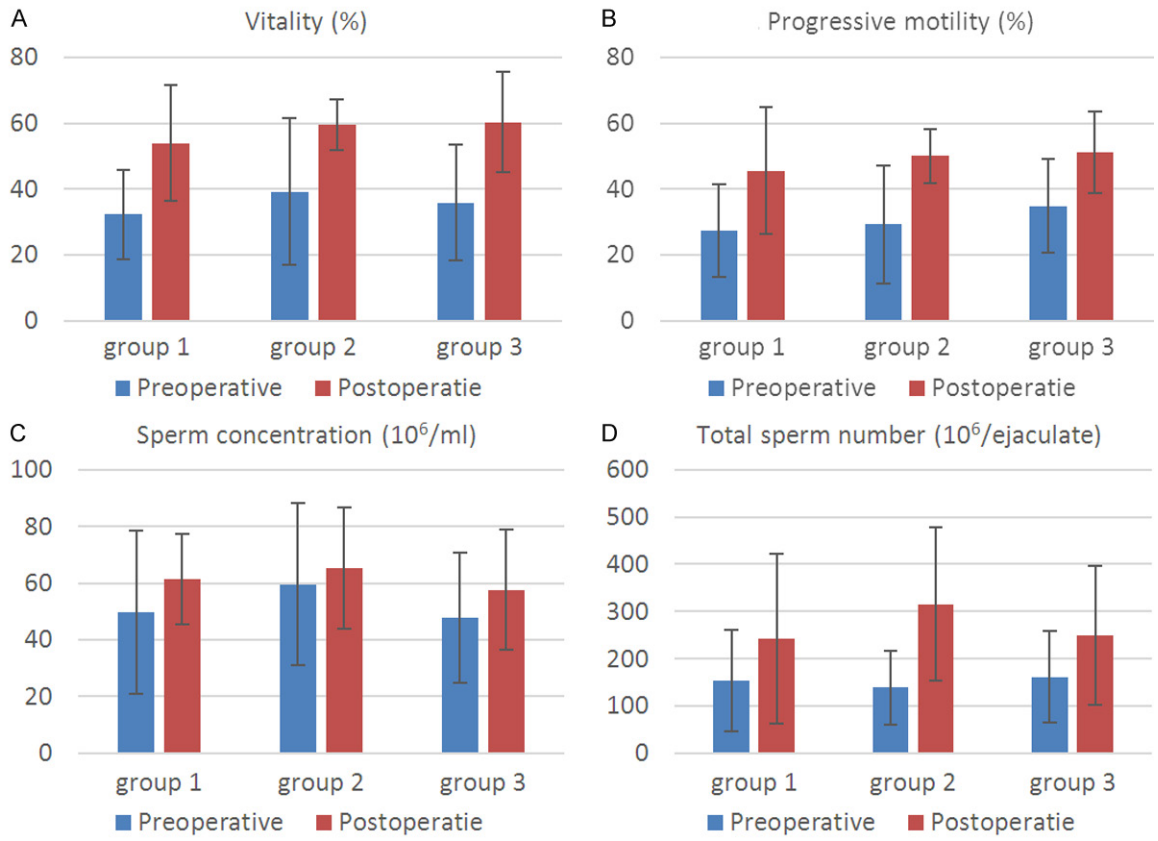


**Figure 1.** Preoperative and postoperative semen characteristics of group 1, group 2, and group 3.

groups in terms of serum hormone levels, left testicular volume, left internal spermatic vein diameter, and semen parameters. After 6 months postoperative, the left internal spermatic vein diameter and reflux time were significantly decreased substantially in all groups. Moreover, the mean sperm vitality, sperm progressive motility, sperm concentration, and total sperm number were significantly improved substantially in all groups (**Figure 1**). No significant difference was observed in left testicular volume, left internal spermatic vein diameter and reflux time among group 1, group 2, and group 3 (**Table 2**). Improvement of sperm vitality, sperm progressive motility, sperm concentration, and total sperm number showed no significant difference in the patients with nutcracker phenomenon-associated varicocele that underwent MV compared with those that underwent bypass surgery (**Table 2**). As well, there was no significant difference in semen parameters postoperative among the three groups. None of the patients reported serious adverse events that were linked to the treatment (**Table 3**). The number of patients reported scrotal edema in group 1, group 2, and group 3 was 2, 1, and 1, respectively (p=0.848).

## Discussion

The prevalence of varicocele in adult men was 11.7% and 25.4% of which had abnormal semen analysis [16]. Now, varicocele has become one of the most common reasons for surgical correction of male infertility [17]. It has been proven that MV is the best choice for patients with varicocele who need surgical intervention [18, 19]. The treatment of patients with mild to moderate or asymptomatic nutcracker phenomenon always tends to be conservative. There is no consistent conclusion about the treatment of asymptomatic or mild to moderate symptomatic nutcracker phenomenon-associated varicocele. Li et al. analyzed 5 infertile men with nutcracker phenomenon-associated varicocele who underwent bypass surgery [13]. They found that the peak velocity ratio significantly decreased, whereas the mean sperm count and sperm motility significantly increased at 6 months postoperative.

**Table 2.** Postoperative outcomes of group 1, group 2, and group 3

| Variable | Group 1, n=35 | Group 2, n=30 | Group 3, n=31 | *P* value |
|---|---|---|---|---|
| Left testicular volume (ml), mean (SD) | 16.0 (4.3) | 15.2 (2.3) | 14.6 (3.2) | 0.237 |
| Left spermatic vein diameter (mm), mean (SD) | 1.9 (0.2) | 1.9 (0.5) | 1.8 (0.3) | 0.241 |
| Reflux time (s), mean (SD) | 0.0 (0.0) | 0.0 (0.0) | 0.0 (0.0) | - |
| Semen parameters, mean (SD) | | | | |
| Vitality (%) | 54.0 (17.6) | 59.6 (7.7) | 60.3 (15.2) | 0.152 |
| Progressive motility (%) | 45.6 (19.2) | 50.0 (8.1) | 51.1 (12.4) | 0.252 |
| Sperm concentration ($10^6$/ml) | 61.4 (15.9) | 65.3 (21.3) | 57.7 (21.2) | 0.312 |
| Total sperm number ($10^6$/ejaculate) | 242.3 (179.8) | 314.9 (162.3) | 249.5 (146.8) | 0.163 |

**Table 3.** Postoperative complications of group 1, group 2, and group 3

| Complication, n | Group 1 | Group 2 | Group 3 | *P* value |
|---|---|---|---|---|
| Hydrocele | 0 | 0 | 0 | - |
| Scrotal edema | 2 | 1 | 1 | 0.848 |
| Wound infection | 0 | 0 | 0 | - |
| Orchitis and epididymitis | 0 | 0 | 0 | - |
| Testicular atrophy | 0 | 0 | 0 | - |
| Recurrence | 0 | 0 | 0 | - |

However, few studies have been performed to compare the effect of MV and bypass surgery in treating patients with nutcracker phenomenon-associated varicocele.

In this study, 96 patients were enrolled. In group 1, 35 patients were included with nutcracker phenomenon-associated varicocele underwent MV. In group 2, 30 patients were included with nutcracker phenomenon-associated varicocele underwent bypass surgery. In group 3, 31 patients were included with varicocele underwent MV. As shown in **Table 1**, patients with nutcracker phenomenon-associated varicocele had a younger age and a lower BMI than patients with varicocele. As patients age increases and BMI increases, the nutcracker phenomenon likely to improve or even disappear. The mean operation time of bypass surgery was 155.3 min, indicating that it involves more complicated techniques than MV. Umul et al. revealed a negative significant difference between BMI and left plexus pampiniform diameter, which is consistent with our findings [20]. Although there was no significant difference in left spermatic vein diameter among group 1, group 2, and group 3, the left spermatic vein diameter of group 3 tended to be smaller and the reflux time of group 3 was shorter than the other two groups. It was concluded that increasing BMI may play a protective role in the development of varicocele and nutcracker phenomenon. However, there was no significant difference among the three groups in term of semen parameters. As we speculated, the nutcracker phenomenon is one of the etiologies of varicocele but not a aggravative factor. Mali et al. reported a good correlation between reflux of the internal spermatic vein and renocaval pressure gradient [21]. We speculated that in patients with nutcracker phenomenon, a persistent elevated renocaval pressure gradient, the reflux of the internal spermatic vein, and the formation of the collateral vein induced by the nutcracker phenomenon might be the mechanism of varicocele formation.

Previously, Gong XY et al. reported that semen parameters were significantly improved, and proteinuria disappeared three months after bypass surgery [22]. Also, Dong W et al. presented bypass surgery for the management of nutcracker phenomenon presenting as left varicocele in 12 adolescent patients [23]. Patients were followed for 24-72 months (mean 48 months). In their study, symptoms of hematuria, proteinuria, scrotum discomfort, and flank pain disappeared, and the mean peak velocity ratio significantly decreased post-surgery in all patients. Furthermore, left testicular volume also significantly increased after surgery. However, there are few studies on whether the MV can be only performed for nutcracker phenomenon-associated varicocele.

The comparison of postoperative outcomes of group 1, group 2, and group 3 was performed in our study. Although semen parameters were significantly improved substantially in all groups, no significant difference in semen param-

eters was observed among the three groups. Above all, this study indicates that the operative effect of bypass surgery and MV is similar in the treatment of nutcracker phenomenon-associated varicocele. Additionally, MV did not significantly increase the incidence of complications. Furthermore, MV may be a preferred option for nutcracker phenomenon-associated varicocele.

There are some limitations in our study. First, this study was retrospective, which might introduce recall bias. Second, the sample size is limited. Third, the duration of follow-up time was not long. Therefore, in conclusion, outcomes of MV and bypass surgery are similar in term of surgical effect and safety for the management of nutcracker phenomenon-associated varicocele.

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## Disclosure of conflict of interest

None.

**Address correspondence to:** Xiao-Dong Jin, Department of Urology, The First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Road, Hangzhou 310003, Zhejiang, China. Tel: +86-13757191398; Fax: +86-571-87236832; E-mail: xiaodong-jin@zju.edu.cn

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