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Ultrasound-assisted microsurgical left spermatic-inferior epigastric vein anastomosis for treating nutcracker syndrome-associated varicocele

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Abstract

Objectives The study summarizes the effectiveness of ultrasound-assisted microsurgical left spermatic-inferior epigastric vein anastomosis for treating nutcracker syndrome (NCS)-associated varicocele.

Methods Cases of NCS-associated varicocele were recruited between December 2012 and December 2018. Prior to the operation, all patients were tested for the internal diameter and blood flow velocity of left renal vein, testicular volume, maximum venous diameter and venous retrograde flow in the pampiniform plexus of veins during the Valsalva maneuver by Color Doppler ultrasound. Moreover, the direction of left spermatic and inferior epigastric vein was marked.

Results All patients underwent ligation of the internal spermatic veins and left spermatic-inferior epigastric vein anastomosis under microscopy. Color Doppler ultrasound, urinary and semen analysis (above age 18 years old) were reviewed during the follow-up period. 53 patients (94.6%) underwent spermatic-inferior epigastric vein anastomosis with the mean operation time of 78.4 ± 14.2 min. The hospital stay was 4–7 days. Scrotal hydrocele, wound infection and testicular atrophy did not occur after operation. However, there were 5 cases of left varicocele recurrence and 2 cases of vascular anastomotic thrombosis. 51 cases had decrease in blood peak flow rate of left renal vein and improvement in nutcracker syndrome while scrotal bulge symptoms resolved in 26 cases. 10 cases had microscopic hematuria disappearance with symptom improvement in 2 cases. 19 cases of left testicular hypotrophy experience no further deterioration after surgery, of which 16 cases had catch-up testicular growth.

Conclusion Ultrasound-assisted microsurgical left spermatic-inferior epigastric vein anastomosis assisted is safe, easy and effective for treating nutcracker syndrome-associated varicocele.

Keywords Left spermatic-inferior epigastric vein anastomosis · Microsurgical · Nutcracker syndrome · Varicocele · Color Doppler ultrasonography

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Introduction

Nutcracker syndrome (NCS), also known as left renal vein entrapment syndrome, refers to the left renal vein hypertension caused by obstruction of renal vein after the mechanical compression of the left renal vein (LRV) between the abdominal aorta (AA) and superior mesenteric artery (SMA) [1]. The disease is common in adolescence and adulthood with the onset ages between 7 and 13 years old [2]. Clinical features of patients with NCS are various. Symptoms include hematuria, varicocele, orthostatic proteinuria, flank pain, abdominal pain, dyspareunia, dysmenorrhea, fatigue and orthostatic intolerance [2–7]. Symptoms are aggravated by physical activity [3]. Varicocele affects 5.5–9.5% of men and usually occurs on the left side. Development of varicocele is related with high LRV pressure and collateral circulation [1].

The treatment of NCS is still controversial. Surgical procedures are used for treatment in patients with severe symptoms. Numerous surgical procedures have been described, including nephropexy, intravascular or extravascular stenting, transposition of the LRV or SMA, gonadocaval bypass and renal auto-transplantation [8–13]. Due to the high operative risk and severe complications, these procedures have some limits in the treatment of the NCS-associated left varicocele. Many surgeons believe that conventional varicocele ligation is not an acceptable treatment for NCS-associated varicocele, owing to the likely postoperative increase in LRV pressure, which would increase varicocele recurrence rate and aggravate other NCS symptoms [14].

In this context, microsurgical left spermatic-inferior epigastric vein anastomosis is developed to treat the NCS-associated left varicocele [15]. In this study, we further attempt to evaluate the safety and effectiveness of this procedure on the assistance of the ultrasonography.

Materials and methods

This prospective study was approved by the ethics committee of the Henan Provincial People's Hospital. All participants gave written informed consent. We treated 56 cases of NCS-associated left varicocele between December 2012 and December 2018. Clinical symptoms were as follows: left scrotal swelling, scrotum bulge, repeated microscopic hematuria and testicular hypotrophy (Table 1). Physical examination and color Doppler ultrasonography were adopted to determine the diagnosis of all patients. Color Doppler sonographic criteria for the diagnosis of nutcracker syndrome consisted of the peak velocity (PV1) of left renal vein near the hilum and PV2 greater than 110 cm/s between aorta and superior mesenteric artery. At the same time, the ratio of

Table 1 Patient characteristics ($n=56$)

Characteristics	Pre-operation	Post-operation	Value
Age, years, mean			14.7 (9–24)
BMI, kg/m^2			16.2 (13.8–19.6)
N (%)			
Varicocele grade			
Left varicocele	56		
II	12 (21.4%)		
III	44 (78.6%)		
Right varicocele	40		
I	10		
II	26		
III	4		
Clinical symptoms			
Left scrotal swelling	44 (78.6%)	44 (78.6%)	
Left scrotum bulge	26 (46.4%)	0	
Left testicular hypotrophy	19 (33.9%)	3 (5%)	
Microscopic hematuria	12 (21.4%)	2 (3.6%)	
Orthostatic proteinuria	15 (26.8%)	5 (8.9%)	
Renal vein parameters	53		*p*
PV1 (cm/s)	140.93 ± 13.37	57.56 ± 17.83	0.000
PV2 (cm/s)	12.54 ± 0.98	12.56 ± 0.94	0.88
PV1/PV2	11.32 ± 1.50	4.57 ± 1.30	0.000

BMI body mass index

PV1/PV2 > 5 was diagnosed as nutcracker syndrome [16]. Varicocele grades were defined as grade I-palpable only with Valsalva, grade II-palpable without Valsalva and grade III-visually evident without Valsalva. Testicular volumes (ml) were obtained by ultrasound using the formula: 0.71 × length (cm) × width (cm) × height (cm). Percentage of testicular asymmetry was calculated as the difference between left and right testis using the following formula: (right testis volume–left testis volume)/right testis volume × 100%. Testicular hypotrophy was defined as 20% volume or greater differential between the testicles [17]. BMI was calculated. Exclusion criteria included: patients who had secondary varicocele, left inguinal surgery history, various glomerular diseases, urinary tract infection and nephroptosis.

The diameter of spermatic and inferior epigastric vein near the left deep inguinal ring were measured by Color Doppler Ultrasound (Acuson S3000, Siemens Medical Solutions USA, Inc., CA, USA) using a linear array transducer (9L4,4–9 MHz, 37 mm broadband linear array). The trends were marked before operation (Figs. 1 and 2). With patients under general anesthesia, an oblique incision paralleling to the groin was made at the center of the marker intersection of veins on body surface (Fig. 3), with the length of 3–4 cm. The aponeurosis of obliquus externus abdominis was incised. A part of the obliquus internus abdominis and musculus trasversus abdominis were also incised. The spermatic cord was found close to deep inguinal ring and fixed outside the incision by the thyroid retractor. Under 10 times magnification with ZEISS OPMI VARIO 700 microscope (Carl Zeiss Meditec AG, Jena, Germany), the external spermatic fascia was cut off, and then the internal spermatic veins were separated, where the veins were mostly 1–2 thicker veins. The largest vein was preserved for anastomosis with the inferior epigastric vein (Fig. 4). Its distal end was ligated and proximal end (3–5 cm) was clipped by microvascular

Fig. 1 Measure the inner diameter and direction of spermatic-inferior epigastric vein

Fig. 2 Mark the direction of internal spermatic-inferior epigastric vein at body surface

Fig. 3 Incision position

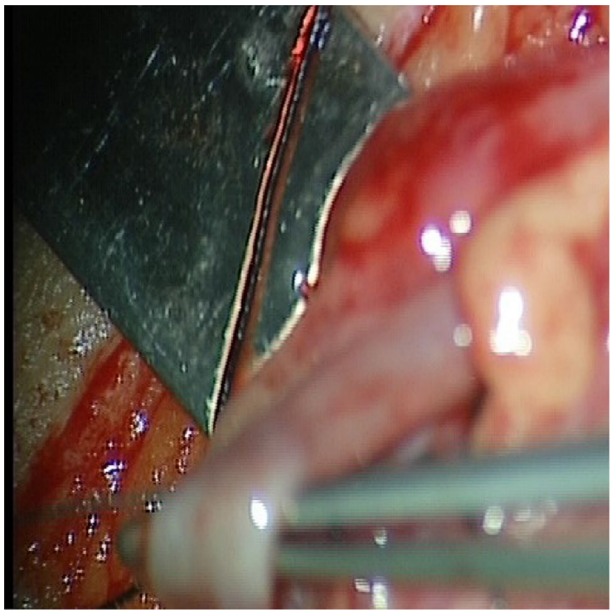

Fig. 4 Free the left spermatic vein

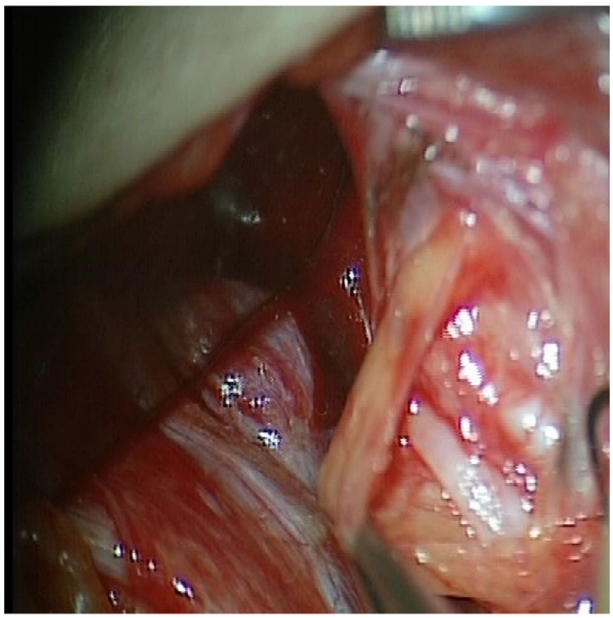

Fig. 5 Reveal the left inferior epigastric vein

clamp. The testicular artery was carefully identified and isolated, and arterial pulse was visible in most cases. The appearance of testicular arteries was blue–white color, its wall was more flexible and thicker than the spermatic vein. It easily tended to bulge out like arch shape and was accompanied by two or several small veins on both sides. After isolating testicular artery, it was marked with 4–0 silk thread traction to avoid injury by subsequent separation. Lymphatic vessels varied in thickness and number and presented canary yellow, transparent, bright in color. The wall of lymphatic vessels was thin and easily broken. After separation of lymphatic vessels, they were pushed aside with micro tweezers, further protection would be needed. The remaining spermatic veins and the veins surrounding testicular artery were separately ligated with 4–0 silk. The spermatic cord was pulled inside by the thyroid retractor and the transverse fascia was separated. The inferior epigastric artery and vein were searched in the deep surface of the deep inguinal ring. And there were usually two veins, which were located at the upper and lower sides of the artery, accompanied by the artery. A suitable inferior epigastric vein was selected according to the diameter of the preserved spermatic vein. The selected inferior epigastric vein (Fig. 5) was freed and ligated the distal end. Its proximal end (opened into the external iliac vein) was freed to about 3 cm long and clipped by microvascular clamp. The lumen of vein was flushed with heparin saline. The selected spermatic vein and the proximal end of inferior epigastric vein were anastomosed using 8–0 non-absorbable polypropylene suture (Ethicon GmbH, Neuenburg, Switzerland) to make continuous or intermittent anastomosis with 6–8 needles (Fig. 6).

If there's size discrepancy in the two blood vessels above 1:1.5 or greater, the broken end of the smaller vessels was cut into slope for anastomosis. After removing the vascular clamp, the vessel filled immediately and patency tests showed lumen unobstructed (Fig. 7). The incision was

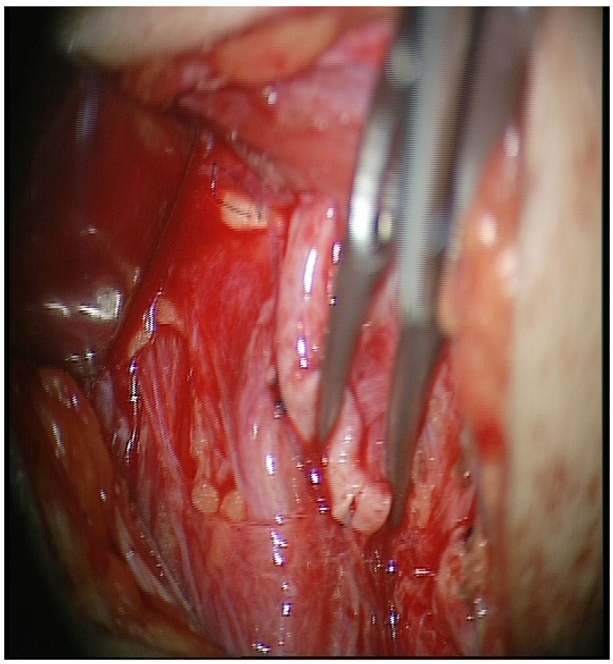

Fig. 6 Anastomose the left spermatic-inferior epigastric vein

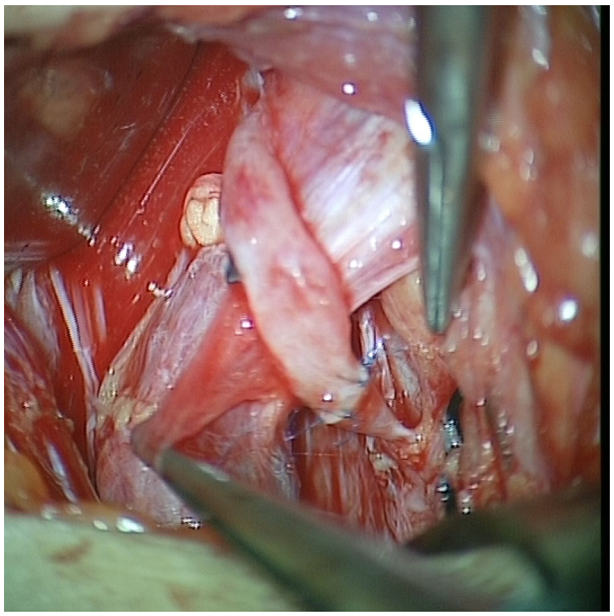

Fig. 7 The left inferior-epigastric vein after anastomosis

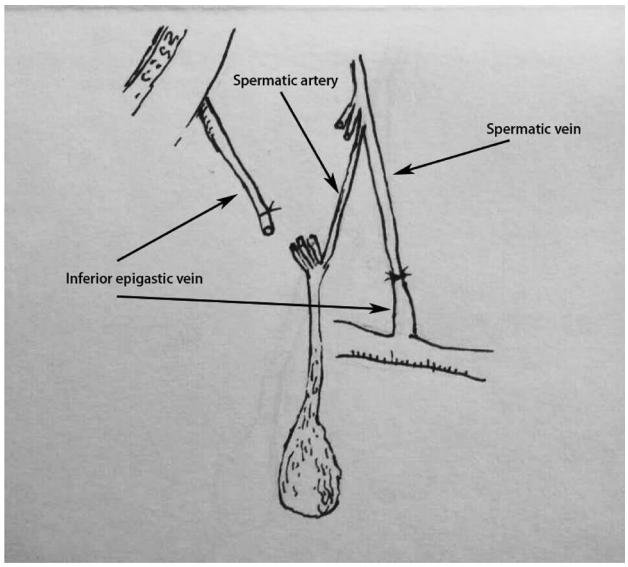

Fig. 8 The proximal end of the inferior epigastric vein is anastomosed in an end-to-end fashion with the proximal end of the spermatic vein; the distal ends of the spermatic veins are ligated, and the spermatic artery is spared

sutured with 4–0 absorbable VICRYL suture (Ethicon, Inc. Jersey, USA) layer by layer. The right varicocele was treated by high ligation of spermatic vein via right groin approach. Preventing the left side wound from compression and low molecular heparin or dextran anticoagulant should be adopted for treatment in 3 days. The successful operation standard of left spermatic-inferior epigastric vein anastomosis is that: patency test showed unobstructed and color Doppler ultrasound postoperative review in 1 months showed that the blood Peak velocity (PV) of left renal vein at the corner of superior mesenteric artery and abdominal aorta decreased than pre-operation. The nutcracker phenomenon improved, i.e., the ratio of (PV1/PV2) decreased. The varicocele disappeared without flood reflux (see Fig. 8).

Operation time and complications were recorded. The patients were followed up from 3 to 24 months. The results were analyzed by software SPSS22.0. A student *t* test was used for group comparison. All statistical tests were 2-sided and a *p* value of less than 0.05 was considered significant.

Results

There was 1 branch of left spermatic vein suitable for anastomosis in 14 cases near the left deep inguinal ring, 2 in 29 cases and 3 in 13 cases. The diameter of the thickest vein of left spermatic vein was 2.5–4.0 mm. There were 2 branches of left inferior epigastric vein in 53 cases, 1 in 1 case. And 2 cases showed reticulum with multibranches. The diameter of the thickest vein of left inferior epigastric vein was 1.5–3.5 mm. And 3 cases (including 2 cases of reticular vein) were less than 2 mm, which there's great difference with the diameter of left spermatic vein (3.5–4 mm). The 3 cases with anastomosis could not be implemented excluding high ligation of left spermatic vein. The bilateral operation time was 85–140 min, of which the left operation time was 65–110 min, average (78.4 ± 14.2) minutes, and hospital stays were 4–7 days. The patients were followed up for 6–24 months, the renal vessels and spermatic vein vessels were reviewed by color Doppler ultrasonography. The urine routine examination, semen analysis (above age 18 years old) and physical examination were reviewed. There were no complications of wound infection, scrotal hydrocele and testicular atrophy. The left spermatic-inferior epigastric vein anastomosis was successfully performed for 53 patients. A total of 5 patients (including 3 cases who were unable to perform vascular anastomosis) were reviewed at 6 months post surgery with flow velocity of renal vein unchanged, and vascular anastomotic thrombosis was confirmed by ultrasonography in 2 cases. There were left varicocele recurrence in 3 cases, right in 2 cases. But there's no Blood reflux phenomenon of the relapsing varicocele examined by Doppler ultrasound in quiet breathing, and reflux appeared only during the Valsalva maneuver. The reflux time was less than or equal to 2 s. The renal vein flow velocity is shown in Table 1. The scrotal bulge symptoms were improved in 23 cases. Ten cases of microscopic hematuria disappeared, and 2 cases of microscopic hematuria reduced. 10 cases of orthostatic proteinuria disappeared, and 5 cases of orthostatic proteinuria improved significantly. 19 cases of left

testicular hypotrophy did not continue to get smaller and softer, of which 16 cases had catch-up testicular growth.

Discussion

Due to rapid physical development during adolescence, the body turns into shape of thin and tall, left renal veins were compressed by the excessive stretching centrum. Abdominal viscera pulling superior mesenteric artery due to gravity factor and the reduction of its initial adipose tissue during the upright activity can lead to the situations of corner narrowing of superior mesenteric artery and abdominal aorta, compression of left renal veins, and then seminalvenous plexus of left renal vein drainage, venous plexus around ureter, congestion and expansion of suprarenal veins. It shows the symptom of left varicocele, hematuresis, chronic fatigue syndrome and orthostatic regulation disturbance [2–8]. NCS is the common cause of severe or secondary varicocele, and which is one of the most clinical features [14, 18]. NCSs with left varicocele of this group of patients were all with grade II or III.

Most scholars tended to choose conservative observation for patients with asymptomatic hematuria or age of younger than 18 years for the treatment of NCS at present [18]. However, recurrent gross hematuria with anemia, severe flank pain, renal functional impairment, and inefficacy or aggravation of conservative treatment of the persistent orthostatic proteinuria after 2 years of follow-up might require surgical treatment [19]. The purpose of surgery is to lift the oppression of left renal vein and to restore the normal blood reflux of left renal vein and its branches. Common surgical procedures include nephropexy, intravascular and extravascular stent implantation, transposition of the LRV or SMA, gonadocaval bypass, renal autotransplantation and nephrectomy [8–12, 20]. Recently, laparoscopic extravascular stent renal vein placement effectively treated NCS [21]. However, due to the existence of severe surgical trauma, more complications and long-term efficacy have been observed in these surgical procedures, so they could only be operated in a few patients with severe symptoms.

A high grade left testicular varicocele was associated with ipsilateral testicular hypotrophy and parallel to worsened sperm parameters [15, 22]. NCS is one of the common reasons of a high grade left varicocele [1, 14]. Several studies revealed that left testicular hypotrophy could improve after varicocele repair and so may represent a testis at risk [23, 24]. Therefore, early surgical treatment of NCS associated varicocele could be beneficial. For the treatment of NCS with varicocele, most urological physicians believe that the conventional ligation of spermatic vein may increase the pressure of left renal vein after operation, and lead to or exacerbate the symptoms of hematuresis and other symptoms related to NCS [25]. At the same time, the simply varicocele ligation might result in the high varicocele recurrence rate at the presence of NCS [14].

Recently, it has been reported that the effect of spermatic-inferior epigastric vein bypass for the treatment of NCS associated with varicocele in infertile male patients is good and the risk of operation is small, however the cases are a few [15]. This procedure does not involve large vessels. The operation is relatively simple and the risk is small. Under the magnification with a microscope, the lumen of the veins was clearly visualized, and the end-to-end anastomosis was finely performed. After operation, the blood in the left renal vein shunted into the iliac vein via the reconstructed spermatic-inferior epigastric vein, which reduced the renal vein pressure. For the decrease of the left renal vein pressure, the related symptoms of NCS like hematuresis improved or disappeared, and the recurrence rate of varicocele decreased. Although the spermatic vein is close to the inferior epigastric vein, searching for the latter is time-consuming during operation and even need longer incision. We firstly used Color Doppler ultrasonography to measure and mark the left spermatic and inferior epigastric vein before operation, in order to accurately position for incision, thereby reducing the length of incision and time of finding the vein. The diameter of inferior epigastric and spermatic vein measured by color Doppler ultrasound before operation is in accordance with finding during operation. The procedure assisted by Color Doppler ultrasonography could also reduce unnecessary vascular injury and predict the success rate of vascular anastomosis because of measuring the discrepancy in the vein diameter. Discrepancy in the vessel size is a main problem for microvascular anastomosis. The sudden change of caliber may cause turbulence to the blood flow and predisposes to platelet aggregation and thrombosis in the anastomotic veins [26]. In this situation, the oblique cut technique was employed in end-to-end anastomosis. This technique is widely used in free flap transfer and transplantation surgery owing to its advantages of high success rates and prevention of intimal separation, especially in discrepancy exceeding 1:1.5 [27]. In our study, 15 patients underwent this technique because of size discrepancy between the inferior epigastric vein and spermatic vein. During the 6-month follow-up, 2 patients unfortunately occurred in thrombosis because of great discrepancy. The diameter of inferior epigastric vein in 18 patients found by ultrasonography was smaller than the spermatic vein near the left deep inguinal ring, which was consistent with the operation. The anastomosis was not performed in 2 cases of reticular inferior epigastric vein and 1 of discrepancy exceeding 1:2.

It is generally accepted that microsurgical technique could preserve testicular artery and spermatic lymphatic vessels [28]. Hydrocele formation and recurrence are common post-operation complications of varicocelectomy. The ligation of

lymphatics leads to obstruction of lymphatic reflux, which easily occurs in post-varicocelectomy hydrocele. The cause of recurrence is inadequate ligation of the spermatic veins. We ligated the veins and preserve lymphatic under optical magnification with a microscope, and no hydrocele formation had occurred in our study. But 3 cases of left varicocele and 2 right occurred recurrence grade I. All the patients were preserved testicular artery, which prevented the testicular atrophy. Certainly, this procedure requires sophisticated mircoscopic surgical skill.

One disadvantage of this technique is that there's certain aberration rate for inferior epigastric veins, and a few amount of veins are with 3 branches and thin diameter, which are not suitable for vascular anastomosis. But these cases of vascular variation are less than 5% in our present study. In addition, because the technique we described is complicated and the benefits of performing this versus simply performing microsurgical varicocelctomy are unclear, we don't suggest the average infertility microsurgeons to perform it.

In a word, preoperative color Doppler ultrasonography measuring the diameter of spermatic-inferior epigastric vein near the left internal ring and marking their direction, contribute to accurately positioning of incision, shortening the length of incision and time of finding the vein, predicting the adaptability of vascular anastomosis. Microscopical ligation of left spermatic vein, anastomotic bypass of proximal end and inferior epigastric vein can effectively lower the back-flow pressure of left renal vein, alleviate the related symptoms to NCS, and reduce the postoperative recurrence rate of varicocele with minimal operation risk, lesser trauma and fewer complications. This operation method is safe, simple and effective for the treatment of patients with varicocele-associated nutcracker syndrome, which is worthy of promotion.

Author contributions TD and HS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: TD, HS. Analysis and interpretation of data: HX, JZ, JZ. Drafting of the manuscript: JH, Tao Du Critical revision of the manuscript for important intellectual content: Supervision: TD, HS. Other: None. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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