

A New Surgical Technique of Laparoscopic Retrograde Inguinal Lymph Node Dissection

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Received: 10 Aug 2021

Accepted: 24 Aug 2021

Published: 30 Aug 2021

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Citation:

Tian L, Xing N. A New Surgical Technique of Laparoscopic Retrograde Inguinal Lymph Node Dissection. Clin Surg. 2021; 6(4): 1-7

Authors' contributions:

Zhao Q, Han H, Lei H, Li Y, Tian L, Xing N and these authors are contributed equally to this work

Abbreviations:

LND: Lymph node dissection; PLND: Pelvic lymph node dissection; LNM: Lymph node metastasis; VEIL: Video endoscopy inguinal lymphadenectomy; OIL: Open inguinal lymphadenectomy

Keywords:

Penile cancer; Scrotal Paget's disease; Laparoscope; Retrograde, Inguinal lymph node dissection

1. Abstract

1.1. Background: To explore the clinical efficacy of a new laparoscopic inguinal retrograde Lymph Node Dissection (LND) in treatment of penile cancer and scrotal Paget's disease.

1.2. Methods: A retrospective analysis was made of 13 female patients who underwent laparoscopic retrograde inguinal LND in two medical centers from July 2018 to September 2020. Thereafter, the basic clinical, perioperative data and postoperative complications were evaluated.

1.3. Results: All the 13 patients were performed laparoscopic retrograde inguinal LND successfully without conversion to open surgery. The operation time was (220.00±33.73) min, (8.92±4.00) lymph nodes were harvested in the left groin, (8.54±5.04) lymph nodes were dissected in the right groin. Meanwhile, (5.00±1.00) lymph nodes were harvested in the left pelvic cavity, and (8.50±6.46) lymph nodes were dissected in the right. The drainage tube removal time was (13.23±3.83) days. The postoperative follow-up time ranged from 7 to 33 months, and no primary lesion, inguinal

or pelvic lymph node relapse or metastasis was reported.

1.4. Conclusion: Laparoscopic retrograde inguinal LND in the treatment of penile cancer and scrotal Paget's disease through trans-hypogastrum subcutaneous approach is safe and feasible. Moreover, inguinal LND and PLND can be performed through the same incision, which is worthy of being promoted in clinic.

2. Background

Penile cancer and scrotal Paget's disease are the two rare malignant tumors in the male urogenital system, and the most common metastatic site is inguinal lymph node, while Lymph Node Metastasis (LNM) usually predicts the poor prognosis [1]. Therefore, inguinal lymph node dissection (LND) is recommended after local treatment for the primary lesion, when there is LNM or a high risk of LNM [2]. However, the traditional open inguinal LND is associated with severe complications, such as wound infection, skin necrosis, lymphocyst and lymphedema [3]. To reduce the incidence of complications, clinicians have improved various techniques, but the postoperative complication rate remains high [4].

With the development and progresses of laparoscopy, laparoscopic inguinal LND has been well developed in recent years. Several studies suggest that, laparoscopic inguinal LND has fewer complications and markedly lower incidence than open surgery [5, 6]. Nonetheless, the traditional trans-huckle subcutaneous approach inguinal LND is also linked with certain limitations; for instance, the puncture channel should be reconstructed in the case of Pelvic Lymph Node Dissection (PLND). Therefore, this paper introduced a new technique, namely, the trans-hypogastrum subcutaneous approach laparoscopic retrograde inguinal LND. We retrospectively analyzed the clinical data from 10 penile cancer cases and 1 scrotal Paget's disease case admitted and treated at the department of urology, Beijing Chaoyang Hospital, Capital Medical University and Cancer Hospital, Chinese Academy of Medical Sciences from July 2018 to September 2020. All patients had received laparoscopic retrograde inguinal LND, and favorable clinical outcomes were achieved after surgery, as reported below.

3. Methods

3.1. Basic Clinical Data

A total of 13 cases were enrolled, including 12 with penile cancer and 1 with scrotal Paget's disease. The age of patients ranged from 38 to 83 years, with the average of (58.85±13.32) years; and the body mass index (BMI) ranged from 18.94 to 34.89 kg/m², with the average of (25.02±3.89) kg/m². Resection of the primary focus was performed in 13 cases and pathological analysis was carried out. Postoperative pathology suggested that 4 with highly differentiated squamous carcinoma cases, 1 with moderately differentiated squamous carcinoma, 4 with highly-moderately differentiated squamous carcinoma, 2 with moderately-lowly differentiated squamous carcinoma, 1 with verrucous carcinoma accompanying with condyloma acuminata, and 1 with skin invasive adenocarcinoma accompanying with Paget's disease. Preoperative physical examination or auxiliary examination revealed inguinal lymph node enlargement, among them, 4 cases had pelvic lymph node enlargement (Table 1).

Table 1: Demographic and clinicopathologic characteristics of all 13 patients

Number of cases	Age/years	BMI#/(kg·m ²)	Clinical Diagnosis	Pathology of primary lesion	Surgical methods for primary lesions
				Verrucous carcinoma accompanying with condyloma acuminata	Excision of penile tumor and penile reconstruction
1	38	26.22	Penile Cancer		
2	70	25.76	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
3	58	27.92	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
4	59	22.86	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
5	75	23.66	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
			Scrotal Paget's disease	Skin invasive adenocarcinoma accompanying with Paget's disease	Excision of penile mass + urethroplasty
6	68	28.37			
7	53	23.4	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
8	38	24.21	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
9	64	23.67	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
10	49	34.89	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
11	52	18.94	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
12	58	21.45	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty
13	83	23.95	Penile Cancer	Squamous cell carcinoma	Excision of penile mass + urethroplasty

BMI=body mass index

3.2. Surgical Method

3.2.1. Patient position and trocar location

The patients were given general anesthesia through tracheal intubation and were in supine position, their heads were 15° higher than their feet, the hips were raised, bilateral lower limbs were subjected to extorsion and abduction for 15°, and the bilateral upper limbs were abducted beside the trunk. After skin preparation in the abdomen and vulva, the catheter was indwelt. A 2-cm longitudinal incision was made below the umbilicus, the skin was then

cut open, the superficial fascia (Camper fascia) was isolated to the deep fascia (Scarpa fascia), the vessel forceps were used for blunt dissection between these two layers, and the balloon was used to dilate this space downward. Then, a 10-mm cannula was indwelt in this incision, and then the laparoscope was placed. Later, the 10-mm Trocar was placed at the midpoint between the umbilicus and the pubis, while two 5-mm Trocar were placed at the midpoints between the left and right anterior superior iliac spines and the umbilicus (bilateral inguinal LND) (Figure 1).

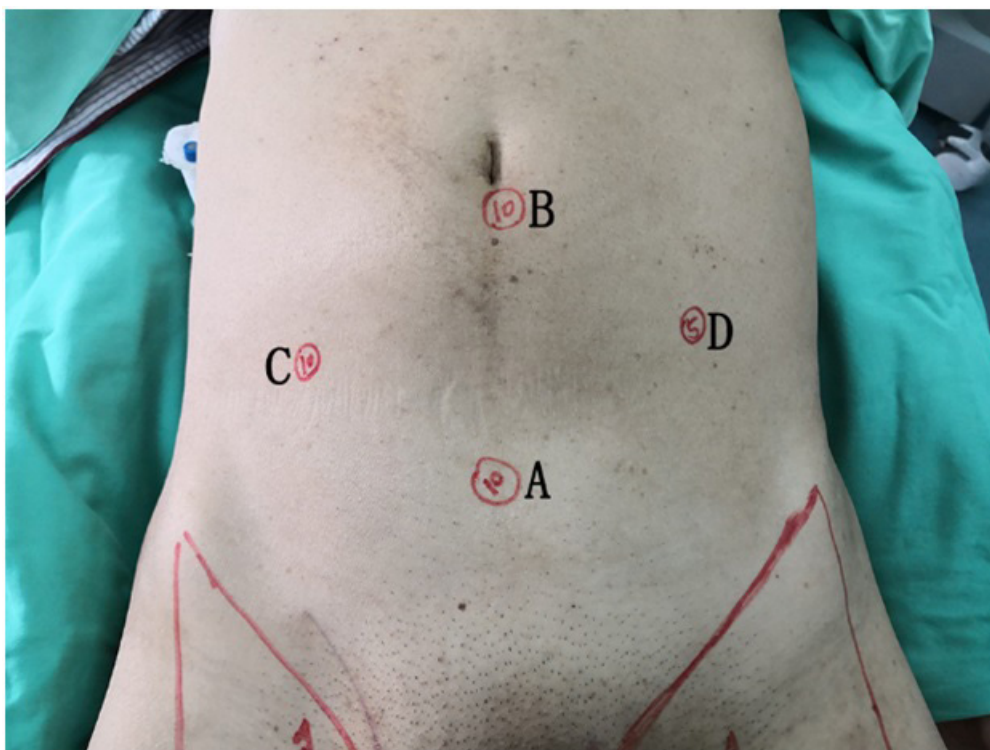


Figure 1: Figure 1. Patient positioning and ports placement. The patients were in supine position, their heads were 15° higher than their feet, the hips were raised. Trocar placement : A 2-cm longitudinal incision was made below the umbilicus (port B), a 10-mm Trocar was placed at the midpoint between the umbilicus and the pubis (port A), two 5-mm Trocars were placed at the midpoints between the left and right anterior superior iliac spines and the umbilicus (port C, port D).

3.2.2. Surgical Procedure

The space between Camper fascia and Scarpa fascia was dissociated (Figure 2A); to be specific, the right inguinal lymph nodes were dissociated first with the bipolar electrocoagulation machine in the left hand and the ultrasonic scalpel in the right hand, the upper boundary reached 2 cm above the inguinal ligament, while the lower boundary was the tip of the femoral triangle the lateral border is the medial edge of the sartorius muscle, and the medial border is the lateral edge of the long adductor muscle (Figure 2B, 2C). Then, the lymph nodes were completely dissected, and the surrounding fat tissues were also dissected to sufficiently expose the local site (Figure 2D); the great saphenous vein, femoral vein and femoral artery were identified in the femoral triangle through exposing the fascia lata behind the saphenous-femoral junction, then the surrounding lymphatic fat tissues were raised and dissociated towards the tip of femoral triangle; the great saphenous vein, superficial iliac circumflex vein, medial femoral vein, lateral femoral vein, external pudendal vein and superficial epigastric vein were protected (Figure 2E); finally, the superficial inguinal lymphatic tissues in the femoral triangle were dissected. Later, the groin was opened along the femoral artery sheath, the deep ingui-

nal lymph nodes were isolated and dissected, and femoral artery, femoral vein and femoral nerve were protected (Figure 2F). Similarly, the left inguinal lymph nodes were dissected according to the same method. The pneumoperitoneum pressure was reduced, and no bleeding was observed in the surgical field; and then the lymphatic tissue specimens were labeled and dissected in succession. Bilateral inguinal drainage tubes were indwelt through the bilateral Trocar points, the vacuum drainage bottles were connected; finally, the incision and skin were sutured.

In the case of concurrent PLND, the original puncture channel was isolated by the vessel forceps to the extraperitoneal space after bilateral inguinal LND, Trocar was placed again into the extraperitoneal space, and the surrounding pelvic lymph nodes were isolated along the external iliac blood vessel.

3.3. Postoperative Treatment and Follow-Up

After surgery, the groin was applied compression with elastic bandage, the inguinal drainage tube maintained vacuum drainage, and the drainage tube was removed when the drainage amount was < 40 ml for three consecutive days. After discharge, the patients were paid for regular clinic follow-up or received subsequent treatment.

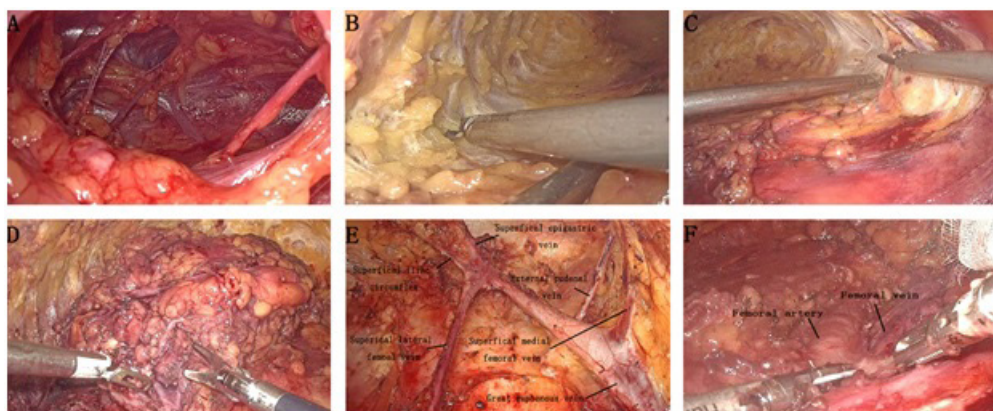


Figure 2: The procedure of laparoscopic inguinal lymph node dissection. Figure 2A, establishment of extraperitoneal space, which is between Camper fascia and Scarpa. Figure 2B, Figure 2C, dissection of the inner and outer boundary of the inguinal triangle. The lateral border is the medial edge of the sartorius muscle, and the medial border is the lateral edge of the long adductor muscle. Figure 2D, dissection of lymph nodes in superficial inguinal region. Then, the lymph nodes were completely dissected, the great saphenous vein and its tributaries are fully exposed (Figure 2E). Figure 2F, deep inguinal lymph node dissection and protection of femoral artery and vein.

4. Results

4.1. Surgery-Related Data

All the 13 patients successfully received laparoscopic retrograde inguinal LND under general anesthesia, among them, 4 received concurrent PLND. Among these patients, 3 cases had invaded subcutaneous connective tissue (T1 stage), 4 had infiltrative corpus spongiosum penis (T2 stage), and 3 had invaded the whole-layer (T3 stage); 1 invaded other adjacent tissues. Meanwhile, 7 cases were at N0 stage, 0 at N1 stage, 1 at N2 stage, and 4 at N3 stage, and 1 had distant metastasis (M1 stage). The operation time was (220.00±33.73) min, which ranged from 155 to 280 min; and the intraoperative blood loss was (15.38±13.76) ml, with the range of 5-50 ml. (8.92±4.00) lymph nodes were harvested in the left

groin, with the range of 4-17; (8.54±5.04) lymph nodes were dissected in the right groin, with the range of 4-21; meanwhile, (5.00±1.00) lymph nodes were harvested in the left pelvic cavity, with the range of 4-6; and (8.50±6.46) lymph nodes were dissected in the right pelvic cavity, with the range of 1-16 (Table 2).

4.2. Postoperative Follow-Up

All the 13 cases had successfully received surgery, among them, only one case developed mild lower limb swelling, and recovered favorably after symptomatic treatment (elevation of the affected limb, wearing stretch socks, and low-fat diet). The drainage tube removal time (13.23-3.83) days, ranging from 7 to 20 days. The postoperative follow-up time ranged from 7 to 33 months, and no primary lesion, inguinal or pelvic lymph node relapse or metastasis was reported (Table 3).

Table 2: Perioperative and pathological results of 13 patients

Number of cases	Operation Method	Operation Time/ (min)	Bleeding Volume/ (ml)	Number of postoperative lymph node dissection (positive / total)	Pathological Stage
1	Laparoscopic bilateral inguinal lymph node dissection	230	20	Left groin 0/11; Right groin 0/8	TaN0M0
2	Laparoscopic bilateral inguinal lymph node dissection	240	30	Left groin 0/4; Right groin 0/11	T1aN0M0
3	Laparoscopic bilateral inguinal lymph node dissection+ pelvic lymph node dissection	280	30	Left groin 0/13; Right groin 0/8; Left pelvic cavity 0/6; Right pelvic cavity 0/11	T1aN0M0
4	Laparoscopic bilateral inguinal lymph node dissection	250	15	Left groin 0/10; Right groin 1/21	T2N2M0
5	Laparoscopic right inguinal lymph node dissection	185	5	Right groin 0/5	T3N0M0
6	Laparoscopic bilateral inguinal lymph node dissection	230	5	Left groin 2/10; Right groin 3/11	-
7	Laparoscopic bilateral inguinal lymph node dissection	210	10	Left groin 0/6; Right groin 0/10	T2N0M0
8	Laparoscopic bilateral inguinal lymph node dissection	220	50	Left groin 6/10; Right groin 8/10	T4N3M1
9	Laparoscopic left inguinal lymph node dissection+ pelvic lymph node dissection	250	10	Left groin 5/11; Left pelvic cavity 2/4; Right pelvic cavity 0/16	T3N3M0

10	Laparoscopic bilateral inguinal lymph node dissection	200	5	Left groin 1/6; Right groin 1/4	T3N3M0
11	Laparoscopic bilateral inguinal lymph node dissection	230	5	Left groin 2/17; Right groin 3/11	T1bN0M0
12	Laparoscopic bilateral inguinal lymph node dissection+ pelvic lymph node dissection	155	5	Left groin 0/4; Right groin 0/4; Left pelvic cavity 0/6; Right pelvic cavity 0/6	T2N0M0
13	Laparoscopic bilateral inguinal lymph node dissection+ pelvic lymph node dissection	180	10	Left groin 3/5; Right groin 2/8; Left pelvic cavity 0/4; Right pelvic cavity 0/1	T2N3M0

Table 3: Postoperative follow-up data of 13 patients

Number of cases	Duration of drain/ days	Follow-up time/ months	Postoperative complications	Treatment of postoperative complications
1	14	9	None	None
2	20	10	None	None
3	18	9	None	None
4		8	Mild lower limb swelling	Raise the affected limb and take the medicine orally
5	10	6	None	None
6	16	6	None	None
7	14	3	None	None
8	15	2.5	None	None
9	13	19.5	None	None
10	10	13	None	None
11	7	11	None	None
12	9	10	None	None
13	10	10	None	None

5. Discussion

Penile cancer is a rare disease, its precise etiology remains unclear, and its risk factors mainly include poor hygiene practices, redundant prepuce- phimosis and long-term stimulation of smegma [7]. Extramammary Paget’s disease is also a rare skin cancer that is mainly observed in the elderly, and it mostly occurs in the vulva and male genital organ; in clinic, it is usually misdiagnosed as dermatitis or eczema of scrotum, thus delaying treatment [8]. The primary lesion is mainly treated by surgical resection, and the surgical resection scope depends on the tumor size, infiltration depth, and the involvements of penis and surrounding tissues; theoretically, negative incisional margin should be guaranteed [9].

Regional lymph node metastasis (LNM) or not, the metastasis degree, and radical resection are the determinants that affect its survival rate. Some research suggests that, the postoperative 5-year survival rate of patients with no regional LNM reaches as high as 95%-100%, while that reduces to 80% in the presence of a single inguinal LNM, to 50% in the presence of multiple inguinal LNM, and to 0% in the case of pelvic or peripheral LNM [10]. Inguinal LNM is the first metastatic region of penile cancer and scrotal Paget’s disease, and about 20%-40% cases have LNM [11]. It is indicated in research that, inguinal LND prior to PN3 stage LNM is of curative effect, which can cure about 80% micro-metastatic cases [12]. Therefore, inguinal LND plays an important role in its treatment, which is a vital indicator that affects patient prognosis and survival rate [12]. For patients with LNM upon preoperative physical examination or imaging examination, inguinal LND should be carried out aggressively. Additionally, for patients with

no LNM but are at high risk of micro-metastasis (① low differentiation (grade G3 and above); ② stage T2 and above; ③ tumor with vascular and lymphatic infiltration), preventive inguinal LND is suggested [13]. Numerous studies demonstrate that, compared with delayed LND, preventive bilateral LND enhances the survival rate of patients with impalpable inguinal lymph nodes [13-15]. However, research indicates that, the traditional open inguinal LND is linked with obvious complications, such as wound infection, skin necrosis, lymphocyst, and lymphedema; the incidence rate is over 50%, which has restricted its clinical application [16]. To reduce the incidence of complications, clinicians have performed various technical improvements, such as reservation of great saphenous vein, prevention of sartorius displacement, dynamic sentinel lymph node biopsy and improved LND, and reduction in the anatomic vision. Nonetheless, these improved techniques may omit micro-metastasis, which may lead to considerable false negative rate and endanger the oncologic control. Additionally, the postoperative complication rate remains high, which ranges from 26.7% to 38.9% [17-19].

To reduce the incidence of open radical LND without affecting oncologic outcomes, minimal-invasively technique of laparoscopic inguinal LND emerges. This technique was first reported by Bishoff et al. in 2003; in 2006, Tobias-Machado further developed and applied laparoscopic inguinal LND in clinic, and the 0% skin morbidity and 20% overall morbidity were reported [20]. Since the introduction of VEIL, different institutions have shared their experience in using this technique, which suggest that VEIL is a safe and effective minimally invasive method. [21] compared the

complications and oncologic outcomes between Video Endoscopy Inguinal Lymphadenectomy (VEIL) and Open Inguinal Lymphadenectomy (OIL) in treating carcinoma of penis in males. Their results found that VEIL was an oncologically safe surgery, which was linked with rather low incidence (especially for leg swelling-related complications) and shortened length of stay. Russell et al. [22] retrospectively analyzed 34 patients with penile cancer undergoing endoscopic inguinal LND, analyzed and assessed the harvested lymph nodes, related perioperative indexes and postoperative complications. Their results discovered that, from the technical perspective, VEIL was feasible, and it was comparable to the open surgery in terms of the number of harvested lymph nodes. Importantly, compared with OIL, VEIL was advantageous in the reduced complication rate and rapid recovery. In our study, among those 13 patients receiving laparoscopic retrograde inguinal LND, (8.92 ± 4.00) lymph nodes were harvested during left inguinal LND, while (8.54 ± 5.04) lymph nodes were harvested in right inguinal LND; the patients were followed up for 2.5 to 19.5 months after surgery, and no tumor relapse or metastasis of primary lesion, inguinal or pelvic lymph node was reported.

Such results further proved the previously reported results, which verified the feasibility and safety of laparoscopic inguinal LND; besides, such technique achieved favorable oncologic control, with rapid recovery, few complication and short length of stay. The main reasons for this result are that, the small incision better preserve the skin blood supply; secondly, the tiny lymph vessels are amplified under laparoscope, which can be more thoroughly clamped, thus reducing the chance of lymph leakage; additionally, the incision is far away from major vessel, avoids sartorius translocation, and markedly reduces the surgical wound.

Through literature review, we found that, the trans-huckle subcutaneous approach VEIL is reported in almost all previous articles on laparoscopic inguinal LND, while the trans-hypogastrum subcutaneous approach VEIL is rarely reported. In the case of pelvic LNM of penile cancer or scrotal Paget's disease that requires simultaneous inguinal and pelvic LND, the traditional trans-huckle subcutaneous approach VEIL requires to disinfect again and to change patient position and the position of Trocar placed, which will inevitably extend the surgical operation time. Therefore, we reported a novel trans-hypogastrum subcutaneous approach inguinal LND in this study, in which only 4 Trocar were necessary to be placed at the puncture points in the hypogastrum (2 cm at the lower umbilical margin, midpoint between umbilicus and pubis, midpoints between the left and right anterior superior iliac spines and the umbilicus) for bilateral inguinal LND. Besides, any change was not required in the case of pelvic LNM, instead, only the Trocar position inside the extraperitoneal space was necessary to carry out PLND through the same incision. Additionally, this surgical approach also possesses the following superiorities: (1) great operation space, clear surgical field, clear anatomical lay-

er, convenient operation, and reduced possibility of intraoperative injury; (2) it thoroughly eliminates the inguinal lymphatic and fat tissues, accurately distinguishes the flap level, preserves blood vessels and lymphatic vessels to provide blood supply for flaps, and reduces the postoperative complications such as flap ischemic necrosis and lymphatic fistula; (3) it also substantially shortens the operation time required for changing the body position and skin preparation; (4) there is no puncture incision in the leg, which is more beautiful and can theoretically further reduce the incidence of lower limb wound complications.

Inguinal lymph nodes include superficial inguinal lymph nodes and deep inguinal lymph nodes, which are located at the upper and medial side of anterior femur. The superficial lymph nodes are located inside the superficial subcutaneous fascia, which are divided into the upper and lower subgroups, among which, the upper subgroup is arranged along the inguinal ligament, while the lower subgroup is arranged along the great saphenous vein. Moreover, the upper subgroup lymph nodes close to the medial side were closely related to urinary surgery, which are located near the great saphenous vein and receive lymph from the external genital and the perineum. The output tubes of superficial inguinal lymph nodes infuse the deep inguinal lymph nodes. The deep inguinal lymph nodes are located at the deep surface of fascia lata of the medial femoral vein, and they are arranged along the upper segments of femoral artery and femoral vein. Apart from receiving the output tubes of superficial inguinal lymph nodes, they also accept the lower limb deep lymphatic vessel, penis, scrotum, and lower anal lymphatic vessels. The output tubes of deep inguinal lymph nodes reach the extra-iliac lymph nodes upwards [23]. Retrograde inguinal LND refers to dissection at the opposite direction of other genital neoplasm LNM, namely, the opposite direction of lymphatic return. Laparoscopic retrograde LND is advantageous in that, it further prevents tumor diffusion along the lymph due to surgical stress; moreover, retrograde operation is more aligned with the operation habit of the operator.

In addition, the trans-hypogastrum subcutaneous approach in this study is superior in that, it allows to directly and conveniently search for the femoral artery and vein and the great saphenous vein from the avascular area behind the adipose lymphatic tissue. When dissecting the superficial inguinal lymph nodes, the skin and great saphenous vein should be protected as far as possible; in the case of deep inguinal LND, the saphenous vein gap should be exposed in anatomical structure to expose the great saphenous vein. Any damage to the great saphenous vein during the surgery can lead to obstructed blood circulation, which may result in postoperative lower limb lymphedema and scrotal edema. Numerous studies suggested that [24-25], preservation of the great saphenous vein and its branch will not affect the thoroughness of LND; on the other hand, it reduces the postoperative complication rates such as incision infection, seroma and lower limb edema.

To avoid or recognize the early deep lymphatic damage and reduce the postoperative lymphatic system-related complications, the homemade real-time fluorescence lymph-mapping developer (indocyanine green) was applied in the latest one surgical patient in this study, which was simple and convenient in intraoperative operation, and allowed for lymphatic vessel visualization. Thus, it is promising to become the conventional tool for inguinal LND. However, randomized controlled trials with larger sample sizes are warranted to further verify the comparative study with the trans-huckle subcutaneous approach VEIL.

6. Conclusion

To sum up, based on our research results and actual clinical practical experience, it is safe and feasible to treat penile cancer and scrotal Paget's disease through the trans-hypogastrium subcutaneous approach laparoscopic retrograde inguinal LND. Moreover, it is of great significance to patients requiring bilateral inguinal LND and PLND.

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