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ORIGINAL PAPER

"Bottoms-up" minimally-invasive approach to inguinal lymph node dissection for penile cancer management. A single-center comparative study versus open approach and review

Vlad Horia Schițcu, Vlad Cristian Munteanu, Mihnea Bogdan Borz, Ion Cojocaru, Sergiu Vasile Labo, Andrei-Ionuț Tișe

Department of Urology, Institute of Oncology "Prof. Dr. Ion Chiricuță", Romania.

Summary *Purpose: Open inguinal lymph node dissection (OILND) plays a crucial role in penile cancer management, but in order to improve patient outcomes, minimally-invasive (MILND) approaches were developed. Our "bottoms-up" MILND is a novel endoscopic technique, changing the way the sequence of dissection is performed. This study aims to compare our approach to the current standard of OILND in terms of oncologic and perioperative outcomes.*

Materials and methods: In our database, from 2016 to 2023, 12 patients underwent OILND and 16 had a "bottoms-up" MILND, which is performed with a three port configuration, starting the dissection under the fascia lata, dissecting the femoral vessels in the most distal part of the femoral fossa, followed by dissection of the proximal and superficial lymph nodes at the top of the femoral triangle.

Results: For MILND, median operation time per groin was shorter (58 vs 64 minutes, p = 0.34), patients presented shorter hospital stays (10 vs 18 days, p = 0.32) and fewer days with drains (14 vs 24 days, p = 0.01). Median lymph node yield per groin was higher for MILND (10 vs 9 nodes, p = 0.7), but OILND had a higher median of positive lymph nodes (4 vs 3 nodes, p = 0.63). MILND patients experienced a lower incidence of major complications (33% vs 58%, p = 0.007). Conclusions: We have proved that our technique of MILND is not inferior to the current standard and we believe that it can further improve patient outcomes with a safer, simplified and easily reproducible approach.

KEY WORDS: *Penile cancer; Inguinal lymphadenectomy; Minimally invasive; Video endoscopic.*

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INTRODUCTION

Penile cancer is a rare disease with an annual incidence below 1 case per 100 000 men, representing less than 1% of malignancies in men (1). Following the routes of anatomical drainage, regional lymphatic metastases first occur at level of the superficial and deep inguinal lymph nodes, usually in medial-superior zone, followed by the pelvic lymph nodes (2, 3). While inguinal spread can be either unilateral or bilateral and crossover to the contralateral groin is possible, distant lymphatic spread above the pelvic lymph nodes to the retroperitoneal nodes is classified as metastatic disease (4). Conversely, metastatic spread from the inguinal lymph nodes to the contralateral pelvic nodes was not reported, nor crossover from the pelvic nodes to the opposite side of the pelvis (5).

Inguinal lymph node dissection (ILND) is indicated for proper cancer staging and has a curative role when the cancer is limited to the penis and regional nodes. The EAU guidelines endorse performing open ILND for clinically node positive patients or after nodal metastasis is confirmed after image-guided biopsy. For cN0 disease with high metastatic risk, surgical staging is recommended, preferably by dynamic sentinel node biopsy rather than ILND (4).

Unfortunately, recovery after ILND is hindered by postoperative complications occurring in up to 77% of cases, including: wound infections, skin or flap necrosis, seroma, lymphoedema, lymphocele, etc. (6). In order to overcome the morbidity of the open ILND, in 2002, Ian M. Thompson developed a minimally invasive endoscopic subcutaneous approach for ILND and the first endoscopic subcutaneous modified ILND was performed in 2003 (7). The endoscopic approach was further developed with the incorporation of 3D and robotic-assisted systems. Compared to open ILND, *minimally-invasive inguinal lymph node dissection* (MILND) improves the lymph-node yield, facilitates a shorter hospital stay with fewer skin complications, lymphoedema and other major complications (8).

The most widespread technique utilized for MILND (7). involves two stages of dissection, first above the fascia lata for the superficial nodes and the second under the fascia lata for the deep inguinal lymph nodes around the femoral vessels. We believe that the MILND procedure can be simplified by first approaching the deep and distal part of the femoral triangle, following the femoral vascular bundle and its branches cranially and superficially for a complete inguinal lymphadenectomy.

The purpose of our study is to assess the results of the ILND procedures performed in our centre, both by open and minimally invasive approach, to determine whether our novel technique of MILND is non-inferior to the current standard of treatment, the OILND.

Materials and methods

We retrospectively reviewed our database of patients who underwent ILND in our center, starting from 2016 to 2023. All patients included in our study were diagnosed with penile cancer with indication for ILND based on the guidelines at that time (cN1/cN2 disease or cN0 with high-risk primary tumor for which dynamic sentinel node biopsy was not available). Patients with bulky or ulcerated inguinal lymph nodes were excluded from the study. During the analyzed period, all ILND procedures were performed by a single surgeon (V. S.), who operated initially only by open approach and then switched to performing only the minimally invasive approach whenever indicated. In case metastatic spreading to the pelvic lymph nodes was suspected on pre-operative imaging (computer tomography or positron emission tomography scan), laparoscopic extended pelvic lymph node dissection was performed in the same session.

For the minimally invasive approach, the patient was placed in dorsal decubitus position with the upper limbs alongside the body, and the lower limbs in a "*frog-legged*" position (Figure 1). A three-port configuration was implemented with one 10 mm port for the camera, and two 5 mm ports for the instruments. The optical port is placed first at 2 cm caudally from the apex of Scarpa's triangle using an open technique and the other two 5 mm ports are placed on the lateral border of the triangle (Figure 2). In order to ensure a wide space for work and a safe introduction of the working trocars, the subcutaneous space is further developed with the Gaur balloon. Dissection was carried out with a bipolar clamp and 5 mm polymer clips that were used to secure lymph vessels.

Figure 1.
Patient positioning and port placement.

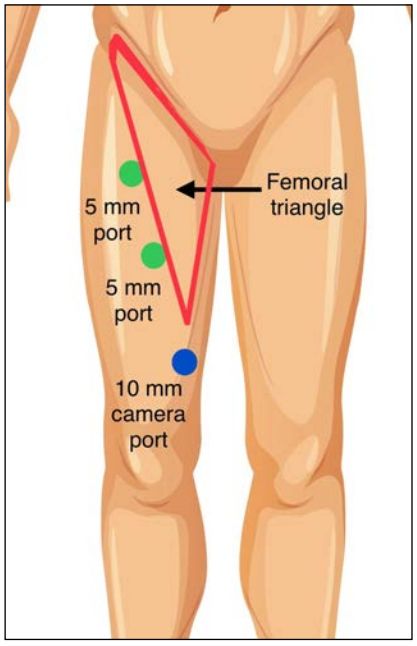


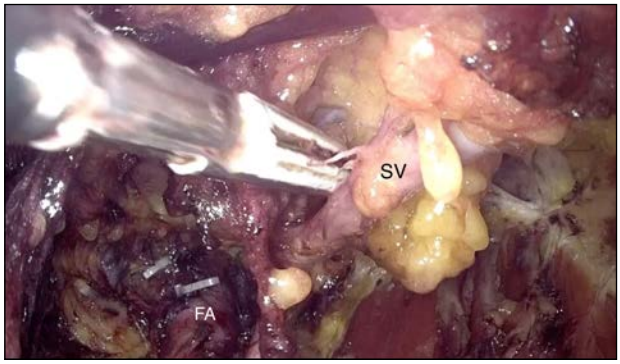
Figure 2.
Port placement relative to the femoral triangle.

The deep lymph nodes around the femoral neurovascular bundle were first dissected (Figure 3), starting at the apex of the femoral triangle, thus ensuring vascular control from the start of the procedure. Following the femoral vessels cranially, the deep lymph node dissection is completed, including the excision of the Cloquet node. The sapheno-femoral junction is isolated and, by following the saphenous vein, the superficial lymph nodes are dissected up to the inguinal ligament. Thus, the ILND is performed starting from the "*bottom*", at the deepest and most caudal region of the femoral triangle, and finishing "*up*" at the level of the inguinal ligament.

Open inguinal lymph node dissection (OILND) was carried out classically, with an incision below and parallel to the inguinal ligament. For both approaches, saphenous vein sparing was performed whenever possible in order to improve post-operative recovery (Figure 4). Negative pressure wound drainages were installed at the end of the surgery and were replaced with passive drains after 3 days. After draining less than 30 mL in 24 hours, passive tubes were removed.

Figure 3.
Minimally invasive lymph node dissection proximal to the femoral vessels. FA: femoral artery; FV: femoral vein; ILN: inguinal lymph nodes.

Figure 4.
Saphenous vein sparing during minimally invasive lymph node dissection. SV: saphenous vein; FA: femoral artery.



Statistics

Statistical analysis was performed using the SPSS software package. Descriptive analysis was carried out using frequencies, means, medians, interquartile ranges and standard deviations. For group comparisons of continuous variables, Student's t-test or the Mann-Whitney U test was performed depending on the results of the Kolmogorov-Smirnov test. The chi-squared test was used to examine categorical variables.

Ethical approval

This retrospective study was conducted using anonymized data retrieved the Institute of Oncology "*Prof. Dr. Ion Chiricuță*" patient registry. Ethical approval for this study was obtained from the institute's Ethics Committee, with waiver of informed consent granted due to the retrospective nature of the study and the use of de-identified data in accordance with local regulations and institutional guidelines.

Results

Our database of ILND is comprised of 28 cases of patients diagnosed with penile cancer requiring inguinal lymph node staging. From 2016 to 2023, 12 patients underwent OILND and 16 had a "*bottoms-up*" MILND.

In total, OILND and MILND were performed on 24 and 32 groins, respectively.

The median age of the patients included in our study was 63 years (range 59-66). For the OILND group, the median age was 61 years (range 54-67) and for the MILND 63 years (range 57-66), with no statistically significant difference (p = 0.69). All cases were diagnosed with penile squamous cell carcinoma and the MILND and OILND groups were comparable in pathological T stage (p = 0.52). Saphenous vein preservation was attempted whenever feasible and was achieved for 12 groins (50%) in the OILND group and 18 (56.25%) in the MILND group, with no significant difference (p = 0.3). Median operation time for one groin was 58 minutes (IQR 48-68 minutes) in the MILND group, shorter that 64 minutes (IQR 55-73 minutes) for OILND, but statistically insignificant (p = 0.34). Patients who underwent MILND had a shorter median hospital stay (10 *vs* 18 days, p = 0.32) and a significantly shorter median number of days until drainage tubes were removed (14 *vs* 24 days, p = 0.01).

Median lymph node yield per groin was slightly higher in the MILND group (10 *vs* 9 nodes, p = 0.7), but OILND yielded a marginally higher median of positive lymph nodes per groin (4 *vs* 3 nodes, p = 0.63) for each groin. Regarding the pathology result, there were no significant differences between pN staging regardless of surgical approach (p = 0.55).

Patients treated with MILND experienced a significantly lower incidence of major complications ranked Clavien-Dindo > II (31.25% *vs* 58.3%, p < 0.007). The complications encountered in the OILND group were three cases of lymphocele that required percutaneous drainage, one case of wound infection and three cases of wound dehiscence. In the MILND group, one patient experienced delayed wound healing due to wound dehiscence and three other cases required percutaneous drainage for lymphocele.

If saphenous vein preservation was accomplished, the median time duration until drainage tubes were removed was significantly shorter compared to cases where saphenous vein sparing was not possible (13 *vs* 23 days, p = 0.03) and the median duration of hospital stay was reduced (11.5 *vs* 18 days, p = 0.06), although insignificantly.

The Table 1 summarizes patient demographics, tumor characteristics, operative parameters, initial patient outcomes and pathological data.

Discussion

ILND represents a critical aspect of cancer treatment and staging for patients with penile cancer. Despite its importance in oncological care, ILND is considered a highly morbid procedure. A systematic review and meta-analysis (9).

Table 1.
Patient demographics, tumor characteristics, operative parameters, initial patient outcomes and pathological data.

	OILND	MILND	P
Median age, years (IQR)	61 (54-67)	63 (57-66)	0.69
Pathological T stage (%)			0.52
pT1	5 (41.7%)	6 (37.5%)	
pT2	1 (8.3%)	4 (25%)	
pT3	5 (41.7%)	5 (31.25%)	
pTx	1 (8.3%)	1 (6.25%)	
Saphenous vein preservation, no of groins (%)	10 (41.6%)	15 (46.8%)	0.3
Median operation time/groin, minutes (IQR)	64 (55-73)	58 (48-68)	0.34
Median hospital stay, days (IQR)	18 (8-20)	10 (7-17)	0.11
Days to drain removal (IQR)	24 (19-30)	14 (8-20)	0.01
Median no. of lymph nodes removed (IQR)	9 (6-14)	10 (8-12)	0.7
Median no. of positive lymph nodes (IQR)	4 (1.5-6.5)	3 (2-5)	0.63
pN staging (%)			0.55
pN0	2 (16.6%)	5 (31.25%)	
pN1	-	1 (6.25%)	
pN2	2 (16.6%)	4 (25%)	
pN3	8 (66.6%)	6 (37.5%)	
Clavien-Dindo Complications > II (%)	7 (58.3%)	4 (31.25%)	0.007
Wound dehiscence (%)	3 (25%)	1 (6.25%)	
Wound infection (%)	1 (8.3 %)	-	
Lymphocele (%)	3 (25%)	3 (18.75%)	

found that perioperative adverse events were common in patients undergoing ILND, with high BMI, comorbidities, and diabetes identified as independent predictors for complications.

Historically, OILND has been the standard of care. However, due to potential complications and morbidity associated with OILND, there has been growing interest in minimally invasive techniques, such as video-endoscopic or robot-assisted ILND. These techniques are suggested to achieve comparable oncologic outcomes to OILND, with lower rates of complications (8, 10).

We present our approach for MILND which is different from the already established MILND technique described in the literature, demonstrating unique advantages. The initial space developed under the fascia lata with the Gaur balloon provides adequate space for safe port placement and tissue manipulation, reducing the need for other aid ports and instruments. By approaching first the apex of the inguinal triangle, early vascular control of the femoral bundle is achieved, thus reducing the hemorrhagic risk of this procedure. Continuing the dissection proximally, around the femoral artery, the femoral vein and the saphenofemoral junction can then be easily and safely isolated, facilitating the preservation of the saphenous vein. Conversely, the invasion of the saphenous vein is easily identified before commencing its dissection, thus making the decision to preserve or to sacrifice quick and early during the procedure.

In our high-volume center, we compared the early results following the adoption of our technique of MILND with the outcomes of the well-established OILND. Our study included 28 patients with penile cancer requiring ILND, with 12 patients undergoing OILND and 16 MILND. The results showed no significant differences between the two groups in age, pathological T stage, saphenous vein preservation rate and median operation time. However, patients who underwent minimally invasive procedures had shorter hospital stays and required fewer days with drains in place. The minimally invasive group also had a slightly higher median lymph node yield per groin, though the open group had a marginally higher median number of positive lymph nodes per groin. No significant differences were observed in pN staging between the two surgical approaches. However, patients in the minimally invasive group experienced a significantly lower incidence of major complications (Clavien-Dindo > II). In addition, successful saphenous vein sparing reduced the duration of hospital stay and decreased the period for wound drainage significantly.

Previous systematic reviews and meta-analyses have reported better perioperative outcomes and comparable short-term oncological outcomes for minimally invasive techniques. A 2019 systematic review and meta-analysis (10). compared *video endoscopic ILND* (VE-ILND) and OILND in the management of penile cancer. The results indicated that the VE-ILND group had less intraoperative blood loss, shorter hospital stay, shorter drainage time, reduced wound infection rate, reduced skin necrosis rate, and lower lymphedema rate compared to the OILND group. However, the number of dissected lymph nodes was slightly higher in the OILND group. Lymphocele rate and recurrence rate were found to be similar between the two groups.

A 2022 systematic review and meta-analysis (8) compared robot-assisted video endoscopic ILND (RAVEIL/VEIL) with OILND in penile carcinoma management. RAVEIL and VEIL techniques increased the operative time (MD = 15.28) but reduced hospital stay (MD = -1.06), and decreased the duration of drainage (MD = -2.82). It also demonstrated lower rates of wound infection (OR = 0.15), skin necrosis (OR = 0.12), lymphedema (OR = 0.41), and major complications (OR = 0.11) compared to OILND. Recurrence rates and number of deaths were comparable, but RAVEIL/VEIL had a slightly larger lymph-node yield (MD = 0.44). RAVEIL/VEIL demonstrated fewer complications and better lymph-node yield, with comparable oncological outcomes to OILND.

Thyavihally et al. (11) compared *video endoscopic inguinal lymphadenectomy* (VEIL) and *open ILND* (O-ILND) in terms of perioperative and survival outcomes. Results from 79 patients showed wound complications were higher in O-ILND (65.6%) than VEIL (27.7%) (p = 0.001). Median overall survival was 80 months for O-ILND and 88 months for VEIL (p = 0.840), with five-year survival rates of 65% and 66.8% (p = 0.636) and disease-specific survival rates of 76.6% and 73.9% (p = 0.96), respectively.

A 2023 systematic review assessed the clinical effectiveness of treatment options available for the management of inguinal and pelvic lymphadenopathy in men with penile cancer and reinforced the idea that early ILND improves survival in nodal disease in penile cancer and, furthermore, MILND may offer comparable survival outcomes to open ILND with lower wound-related morbidity (12).

As observed, minimally invasive surgery provides an economic benefit in reducing costs of hospitalization and an earlier return to activity, when compared with open surgery (13). It is very probable that this is as also the case for MILND, but we also believe that our method of VEIL can provide further financial advantage when compared to the associated costs of RAVEIL. Although additional studies would be needed to demonstrate this hypothesis, a lower financial-impact procedure that is simplified and with reproducible favorable outcomes would serve as additional reasons for adoption, especially in developing countries.

Following the latest recommendations by the EAU-ASCO guidelines, for cN0 disease that requires inguinal lymph node staging, *dynamic sentinel node biopsy* (DSNB) is preferred in order to avoid unnecessary formal ILND and its associated morbidity (4). An updated systematic review and meta-analysis by *Zou et al.* (14) assessed the accuracy of radiocolloid-based DSNB in penile cancer with clinically negative groin (cN0) disease and found a pooled sensitivity of 88% and a negative predictive value of 99%. Factors such as preoperative *ultrasonic scan* (USS), *fine-needle aspiration cytology* (FNAC), surgical exploration of the wound for suspicious lymph nodes, immunohistochemistry and extensive experience were associated with improved DSNB sensitivity.

A 2022 systematic review, *Fallara et al.* (15) assessed the diagnostic accuracy of DSNB and ILND in detecting lymph node metastasis in penile cancer patients with cN0 disease. It found that DSNB had a pooled weighted sensitivity of 0.87, but for detecting further positive lymph nodes at ILND, DSNB had a pooled weighted sensitivity of 0.50. The study concluded that a positive DSNB is poorly able to

discriminate which patients will have further metastatic involvement at the completion of ILND, suggesting that better patient stratification could help avoid unnecessary overtreatment and postoperative comorbidities. For this, *Kumar et al.* demonstrated that outcomes can be further improved with additional inguinal ultrasound, fine needle aspiration and cross-sectional imaging to select patients for either INLD or DSNB, leading into a DSNB procedure with a sensitivity of 100% at a mean follow-up of 5 years (16).
Our study demonstrates that our novel technique for MILND provides benefits such as shorter hospital stay and reduced complications compared to the well-established open approach. The findings align with those of previous systematic reviews and meta-analyses, which have also reported better perioperative outcomes and comparable short-term oncological outcomes for minimally invasive techniques. However, our study has several limitations. The sample size is relatively small and the data is provided from a single center with a single surgeon, which may hinder the extrapolation of the results. Additionally, our study focused on early post-operative results and did not assess long-term oncological outcomes. Future research should involve larger, multicenter studies with more diverse patient populations and longer follow-up periods to better understand the safety, efficacy, and long-term outcomes of minimally invasive approaches for ILND.

Conclusions

Our study compared our novel 'bottoms-up' minimally invasive inguinal lymph node dissection in penile cancer management with the current standard of treatment, the open approach. Our approach is less invasive, resulting in a shorter operating time (58 *vs* 64 mins, IQR 55-73 minutes *vs* 48-68 minutes), shorter hospital stays (10 *vs* 18 days, IQR 7-17 days *vs* 8-20 days), fewer days with drains (14 *vs* 24 days, IQR 8-20 *vs* 19-30 days), and fewer major complications (33% *vs* 58%). We retrieved more lymph nodes (10 *vs* 9) but had similar cancer-related outcomes. This suggests our approach is non-inferior to the standard of treatment, but safer and simpler for patients and surgeons alike.

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Correspondence

Vlad Horia Schițcu, MD - schitcu@yahoo.com

Vlad Cristian Munteanu, MD - vladcristian.munteanu@gmail.com

Mihnea Bogdan Borz, MD - borz.m.bogdan@gmail.com

Ion Cojocaru, MD - cojocaruion90@yahoo.com

Sergiu Vasile Labo, MD - atolica@gmail.com

Andrei-Ionuț Țișe, MD (Corresponding Author)
andreitisemd@gmail.com

Department of Urology, Institute of Oncology "Prof. Dr. Ion Chiricuță", Romania - Str. Republicii 34-36, Cluj-Napoca 400015, Romania

Conflict of interest: The authors declare no potential conflict of interest.