Low pressure video endoscopic inguinal lymphadenectomy in the treatment of penile cancer: a historical control study

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Keywords: Penile cancer, Lymph node excision, Laparoscopy

DOI: https://doi.org/10.21203/rs.3.rs-71543/v1

Abstract

Background and Objective

To decrease the risk of complications of inguinal lymphadenectomy by investigating the value of low CO_2 pressure video endoscopic inguinal lymphadenectomy in the treatment of penile cancer.

Methods

The clinical data of a total of 44 patients who underwent video endoscopic inguinal lymphadenectomy (VEIL) were collected for statistical analysis.

Results

The average operation time was (106.88 ± 17.93) min in low CO_2 pressure (LP) group and (115.79 ± 20.29) min in normal CO_2 pressure (NP) group. The average number of lymph nodes was (10.83 ± 2.14) in LP group and (11.16 ± 1.77) ml in NP group. The intraoperative $PaCO_2$ value was (45.51 ± 4.57) mmHg in LP group and (50.77 ± 6.50) ml in NP group. The PH value of blood gas analysis was (7.35 ± 0.05) in LP group and (7.31 ± 0.04) ml in NP group. The incidence of emphysema was 2/25 in LP group while it was 9/19 in NP group. 2 cases of skin metastasis and 1 lung metastasis were observed in NP group, but not in LP group.

Conclusions

Decrease of CO_2 pressure during operation will not increase the difficulty of the surgery. LP VEIL can reduce the risk of complications including hypercapnia and the subcutaneous or lung recurrence.

Introduction

Penile cancer is a rare malignant tumor of male reproductive system. But the incidence of penile cancer is unbalanced in different areas. It is much common in less developed area such as rural areas in western China. Surgery is the main treatment for penile cancer. Lymph node metastasis is the main route of metastasis of penile cancer. Whether regional lymph node metastasis exists or not and whether radical regional lymphadenectomy can be performed is the most important factor affecting the prognosis of penile cancer [1]. For patients with no definite lymph node metastasis on physical examination or imaging examination, preventive lymphadenectomy can find some patients with micro-metastasis and perform radical lymph node dissection, which can benefit some patients' survival [2]. However, the conventional inguinal lymphadenectomy has large incision, wide dissection range, large trauma and high incidence of complications [3, 4]. Therefore, it is still controversial whether routine inguinal lymphadenectomy is necessary for penile cancer patients. In recent years, with the development of science and technology, endoscopy technology has been gradually applied to inguinal regional lymphadenectomy (video endoscopic inguinal lymphadenectomy, VEIL) and has achieved some positive results [5, 6]. However,

some complications can be caused by intra-operative pressure and other factors. From May 2015, we try to make some development to this operation, especially completing the surgery with low CO_2 pressure. To evaluate the safety and the efficiency of this technical improvement, we prospectively determined the clinical date of the patients after technical improvement. We compared our findings with a historical control group which was operated in the same department before May 2015.

Patients And Methods

This study was planned in accordance with the ethical principles for medical research and has been approved by the Ethical Committee of the Chongqing University Cancer Hospital. It is a retrospective study of a prospectively collected database. The clinical data of patients underwent operation with low CO_2 pressures (5-7mmHg) during October 2015 to September 2018 were prospectively collected, which were included in the low pressure group (LP group). All patients met the following inclusion criteria: age from 18-80; pathological diagnosis of penile carcinoma for T1-T3;CT/MRI imaging diagnosis of inguinal lymph node N0-1; no pelvic lymph node metastasis or lung metastasis was found in imaging examination; no fixed enlarged lymph nodes can be reached by palpation of the inguinal region; physical condition suitable for general anesthesia; The clinical data of patients underwent operation with normal CO_2 pressure(12-15mmHg) during March 2013 to September 2015 were retrospectively collected, which were included in the normal pressure group(NP group).

Treatment

All patients underwent VEIL surgery under general anesthesia with tracheal intubation. The patients were supine with bilateral abduction flexion of the hip joint and slight flexion of the knee joints. First, make a transverse incision 2 ~ 3cm at 25cm below the inguinal ligament. The subcutaneous tissue was separated with a low-power electric knife until the Camper's fascia. The tissue between the Camper's fascia and the Scapa fascia was separated. Blunt, sharp release to the sides and upwards with fingers and electric knife. So an isosceles triangle is formed with the midpoint of the incision as the vertex and 5cm above it as the bottom. It doesn’t matter whether this space is exactly between the two layers. Then place the endoscope trocars at the three vertices of the triangle. After closing the lower incision, the operating space was filled with CO_2 and maintain the pressure at 5-7mmHg (1mmHg = 133.3Pa). In the NP group, the CO_2 pressure was maintained between 12-15mmHg, which was same as conventional laparoscopy. The observation endoscope was put in the lower trocar, and the other instruments such as the ultrasonic knife, separation forceps were put in the other two trocars. First the space between the Camper’s fascia and the Scapa fascia was continued to expand along the previously separated gap. If the previous separated gap is not at the accurate level, you can use the ultrasonic knife to find the accurate level from the bottom of the cleaning range and then start the operation. After the operating space was fully established and suitable for operating, the CO_2 pressure was reduced and maintained at 5mmHg. Free up to 3cm above the inguinal ligament, the lateral upper boundary reaches the anterior superior iliac spine, the lateral lower boundary is 20cm vertically downward, the medial upper boundary

reaches the pubic tubercle, and the lateral lower boundary 15cm vertically. The trocars' location and dissection range are shown in Figure 1. All the fatty lymph tissues below Camper's fascia and above the broad fascia were removed with an ultrasonic knife (Fig. 2). The main saphenous vein trunk was routinely retained during the dissection, and its branches were clipped by ultrasound knife or bipolar electrocoagulation (Fig. 3). If there were obvious enlarged lymph nodes near the saphenous vein hole, the large saphenous vein was not retained. The superficial inguinal lymph nodes were bagged with homemade specimens bag. Continued to open the femoral sheath along the saphenous vein hiatus and dissect the deep inguinal lymph nodes around the femoral vessels. All specimens were bagged and removed through the lower incision. A drainage tube was placed for continuous negative pressure drainage after operation, and each incision was closed.

Primary and secondary outcome measures

The primary outcome measures was the surgery-related data, including the surgery duration, the intra-operative blood loss, the number of lymph node dissected, the intra-operative blood gas analysis, the postoperative hospital stay, the postoperative drainage catheter retention time and drainage volume, and the incidence of postoperative complications. The secondary outcome measures were postoperative pathological findings, postoperative follow-up recurrence and survival.

Data collection and Statistics

Data from the LP group were collected prospectively by the surgeons. Data from the NP group were collected retrospectively from the electronic patient records. SPSS version 18.0 was used for data analysis. Continuous variables were described using mean ± standard deviation and categorical variables were described using frequency measures. Continuous variables were compared by the Student's t-test. Comparison of categorical variables was performed by Chi-square test or Fisher's test. Statistical significance was assumed if P value less than 0.05.

Result

Patient characteristics

A total of 25 patients who underwent endoscopic inguinal lymphadenectomy between October 2015 and September 2018 were operated with low CO_2 pressures (5–7 mmHg), which were included in the LP group. A total of 19 patients who underwent endoscopic inguinal lymphadenectomy between March 2014 and September 2015 were operated with normal CO_2 pressures (12–15 mmHg), which were included in the RP group. The main patient characteristics are shown in Table 1.

Table 1
Pathological features of the patients

	LP Group	NP Group	P value
Number of patients	25	19	
Age	64.08 ± 10.52	63.11 ± 9.05	0.749
BMI	23.04 ± 2.79	22.26 ± 2.80	0.370
Phimosis history (%)	16/25 (64.0)	13/19 (68.4)	0.759
Circumcision history (%)	8/25 (32)	7/19 (36.8)	0.737
Duration of disease(months)	7.42 ± 4.44	6.95 ± 3.32	0.704
Pathological T stage (%)	1 (4.0)	0 (0.0)	
Tis	12 (48.0)	10 (52.6)	
T1	10 (40.0)	8 (42.1)	
T2	2 (8.0)	1 (5.3)	
T3			
Clinical N stage (%):	15 (60.0%)	10 (52.6%)	
N0	10 (40.0%)	9 (47.4%)	
N1			
Pathological type (%)	24 (96.0%)	19 (100.0%)	0.378
Squamous cell carcinoma	1(melanoma)	0 (0.0)	
Other			

Patients' data in the two groups were similar in BMI, Phimosis history, Circumcision history and disease duration, which is comparable. All the patients were squamous cell carcinoma except 1 case with melanoma in LP group. There was no significant difference in the composition ratio of clinical stages between the two groups.

Intra-operative data and pathological results

All patients underwent VEIL surgery successfully without converting to open surgery. No serious complications or death occurred during perioperative period in both groups. No significant difference observed between two groups in terms of surgery duration, blood loss during surgery, lymph nodes resected, number of metastatic lymph nodes. However, significant difference observed between two groups in terms of blood gas analysis at the end of surgery. Compared to patients in NP group, no matter in PH value, partial pressure of carbon dioxide or base excess, patients in LP group were closer to normal($p < 0.05$) (Table 2).

Table 2
Surgery related features of the patients

	LP Group	NP Group	P value
Number of patients	25	19	
Duration of surgery (each side)	106.88 ± 17.93 min	115.79 ± 20.29 min	0.134
Blood loss (each side)	27.71 ± 11.61 ml	25.79 ± 8.21 ml	0.546
Number of lymph nodes resected (each side)	10.83 ± 2.14	11.16 ± 1.77	0.598
Number of metastatic lymph nodes resected (each side)	0.63 ± 0.92	0.53 ± 0.77	0.711
PH value of blood gas analysis (at the end of surgery)	7.35 ± 0.05	7.31 ± 0.04	0.001
PCO_2 of blood gas analysis (at the end of surgery)	45.51 ± 4.57	50.77 ± 6.50	0.003
BE of blood gas analysis (at the end of surgery)	-0.57 ± 1.66	-2.05 ± 2.03	0.012

Postoperative data and follow up

After surgery, all patients in both groups recovered smoothly without necrosis of skin flap and incision dehiscence. No significant difference observed between two groups in terms of postoperative drainage volume/time and postoperative hospital stay.5 patients in LP group and 6 patients in NP group were observed lymphocystis/lymphitis after surgery, which were cured after anti infection and symptomatic treatment. Over an average follow-up period of 32months (range, 12 to 64), 5patients in each group had tumor recurrence or progression. Among LP group, all the recurrences occurred in pelvic regions with lymph metastasis, whereas 2 patients experienced with inguinal skin recurrence, the other 2 patients relapsed with pelvic lymph metastasis and the rest 1 patient with lung metastasis (Fig. 4). 3 patients in LP group and 4 patients in NP group finally died of cancer progression during the follow-up period. The post-operative data of the patients were showed in Table 3.

Table 3
Post-operative data of the patients

	LP Group	NP Group	P value
Postoperative drainage time(days)	10.04 ± 2.14	10.21 ± 2.04	0.794
Postoperative drainage volume(ml/day)	45.42 ± 10.62	42.11 ± 9.02	0.284
Postoperative hospital stays(day)	13.04 ± 1.52	12.53 ± 1.50	0.273
Postoperative subcutaneous emphysema	2(8%)	9(47.3%)	0.003
Postoperative lymphocystis/lymphitis	5(20%)	6(31.6%)	0.598
Tumor recurrence during follow-up	5(20%)	5(26.3%)	0.895
Inguinal skin	0(0)	2(10.5%)	
Pelvic lymph node	5(20%)	2(10.5%)	
Lung metastasis	0(0)	1(5.3%)	
Median time to recurrence (months)	15	15.8	
Death during follow-up	3/25	4/19	0.691

Discussion

Whether standard regional lymphadenectomy can be performed is an important factor affecting the prognosis of patients with penile cancer. It is general believed that patients with staging/grades exceeding T1/G2 should undergo preventive inguinal lymphadenectomy. Some studies suggest that dynamic sentinel node biopsy (DSNB) should be performed first, and patients with positive results then undergo lymphadenectomy [7]. However, the operation of DSNB is complicated and it is difficult to carry out routinely in China. No matter what kind of incision is used in open inguinal lymphadenectomy, there is a higher chance of complications such as flap necrosis and incision infection [8, 9]. Since 2003, some studies have reported the use of VEIL, and this technique is considered safe and effective [10–12]. We carried out video endoscopic inguinal lymphadenectomy since 2013, and analyzed the results of the surgery. It does have the advantages of reducing the incidence of flap necrosis, reducing the infection rate of the incision, and speeding up the postoperative recovery. However, we found some shortcomings. We observed that patients may have subcutaneous emphysema, hypercapnia and other complications during and after surgery. In particular, we have observed local skin metastases in two patients underwent VEIL. Analyzing the reasons may be related to the use of conventional carbon dioxide gas pressure (12–15 mmHg) during the surgery. In previous studies of VEIL, the intraoperative CO_2 pressure is usually maintained at 12–15 mmHg [13, 14], which is usually used in laparoscopy. Since October 2015, we have improved the technology of VEIL, using low pressure (5–7 mmHg) during surgery, and the operation results are good. Because of the anatomical characteristics of the groin area, the local tissue is loose, and

the broad fascia extends upwards above the inguinal ligament and extends to the external oblique tendon and extends inward and outward to the perineal fascia and gluteal fascia, respectively. Carbon dioxide under high pressure can easily diffuse through these loose spaces, especially the abdomen and scrotum, and be absorbed to form different degrees of subcutaneous emphysema, which may cause complications such as elevated airway pressure and hypercapnia. Pahwa reported 10/10 cases of subcutaneous emphysema after VEIL [15]. Delman reported in 32 patients underwent VEIL, three patients experienced elevated end-expiratory CO_2 partial pressure, and one patient was converted to open surgery for this reason. Six patients developed cellulitis after surgery [16]. We reduced the intraoperative carbon dioxide pressure to about 5 mmHg and found that the intraoperative space and visual field did not become restricted. The difficulty and duration of operation did not increase.

In this study, all surgeries are performed by two experienced surgeons. Since the intraoperative carbon dioxide pressure reduction did not increase the difficulty of the operation, the operation duration was not prolonged. In terms of surgical results, no matter the amount intraoperative of bleeding, the number of lymph nodes cleaned or the drainage after the operation, there was no statistical difference between the two groups. We found that in the LP group, the effect of carbon dioxide accumulation during surgery on the body was significantly smaller. It can be seen from the pH value, partial pressure of carbon dioxide, be value and other indexes in the blood gas analysis at the end of operation that the influence of carbon dioxide accumulation in NP group is more significant. Nearly half of the patients in the NP group (9/19) developed varying degrees of subcutaneous emphysema after surgery, which is rare in the LP group (2/25). More importantly, we observed 2 patients with skin metastasis after VEIL in the NP group and 1 patients with lung metastasis, but not in the LP group. Skin implant metastasis has also been reported in other VEIL studies [17].The appearance of skin metastasis is scattered nodules in the scope of cleaning. We consider that there may be a relationship between high intraoperative carbon dioxide pressure and skin implant metastasis as well as hematogenous metastasis. Reducing the intraoperative carbon dioxide pressure is not only beneficial for reducing the chance of postoperative complications, but also for tumor control.

Studies have shown that seven or more lymph nodes removed each side, or 15 lymph nodes removed bilaterally can be considered a reliable threshold [18, 19]. Regardless of the LP group or the NP group, the number of lymph nodes removed during the operation averaged more than 10 each side, which could achieve the purpose of preventive lymphadenectomy. All the patients in the two groups had incisions healed after the operation without flap necrosis and incision splitting, which was the biggest advantage of VEIL. Only a small number of patients have postoperative lymphocystis or lymphangitis, which can be cured after simple treatment. These minor complications do not affect the length of postoperative hospital stay.

When setting up the operating space, it is difficult to reach the accurate layer for operation with a finger through a small incision through blunt separation, especially in areas that cannot be seen directly. If the operation layer is completely separated under direct vision, the skin incision will be larger. First, we to use

fingers to bluntly separate operating space in the area below the cleaning range though a small incision. If this space is exactly at the right layer is the best. If not, we can use the ultrasonic knife to find the accurate level from the bottom of the cleaning range and then start the operation. Such procedure can make the incision smaller and not take much time in the early stage of the surgery.

This study is not a prospective randomized controlled study and the patients in the NP group were all retrospective data, so there are inevitable biases in the choice of patients. The surgeries of the two groups were not in the same period. When completing surgeries for LP group patients, the surgeons' technical proficiency in VEIL may be better, which may cause bias in the final result. The total number of patients was relatively small, and some patients were lost to follow-up after a period after surgery. Therefore, the reliable results of long-term recurrence rate and survival rate cannot be obtained. Only the statistics of recurrence and death cases were listed.

Conclusion

Video endoscopic inguinal lymphadenectomy might be an effective, safe and minimally invasive method for penile cancer patients. The use of lower intraoperative pressure will not affect the operation difficulty nor increase the operation time. It is important that the operation under low pressure can significantly reduce the complications caused by carbon dioxide accumulation during surgery. More data is needed to verify the long-term effect of tumor control.

Declarations

Acknowledgments

No applicable.

Funding

This work was supported by grants from the Chongqing Municipal science and Technology Bureau and Health Bureau Joint Medical Research Project (No. 2018MSXM033), the Natural Science Foundation of Chongqing (No. cstc2019jcyj-msxmX0420).

Competing interests

The authors declare that they have no competing interests.

Ethics approval

This study was approved by the Ethics Committee of Chongqing cancer hospital. Every person who participated in the study had signed the consent of using his clinical data and materials for the purpose of study research.

Availability of data and materials

The details of data and materials involved in this study could be asked from the authors if necessary.

Authors' contributions

PX, HL and NL involved in the study concept and design; PX and GJY drafted this manuscript; XLT, FY and YPS performed statistical analysis; JL, YL and JYD collected data and materials. All authors read and approved the final

manuscript.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

References

1. Leone A, Diorio GJ, Pettaway C, et al. Contemporary management of patients with penile cancer and lymph node metastasis. Nature Reviews Urology. 2017;14:335.
2. Andres F, Correa E, Handorf SS, Joshi, et al. Differences in Survival Associated with Performance of Lymph Node Dissection in Patients with Invasive Penile Cancer: Results from the National Cancer Database. J Urol.2018 05;199(5):1238–44.
3. Koifman L, Hampl D, et al. Radical open inguinal lymphadenectomy for penile carcinoma: surgical technique, early complications and late outcomes. Journal of Urology, 190(6), 2086–92.
4. Spiess PE, Hernandez MS, Pettaway CA. Contemporary inguinal lymph node dissection: minimizing complications. World J Urol. 2009;27(2):205–12.
5. Nabavizadeh R, Master V. Minimally invasive approaches to the inguinal nodes in cN0 patients. Curr Opin Urol. 2019;29(2):165–72.
6. Meneses AD, Mattos PAL, Eulálio WMN, Filho, et al. Initial experience of video endoscopic inguinal Lymphadenectomy in a center located at northeast brazilian region. International Braz J Urol Official Journal of the Brazilian Society of Urology. 2019;45(2):325–31.
7. Varun S. Maarten, et al. Management of non-visualization following dynamic sentinel lymph node biopsy for squamous cell carcinoma of the penis. BJU Int.2017 04;119(4):573–78.
8. Gopman JM, Djajadiningrat RS, Baumgarten AS, et al. Predicting postoperative complications of inguinal lymph node dissection for penile cancer in an international multicentre cohort. Bju International. 2015;116(2):196–201.
9. Stuiver MM, Djajadiningrat RS, Graafland NM, et al. Early Wound Complications After Inguinal Lymphadenectomy in Penile Cancer: A Historical Cohort Study and Risk-factor Analysis. Eur Urol. 2013;64(3):486–92.

10. Bishoff JT, Basler JW, Teichman JM, et al. Endoscopic subcutaneous modified inguinal lymph node dissection (ESMIL) for squamous cell carcinoma of the penis. J Urol. 2003;169:78.
11. Tobias-Machado M, Tavares A, Molina WR Jr, et al. Video endoscopic inguinal lymphadenectomy (VEIL): Minimally invasive resection of inguinal lymph nodes. Int Braz J Urol. 2006;32:316–21.
12. Pompeo A, Tobias-Machado M, Molina WR, et al. Extending boundaries in minimally invasive procedures with simultaneous bilateral video endoscopic inguinal lymphadenectomy (veil) for penile cancer: initial Denver health medical center and ABC school of medicine experience and surgical considerations. Int Braz J Urol. 2013;39(4):587–92.
13. Chaudhari R, Khant SR, Patel D. Video endoscopic inguinal lymphadenectomy for radical management of inguinal nodes in patients with penile squamous cell carcinoma. Urology Annals. 2016;8(3):281–5.
14. Kumar V, Sethia KK. Prospective study comparing video-endoscopic radical inguinal lymph node dissection (VEILND) with open radical ILND (OILND) for penile cancer over an 8-year period. BJU Int.2017 04;119(4) :530–534.
15. Pahwa HS, Misra S, Kumar A, et al. Video Endoscopic Inguinal Lymphadenectomy (VEIL) -a prospective critical perioperative assessment of feasibility and morbidity with points of technique in penile carcinoma. World Journal of Surgical Oncology. 2013;11(1):42.
16. Delman KA, Kooby DA, Rizzo M, et al. Initial Experience with Videoscopic Inguinal Lymphadenectomy. Ann Surg Oncol. 2011;18(4):977–82.
17. Zunguang Bai Z, Wang R, Dai, et al. standardization and practice of video endoscopic inguinal lymphadenectomy. Journal of Modern Urology,2015(11):790–793. (in Chinese).
18. Spillane AJ, Cheung BL, Stretch JR, et al. Proposed quality standards for regional lymph node dissections in patients with melanoma. Ann Surg. 2009;249:473–80.
19. Soodana-Prakash N, Koru-Sengul T, Miao Fet al. Lymph node yield as a predictor of overall survival following inguinal lymphadenectomy for penile cancer. Urol Oncol.2018 10;36(10) :471.e19-471.e27.

Figures

Figure 1

Operation position and trocars' position. A: trocar position for eyepiece; BC: Trocar position for instruments; D: Region of lymph node dissection.

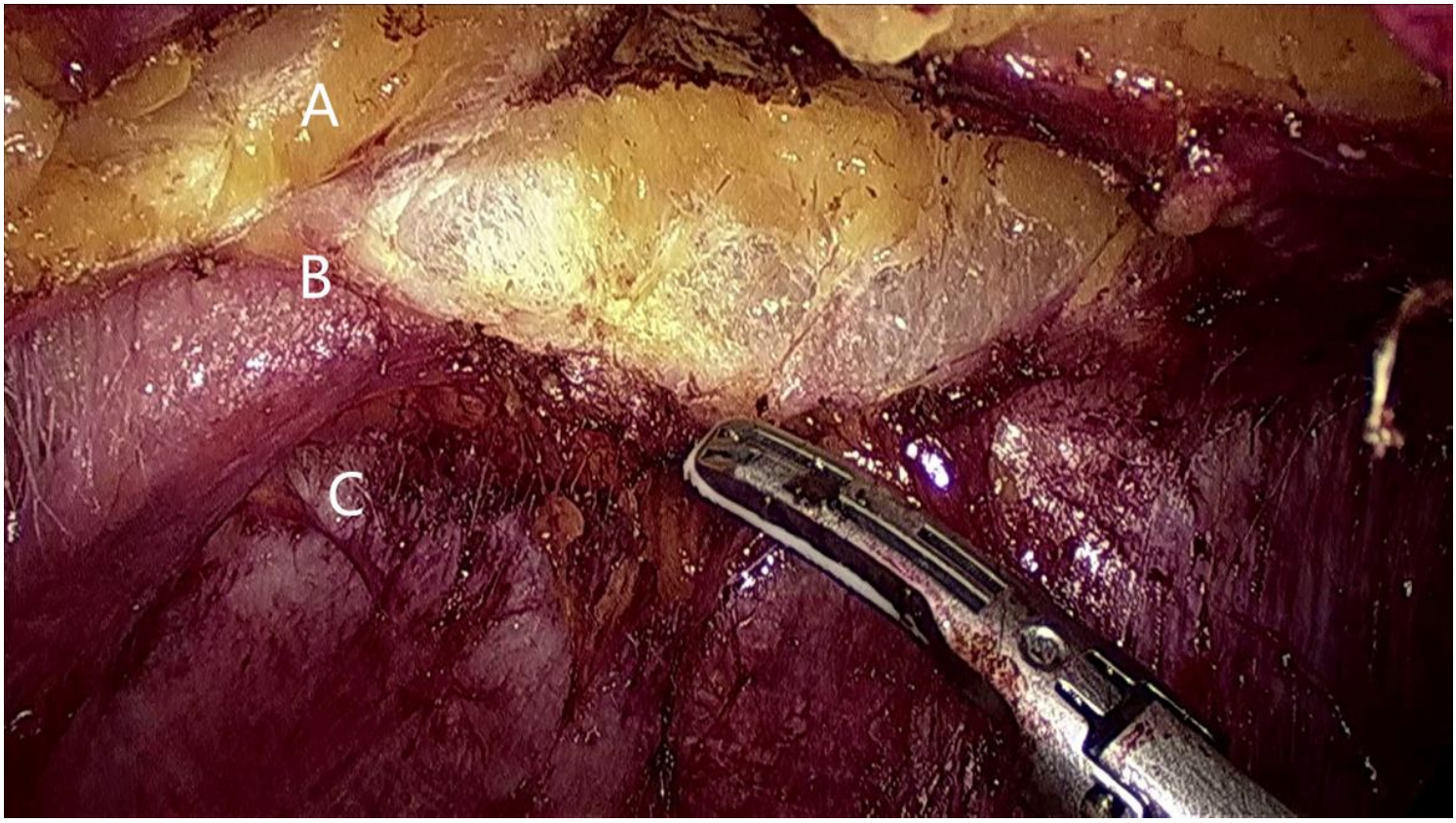

Figure 2

Initial anatomical level recognition. A: Camper’s fascia; B: Scarpa’s fascia; C: Fascia lata.

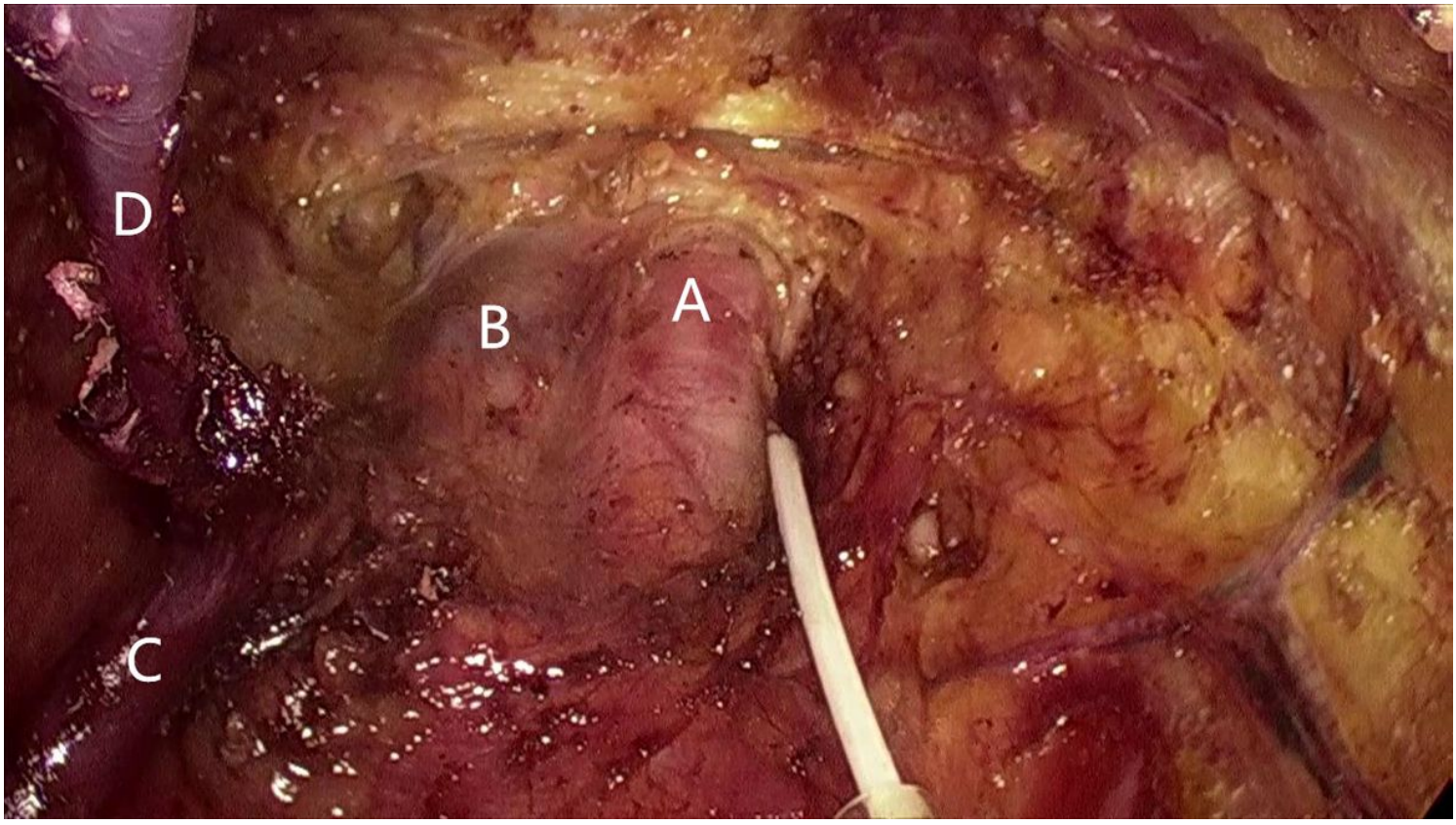

Figure 3

Intraoperative anatomical markers. A: Femoral artery; B: Femoral vein; C: Great saphenous vein; D: Branches of great saphenous vein.

Figure 4

Metastasis of penile cancer. A: Skin metastasis of penile cancer; B: Skin metastasis of trocar channel; C: Lung metastasis of penile cancer.