#### **ORIGINAL ARTICLE**



# Morbidity and risk factors for complications of inguinal lymph node dissection in penile cancer

Antoine Jeanne-Julien<sup>1</sup> · Olivier Bouchot<sup>1</sup> · Stéphane De Vergie<sup>1</sup> · Julien Branchereau<sup>1</sup> · Marie-Aimée Perrouin-Verbe<sup>1</sup> · Jérôme Rigaud<sup>1</sup>

Received: 23 June 2022 / Accepted: 23 September 2022 / Published online: 8 October 2022 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

#### Abstract

**Purpose** To assess the morbidity of inguinal lymph node dissection (ILND) in penile cancer, then to compare this morbidity with that of ILND performed in the context of skin cancer treatment.

**Methods** We retrospectively included all patients having undergone ILND between 1 January 2004 and 31 December 2019 in our centre's urology department in the context of treatment of penile cancer or skin cancer. Postoperative complications were reported in accordance with the Clavien–Dindo classification system.

**Results** Two hundred forty-two ILNDs were performed in 122 patients with penile cancer and 56 ILNDs were performed in 56 patients with skin cancer. The most common early complication was postoperative fluid collection (lymphocele or haematoma), which complicated 44% of ILNDs overall and 60% of radical lymphadenectomies. The most common late complication was leg lymphoedema, found in up to 36% of radical lymphadenectomies. Major complications (grade  $\geq$  III) were very rare (4% of radical lymphadenectomies). Radical lymphadenectomies resulted in significantly more cases of postoperative fluid collection, skin necrosis and dehiscence, as well as leg lymphoedema, than modified lymphadenectomy techniques. Two factors significantly increasing postoperative morbidity were demonstrated: ASA score = 3 (OR = 3.09) and operating time (OR = 1.01).

**Conclusion** ILNDs are morbid surgical procedures for which the indications must be well defined. However, the complications are almost exclusively minor, for a major oncological benefit.

Keywords Penile cancer · Inguinal lymphadenectomy · Inguinal lymph node dissection · Morbidity · Risk factor

# Introduction

Penile cancer is rare, representing less than 1% of all urological cancers. In more than 95% of cases, the cancer is a squamous cell carcinoma, often related to Human Papillomavirus infection [1]. The histological characteristics of this cancer make it a disease with lymphatic spread and the inguinal lymph nodes are always the first relay route [2]. Progression is local for a prolonged period, then secondarily locoregional, first in the inguinal then the pelvic lymph node regions.

Good lymph node staging is therefore essential at the time of initial diagnosis, with sentinel lymph node biopsy and/or

Antoine Jeanne-Julien antoine.jeannejulien@gmail.com the performance of inguinal lymph node dissection (ILND) [3, 4]. This is particularly important given that the lymph node status has an impact on patients' prognosis and survival as an independent factor [4, 5]. But the morbidity associated with ILND means that it is necessary to clearly define the indications and remain as minimally invasive as possible [3]. Skin complications (necrosis, infection, dehiscence) and lymphatic complications (lymphocele, lymphoedema) are reported in the literature. In this context, the European Association of Urology (EAU) proposes five management options for inguinal lymph node regions: surveillance, fine needle aspiration cytology, dynamic sentinel node biopsy, modified inguinal lymphadenectomy (MIL) or radical inguinal lymphadenectomy (RIL).

ILND also plays an important role in the management of skin cancers, with a direct benefit in terms of patient assessment and treatment. This RIL is similar but in a different context, with skin cancers less frequently being a

<sup>&</sup>lt;sup>1</sup> Clinique Urologique, Hôpital Hôtel Dieu, CHU de Nantes, 1 place Alexis Ricordeau, 44093 Nantes, France

source of infection and patients sometimes having fewer comorbidities.

The objective of this single-centre study was to conduct a retrospective assessment of morbidity related to ILND in penile cancer and to compare it with that of ILND in skin cancers. We also analysed the risk factors for postoperative complications.

# **Materials and methods**

# Population

#### Penile cancer

We conducted a retrospective analysis of the files of patients having undergone ILND in the context of penile cancer between 1 January 2004 and 31 December 2019 in our urology department. Only patients with squamous cell carcinoma were included. Patients for whom ILND was palliative were excluded.

#### Skin cancers

We conducted a retrospective analysis of the files of patients having undergone ILND in the context of skin cancer over the same period in our urology department. All the patients were included, irrespective of the histology of their primary tumour (melanoma, squamous cell carcinoma, Merkel cell carcinoma).

# **Assessment of extension**

Assessment of penile cancer extension consisted in examination of the inguinal lymph node regions during a consultation, with bilateral palpation of the groin regions and inguinal ultrasound. Needle aspiration was performed when lymph node enlargement was palpable (cN1-2). Imaging was performed by CT scan of the chest, abdomen and pelvis before 2007, then by 18-FDG PET/CT thereafter.

For skin cancers, the assessment of extension was similar, with physical examination and imaging by CT scan of the chest, abdomen and pelvis or 18-FDG PET/CT.

# **ILND indications**

The indications for ILND in penile cancer have evolved a little over the years and as successive guidelines have been issued. However, the main indications are:

• Dynamic sentinel node biopsy (DSNB) when the primary tumour was in place with signs of local infiltration and with no palpated lymph node enlargement (cN0)

- MIL when the primary tumour was in place with signs of local infiltration and with no palpated lymph node enlargement (cN0) before the widespread use of DSNB in the centre (2013)
- RIL in the event of palpable lymph node enlargement (cN+), particularly in the event of positive needle aspiration cytology or positive 18-FDG PET/CT
- If DSNB or MIL demonstrated metastatic involvement (pN+), it was supplemented by either RIL alone or chemotherapy followed by RIL.

# Surgical techniques for ILND

89% of lymphadenectomies were performed by two expert surgeons. The remainder was done by younger surgeons, always supervised by one of the two expert surgeons.

#### Dynamic sentinel node biopsy

DSNB was always performed with the primary tumor in place. Isotopic detection of the sentinel node(s) by scintigraphy following injection of a Tc99m-labelled radiotracer into the area around the tumour was performed prior to the procedure. The incision was made above the lymph node(s), which was/were then removed after perioperative detection using a gamma probe.

#### Modified inguinal lymphadenectomy

MIL included removal of the nodes in the upper inner and central quadrants. The incision was made 2–4 cm below the inguinal ligament, following the same line. The boundaries were the inguinal ligament superiorly, the femoral vein externally, the adductor longus muscle medially, the anterior sheet of the fascia inferiorly, the fascia superficialis anteriorly, and the pectineus muscle and femoral vessels posteriorly.

#### **Radical inguinal lymphadenectomy**

RIL consisted of dissection of all the lymph nodes in the groin. The incision was made 2 to 4 cm below the inguinal ligament and was a little larger than for MIL. The boundaries were the inguinal ligament superiorly, the sartorius muscle externally, the adductor longus muscle or the spermatic cord medially, the tip of the femoral triangle inferiorly, the fascia superficialis anteriorly, and the pectineus muscle and femoral vessels posteriorly. The cribiform fascia was not opened.

#### Other points

• Wherever possible, the long saphenous vein was preserved to improve venous return.

- Haemostasis and lymphostasis were achieved with sutures, clips, an electric scalpel and/or tissue fusion device.
- At the end of the procedure, transposition of the sartorius muscle following RIL, the use of biological glue and drainage were left to the discretion of the surgeon.
- Open or laparoscopic iliac lymph node dissection could be performed in the event of associated iliac lymph node enlargement.
- Patients were allowed to mobilise on D1 for MIL techniques and DSNB, and on D5 for RIL, with flexion of the thigh from D15.
- Preventive anticoagulant therapy was prescribed for 2–3 weeks, along with wear of compression hosiery for 3 months, particularly in the event of RIL.

# **Postoperative surgical complications**

Surgical complications were classified using the Clavien–Dindo classification system [6] and based on their early or late nature. An early complication was defined as a complication observed during the first month postoperatively or occurring during the initial hospitalisation, whereas a late complication occurred after the first month (and up to one year later). Complications were defined as follows:

- *Fluid collection (lymphocele or haematoma)*: subcutaneous collection of lymph or blood at the surgical site requiring or otherwise needle aspiration/reopening of the wound in the ward or during a consultation (grade I), or requiring surgical removal/drainage in the operating theatre (IIIb)
- *Skin infection*: skin inflammation associated with sepsis requiring local care (I), antibiotic therapy (II) or surgical drainage of an abscess in the operating theatre (IIIb)
- *Wound dehiscence:* reopening of the wound requiring local care (I) or surgical management (IIIb)
- *Skin necrosis*: necrosis of the skin around the wound requiring local care (I) or surgical management, with skin graft if necessary (IIIb)
- *Deep vein thrombosis*: thrombosis of a deep vein in the lower limb on Doppler ultrasound requiring curative anti-coagulant therapy (II)
- Leg lymphoedema and pelvic/scrotal lymphoedema: increase in lower limb circumference or scrotal/perineal volume (I)

# Statistics

Statistical analysis was performed using R $\circledast$  software. For descriptive statistics, quantitative variables were expressed as a mean (standard deviation) or median (range), and qualitative variables as a frequency or proportion. Student's *t* 

tests, Fisher's exact tests and Chi<sup>2</sup> tests were used for univariate analyses, and logistic regression for multivariate analyses. The *p* value used to consider statistical tests significant was p < 0.05.

The project was registered with our centre's Clinical Research department and validated by the local ethics committee.

# Results

# **Population characteristics**

Between 1 January 2004 and 31 December 2019, we included,

- 122 patients having undergone ILND in the context of penile cancer. Of these, 15 patients underwent two procedures and one patient underwent three procedures. A total of 139 procedures were, therefore, performed.
- 56 patients underwent unilateral RIL in the context of skin cancer.

The population characteristics are described in Table 1. A significant difference in BMI should be noted, this being higher in the "penile cancer" group compared to the "skin cancer" group.

As regards penile cancers, and based on the 2016 TNM classification, 19% of the primary tumours were graded pT1, 44% pT2, 33% pT3 and 2% pT4. According to the EAU risk group classification, 84% of tumours were at high risk of inguinal lymph node spread, 4% at intermediate risk and 12% at low risk.

# **ILND characteristics**

#### Penile cancer

For the management of penile cancer, 139 procedures were performed, with bilateral ILND in 74% of cases. A total of 242 ILNDs were performed: 15 DSNB, 131 MIL and 96 RIL (Table s1).

In 42% of cases, ILND was performed at the same time as penile surgery. When ILND was performed after surgery, it was performed  $127\pm147$  days afterwards on average.

It should be noted that drainage was put in place almost exclusively in the event of RIL (67 cases of drainage in total, of which 62 in RIL).

The mean number of lymph nodes removed was correlated with the dissection type. Hence, the mean was 1.5 nodes in the event of DSNB, 3 nodes in the event of MIL and 8.8 nodes in the event of RIL. Table 1Populationcharacteristics

Total (N=178)	Penile carcinoma (N=122)	Skin cancer ( $N = 56$ )	p value
63,4±12,9	63,8±11,0	62,4±16,3	0.55
19% (33)	0	59% (33)	0,0001
81% (145)	100% (122)	41% (23)	
$27,6 \pm 5,1^{\$}$	$28,5 \pm 5,0*$	$25,6 \pm 4,9*$	0.001
25% (45)*	30% (36)	16% (9)*	0,09
18% (32)*	21% (26)	11% (6)*	0,15
20% (36)*	24% (29)	13% (7)*	0,14
46% (81)*	46% (56)	45% (25)*	1
5% (8)*	6% (7)	2% (1)*	0,44
\$		\$	
23% (41)	25% (30)	20% (11)	0,68
60% (106)	57% (70)	67% (36)	0,32
16% (29)	18% (22)	13% (7)	0,54
	Total ( $N = 178$ ) $63,4 \pm 12,9$ 19% (33) 81% (145) $27,6 \pm 5,1^{\$}$ 25% (45)* 18% (32)* 20% (36)* 46% (81)* 5% (8)* \$ 23% (41) 60% (106) 16% (29)	Total $(N=178)$ Penile carcinoma $(N=122)$ $63,4\pm12,9$ $63,8\pm11,0$ $19\%$ (33) $0$ $81\%$ (145) $100\%$ (122) $27,6\pm5,1^{\$}$ $28,5\pm5,0^{\ast}$ $25\%$ (45)* $30\%$ (36) $18\%$ (32)* $21\%$ (26) $20\%$ (36)* $24\%$ (29) $46\%$ (81)* $46\%$ (56) $5\%$ (8)* $6\%$ (7) $$$ $23\%$ (41) $25\%$ (30) $60\%$ (106) $57\%$ (70) $16\%$ (29) $18\%$ (22)	Total $(N=178)$ carcinoma $(N=122)$ Skin cancer $(N=56)$ carcinoma $(N=122)$ $63,4\pm12,9$ $63,8\pm11,0$ $62,4\pm16,3$ $19\%$ $(33)$ 0 $59\%$ $(33)$ $81\%$ $(145)$ $100\%$ $(122)$ $81\%$ $(145)$ $100\%$ $(122)$ $41\%$ $(23)$ $27,6\pm5,1^{\$}$ $28,5\pm5,0^{\ast}$ $25,6\pm4,9^{\ast}$ $25\%$ $(45)^{\ast}$ $30\%$ $(36)$ $16\%$ $(9)^{\ast}$ $20\%$ $(36)^{\ast}$ $24\%$ $(29)$ $13\%$ $(7)^{\ast}$ $46\%$ $(81)^{\ast}$ $46\%$ $(56)$ $45\%$ $(25)^{\ast}$ $5\%$ $(8)^{\ast}$ $6\%$ $(7)$ $2\%$ $(1)^{\ast}$ $23\%$ $(41)$ $25\%$ $(30)$ $20\%$ $(11)$ $60\%$ $(106)$ $57\%$ $(70)$ $67\%$ $(36)$ $16\%$ $(29)$ $18\%$ $(22)$ $13\%$ $(7)$

\*1 missing data

<sup>\$</sup>2 missing data

p value: comparison between "Penile carcinoma" and "Skin cancer"

Bold italics indicates p value < 0.05

Obesity:  $BMI > 30 \text{ kg/m}^2$ 

Vascular diseases: hypertension, peripheral artery disease, carotid stenosis

Chronic kidney disease: glomerular filtration rate < 60 mL/min

Of the 122 patients, there were 71 pN0 (58%), 9 pN1 (7%), 4 pN2 (3%) and 38 pN3 (31%).

#### Skin cancers

For the management of skin cancers, 56 procedures were carried out, during which 56 ILNDs were performed, all unilateral and radical. In 2/3 of cases, the ILND were combined with iliac dissection (table s1).

#### Morbidity of all ILNDs by procedure

Table 2 indicates early and late postoperative complications by procedure for all ILNDs (139 procedures for penile cancer and 56 procedures for skin cancer).

The most common early complication, irrespective of the type of lymphadenectomy performed, was the formation of at least one postoperative fluid collection (lymphocele or haematoma). These complications were almost exclusively minor (grade  $\leq$  II). Major complications (grade  $\geq$  III) were very rare (fewer than 5%).

The most common late complication, irrespective of the type of lymphadenectomy performed, was at least unilateral leg lymphoedema. This was particularly common in the event of at least one RIL (38 to 67%). Pelvic/scrotal

lymphoedema was rare, except in the event of bilateral RIL, in which 43% of patients developed it. All the late complications were minor.

#### Morbidity of all ILNDs by procedure type

Table 3 reports early and late postoperative complications by procedure type for all ILNDs (242 ILNDs for penile cancer and 56 ILNDs for skin cancer).

Overall, 69% of RIL had early complications, compared to 31% of MIL and 27% of DSNB. However, these complications were almost exclusively minor (grade  $\leq$  II). Only 2% of MIL had a serious complication and 4% of RIL.

The most common late complication was leg lymphoedema, which was demonstrated in up to 36% of cases on the leg having undergone RIL.

Comparison of MIL and RIL revealed a significantly higher frequency of postoperative fluid collection, necrosis, skin dehiscence and lymphoedema for RIL.

# Morbidity of radical inguinal lymphadenectomy by cancer type

No significant difference in early or late complications was demonstrated between RIL in penile cancer and RIL in skin cancer (Table s2). It should be noted that 2/3 of RIL for skin

	Total $(N = 195)^{\#}$	Bilateral DSNB $(N=7)$	Unilateral MIL $(N=7)$	Bilateral MIL (N=59)	Unilateral RIL (N=84)	Bilateral RIL $(N=31)$	MIL/RIL (N=6)
Length of hospi- tal stay (days, median M or mean m)	$m = 9,0 \pm 6,1$	<i>M</i> =6	<i>M</i> =5	$m = 6,1 \pm 3,6$	$m = 10,4 \pm 6,0$	$m = 11,6 \pm 5,9$	<i>M</i> =8,5
Grade I—% (N)							
Seroma formation, lymphorrea, hematoma	53% (103)*	43% (3)	43% (3)	37% (22)	57% (47)*	77% (24)	67% (4)
Skin necrosis	5% (9)*	0	0	2% (1)	4% (3)*	13% (4)	17% (1)
Wound dehis- cence	16% (32)*	0	14% (1)	8% (5)	24% (20)*	16% (5)	17% (1)
Wound infec- tion	6% (11)*	0	14% (1)	3% (2)	5% (4)*	6% (2)	33% (2)
Grade II—% (N)							
Deep venous thrombosis	0,5% (1)*	0	0	0	0*	0	17% (1) (PE)
Wound infec- tion	8% (16)*	14% (1)	14% (1)	7% (4)	6% (5)*	16% (5)	0
Grade IIIa—% (N)	0	0	0	0	0	0	0
Grade IIIb—% (N	)						
Seroma formation, lymphorrea, hematoma	2% (4)*	0	0	2% (1)	2% (2)*	3% (1)	0
Wound dehis- cence	1% (2)*	0	0	0	2% (2)*	0	0
Wound infec- tion	1% (2)*	0	0	2% (1)	1% (1)*	0	0
Grade IV—% ( <i>N</i> )	0	0	0	0	0	0	0
Grade V—% ( <i>N</i> )	0,5% (1)*	0	0	0	1% (1)	0	0
Most severe comp	lication—% (N)						
Grade I	51% (99)	29% (2)	43% (3)	34% (20)	60% (50)	65% (20)	67% (4)
Grade II	8% (15)	14% (1)	14% (1)	5% (3)	6% (5)	13% (4)	17% (1)
Grade III	4% (7)	0	0	3% (2)	5% (4)	3% (1)	0
Grade IV	0	0	0	0	0	0	0
Grade V	0,5% (1)	0	0	0	1% (1)	0	0
Grade I—% ( <i>N</i> )							
Leg oedema	28% (50) <sup>\$</sup>	17% (1)*	0*	6% (3) <sup>@</sup>	38% (29)^	43% (13)*	67% (4)
Pelvic/scrotal oedema	11% (19) <sup>\$</sup>	0*	0*	6% (3) <sup>@</sup>	3% (2)^	43% (13)*	17% (1)
Grade II—% (N)				_			
Deep venous thrombosis	2% (3) <sup>\$</sup>	0*	0*	$0^{@}$	1% (1)^	7% (2)*	0
Grade IIIa—% (N)	0	0*	0*	0@	0^	0*	0
Grade IIIb—% (N	)						
Skin necrosis	0,6% (1) <sup>\$</sup>	0*	0*	$0^{@}$	0^	3% (1)*	0
Grade IV—%	0	0	0	0	0	0	0

Table 2 (continued)

	Total $(N = 195)^{\#}$	Bilateral DSNB (N=7)	Unilateral MIL (N=7)	Bilateral MIL (N=59)	Unilateral RIL (N=84)	Bilateral RIL (N=31)	MIL/RIL $(N=6)$
Grade V—% ( <i>N</i> )	0	0	0	0	0	0	0
Patient without complica- tion—% (N)	67% (120) <sup>\$</sup>	83% (5)*	100% (6)*	91% (49) <sup>@</sup>	61% (46)^	37% (11)*	33% (2)

DSNB dynamic sentinel node biopsy, MIL modified inguinal lymphadenectomy, RIL radical inguinal lymphadenectomy, PE pulmonary embolism

\*1 missing data

@5 missing data

^8 missing data

<sup>\$</sup>16 missing data

<sup>#</sup>"Unilateral DSNB (N=1)", without complication, was not represented in the table

cancer were combined with iliac lymphadenectomy compared to 8% in the event of penile cancer.

# Morbidity of ILND in penile cancer

Considering only ILND in penile cancer (Table s3), there were significantly more cases of postoperative fluid collection, necrosis and skin dehiscence in RIL, but also a longer mean drainage time (4.3 vs. 0.1 days). Leg lymphoedema was significantly more present in RIL (36% vs. 3%). No difference in major complications was revealed, with only two grade III complications per group.

# Risk factors for complications of ILND in penile cancer

Following univariate analysis (Table 4), 11 factors had a significant influence on ILND complications in penile cancer: ASA score = 3, neo-adjuvant chemotherapy, simultaneous performance of penectomy and ILND, MIL, RIL, ILND of the contralateral side, sartorius muscle transposition, associated iliac lymphadenectomy, operating time, drainage and number of nodes removed.

Following multivariate analysis, two factors significantly increasing postoperative morbidity were revealed: ASA score = 3 (OR = 3.09) and operating time (OR = 1.01). Age, bilateral ILND and simultaneous performance of penectomy along with ILND were associated with a reduction in complications (odds ratios of 0.95, 0.27 and 0.42, respectively).

# Discussion

In our series of 195 ILND procedures in a context of penile cancer (N=139) or skin cancer (N=56), resulting in a total of 298 ILNDs, we revealed several points:

- 69% of RIL had early complications, versus 31% of MIL.
- All these complications were almost exclusively minor.
- The most common early complication was the formation of at least one postoperative fluid collection (lymphocele or haematoma).
- The most common late complication was leg lymphoedema.
- No significant difference for early or late complications was demonstrated on the basis of cancer type (penile versus skin).
- In the penile cancer group exclusively (242 ILNDs); ASA score = 3 (OR = 3.09) and operating time (OR = 1.01) were significant factors for increased morbidity. Conversely, age (OR = 0.95), bilateral ILND (OR = 0.27) and the simultaneous performance of penectomy along with ILND (OR = 0.42) were significant factors for decreased morbidity.

Over the past 20 years, 11 publications concerning the morbidity of RIL have been reported [7-17] (Table s4). These indicate overall complication rates for lymphadenectomy of up to 68% (77% in our series), but with the very great majority of these complications being minor. It is interesting to note that, despite the potentially increased thrombogenic risk in oncological surgery, deep vein thrombosis remains very rare (<1%).

The morbidity of MIL procedures has been less described since DSNB has partially replaced these. The main series reported more limited morbidity thanks to less extensive dissection than for RIL [7, 18, 19]. Lymphatic complications remained relatively common, with lymphoceles in 3–27% of cases and lymphoedema in 3–21% of cases (27% and 3% respectively in our series). Skin complications were more rare, with infections in 1 to 14% of cases and necrosis in around 3% of cases (8% and 1% respectively in our series).

Table 3Early and latepostoperative complicationsof ILNDs by procedure type(according to Clavien-Dindoclassification)

	DSNB ( $N = 15$ )	MIL $(N = 131)$	RIL $(N = 152)$
Drainage duration (days, mean $\pm$ SD)	0	$0,1 \pm 0,6$	4,3 ± 3,4\$
Grade I—% ( <i>N</i> )			
Seroma formation, lymphorrea, hematoma	27% (4)	26% (34)	58% (88)*
Skin necrosis	0	1% (1)	6% (9)*
Wound dehiscence	0	6% (8)	18% (27)*
Wound infection	0	3% (4)	5% (8)*
Grade II—% (N)			
Deep venous thrombosis	0	1 PE	
Wound infection	7% (1)	5% (6)	7% (11)*
Grade IIIa—% (N)	0	0	
Grade IIIb—% (N)			
Seroma formation, lymphorrea, hematoma	0	1% (1)	2% (3)*
Wound dehiscence	0	0	1% (2)*
Wound infection	0	1% (1)	1% (1)*
Grade IV—% ( <i>N</i> )	0	0	0
Grade V—% ( <i>N</i> )	0	0	1% (1)
Most severe complication—% (N)			
Grade I	20% (3)	24% (32)	59% (89)
Grade II	7% (1)	5% (6)	7% (10)
Grade III	0	2% (2)	3% (5)
Grade IV	0	0	0
Grade V	0	0	1% (1)
Grade I—% ( <i>N</i> )			
Leg oedema	13% (2) <sup>@</sup>	3% (4)€	36% (51)^
Grade II—% (N)			
Deep venous thrombosis	0	0	2% (3) <sup>£</sup>
Grade IIIa—% (N)	0	0	0
Grade IIIb—% (N)			
Skin necrosis	0	0	$1\% (1)^{@}$
Grade IV—% (N)	0	0	0
Grade V—% ( <i>N</i> )	0	0	0

DSNB dynamic sentinel node biopsy, MIL modified inguinal lymphadenectomy, RIL radical inguinal lymphadenectomy, PE pulmonary embolism

<sup>\$</sup>: only on penile carcinoma data

\*1 missing data

@6 missing data

 $\pounds 8$  missing data

^9 missing data

€11 missing data

For DSNB in penile cancer, Lam and al. observed a complication rate of 7.6%, almost all minor, with lymphocele in 3.4% of cases and skin infection in 1.9% of cases [20]. Two recent studies have suggested much higher figures: 21.4% for Dimopoulos and al. [21] and 22% for Dell'Oglio and al. [22].

The main risk factors for complications described were sarcopenia [23], BMI, sartorius muscle transposition [8] and the number of nodes removed [12]. However, since

sartorius muscle transposition is often performed to cover vessels in patients considered to be at risk of complications and having undergone extensive dissection, this constitutes a major bias. Similarly, since the number of nodes removed is a bias reflecting the extent of dissection and, above all, is a prognostic factor for 5-year overall survival [24], it should not be modified.

In our series, we demonstrated two new risk factors for complications: ASA score = 3 and operating time. This

Table 4 I	Risk fac	ctors for	compl	lications	of ILND	in	penile cancer	
-----------	----------	-----------	-------	-----------	---------	----	---------------	--

	No complication	Complication	Univariate	Multivariate	
	(N=122)	(N=120)	p value	odds-ratio	p value
Age (years, mean)	64.6	62	0.0695	0.95	0.0078
ASA score = $3-\%$	10%	25%	0.0039	3.09	0.0248
Body mass index (kg/m <sup>2</sup> , mean)	27.8	28.7	0.159	1.01	0.8403
Smoking (current)—%	26%	22%	0.6064	0.70	0.4192
Diabetes—%	21%	25%	0.5636	0.83	0.6914
Chronic kidney disease—%	4%	9%	0.1326	1.59	0.5399
Neo-adjuvant chemotherapy—%	4%	13%	0.0389	0.94	0.9308
Concomitant penectomy—%	46%	28%	0.0071	0.42	0.0337
MIL—%	75%	36%	0.0001	0.44	0.2412
RIL—%	17%	60%	0.0001	1.21	0.8335
Bilateral inguinal lymphadenectomy—%	94%	79%	0.0017	0.27	0.0267
Sartorius muscle transposition—%	5%	21%	0.0013	0.61	0.4538
Concomitant pelvic lymph node dissection—%	3%	10%	0.0397	0.45	0.4011
Drainage—%	15%	42%	0.0001	0.89	0.8415
Operating time (minutes, mean)	103	147	0.0001	1.01	0.0202
No. of removed nodes (mean)	3.4	6.8	0.0001	1.11	0.068

MIL modified inguinal lymphadenectomy, RIL radical inguinal lymphadenectomy

p value < 0.05

should lead us to be even more meticulous and rigorous in highly comorbid patients since they are the population most at risk of postoperative complications, and perhaps to entrust this surgery to experienced surgeons or expert centres.

A few factors reducing morbidity have already been reported with, in particular, sparing of the long saphenous vein [25] and omentoplasty in the event of concomitant iliac lymph node dissection [25]. Epidermal vacuum wound dressings have not demonstrated any efficacy on lymphatic and cutaneous complications or on reinterventions [26]. Similarly, fibrin sealants have not been shown to be useful, particularly as concerns lymphatic complications [27].

Furthermore, endoscopic procedures—robot-assisted or otherwise—have been shown to be effective to reduce morbidity, while remaining reliable in oncological terms [16, 28, 29]. These reduce the rate of necrosis and infections, as well as of lymphocele and lymphoedema. Major complications are observed in a maximum of 9% of cases.

However, in our series, we demonstrated that in the event of penile cancer, the simultaneous performance of ILND and penectomy reduced the risk of complications. This should encourage us to perform the two procedures during the same surgery rather than separately. Once again, this requires immediate referral of these patients to expert centres for one-stage treatment. In addition, it can also be noted that if iliac lymph node dissection is indicated in addition to RIL, this can also be performed at the same time without any impact on morbidity.

The limitations of our study lie in its retrospective nature, which results in numerous biases inherent to this type of study, with a lack of precise information on the haemostasis and lymphostasis methods used during the procedure (sutures, clips, electric scalpel or tissue fusion device), and the non-exhaustive and non-objective collection of postoperative data.

# Conclusion

ILNDs are morbid procedures but with almost exclusively minor complications and an indisputable oncological benefit.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00345-022-04169-y.

Author contributions AJ-J: project development, data collection, data analysis, and manuscript writing. OB: data collection. SDV: data collection. JB: data collection. MAP-V: data collection. JR: project development, data collection, data analysis, and manuscript writing.

Funding No funding was received for conducting this study.

Availability of data (data transparency) Data are available from the corresponding author on request.

#### Declarations

**Conflict of interest** The authors have no competing interests to declare that are relevant to the content of this article.

**Ethical approval** This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Local Ethics Committee (Groupe Nantais d'Ethique dans le Domaine de la Santé, 2021).

**Consent to participate** For this type of study, an approval or informed consent is not required (retrospective study). Analysed data were completely anonymized.

#### References

- Olesen TB, Sand FL, Rasmussen CL et al (2019) Prevalence of human papillomavirus DNA and p16INK4a in penile cancer and penile intraepithelial neoplasia: a systematic review and metaanalysis. Lancet Oncol 20:145–158. https://doi.org/10.1016/ S1470-2045(18)30682-X
- Jakobsen JK, Høyer S, Bouchelouche K, Jensen JB (2021) DaPeCa-8: drawing the map of lymphatic drainage in patients with invasive penile cancer—evidence from SPECT/CT and sentinel node surgery. Scand J Urol. https://doi.org/10.1080/21681 805.2021.1882560
- 3. O'Brien JS, Perera M, Manning T et al (2017) Penile cancer: contemporary lymph node management. J Urol 197:1387–1395. https://doi.org/10.1016/j.juro.2017.01.059
- Correa AF, Handorf E, Joshi SS et al (2018) Differences in survival associated with performance of lymph node dissection in patients with invasive penile cancer: results from the National Cancer Database. J Urol 199:1238–1244. https://doi.org/10.1016/j.juro.2017.11.121
- Wen S, Ren W, Xue B et al (2018) Prognostic factors in patients with penile cancer after surgical management. World J Urol 36:435–440. https://doi.org/10.1007/s00345-017-2167-5
- Dindo D, Demartines N, Clavien P-A (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213. https://doi.org/10.1097/01.sla.0000133083.54934.ae
- Bouchot O, Rigaud J, Maillet F et al (2004) Morbidity of inguinal lymphadenectomy for invasive penile carcinoma. Eur Urol 45:761–765. https://doi.org/10.1016/j.eururo.2003.12.003 (discussion 765–766)
- Stuiver MM, Djajadiningrat RS, Graafland NM et al (2013) Early wound complications after inguinal lymphadenectomy in penile cancer: a historical cohort study and risk-factor analysis. Eur Urol 64:486–492. https://doi.org/10.1016/j.eururo.2013.02.037
- Kroon BK, Lont AP, Valdés Olmos RA et al (2005) Morbidity of dynamic sentinel node biopsy in penile carcinoma. J Urol 173:813–815. https://doi.org/10.1097/01.ju.0000156733.99684. 9c
- Perdonà S, Autorino R, De Sio M et al (2005) Dynamic sentinel node biopsy in clinically node-negative penile cancer versus radical inguinal lymphadenectomy: a comparative study. Urology 66:1282–1286. https://doi.org/10.1016/j.urology.2005.06.085
- Nelson BA, Cookson MS, Smith JA, Chang SS (2004) Complications of inguinal and pelvic lymphadenectomy for squamous cell carcinoma of the penis: a contemporary series. J Urol 172:494– 497. https://doi.org/10.1097/01.ju.0000131453.52463.8f

- Gopman JM, Djajadiningrat RS, Baumgarten AS et al (2015) Predicting postoperative complications of inguinal lymph node dissection for penile cancer in an international multicentre cohort. BJU Int 116:196–201. https://doi.org/10.1111/bju.13009
- Yao K, Tu H, Li Y-H et al (2010) Modified technique of radical inguinal lymphadenectomy for penile carcinoma: morbidity and outcome. J Urol 184:546–552. https://doi.org/10.1016/j.juro.2010. 03.140
- Koifman L, Hampl D, Koifman N et al (2013) Radical open inguinal lymphadenectomy for penile carcinoma: surgical technique, early complications and late outcomes. J Urol 190:2086–2092. https://doi.org/10.1016/j.juro.2013.06.016
- Yao K, Zou Z, Li Z et al (2013) Fascia lata preservation during inguinal lymphadenectomy for penile cancer: rationale and outcome. Urology 82:642–647. https://doi.org/10.1016/j.urolo gy.2013.05.021
- Singh A, Jaipuria J, Goel A et al (2018) Comparing outcomes of robotic and open inguinal lymph node dissection in patients with carcinoma of the penis. J Urol 199:1518–1525. https://doi. org/10.1016/j.juro.2017.12.061
- Yadav SS, Tomar V, Bhattar R et al (2018) Video endoscopic inguinal lymphadenectomy vs open inguinal lymphadenectomy for carcinoma penis: expanding role and comparison of outcomes. Urology 113:79–84. https://doi.org/10.1016/j.urology. 2017.11.007
- Bevan-Thomas R, Slaton JW, Pettaway CA (2002) Contemporary morbidity from lymphadenectomy for penile squamous cell carcinoma: the M.D. Anderson Cancer Center Experience. J Urol 167:1638–1642
- Milathianakis C, Bogdanos J, Karamanolakis D (2005) Morbidity of prophylactic inguinal lymphadenectomy with saphenous vein preservation for squamous cell penile carcinoma. Int J Urol 12:776–778. https://doi.org/10.1111/j.1442-2042.2005.01137.x
- Lam W, Alnajjar HM, La-Touche S et al (2013) Dynamic sentinel lymph node biopsy in patients with invasive squamous cell carcinoma of the penis: a prospective study of the long-term outcome of 500 inguinal basins assessed at a single institution. Eur Urol 63:657–663. https://doi.org/10.1016/j.eururo.2012.10.035
- Dimopoulos P, Christopoulos P, Shilito S et al (2016) Dynamic sentinel lymph node biopsy for penile cancer: a comparison between 1- and 2-day protocols. BJU Int 117:890–896. https:// doi.org/10.1111/bju.13389
- 22. Dell'Oglio P, de Vries HM, Mazzone E et al (2020) Hybrid indocyanine green-99mTc-nanocolloid for Single-photon emission computed tomography and combined radio- and fluorescenceguided sentinel node biopsy in penile cancer: results of 740 inguinal basins assessed at a single institution. Eur Urol 78:865–872. https://doi.org/10.1016/j.eururo.2020.09.007
- Sharma P, Zargar-Shoshtari K, Caracciolo JT et al (2015) Sarcopenia as a predictor of complications in penile cancer patients undergoing inguinal lymph node dissection. World J Urol 33:1585– 1592. https://doi.org/10.1007/s00345-014-1471-6
- Chipollini J, Azizi M, Lo Vullo S et al (2020) Identifying an optimal lymph node yield for penile squamous cell carcinoma: prognostic impact of surgical dissection. BJU Int 125:82–88. https:// doi.org/10.1111/bju.14883
- Abbas S, Seitz M (2011) Systematic review and meta-analysis of the used surgical techniques to reduce leg lymphedema following radical inguinal nodes dissection. Surg Oncol 20:88–96. https:// doi.org/10.1016/j.suronc.2009.11.003
- 26. Schmid SC, Seitz AK, Haller B et al (2021) Final results of the PräVAC trial: prevention of wound complications following inguinal lymph node dissection in patients with penile cancer using epidermal vacuum-assisted wound closure. World J Urol 39:613–620. https://doi.org/10.1007/s00345-020-03221-z

- 27. Tranoulis A, Georgiou D, Sayasneh Mrcog A et al (2020) A metaanalysis evaluating the intra-operative use of collagen-fibrin sealants during inguino-femoral lymphadenectomy: a new direction in reducing post-operative morbidity or another disappointment? Eur J Surg Oncol 46:1795–1806. https://doi.org/10.1016/j.ejso. 2020.06.001
- Kumar V, Sethia KK (2017) Prospective study comparing videoendoscopic radical inguinal lymph node dissection (VEILND) with open radical ILND (OILND) for penile cancer over an 8-year period. BJU Int 119:530–534. https://doi.org/10.1111/bju.13660
- Master VA, Jafri SMA, Moses KA et al (2012) Minimally invasive inguinal lymphadenectomy via endoscopic groin dissection: comprehensive assessment of immediate and long-term complications. J Urol 188:1176–1180. https://doi.org/10.1016/j.juro.2012.06.038

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.