Mini-Review: Urological Surgery

Minimally invasive techniques to reduce complications of inguinal lymphadenectomy

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Contributions: (I) Conception and design: AA Ali, VA Master, R Nabavizadeh; (II) Administrative support: All authors; (III) Provision of study materials or patients: VA Master; (IV) Collection and assembly of data: AA Ali; (V) Data analysis and interpretation: AA Ali; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Appropriate management of lymph nodes is critical in patients with malignancy of the inguinal region, particularly penile cancer which has a propensity for regional dissemination from inguinal to pelvic lymph nodes then distant spread. Lymphadenectomy is the gold standard for staging and treatment of locally advanced penile cancer. This procedure has conventionally been performed in an open fashion and is associated with significant morbidity and complication rates. Many physicians and patients are reluctant to perform inguinal lymph node dissection (ILND) due to such high rates of morbidities. Minimally invasive technologies such as video endoscopic inguinal lymphadenectomy (VEIL) and robot-assisted VEIL have emerged as feasible alternatives that reduce complications (i.e., skin necrosis, wound infections, blood loss) while maintaining oncological outcomes similar to those of open ILND. Current studies show that these modalities are safe and feasible in both node-negative and node-positive penile cancer patients. Template modifications have also been developed to minimize complications. These innovations in ILND can subsequently allow patients to better tolerate the procedure, and surgeons can offer surgery to those who would otherwise not be candidates or willing to have surgery. Our aim is to highlight the minimally invasive methods to reduce complications for inguinal lymphadenectomy in penile cancer and review their perioperative morbidity and oncological equivalency.

Keywords: Penile cancer; inguinal lymphadenectomy; minimally invasive; robotic; video endoscopic

Received: 02 February 2023; Accepted: 25 April 2023; Published online: 12 May 2023.

doi: 10.21037/amj-23-26

View this article at: https://dx.doi.org/10.21037/amj-23-26

Introduction

Carcinoma of the penis is an exceedingly rare malignancy, accounting for less than 1% of cancers in men with an incidence of less than 1/100,000 (1). Like other genitourinary neoplasms and cutaneous malignancies, penile cancer has a propensity to spread to the first echelon of nodes in the groin, making nodal status a key prognosticator in these patients (2). Treatment with lymphadenectomy can potentially cure patients with nodal confined disease and prevent distant metastases (3). Furthermore, retrospective studies show that patients who had eight or more lymph nodes removed during lymphadenectomy had improved 5-year overall survival compared to less extensive lymphadenectomy (3). Current National Comprehensive Cancer Network guidelines recommend bilateral inguinal lymph node dissection (ILND) for patients with palpable inguinal nodes and also cN0 patients with primary tumor staged at T1b stage or higher. Patients with pTa or pT1a

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and non-palpable inguinal lymph nodes who have positive dynamic sentinel node biopsy (DSNB) should also undergo ILND.

Five-year survival is significantly higher in patients undergoing ILND compared to those who do not in both stage II (88% *vs.* 38%) and stage III (66% *vs.* 0%) penile cancer (4). Furthermore, the survival benefit of ILND is greater when conducted earlier in the disease process with 3-year survival estimates of 85% versus 35% for prophylactic ILND as compared to ILND for palpable nodes, respectively (5).

While ILND offers a clear survival benefit in penile cancer patients, only a third of eligible patients undergo the procedure, likely attributable to the severe perioperative morbidity associated with ILND (6). Open inguinal lymphadenectomy (O-ILND) is associated with significant perioperative morbidity and complication rates, which range from 50% to 90% (7). Most of these complications are wound-related, such as skin necrosis, lymphocele, dehiscence, and infection (8). Disrupting lymphatic draining from the lower limb and groin can also result in significant lymphedema and lymphorrhea, however this complication rate may not differ across certain ILND techniques due to comparable nodal yields (9). A comparison of multiple studies revealed similar lymphedema incidence between O-ILND an minimally invasive techniques, however this complication rate varies across studies; ranging from 0–38% (10). As a result both surgeons and patients may be reluctant to choose ILND despite the significant oncologic and survival benefit of this surgery for indicated cases.

In an effort to reduce complication rates and morbidity of O-ILND, various technical modifications have been developed. In particular, template modifications and minimally invasive technologies for ILND, such as robot-assisted video endoscopic inguinal lymph node dissection (RA-VEIL) and video endoscopic inguinal lymph node dissection (VEIL), have gained popularity due to their favorable safety and complication profile as well as oncological outcomes (7).

Template modifications

Superficial ILND (sILND) and modified templates for ILND (mILND) have been proposed as approaches to minimize complication risks. The modified technique limits surgical dissection above the fascia lata where superficial lymph nodes lie. Modifications include using a smaller skin incision, eliminating sartorius muscle transposition, and preserving the greater saphenous vein as well as the area lateral to the femoral artery and below the fossa ovalis (11). Similar to mILND, sILND preserves the saphenous vein but extends boundaries of dissection while maintaining the fascia lata and removing all nodal tissue anteriorly. Both these approaches show reduced morbidity when compared to radical O-ILND (9,12). In the largest contemporary series reported for patients who received mILND, Gopman *et al.* report a complication rate of 55%, similar to other historical series (9,13). A third of these complications were deemed major, such as wound infection requiring intravenous antibiotics, skin flap necrosis, or lymphocele requiring intervention (9). Skin necrosis can depend on surgical technique; if all the subcutaneous fat is retained above Camper's fascia, then necrosis can be minimized with an open operation. While these modified template dissections may reduce perioperative morbidity, patients may be at risk for increased false negative samplings and inguinal recurrence (14).

Endoscopic dissections

In addition to template modifications, minimally invasive approaches to ILND have been introduced in efforts to further minimize morbidity associated with ILND. A detailed description of the surgical setup and technique of these endoscopic dissections have been reported previously (15). Here, we highlight the improved morbidity and comparable outcomes for less invasive approaches. For a representative summary of perioperative outcomes associated with ILND techniques identified in the literature from various contemporary series, refer to *Table 1*.

VEIL

The study proposed an endoscopic approach to perform inguinal lymphadenectomy on human cadavers in 2003 (29). This was subsequently refined by Tobias-Machado *et al.* who described a comparative case series of video endoscopic inguinal lymphadenectomy (VEIL) compared to the traditional open technique, revealing a 20% and 70% complication rate, respectively, and equivalent nodal yield (21,30). Other case series similarly established the feasibility of this laparoscopic technique, with a wide range of incidence of complications across these studies, from 10% to 70% (22,25-27,30). Notably, complication differences may be attributed to different reporting criteria.

When assessing safety of the VEIL approach, short-

Table 1 Summary of perioperative outcomes of modified, VEIL, and RA-VEIL studies reported in the literature

Study	Technique	Patients [limbs]	Nodal yield	Hospital LOS, days	Operative time (min)	Post-operative complications
Tsaur *et al.*, 2015 (12)	LIL	29 [57]	Mean 8.1±3.7	Mean 14.2±6.1 days	Mean 89±37.3 (unilateral LIL)	Total: 54.4% of dissections; major 26.3%; minor 28.1%; leg edema 15.8%
Russell *et al.*, 2017 (16)	RA-VEIL and VEIL	18 [27 RA-VEIL, 7 VEIL]	VEIL: median 10 (7.5 to 12) RA-VEIL: median 8 (6 to 12)	Median 1 (1 to 3)	Mean 141 (120 to 162)	Total: 33% of patients; wound infection 17%; major 9%; minor 9%
Thyavihally *et al.*, 2021 (17)	VEIL *vs.* O-ILND	VEIL: 47 [88] O-ILND: 32 [59]	VEIL: median 10 (7 to 18) O-ILND: 10 (7 to 16)	VEIL: mean 6.1 (4 to 12) O-ILND: 9.6 (5 to 20)	Mean 90 (50 to 140)	VEIL *vs.* O-ILND: total 27.7% *vs.* 65.6% (P=0.0001) of groins; wound infection 7.95% *vs.* 27.12%; lymphocele 20.45% *vs.* 23.73; lymphorrhea 26.14% *vs.* 27.12%; skin-flap necrosis 0% *vs.* 23.73%
Matin *et al.*, 2013 (18)	RA-VEIL	10 [20]	Mean 9 (5 to 21)	–	90–120 per dissection	Total: 60%; skin necrosis 10%; wound breakdown 10%; lymphocele 20%; cellulitis 20%; abscess 10%
Singh *et al.*, 2018 (19)	RA-VEIL *vs.* O-ILND (with and without sartorius transposition)	RA-VEIL: 51 [102] O-ILND: 100	RA-VEIL: median 13 (11 to 14.5) O-ILND: 12.5 (10.5 to 14.25)	RA-VEIL: median 3 (3 to 3.75) O-ILND: 4	RA-VEIL: median 75 (70 to 85) O-ILND: 60	RA-VEIL *vs.* O-ILND: major complications 2% *vs.* 17% (P=0.0067); edge necrosis 9.8% *vs.* 23% (P=0.048); flap necrosis 2% *vs.* 13% (P=0.035); severe limb edema 0% *vs.* 9% (P=0.029)
Josephson *et al.*, 2009 (20)	RA-VEIL	1 [2]	Median 10	Median 1	Mean 125 (120 to 130)	0%
Tobias-Machado *et al.*, 2008 (21)	VEIL and O-ILND	VEIL: 15 [20] O-ILND: 5 [10]	VEIL: mean 10.8 (6 to 16) O-ILND: 9.7 (6 to 14)	–	VEIL: mean 120 (90 to 160) O-ILND: 92 (80 to 110)	VEIL *vs.* O-ILND: total 20% *vs.* 70% (P=0.011); hematoma 5% *vs.* 0% (P=1); lymphatic complications 10% *vs.* 20% (P=0.58); skin-related 5% *vs.* 50% (P=0.009)
Stuiver *et al.*, 2013 (13)	Modified O-ILND (40% sartorius muscle transposition), 57% sparing saphenous vein	163 [237]	Median 9 (1 to 25)	Median 9 (1 to 62)	–	Total 58% of dissections; wound infection 43%; seroma 24%; skin-flap problems 16%
Gopman *et al.*, 2015 (9)	Modified or extended ILND	327 [374]	Median 18 (2 to 67)	Median 8 (0 to 62)	–	Total 55.4% of patients; major 34.3%; minor 65.7%; wound infection with IV abx 22.1%; skin-flap necrosis 39.2%; seroma 26.5%; lymphocele 13.7%
Sotelo *et al.*, 2007 (22)	VEIL	8 [14]	Mean 9 (4 to 15)	–	Median 91 (50 to 150)	Lymphocele 23% of groins; wound-related 0%
Sotelo *et al.*, 2013 (23)	RA-VEIL	1 [2]	Left 19; right 14	3	Left 90; right 150	Total: 50%; lymphocele 50%
Sanchez *et al.*, 2016 (24)	RA-VEIL	1 [1]	8	2	130	–
Master *et al.*, 2009 (25)	VEIL	16 [25]	Mean: left 10.2; right 9.7	–	Mean 147	Total: 12% of dissections; cellulitis: 1 case requiring readmission with antibiotics and another case immediately post-operative, 1 seroma
Master *et al.*, 2012 (26)	VEIL	29 [41]	Median 11 (3 to 24)	Median 1 (1 to 14)	Median 175 (75 to 398)	Major 14.6%; minor 27%; lymphatic 12%; flap necrosis 2.6%; readmission for IV abx 10.5%
Delman *et al.*, 2010 (27)	VEIL	5	Median 10 (4 to 13)	Median 1 (1 to 5)	Median 180 (142 to 223)	Cellulitis 40%
Jain *et al.*, 2017 (28)	RA-VEIL	12 [22]	Mean 11 (4 to 26)	Mean 4.5 (4 to 7)	Mean 69.3 (45 to 95)	Lymphatic 33.3%; cellulitis 16.7%

LIL, limited open inguinal lymphadenectomy; LOS, length of stay; RA-VEIL, robot-assisted video endoscopic inguinal lymph node dissection; VEIL, video endoscopic inguinal lymph node dissection; ILND, inguinal lymph node dissection; O-ILND, open inguinal lymph node dissection.

term perioperative outcomes can be reviewed to better understand the potential risks associated with VEIL. Mean operative time of VEIL in most reported series is often higher than O-ILND (mean 141.5 *vs.* 94 min per limb), however, no difference is noted between VEIL and RA-VEIL operative times across various series per Russel *et al.* (16). Furthermore, length of stay has been reported as roughly 1 day for both minimally invasive techniques but ranges from 6.4 to 9 days for O-ILND (16). This shortened stay may be attributed to the modified surgical technique moving incisions away from the groin crease. Despite faster recovery, time to drain removal was noted to be higher in both VEIL and RA-VEIL, suggesting the need for techniques to improve lymphostasis (13).

Node positive patients undergoing VEIL experience a comparable or higher nodal yield compared to O-ILND, ranging from 5 to 16 (17). Nodal yield is considered to be a surrogate for oncological adequacy (1). While oncological adequacy may be achieved using this approach, few studies have reported on follow-up and long-term oncological outcomes in these patients and more data is needed in the future to close this knowledge gap.

RA-VEIL

Josephson was the first to describe the robotic platform with successful application in 2009 (20). In the largest reported prospective series on RA-VEIL, Matin *et al.* conducted a phase 1 prospective study evaluating outcomes of 10 patients with subsequent open assessment of dissection adequacy (18). In this study, after RA-VEIL was completed on each of 19 thighs, a separate surgeon created an open incision to verify complete resection of lymph nodes. Eighteen of the 19 inguinal areas (94.7% in nine patients) were considered adequate dissections, albeit two benign nodes were discovered above the inguinal dissection field (18). This and other studies report adequate clearance with acceptable nodal yield, with a mean of at least nine lymph nodes per thigh (23,28).

The robotic approach is also appealing considering it offers improved 3D visualization and dexterity over laparoscopic tools which is especially useful considering the already limited working space in the inguinal region (24). Various series confirm the oncological adequacy of RA-VEIL when compared to O-ILND, although nodal yield may differ depending on the series (19). Similar to VEIL, the complication rates for RA-VEIL is lower than the traditional O-ILND (19). Lymph node stage/status was noted to be an independent risk factor associated with more complications.

The operative time of RA-VEIL is significantly higher than O-ILND (75 *vs.* 60 min) (19). Of note, there is a financial constraint with RA-VEIL, with various patients often choosing the open approach versus robotic citing the prohibitive cost of robotic surgery as the primary reason in countries where patients pay for consumable costs (19). Another considerable limitation with minimally invasive techniques is the sparsity of literature that evaluates long-term follow-up and oncologic outcomes in these patients.

Conclusions

VEIL and RA-VEIL are attractive minimally invasive strategies when treating penile cancer patients with non-palpable inguinal nodes to reduce the significant perioperative morbidity associated with traditional O-ILND. Long-term and large volume studies are still needed to confirm oncological efficacy and lower morbidity, however currently available data suggest that endoscopic ILND (E-ILND), including both VEIL and RA-VEIL, decrease postoperative complications while achieving adequate short and intermediate oncological outcomes.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Stênio de Cássio Zequi) for the series "Penile Cancer" published in *AME Medical Journal*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://amj.amegroups.com/article/view/10.21037/amj-23-26/coif). The series "Penile Cancer" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

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doi: 10.21037/amj-23-26
Cite this article as: Ali AA, Schmeusser BN, Nabavizadeh R, Master VA. Minimally invasive techniques to reduce complications of inguinal lymphadenectomy. AME Med J 2023;8:16.