

Minimal invasive approaches in lymph node management of carcinoma of penis: A review

Shreedhar Gurunathan Kandasamy, Kosur Ravi Chandran, Ginil Kumar Pooleri*

Department of Urology, Amrita Institute of Medical Sciences, Kochi, Kerala, India

*E-mail: drginil@gmail.com

ABSTRACT

Introduction: Inguinal lymph node dissection (ILND) is an integral part in the management of carcinoma penis. The concerns about the postoperative morbidity associated with open ILND led to modification in the template of dissection and adoption of minimally invasive techniques such as video endoscopic inguinal lymphadenectomy (VEIL) and robotic-assisted VEIL (R-VEIL). In this review, we aim to describe the techniques, case selection, perioperative outcomes, and oncological outcomes of VEIL and R-VEIL and to compare it with open ILND.

Methods: Databases of PubMed, Embase, and Google Scholar were searched to identify the articles for VEIL and R-VEIL. Using PRISMA guidelines, literature search yielded 3783 articles, of which 32 full-text articles relevant to the topic were selected and reviewed, after consensus from authors.

Results: After the first description of VEIL, various modifications in port placements and approaches were described. Several studies have shown, VEIL and R VEIL are safe and feasible in both node-negative and node-positive Ca penis patients. Compared to open ILND, VEIL had fewer wound infections and skin necrosis, minimal blood loss, shorter mean hospital stays, and reduced duration of drain kept. There is no difference in mean lymph node yield and recurrence rates between open ILND, VEIL, R-VEIL.

Conclusion: VEIL and R-VEIL are safe and have comparable oncological outcomes with open ILND.

INTRODUCTION

Penile cancer accounts for about 0.5% of the cancers occurring in men worldwide, with India, Brazil, and South Africa being the countries with the highest incidence.^[1-3] Inguinal lymphadenectomy (ILND) is an integral part in the management of the disease as it serves as a diagnostic, therapeutic, and prognostic tool. ILND is recommended in patients with intermediate/high-risk Ca Penis with nonpalpable inguinal nodes and unilateral/bilateral palpable inguinal lymph nodes.^[4] Since ILND is associated with significant complications,^[5] various techniques such as modifying the template of dissection, video endoscopic inguinal dissection (VEIL), and robotic VEIL (R-VEIL) have been described. Despite the VEIL and Robotic VEIL gaining momentum in recent years, there is a paucity

of data on their utility. We reviewed techniques, case selection, perioperative outcomes, and oncological outcomes of VEIL and R-VEIL in penile cancer.

METHODOLOGY

Study design

We performed a review of medical literature to identify the articles relevant to VEIL and R-VEIL. Preferred Reporting Items for Systematic reviews and Meta-Analysis^[6] guidelines were followed while conducting this study.

Search strategy

Online search using MeSH terms “Video Endoscopic Inguinal Dissection or VEIL or Robot-assisted Inguinal dissection or

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R-VEIL or RAVEIL or Minimal invasive Inguinal dissection” using ENDNOTE X9 in PubMed, Goolge Scholar and Embase library on June 2021. Search was limited to articles published after the year 2000.

Selection criteria

Two authors reviewed all the articles confirming to search criteria. All non-English, conference poster presentations, letters to editor, and case reports were excluded. Articles remaining after exclusion were analyzed under one of these heads: technique, case selection, perioperative outcomes, and oncological outcomes.

DISCUSSION

Initial search in PUBMED and EMBASE using Endnote X9, yielded 2479 and 878 results respectively. Google scholar yielded 426 results. Citations of all these were loaded in citation manager and duplicates removed. Title and abstracts relevant to the topic were scrutinized by two authors and after filtering with inclusion criteria, yielded 92 full-text articles. After excluding the VEIL in malignancies other than Carcinoma Penis yielded 32 articles [Figure 1]. These articles will be discussed in this manuscript under the heads as described.

Technique

VEIL

After initial report of Bishoff *et al.*^[7] in 2003 on few cadaveric dissections and one patient, Machado *et al.* in 2006 described this approach after a feasibility study in 7 patients.^[8] The patient is positioned with knee flexed, hip externally rotated, and abducted (frog-leg position). An incision is made 2 cm caudal to the apex of femoral triangle. Finger dissection is used to create the working space deep to Scarpa’s fascia through which the Camera is inserted. Two working ports are placed

superolateral and superio-medial to the camera port, ensuring a distance of 6–8 cm between the ports to avoid clashing of the instruments [Figure 2]. Ports are fixed to the skin to prevent slipping out. The dissection is extended under vision using laparoscopic camera. During this step, transillumination of the skin helps in maintaining the adequate thickness of the camper’s fascia in skin and to avoid a buttonhole [Figure 3]. The blood vessels in camper’s fascia seen during transillumination should be preserved to prevent the necrosis of the skin flap. Template of dissection is similar to that of open ILND. The saphenous vein is sacrificed if it is surrounded by nodes.^[9] After completing the superficial Inguinal dissection, the fascia lata is divided and deep inguinal lymph nodes including pectineus group and Cloquet nodes are removed after identifying and preserving femoral vessels[Figure 4]. The specimen is retrieved through the initial incision or in an endo bag [Figure 5]. Port sites are closed after placing a suction drain and a compressive bandage is applied over the limb and the operative area to avoid lymphorrhea.

Various modifications in port placements and approach have been described. Wang *et al.*^[10] described hypogastric approach in VEIL for Vulvar cancer which was later adopted for penile cancer as well. Yuan *et al.*^[11] compared hypogastric approach with standard approach and found no difference in outcomes. Nayak *et al.*^[12] described lateral approach (L-VEIL) in which all the three ports are placed lateral to the sartorius muscle and the dissection carried out from lateral to medial in the femoral triangle. The short-term oncological outcomes of L-VEIL are comparable to standard VEIL.^[13] Authors claim the shortcomings of the standard approach such as restriction of camera movement and difficulty for assistant to hold the camera could be avoided with L-VEIL. Tamhankar *et al.* described initial space creation using a balloon.^[14] Pahwa *et al.* described cannula-assisted port placement, where the working ports are placed by using the primary port cannula as a guide.^[15]

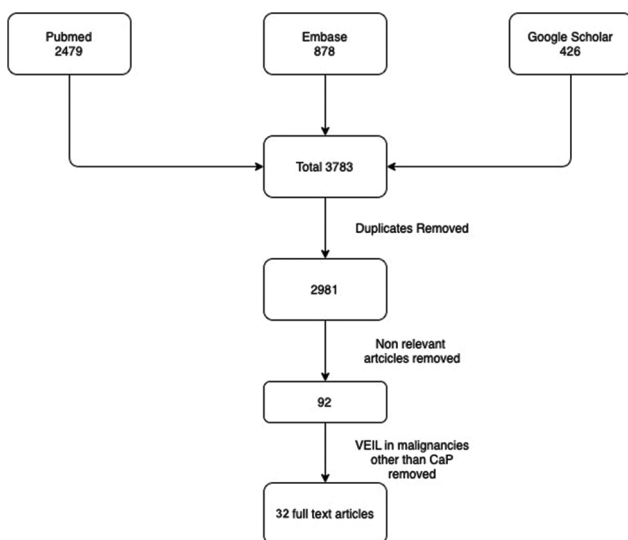


Figure 1: Literature Search



Figure 2: Patient position and port placement

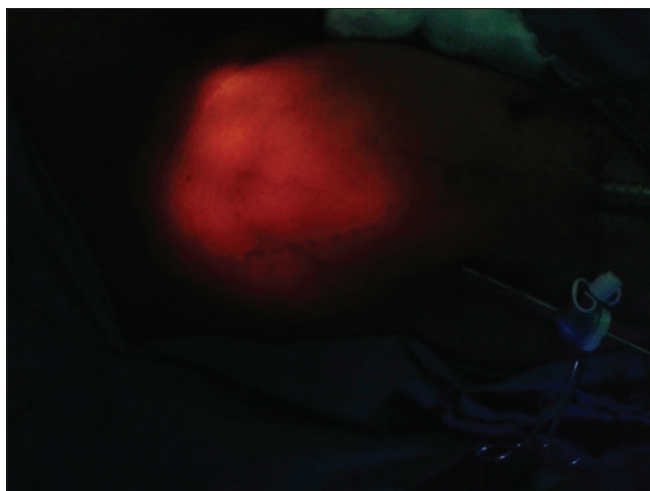


Figure 3: Transillumination of the skin flap

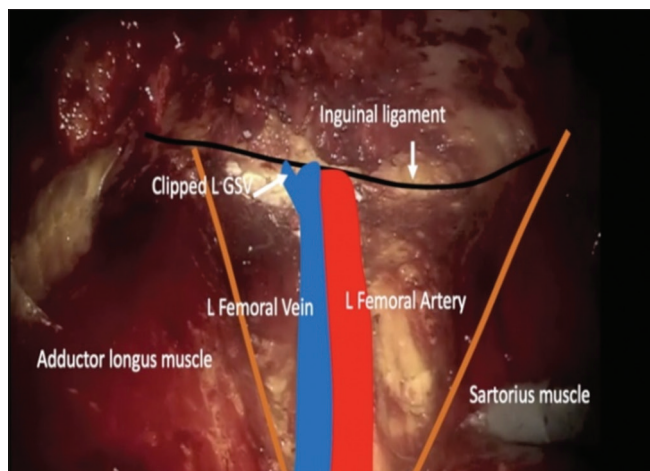


Figure 4: View after lymphadenectomy



Figure 5: After specimen retrieval

Many authors describe initial plane creation deep to deep fascia followed by dropping the fibrofatty layer from the Camper's fascia.^[16,17] Saphenous vein sparing and nonsparing are also described.^[16,18] Machado *et al.*^[19] described the laparo-endoscopic single-site VEIL (LESS VEIL or SS VEIL)

technique in 2011, which requires specialized angulated instruments and is technically demanding. LESS Veil is claimed to be better cosmetically. Herrel *et al.* in 2012 and Pompeo *et al.* in 2013, came out with the feasibility of simultaneous bilateral VEIL in an effort to reduce the anesthesia and operative time.^[20,21]

Robotic VEIL

Josephson *et al.* described R-VEIL in 2009.^[22] DaVinci Si, X and Xi platforms are commonly used in R-VEIL. The first robotic port (Camera) is placed 25 cm caudal to the mid inguinal port. After creating the space, two robotic ports are placed 6–8 cm lateral and medial to the camera port. The fourth robotic port is usually omitted, due to small working space. A 12 mm port for assistant can be placed between and lateral to camera port and lateral port. Rest of the dissection is similar to the standard VEIL.

The advantages with R-VEIL are similar to any robotic procedures such as 3D vision, better dexterity for dissection, and ergonomics for the surgeon. This procedure needs a trained bedside assistant to monitor the skin flap thickness as the surgeon is not in the direct vision of the flap. Yu *et al.*^[23] advocate a hypogastric approach for R-VEIL with utilizing skin incisions for the ports for pelvic lymphadenectomy if needed. Injecting indocyanine green at the base of the tumor during partial penectomy and dissecting the nodes using near infrared fluorescence (firefly) during R-VEIL has also been described.^[24]

Case selection

Although VEIL is done in vulval cancers, urethral cancer, cutaneous malignancies of lower limb, and penile cancer, we have confined our search to VEIL in penile cancer. The first described VEIL procedure by Tobias *et al.*^[8] was in node-negative groin. Carlos *et al.*^[25] did a feasibility study and proved VEIL can be safely done in node-positive groin as well. Except for few studies,^[26-28] most of the studies on VEIL are on mixed population of node-negative and positive patients with >70% the patients in former category. With the advent of robotic assistance, more node-positive patients were subjected to VEIL.^[16,18,29] Ahlawat *et al.*^[17] did robotic bilateral VEIL with bilateral pelvic lymphadenectomy in a single setting, expanding the feasibility.

Perioperative outcomes

Perioperative outcomes including the complications were evaluated in multiple studies [Table 1]. The mean operative duration of VEIL varies from 68 to 194.86 min. Compared to node-negative patients, the mean duration for VEIL was 30 min more for node-positive patients.^[25] The reported mean operative duration in RVEIL was less than standard VEIL (68-151 min vs. 85-180 min).^[16,18] Ahlawat *et al.* reported mean operative duration of 453 min, in the study where the feasibility of B/L VEIL and Pelvic lymphadenectomy was assessed.

Table 1: Perioperative outcomes

Author, year	Technique	Number of patients	Operative duration	Blood loss	Lymph node yield	Days drain kept	Hospital stay	Complications
Meneses et al., 2019 ^[30]	VEIL	11	85 (60-120)	<50 ml	5.8 (1-12)	Mean 8	4 (2-11)	Skin complications 10%, lymphatic complications 25% Global complications 2.6% x 36%, cellulitis 0% x 4.5%, lymphocele 23% in both groups, skin necrosis 3% x 1%, myocutaneous necrosis 0% x 4.5%
Carlos et al., 2013 ^[25]	VEIL (NovoN1)	40	N0-95.5, N1-126.8	N/A	9	N0-5.7, N1-6.7	N0-3.1, N1-5.1	
Pahwa et al., 2013 ^[31]	VEIL	10	144 (120-180)	N/A	5.6 (7-12)	5.1 (5-8)	N/A	Subcutaneous emphysema (self-resolving) - all patients, skin complications - nil, lymphocele - 20% Skin complications 10%, lymphocele 20%, cellulitis 10%
Matin et al., 2013 ^[32]	R VEIL	10	100 (90-120)	100 (10-200)	9 (5-21)	N/A	N/a	
Chiapparrone et al., 2018 ^[33]	VEIL	1	180 min	N/A	16	7	8	Skin complication: 10%
Elsamra and Poch 2017 ^[34]	R VEIL	10	151.4 (99.0-224.0)	30 (12.5-50.0)	10.4 (6.0-16.0)	N/A	N/A	
Sudhir et al., 2012 ^[35]	VEIL	22	N/A	N/A	N/A	N/A	N/A	Skin necrosis: 2.53%, lymphocele 10.45, delayed bleed - 2.53%
Yuan et al., 2018 ^[11]	VEIL	72	107 (90-185)	100 (85-120)	20 (12-29)	4 (3-12)	5 (3-13)	
Elbalka et al., 2020 ^[3]	VEIL	15	128+/-28	20 (15-35)	10.73+/-3.60	3 (3-21)	3 (3-14)	Wound infection 8.42%, seroma - 6.91%, lymphorrhea - 5.66%, cellulitis - 2.66%
Jindal and Meena 2021 ^[26]	VEIL and R VEIL	30	100 (80-140)	N/A	7 (5-9)	7 (5-12)	3.1 (2-5)	
Russell et al., 2017 ^[27]	R VEIL and VEIL	18	141 (120-162)	50 (15-50)	10 (6-12.5)	2 (2-5)	N/A	Wound complication: 9%, lymphocele 6%, DVT 3%
Tobias-Machado et al., 2017 ^[28]	VEIL	10	126 (80-130)	N/A	9.7 (6-14)	Mean 4.9 days	N/A	
Yu et al., 2019 ^[23]	R VEIL	9	68+/-13	N/A	12 (5-21)	N/A	N/A	Lymphorrhea - 10%, Hematoma - 10%
Singh et al., 2018 ^[8]	R VEIL	51	75 (70-85)	75 (65-80)	13 (11-14.5)	12 (10-15)	3 (3-3.75)	
Thyaviahally et al., 2021 ^[6]	RVEIL	47	90 (50-140)	30 (10-70)	10 (7-14)	N/A	6.1 (4-12)	Wound complications: 11.8%, lymphocele - 49%, cellulitis 9.8%
Yadav et al., 2018 ^[29]	VEIL	29	162.83	N/A	7.6	N/A	6.1 (4-12)	
Ahlawat et al., 2016 ^[17]	R VEIL + ILND	3	453	N/A	16.3	44 days	4.6 (4-8)	Wound complications: 7.95%, lymphocele 20.45%, no flap necrosis
Kumar and Sethia 2017 ^[36]	VEIL	20	97	N/A	9.36	N/A	4	
Romanelli et al., 2013 ^[37]	VEIL	20	119 (55-210)	N/A	8 (3-16)	N/A	5 (2-10)	Skin necrosis: 2.8%, lymphocele 10.3%, lymphedema: 10.3%, no wound infection and skin necrosis No skin complications, lymphocele in 33% Wound complications 6%, prolonged lymphocele 27% Wound complications 6%, lymphatic complications: 27.2%
Chaudhari et al., 2016 ^[38]	VEIL	14	194.86 (178-210)	N/A	7.68 (5-11)	N/A	N/A	

VEIL = Video endoscopic inguinal lymph adenectomy, R VEIL = Robotic assisted VEIL, N/A = Not available, ILND = Inguinal lymph node dissection

Estimated blood loss in VEIL ranges from 20 to 100 ml. Singh *et al.*^[18] reported comparable estimated blood loss (about 75 ml) for R-VEIL and open ILND. Thyavihally *et al.* reported less mean estimated blood loss in RVEIL than in Open ILND (30 ml vs. 100 ml, $P=0.005$). Thus, the estimated blood loss in VEIL is comparable or less than that of open procedure.

Mean hospital stay was 3–5 days. This is in contrast to the mean hospital stay of about 10 days in Open ILND.^[16,29] Singh *et al.*^[18] reported mean hospital stay of 4 days in ILND group and 3 days on VEIL group ($P = 0.008$). Thus, VEIL offers quick recovery and earlier discharge from the hospital. This trend is also seen with mean duration of drain kept.

Similar to the open ILND, the complications encountered in minimal invasive surgery are wound infection including cellulitis, lymphocele requiring repeated aspirations, early and delayed lymphedema, and skin necrosis ranging from edge necrosis to flap necrosis. The incidence of the complications in VEIL differs widely between various studies [Table 2]. It can be as low as 10%^[28] and as high as 78.4%^[18]. Large variability between the complications in different studies could be partly due to the difference in reporting criteria used.

Wound infection and skin necrosis are rarely encountered in VEIL when compared to open surgery.^[16,23,28] The incidence of lymphocele and lymphedema were similar in both the groups.^[16,18,23] Complications reported with VEIL, were few in number and of less severity requiring conservative management.^[18] More severe complications particularly wound infection and cellulitis were reported in groin node-positive patients.^[18,25,29] In multivariate analysis of risk factors, nodal stage and open ILND had a significant association with complications after lymphadenectomy.^[16]

Oncological outcomes

Lymph node yield and recurrence rates are the indicators for assessing the oncologic adequacy. Lymph node yield in VEIL varies from 5 to 16. Lymph node yield did not differ between the node-positive and node-negative patients.^[25] Higher lymph node yield with VEIL was reported in the prospective

study which compared open ILND and VEIL (7.11 vs. 9.36, $P = 0.013$).^[36] In other studies, lymph node yield is comparable between VEIL and open surgery [Table 3]. The only study which directly compared VEIL ($n = 7$) and R-VEIL ($n = 27$) showed no difference in lymph node yield.^[27] In node-negative patients, the open approach uses either DSNB or modified ILND but in the VEIL approach, a complete ILND is performed. Hence the lymph node yield may not be comparable.

There is a paucity of data on the long-term outcome after VEIL. Meneses *et al.*^[30] followed up 11 patients for a mean period of 28 months and 2 patients had recurrence. Carlos *et al.*^[25] reported cancer-specific mortality of 5% at 35.3 months of follow-up in node-negative patients and 70% at 17.3 months follow-up in node-positive patients. Singh *et al.*^[18] had the longest follow-up of 41 months for 51 patients after VEIL and 100 patients of open ILND, with no recurrence during the period. In the study by Yu *et al.*, 2 out of 9 patients (18%) developed pelvic and abdominal metastasis, compared to 4 out of 10 patients in open ILND ($P=0.536$). All the patients with recurrence had advanced pathological node status.^[23]

With similar lymph node yield and recurrence rates, VEIL can be considered non inferior to open ILND. The efficacy of VEIL in high volume disease is not answered with current literature. VEIL has a shorter recovery period which enables early institution of adjuvant treatment in deserving patients with possible improvement of outcome.^[39] All the papers reviewed here were of retrospective nature, carrying its inherent limitation in uniformity of case selection and reporting. Prospective large volume studies with long-term follow-up are required to fill the existing lacunae in evidence.

CONCLUSION

Inguinal lymphadenectomy is the cornerstone in the management of carcinoma of penis. Minimally invasive procedures such as VEIL and R VEIL are safe and feasible in both node-negative and node-positive patients. Compared to open ILND, VEIL is associated with low morbidity, less convalescence and similar oncological outcomes, making it

Table 2: Comparison of complications between open and video endoscopic inguinal lymph adenectomy

Author, year	Comparison	Wound infection (%)		Lymphocele (%)		Lymphedema (%)		Skin necrosis (%)	
		Open	MIS	Open	MIS	Open	MIS	Open	MIS
Tobias-Machado 2017 ^[28]	Open versus VEIL	20	0	20	10	20	0	20	0
Yu <i>et al.</i> , 2019 ^[23]	Open versus R VEIL	45	0	20	12.50	0	0	20	0
Singh <i>et al.</i> , 2018 ^[18]	Open versus R VEIL	20	9.80	55	49	38	23.50	36	11.80
Thyavihally <i>et al.</i> , 2021 ^[16]	Open versus R VEIL	42.30	7.90	23.73	20.45	13.56	11.36	23.73	0.00
Yadav <i>et al.</i> , 2018 ^[29]	Open versus VEIL	13.70	0	24.10	10.30	13.70	10.30	27.58	6.89
Kumar and Sethia 2017 ^[36]	Open versus VEIL	68	6	20	27	37	3	N/A	N/A

N/A=Not available, VEIL=Video endoscopic inguinal lymph adenectomy, R VEIL=Robotic assisted VEIL, MIS=Minimally Invasive Surgery

Table 3: Comparison of lymph node yield

Article	Open	VEIL/R VEIL	P
Tobias-Machado 2017 ^[28]	9.7 (6-14)	10 (6-16)	0.52
Yu <i>et al.</i> , 2019 ^[23]	12 (5-21)	11 (2-27)	0.84
Singh <i>et al.</i> , 2018 ^[18]	12.5 (10.5-14.25)	13 (11-14.5)	0.44
Thyavihally <i>et al.</i> , 2021 ^[16]	11 (7-16)	10 (7-14)	0.325
Yadav <i>et al.</i> , 2018 ^[29]	8.3	7.6	0.68
Kumar and Sethia 2017 ^[36]	7.11	9.36	0.013

VEIL=Video endoscopic inguinal lymph adenectomy, R VEIL=Robotic assisted VEIL

a promising alternate to open ILND in selected cases. The safety of minimally invasive procedures like VEIL and R VEIL in high volume lymph node disease is yet to be proved with better evidence.

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