

MODERATOR

SOUTHWEST RE

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INTRODUCTION

- Cancers of the penis are uncommon tumors that are often devastating for the patient and frequently diagnostically and therapeutically challenging for the urologist.
- Although rare in North America and Europe, penile malignant neoplasms constitute a substantial health concern in many African, South American and Asian countries.
- Penile carcinoma accounts for 0.4% to 0.6% of all malignant neoplasms among men in the United States and Europe;

- it may represent up to 10% of malignant neoplasms in men in some Asian, African, and South American countries
- Penile cancer is a disease of older men, with an abrupt increase in incidence in the sixth decade of life.
- The tumor is not unusual in younger men; 22% of patients are younger than 40 years and 7% are younger than 30 years
- the disease has also been reported in children
- more than <u>95% of the lesions are squamous cell carcinoma (SCC)</u>

PREMALIGNANT LESIONS

- CUTANEOUS HORN
- PSEUDOEPITHELIOMATOUS MICACEOUS AND KERATOTIC BALANITIS



BOWENOID PAPULOSIS



CONDYLOMA ACUMINATA



----KAPOSI'S SARCOMA



LEUCOPLAKIA

- Present as solitary or multiple whitish plaques that often involves the meatus
- Surgical excision and radiation are the treatment



BALANITIS XEROTICA OBLITERANS

- Presents as whitish patch on prepuce or glans often involving meatus
- Glanular erosions, fissures and meatal stenosis may occur
- Treatment by topical steroid cream, injectable steroids and surgical excision
- Meatal stenosis is common problem

Buschke-Lowenstein Tumour (Verrucous Carcinoma)

- True incidence is unknown.
- Invades locally.
- Compresses the adjacent tissues causing urethral erosion & fistulisation
- NEVER METASTASIZE
- SHOWS NO SIGN OF MALIGNANT CHANGE
- · C.F.: bleeding, discharge & foul odour

- Treatment is excision. Total penectomy may be required.
- Laser therapy may be effective in some cases.
- Recurrence is common.
- Topical therapy with Podophyllin, 5FU, radiation and chemotherapy have all been tried with no great success.
- Radiotherapy has rather been associated with malignant degeneration of the tumor at other sites

PENILE CANCER

- Squamous cell carcinoma. > 95%
- Mesenchymal tumors. < 3%
 e.g Kaposi sarcoma, angiosarcoma etc
- Malignant Melanoma.
- Basal cell carcinoma.
- Metastasis.



CARCINOMA IN SITU

- Carcinoma in situ (Tis) of the penis is called <u>erythroplasia of</u>
 <u>Queyrat</u> if it involves the glans penis and prepuce or
- Bowen's disease if it involves the penile shaft or the remainder of the genitalia or perineal region.
- Both are histologically similar.

- Clinically <u>erythroplasia of Queyrat</u> consists of a red, velvety, well-marginated lesion of the glans penis or, less frequently, the prepuce of the uncircumcised man.
- It may ulcerate and may be associated with discharge and pain
- Bowen's disease is characterized by sharply defined plaques of scaly erythema on the penile shaft. Crusted or ulcerated variants can occur.
- The appearance can be confused with bowenoid papulosis, nummular eczema, psoriasis, and superficial basal cell carcinoma.



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ERYTHROPLASIA OF QUEYRAT

BOWEN'S DISEASE

- Invasive carcinoma may occur in about 5% to 33% of cases.
- Metastasis is extremely rare.

TREATMENT:

- PREPUTIAL LESION circumcision or excision with a 5-mm margin
- GLANULAR LESION topical 5-fluorouracil cream; 5% imiquimod cream; or ablation therapy
- RADIOTHERAPY is for resistant cases

INVASIVE CARCINOMA

- 0.1 0.9 per 100,000 in USA, Europe.
- Upto 10% in some asian, african and south american countries
- Primary tumor localized to glans (48%), prepuce (21%), both glans & prepuce (9%), coronal (6%), shaft (<2%).</p>

ETIOLOGY

- Lack of neonatal circumcision
- Poor hygiene standards
- Phimosis.
- HPV infection.
- Exposure to tobacco products
- Penile trauma mutilating circumcision, penile tears, etc.
- No convincing association with occupation, gonorrhea, syphillis & alcohol intake.

NATURAL HISTORY

- Begins as small lesion, papillary & exophytic or flat & ulcerative.
- Lymphatic spread main pathway of spread to the regional femoral and iliac nodes.
- Flat & ulcerative lesions > 5cm and extending > 75% of the shaft have higher incidence of metastasis and poor survival.
- Buck's fascia acts as a temporary natural barrier to local extension of the tumor, protecting the corporeal bodies from invasion.

- Penetration of Buck's fascia and the tunica albuginea permits invasion of the vascular corpora and establishes the potential for vascular dissemination.
- Urethral and bladder involvement are rare
- Distant metastasis uncommon 1 10%
- Death within 2 years for most untreated cases.

CLINICAL FEATURES

SYMPTOMS

- Pt. present with ulcer or a swelling on penis
- Pain does not develop in proportion to the extent of the local destructive process and usually is not a presenting complaint.
- Weakness, weight loss, fatigue, and systemic malaise occur secondary to chronic suppuration.
- On occasion, significant blood loss from the penile lesion, the nodal lesion, or both may occur.
- Symptoms referable to metastases are rare.

SIGNS

- The presentation ranges from a relatively subtle induration or small excrescence to a small papule, pustule, warty growth, or exophytic lesion.
- It may appear as a shallow erosion or as a deeply excavated ulcer with elevated or rolled-in edges.
- Erosion through the prepuce, foul preputial odor, and discharge with or without bleeding

- Mass, ulceration, suppuration, or hemorrhage in the inguinal area may be due to nodal metastases.
- Urinary retention or urethral fistula due to local corporeal involvement is a rare presenting sign.

INVESTIGATIONS

1) LABORATORY STUDIES

- Anemia,
- Leukocytosis
- Hypoalbuminemia
- Azotemia
- Hypercalcemia

2) BIOPSY

- Confirmation of the diagnosis of carcinoma of the penis
- Asessment of the depth of invasion,
- Presence of vascular invasion, and
- Histologic grade of the lesion

3) RADIOLOGIC STUDIES

A) CXR - for lung metastasis

B) PENILE ULTRASONOGRAPHY

- -sensitivity 57% and specificity 91%
- -can not delineate invasion into the subepithelial connective tissue of the glans penis from corpus spongiosum involvement

C) CT SCAN

- sensitivity and specificity of CT are 36% and 100%

- -Mainly for assessment of inguinal & pelvic LNs and abd. sec.
- role in examination of the inguinal region in obese patients or in those who have had prior inguinal surgery, for whom the physical examination may be unreliable.
- CT-guided biopsy of enlarged pelvic nodes

D) MRI

- -sensitivity and specifity of 100% and 91% respectively
- assesses local staging of the tumor
- assessment of inguinal & pelvic LNs
- -better with artificial erection

E) NEWER MODALITIES

Nanoparticle (Ferumoxtran-10 particles) and PET/CT of the inguinal region have shown promising results in the detection of <u>minimal inguinal metastases when LNs are normal</u> <u>on CT/MRI</u> but validation in larger series is required

STAGING

AMERICAN JOINT COMMITTEE ON CANCER STAGING FOR PENILE CANCER

PRIMARY TUMOR (T)

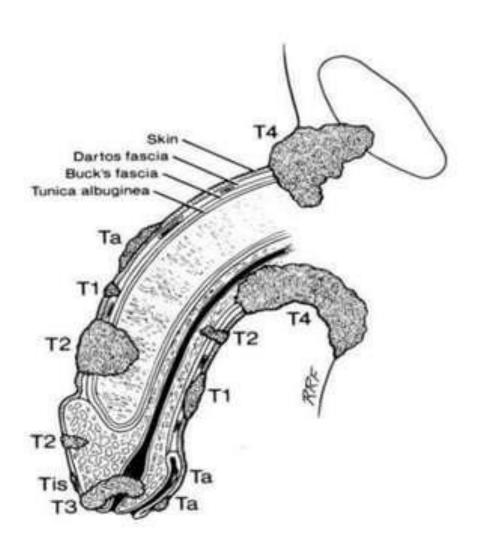
- TX Primary tumor cannot be assessed
- TO No evidence of primary tumor
- Tis Carcinoma in situ
- Ta Noninvasive verrucous carcinoma
- T1a Tumor invades subepithelial connective tissue without lymph vascular invasion and is not poorly differentiated (i.e., grade 3-4)
- T1b Tumor invades subepithelial connective tissue without LVI and is poorly differentiated
- T2 Tumor invades corpus spongiosum or cavernosum
- T3 Tumor invades urethra
- T4 Tumor invades other adjacent structures

LYMPH NODES (N)

- NX Regional nodes cannot be assessed
- NO No palpable or visibly enlarged inguinal lymph nodes
- N1 Palpable mobile unilateral inguinal lymph node
- N2 Palpable mobile multiple or bilateral inguinal lymph nodes
- N3 Palpable fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral

DISTANT METASTASIS (M)

- M0 No distant metastasis
- M1 Distant metastasis



STAGE GROUPING

Stage 0	Tis	NO	MO
	Ta	NO	MO
Stage I	Tla	NO	MO
Stage II	TIb	NO	MO
	T2	NO	MO
	T3	NO	MO
Stage IIIa	T1-3	N1	MO
Stage IIIb	T1-3	N2	MO
Stage IV	T4	Any N	MO
	Any T	N3	MO
	Any T	Any N	M1

BRODER CLASSIFICATION FOR GRADING OF SQUAMOUS CELL CARCINOMA

Grade Histologic Features

> II−III

Cells well differentiated with keratinization

Prominent intercellular bridges

Keratin pearls

Increased mitotic activity

Fewer keratin pearls

Marked nuclear pleomorphism

Many mitoses

Necrosis

Lymphatic and perineural invasion

Absence of keratin pearls

Deeply invasive

TREATMENT OF PENILE LESION

ORGAN PRESERVATION

II) PENILE AMPUTATIONS

ORGAN PRESERVATION

GOAL

- to preserve glans sensation where possible
- to maximize penile shaft length

INDICATIONS

- primary tumors exhibiting favorable histologic features
- stages Tis, Ta, T1; grade 1 and grade 2 tumors

SURGERIES INCLUDE

- Limited excision strategies
- Radiation therapy,
- Mohs surgery, and
- Laser ablation

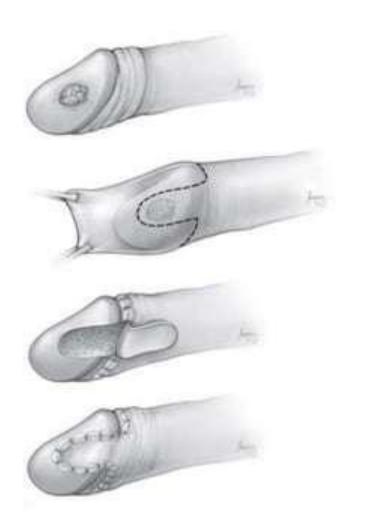
1) CIRCUMCISION AND LIMITED EXCISION STRATEGIES

- 2-cm surgical margin required for all patients undergoing partial penectomy has been challenged
- The maximum proximal histologic extent of 5 mm for grade 1 and grade 2 tumors and 10 mm for grade 3 tumors is recommended.

Limitations of this approach include

- Proximal and distal deeply invasive tumors,
- High-grade tumors,
- Skip lesions and
- Patients with poor compliance who would not be candidates for salvage procedures

Recurrence rate is 4-6 % nowadays



Surgical glans defect covered with outer preputial flap as described by Ubrig and colleagues. A, Superficial glans tumor.

B, Outer preputial flap outlined.

C, Tumor excised and circumcision performed.
D, Glans defect filled with outer preputial flap.



Finely meshed extragenital split-thickness skin graft quilted to glans defect after superficial tumor excision.

2) MOHS MICROGRAPHIC SURGERY

- It involves layer-by-layer complete excision of the penile lesion in multiple sessions (fixed tissue technique), with microscopic examination of the under surface of each layer until the lesion is completely excised.
- Local recurrences rate of 8- 32% were highly associated with
 - tumor size (3 cm),
 - advanced stage, and
 - failure of previous definitive therapy
- Mohs micrographic surgery best suited for patients with <u>carcinoma in</u> <u>situ or small superficially invasive tumors</u>, with cure rates comparable to partial penectomy.
- Complications include meatal stenosis and glans disfigurement.

3) LASER ABLATION

- Circumcision is generally recommended at the time of laser therapy, if it has not already been done.
- The four most widely used laser energy sources are:

A) CO2:

- skin depth of 0.01 mm
- CO2 laser represents optimal therapy for carcinoma in situ; however, a local recurrence rate of up to 33%

B)Nd:YAG: most commonly used

- depth of penetration of 3 to 6 mm
- for treating small superficial penile lesions.
- local recurrence rate has been approximately 20%

C) KTP lasers:

- intermediate depth of penetration
- better hemostasis than the CO2 laser

DISADVANTAGES OF LASER THERAPY

- tissue for tumor grading and assessment of margins is not provided
- difficulty in determining the exact depth of laser coagulation;
- inability to treat larger lesions; and
- potentially difficult healing in patients who are obese, immunocompromised, or receiving anticoagulation therapy

CONTEMPORARY PENILE AMPUTATION

- Penile amputation remains the standard therapy for patients with deeply invasive or high-grade cancers.
- Partial or total penectomy should be considered in patients with
 - tumors of size 4 cm or more,
 - grade 3 lesions, and
 - those invading deeply into the glans urethra or corpora cavernosa

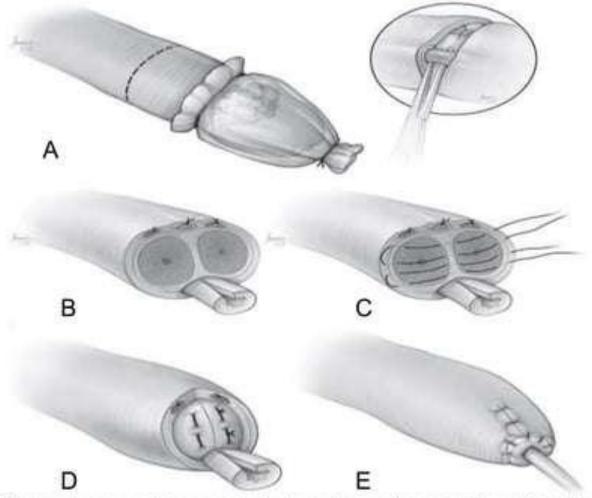
PARTIAL PENECTOMY

- Partial penectomy remains the most common surgical procedure for treatment of the primary tumor in patients with invasive squamous cell carcinoma.
- Successful local control is accomplished in the majority of patients by amputation of the penis at least 2 cm proximal to the tumor.
- Additional goals of the procedure are to preserve the <u>ability to void</u> in a standing position and possibly to allow sexual function.

 Local recurrence rate after partial or total penectomy ranges from 0% to 8%

COMPLICATIONS

- urethral meatal stenosis
- inability to void in upright position
- spraying of the urinary stream
- inadequate sexual function



A, Incision with ligation and division of dorsal penile vessels within Buck fascia (inset). B, Corpora transected and urethra spatulated. C and D, Closure of corpora cavernosa. E, Final closure with construction of urethrostomy.

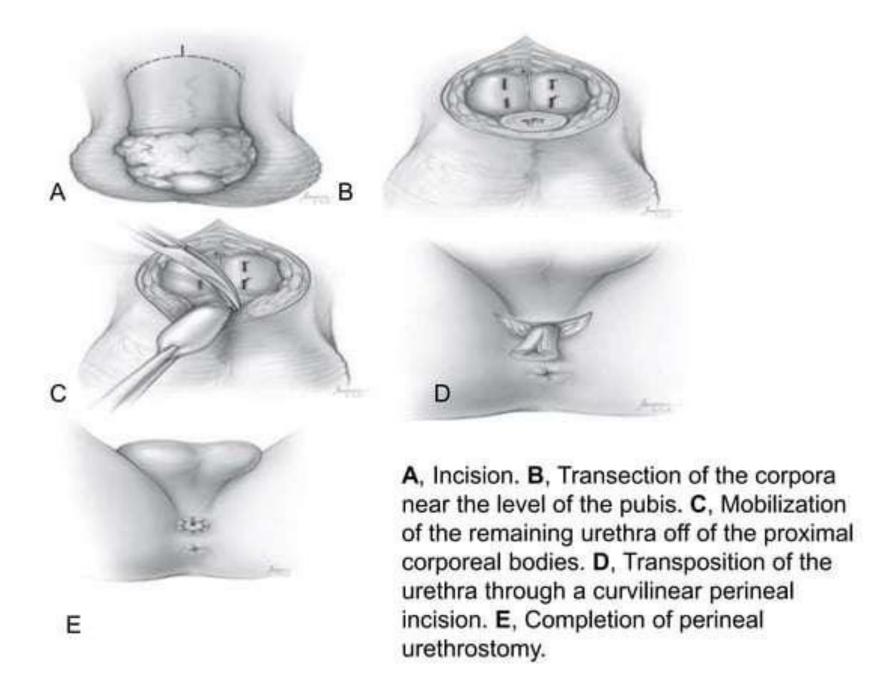


Penile stump after partial penectomy.

TOTAL PENECTOMY

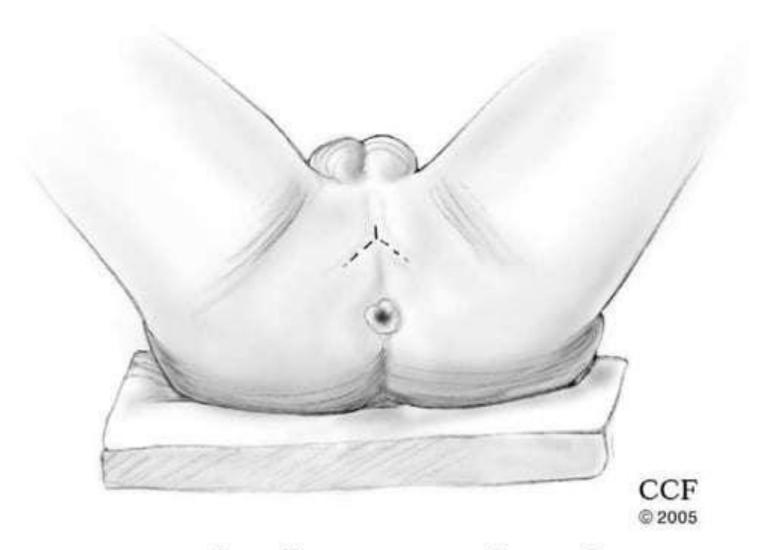
 Total penectomy is a bit of a misnomer, because the penis is amputated at or near the level of the suspensory ligament of the penis without removal of the corpora cavernosa more proximally.

It is indicated for penile tumors whose size or location would not allow excision with an adequate surgical margin and preservation of a remnant sufficient for upright voiding.

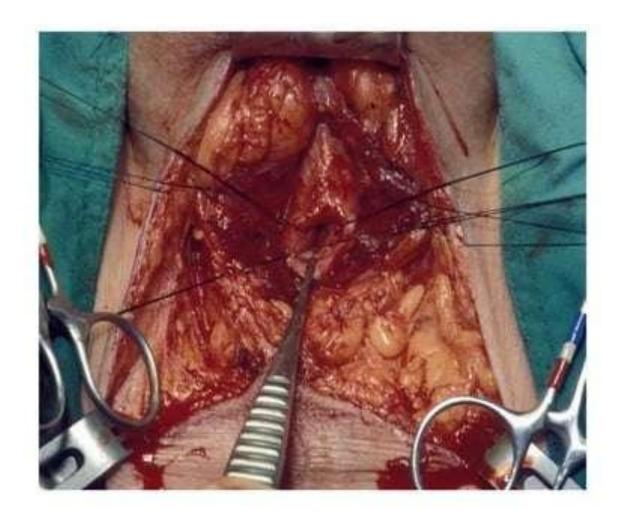




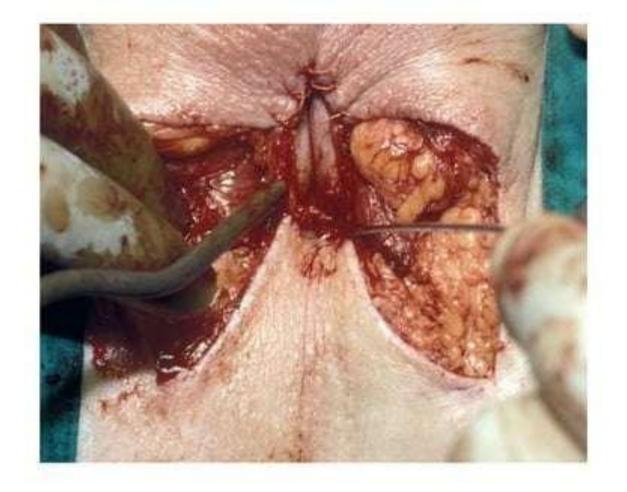
Intraoperative photograph demonstrating the bulbous urethra mobilized dorsally off of the corporeal bodies before transposition. C, proximal corporeal bodies; U, urethra.



Incision for flap perineal urethrostomy.



Ventral urethrotomy incision in the mid- to proximal bulbous urethra.



Perineal flap being sutured into place.



Completed perineal urethrostomy.

TREATMENT OF REGIONAL NODES

INGUINAL ANATOMY

 Inguinal LNs are divided into superficial & deep groups separated by fascia lata of thigh.

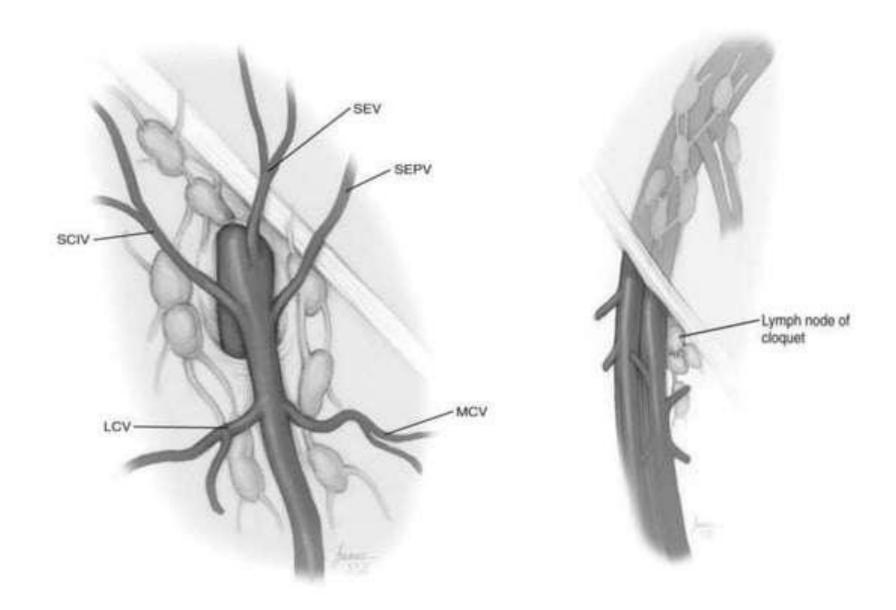
Superficial group

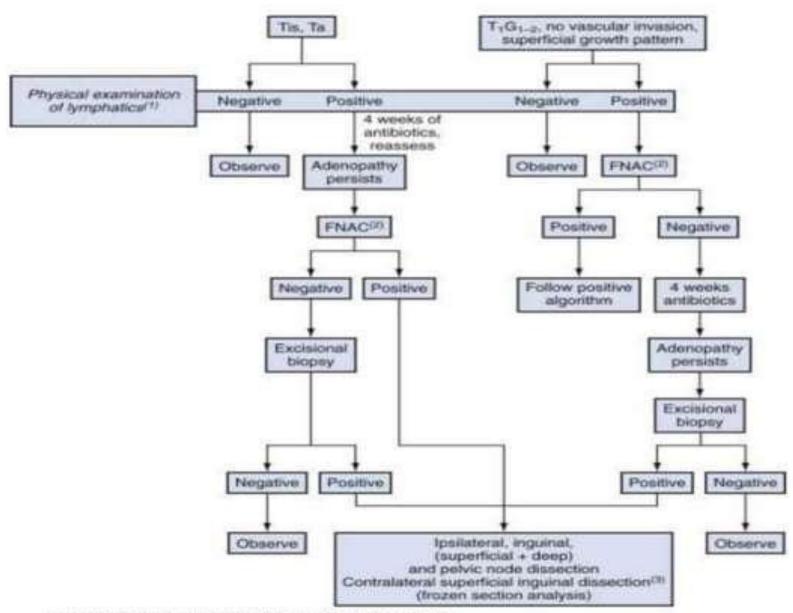
- composed of 4–25 LNs
- Five anatomic group :
 - 1) central nodes arnd SFJ
 - 2) superolateral nodes arnd sup. Circumflex vein
 - 3) inferolateral nodes arnd lat. Femoral cut. V.
 - 4) superomedial nodes arnd sup. Ext. pudendal v.
 - 5) inferomedial nodes arnd gr.saphenous v.

Deep group:

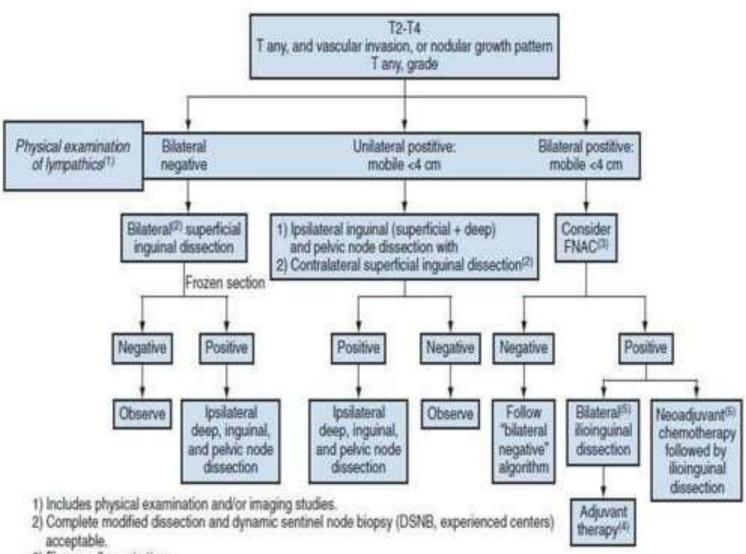
- lie medial to Femoral V. in femoral canal
- node of Cloquet is most cephalad of the group

External iliac LNs receive drainage from the deep inguinal, obturator and hypogastric groups and drain to common iliac and para-aortic nodes.

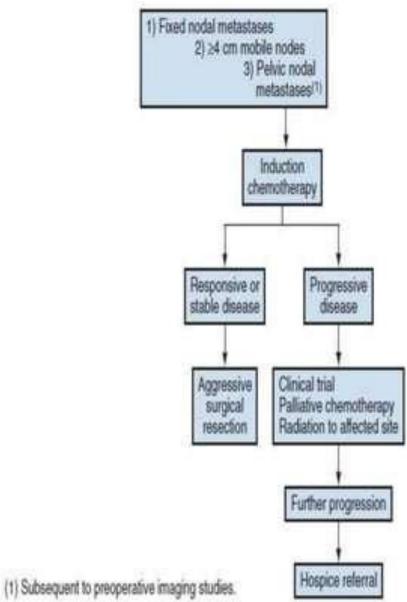




- Includes physical examination and/or imaging studies.
- Fine needle aspiration cytology.
- Complete modified dissection and dynamic sentinel node biopsy (DSNB, experienced centers) acceptable.



- 3) Fine needle aspiration.
- Consider if >2 positive lymph nodes, or bilateral metastases, extranodal extension of cancer, or positive pelvic lymph nodes.
- Either approach is acceptable.



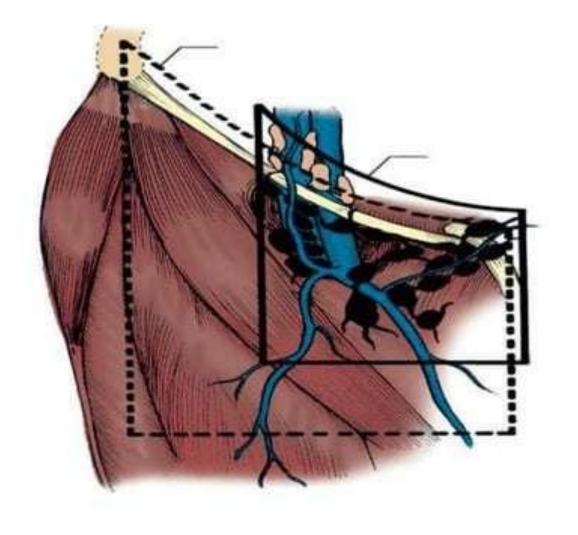
RADICAL ILIOINGUINAL LYMPHADENECTOMY

INDICATIONS

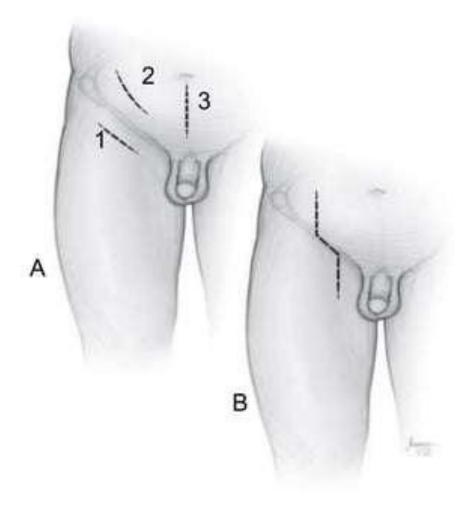
- resectable metastatic adenopathy
- may be curative when the disease is limited to the inguinal nodes
- as a palliative procedure in patients with documented inguinal metastasis who are fit for surgery.

PROCEDURE

- The procedure is carried out 4 to 6 weeks after surgical treatment of the primary tumor.
- Antibiotics are administered during this time.
- The inguinofemoral dissection is designed to cover an area outlined superiorly by a line drawn from the superior margin of the external ring to the anterior superior iliac spine, laterally by a line drawn from the anterior superior iliac spine extending 20 cm inferiorly, and medially by a line drawn from the pubic tubercle 15 cm down the medial thigh.

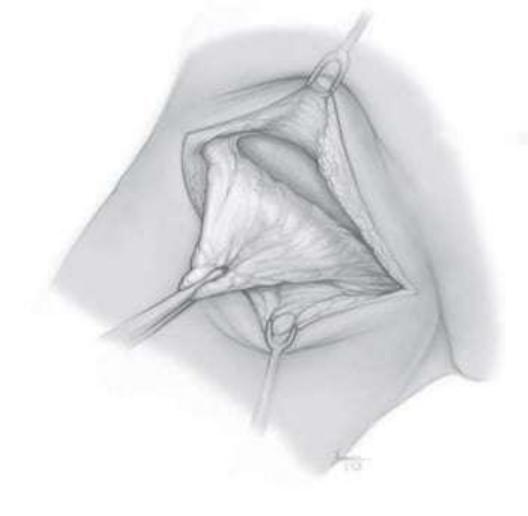


Limits of standard and modified groin dissection



Ilioinguinal lymph node dissection. **A**, Incisions for inguinofemoral lymph node dissection (1), unilateral pelvic lymph node dissection (2), and bilateral pelvic lymph node dissection (3). **B**, Single-incision approach for ilioinguinal lymph node dissection.

- an oblique incision approximately 3 cm below and parallel to the inguinal ligament and extending from the lateral to the medial limit of the dissection
- Superior and inferior skin flaps are developed in the plane just below the Scarpa fascia.
- The superior flap is elevated cephalad to a point 4 cm above the inguinal ligament, and the inferior flap to the limit of the dissection.
- The fat and areolar tissues are dissected from the external oblique aponeurosis and the spermatic cord to the inferior border of the inguinal ligament, forming the superior boundary of the lymph node packet

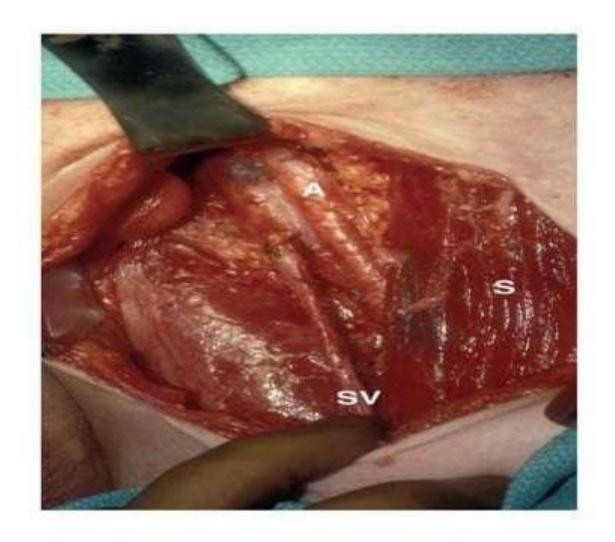


Initial dissection for radical inguinofemoral lymph node dissection with exposure of superior border defined by the external oblique fascia.

- The inferior angle of the inguinofemoral exposure is at the apex of the femoral triangle, where the long saphenous vein is identified and divided
- The saphenous vein is divided at the saphenofemoral junction, and the dissection is continued superiorly to include the deep inguinal nodes medial and lateral to the femoral vein until continuity with the pelvic dissection is attained at the femoral canal.

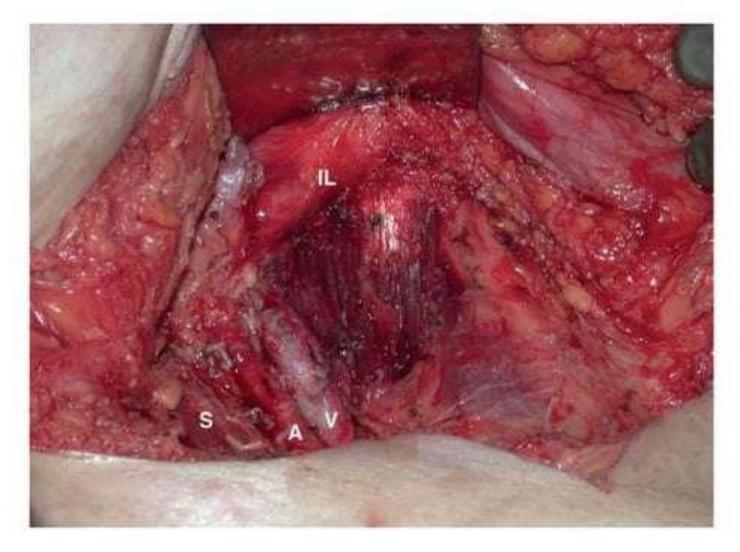


Inferior dissection during radical inguinofemoral lymph node dissection with removal of lymph node packet from the inferior border of the femoral triangle. After further lateral and medial dissection, the packet will remain in continuity with the pelvic dissection in the area of the femoral canal.

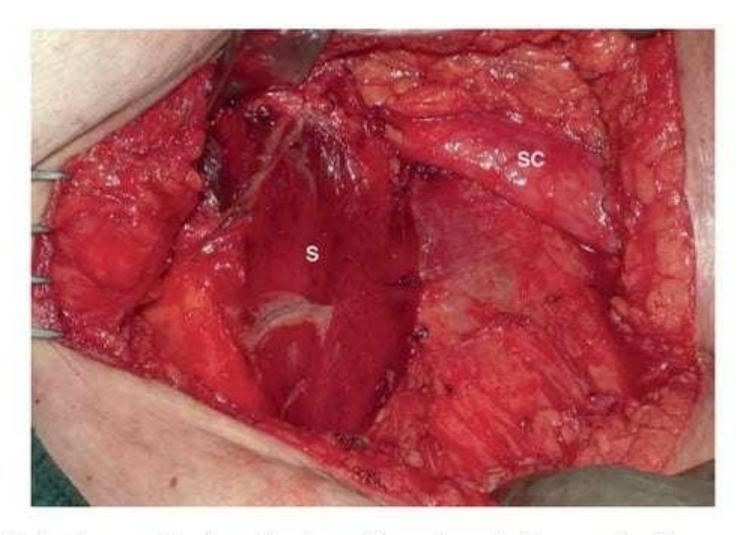


Intraoperative photograph after saphenous-sparing, radical, left inguinofemoral lymph node dissection. A, femoral artery; S, sartorius muscle; SV, saphenous vein.

- After the femoral triangle is dissected, the sartorius muscle is mobilized from its origin at the anterior superior iliac spine and either transposed or rolled 180 degrees medially to cover the femoral vessels.
- The muscle is sutured to the inguinal ligament superiorly, and its margins are sutured to the muscles of the thigh immediately adjacent to the femoral vessels.
- The femoral canal is closed, if necessary, by suturing the shelving edge of the inguinal ligament to the Cooper's ligament



Intraoperative photograph after right radical inguinofemoral lymph node dissection in an obese patient. A, femoral artery; IL, inguinal ligament; S, sartorius muscle; V, femoral vein



Sartorius muscle after detachment from the anterior superior iliac spine and 180-degree rotation medially, with suture fixation to the fascia of the inguinal ligament and the adductor longus. S, sartorius muscle; SC, spermatic cord.

- Closed-suction drains are placed under the subcutaneous tissue and brought out inferiorly.
- During closure, the skin flaps are sutured to the surface of the exposed musculature to decrease dead space.
- The skin is closed with absorbable subcutaneous sutures and staples.
- The patient is maintained at bed rest for 2 or 3 days, and pneumatic compression stockings are used.
- The drains are removed after 5 to 7 days, when drainage is less than 30 to 40 mL/day.
- Compression stockings are recommended postoperatively.
 - suppressive dose of a cephalosporin for 2 mths

- Pelvic lymphadenectomy should include the distal common iliac, external iliac, and obturator nodes.
- No further benefit is gained from proximal iliac or para-aortic dissection.

COMPLICATIONS

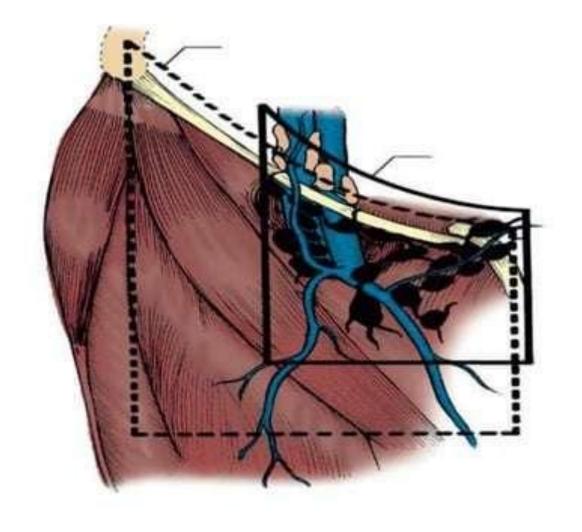
- seroma
- lymphocele
- wound infection or necrosis,
- lymphedema.
- debilitating lymphedema,
- flap necrosis
 occur in 5% to 21% of cases

MODIFIED INGUINAL LYMPHADENECTOMY

Key aspects of the procedure are

- (1) shorter skin incision,
- (2) limitation of the dissection by excluding the area lateral to the femoral artery
- (3) preservation of the saphenous vein, and
- (4) elimination of the need to transpose the sartorius muscle.

- Primary use of modified inguinal lymphadenectomy currently is in patients with a primary tumor that places them at increased risk for inguinal metastasis and <u>clinically negative groins on examination</u> (stage T2 or greater, presence of vascular/lymphatic invasion, or high grade).
- If nodal metastasis is detected on frozen-section examination of the specimen, the procedure is converted to a standard extended lymphadenectomy.
- The false-negative rate for this procedure, in terms of detecting inguinal metastatic disease, ranges from 0% to 5.5%



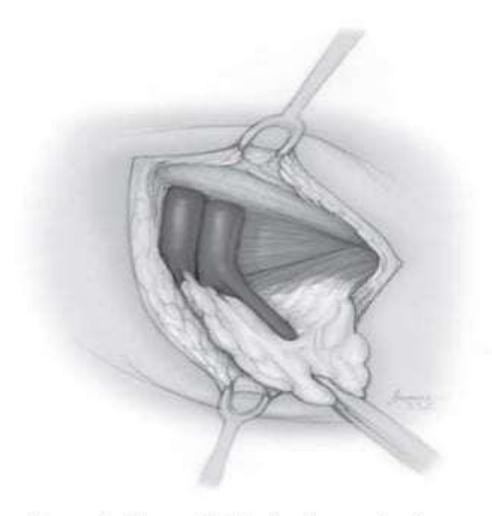
Limits of standard and modified groin dissection

PROCEDURE

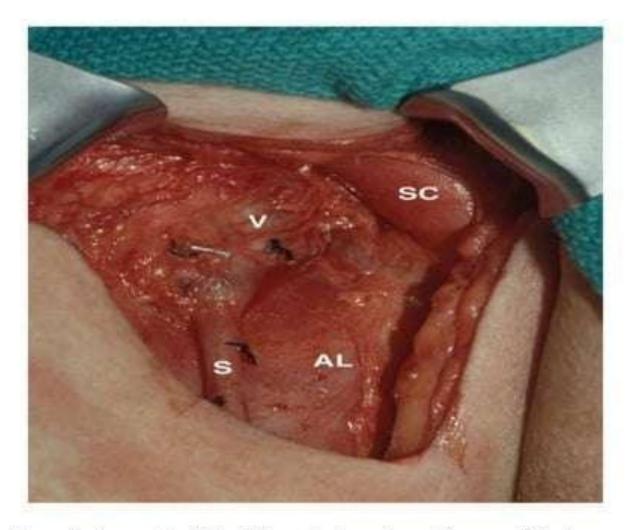
- The procedure begins by placing the patient into a frog-legged position.
- A 10-cm skin incision is made approximately 1.5 to 2 cm below the inguinal crease.
- Skin flaps are developed in the plane just beneath the Scarpa fascia for a distance of 8 cm superiorly and 6 cm inferiorly.
- The superior dissection is carried to the level of the external oblique fascia with exposure of the spermatic cord.

- Dissection commences in a caudad direction with removal of the superficial and deep inguinal nodes, with the boundaries consisting of the adductor longus muscle medially and the femoral artery laterally.
- The saphenous vein is identified and preserved, although a number of branches draining into it will need to be sacrificed.

 A closed-suction drain is placed, and the incision is closed in standard fashion.



Lymph node packet is medial to the femoral artery and includes superficial and deep inguinal nodes.



Intraoperative photograph of right inguinal region after modified lymphadenectomy. AL, adductor longus; S, saphenous vein; SC, spermatic cord; V, femoral vein.

COMPLICATIONS

- seroma (25% to 27%),
- lymphorrhea (9% to 10%), and
- wound infection or skin necrosis (0% to 9%).
- Temporary lower extremity edema 20%
- Flap necrosis

FOLLOW-UP FOR PATIENTS WITH NO EVIDENCE OF INGUINAL ADENOPATHY WHO DO NOT UNDERGO INITIAL LYMPHADENECTOMY

YEAR		Interval	
		Low-Risk Group*	High-Risk Group†
	1-2	3 months	2 months
	3	4 months	3 months
+	4	6 months	6 months
	5+	Annually	Annually

- *Tis, Ta, and T1, grade 1 or grade 2; no vascular invasion with superficial growth pattern.
- †T1, grade 2 with nodular growth or stage T2 or higher, grade 3, with vascular invasion.

CHEMOTHERAPY

INDICATIONS

- Advanced penile cancer presenting as either bulky or unresectable regional disease or
- visceral metastases at initial presentation or
- disease recurrence
- cis platin 5FU, VMB, CMB.
- Adjuvant following RLND, 82% 5 yr survival.
- Neo adjuvant, fixed inguinal nodes, 56% resectable & 31% cured.
- Advanced disease, 32% response rate, 12% Rx related deaths.

RADIOTHERAPY

PRIMARY TUMOR

- EBR, response rate 56%, failure 40%.
- Brachytherapy, response rate 70%, failure 16%.
- Tumor size < 4 cm.</p>

Complications

telengiectasia >90%, meatal stenosis 30%, urethral strictures / fistula 35%, penile necrosis. pain, and edema

Prophylaxis

 NOT recommended. (fails to prevent mets, morbidity, difficult to follow)

Neo adjuvant

can render fixed nodes operable.

<u>Adjuvant</u>

- may be used to reduce local recurrence.
- Radiation to the inguinal area is not as effective as surgery for treatment of the inguinal nodes.

NONSQUAMOUS PENILE MALIGNANT NEOPLASMS

BASAL CELL CARCINOMA

- Rare
- highly curable variant with low metastatic potential
- Treatment is by local excision, which is virtually always curative.



MELANOMA

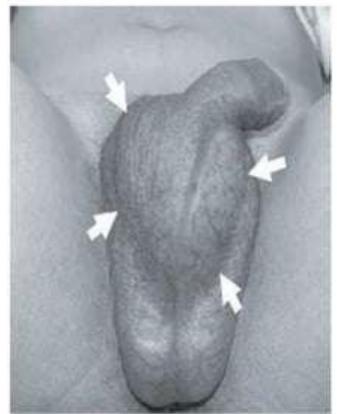
- Melanoma presents as a blue-black or reddish brown pigmented papule, plaque, or ulceration on the glans penis.
 - It occurs on the prepuce less frequently.
 - Surgery is the primary mode of treatment;
- Radiation therapy and chemotherapy are of only adjunctive or palliative benefit.
- Bilateral modified inguinal lymph node dissections in all patients with lesions that are Breslow depth 1 mm or greater, with ulceration, or with Clark level IV or V involvement.



superficial spreading melanoma (large arrowheads), melanoma in situ (arrow), and two areas of possible melanosis (small arrowheads).

SARCOMAS

- Malignant lesions were found more frequently on the proximal shaft (see Fig. 34-6C);
- benign lesions were more often located distally.
- The most common malignant lesions were those of vascular origin (hemangioepithelioma), followed in frequency by those of neural, myogenic, and fibrous origin
 - Surgery treatment of choice
 - Local recurrences are characteristic of sarcomas



EXTRAMAMMARY PAGET DISEASE

It appears grossly as an erythematous, eczematoid, well-demarcated area that cannot be clinically distinguished from erythroplasia of Queyrat, Bowen disease, or carcinoma in situ of the penis.



- On microscopic examination, identification is clearly made by the presence of large, round or oval, clear-staining hydropic cells with hypochromatic nuclei (i.e., Paget cells).
- In most cases only the skin and dermis must be resected with a gross margin of up to 3 cm.

METASTASES

- bladder, prostate, and rectum
- The most frequent sign of penile metastasis is priapism; penile swelling, nodularity, and ulceration have also been reported
- Prognosis is poor, and therapy should be directed toward the primary tumor's histology or local palliation is advised.
- Successful treatment may occasionally be possible in the case of solitary nodules or localized distal penile involvement if complete excision by partial amputation succeeds in removing the entire area of malignant infiltration

