Tumors of the Penis

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Carcinoma in Situ

Carcinoma in situ (Tis) of the penis is called *erythroplasia of Queyrat* by urologists and dermatologists if it involves the glans penis and prepuce or Bowen disease if it involves the penile shaft or the remainder of the genitalia or perineal region.

The erythroplasia of Queyrat 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. Progression to invasive carcinoma can occur in 10% to 33% of patients.

Bowen disease is characterized by sharply defined plaques of scaly erythema on the penile shaft. Crusted or ulcerated variants can occur. If it is not treated, then invasive carcinoma may arise in about 5% of patients. When all cases of carcinoma in situ are considered, metastasis is extremely rare but has been repor

TREATMENT:

Cancer eradication with organ-preserving strategies is the goal of therapy.

Treatment is based on proper histopathologic confirmation of malignancy with multiple biopsies of adequate depth to rule out invasion. When lesions are located on the foreskin, circumcision or excision with a 5-mm margin is adequate for local control.

In this regard, lesions on the glans penis are difficult to treat by excisional strategies while maintaining normal penile anatomy. Alternative strategies include topical 5-fluorouracil cream, 5% imiquimod cream and ablation with the neodymium:yttrium-aluminum-garnet (Nd:YAG), potassium titanyl phosphate (KTP) 532-nm, or carbon dioxide lasers.

Such strategies have been shown to produce excellent cosmetic and functional results.

Radiation therapy can be used to treat tumors that are resistant to topical treatment, especially among patients who are not surgical candidates.

INVASIVE CARCINOMA PENIS

- In urban India, the incidence of penile cancer ranges from 0.7-2.3 cases per 100,000 men.
- In rural India, the rate of penile cancer is 3 cases per 100,000 men, accounting for more than 6% of all malignancies in this population.
- The lowest incidence is in Jewish men born in Israel with rates close to zero.
- The incidence of carcinoma of the penis varies according to circumcision practice, hygienic standard, phimosis, number of sexual partners, HPV infection, exposure to tobacco products.
- Penile cancer is most frequent in the sixth decade of life

- Neonatal circumcision has been well established as a prophylactic measure that virtually eliminates the occurrence of penile carcinoma because it eliminates the closed preputial environment where penile carcinoma develops.
- Phimosis is found in 25% to 75% of patients described in most large series. Adult circumcision appears to offer little or no protection from subsequent development of the disease. Male circumcision has also been shown to be effective against HIV type 1 (HIV-1) infection.
- There was no protective effect of circumcision for other sexually transmitted diseases

In contrast, HPV types 16,
18, 31, and 33 are associated with in situ and invasive carcinomas (Wiener and Walther, 1995). HPV-16 appears to be the most frequently detected type in primary carcinomas and has also been detected in metastatic lesions.

all forms of tobacco
products, including cigarettes, chewing tobacco, and snuff, were significantly and independently related to the incidence of penile Cancer.

Penile trauma may be another risk factor for penile cancer. The development of carcinoma in the scarred penile shaft after mutilating circumcision has been reported as a distinct entity (Bissada et al, 1986). Furthermore, Maden and colleagues (1993) found a greater than threefold risk of penile cancer in men with penile tears and rashes.

Lichen Sclerosus (also known as **Balanitis Xerotica Obliterans**) is a risk factor for the development of penile cancer. There is incidence of cancer with long-term follow-up to be between 2.3% and 9% of men with LS.

Male lichen sclerosus (LS) (balanitis xerotica obliterans), a genital variation of lichen sclerosus et atrophicus, manifests as a whitish patch on the prepuce or glans, often involving the meatus and

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Modes of Presentation

- It is the penile lesion itself that usually alerts the patient to the presence of penile cancer. The presentation ranges from a relatively subtle induration or small excrescence to a small papule, pustule, warty growth, or more luxuriant exophytic lesion. Phimosis may obscure a lesion and allow a tumor to progress silently. Eventually, erosion through the prepuce, foul preputial odor, and discharge with or without bleeding call attention to the disease.
- Penile tumors may arise anywhere on the penis but occur most commonly on the glans (48%) and prepuce (21%). Other tumors

Biopsy

Confirmation of the diagnosis of carcinoma of the penis and assessment of the depth of invasion, the presence of vascular invasion, and the histologic grade of the lesion by microscopic examination of a biopsy specimen are mandatory before the initiation of any therapy.

- **Memorial Sloan Kettering Cancer Center classified the histologic types as follows: usual type, 59% of cases; papillary, 15%; basaloid, 10%; warty (condylomatous), 10%; verrucous, 3%; and sarcomatoid, 3%.**
- **Squamous cell carcinomas have classically been graded using the Broders classification to define the level of differentiation on the basis of keratinization, nuclear pleomorphism, number of mitoses, and several other features.**
- **Low-grade lesions (grade 1 and grade 2) constitute 70% to 80% . Almost half the tumors originating in the shaft are poorly differentiated (grade 3 and grade 4, depending on scale), whereas only 10% of tumors located in the prepuce are high-grade tumors.**
- **Vascular invasion and Perineural invasion are strong predictor of lymph node**

Radiologic Studies

Primary Penile Tumor.

In patients with penile cancer both the primary tumor and the inguinal lymph nodes are readily assessed by palpation.

Penile ultrasonography: USG can not differentiate between glanular stage T1 vs. glanular stage T2).

However, the tunica albuginea separating the corpus cavernosum from the glans was easily identified in all patients, and the sensitivity for detecting corpus cavernosum invasion was 100%.

Thus, for small-volume glanular lesions, imaging studies add virtually no additional information to palpation in most patients. However, for lesions thought to invade the corpus cavernosum, contrast-enhanced MRI (perhaps augmented with artificial erection) may provide unique information, especially when physical examination findings are equivocal and organ-sparing techniques are being considered.

Inguinal and Pelvic Region

Current Imaging Strategies among Clinical Node–Negative Patients.

CT has often been the imaging modality chosen in penile cancer to examine the inguinal and pelvic areas as well as to rule out more distant metastases. However, **CT and lymphangiography offer no useful additional information over physical examination, especially in patients with no palpable adenopathy.**

- Physical examination of the inguinal region remains the clinical gold standard for evaluating the presence of metastasis in the nonobese patient.
- CT or MRI can be useful in evaluating the inguinal region of obese patients and in those who have had prior inguinal surgery.
- Among patients with proven inguinal metastases, CT scan of the abdomen and pelvis may help to determine those patients with poor prognostic features for cure with surgery alone.
- PET/CT may be useful among patients with clinically detected inguinal metastases to define the presence of pelvic or distant metastasis.

T Category	T Criteria
TI	Glans: Tumor invades lamina propria. Foreskin: Tumor invades dermis, lamina propria, or dartos fascia. Shaft: Tumor invades connective tissue between epidermis and corpora regardless of location. All sites with or without lymphovascular invasion or perineural invasion and is or is not high grade.
T Ia	Tumor is without lymphovascular invasion or perineural invasion and is not high grade (i.e., grade 3 or sarcomatoid).
T lb	Tumor exhibits lymphovascular invasion and/or perineural invasion or is high grade (i.e.. grade 3 or sarcomatoid).
T2	Tumor invades into corpus spongiosum (either glans or ventral shaft) with or without urethral invasion.
T3	Tumor invades into corpora cavernosum (including tunica albuginea) with or without urethral invasion.
T4	Tumor invades into adjacent structures (i.e. scrotum, prostate, pubic bone)

Definition of Regional Lymph Node (N)

Clinical N (cN)

cN Category	cN Criteria
cNX	Regional lymph nodes cannot be assessed.
cN0	No palpable or visibly enlarged inguinal lymph nodes.
cN1	Palpable mobile unilateral inguinal lymph node.
cN2	Palpable mobile > 2 unilateral inguinal nodes or bilateral inguinal lymph nodes.
cN3	Palpable fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral.

Pathological N (pN)

pN Category	pN Criteria
pNX	Lymph node metastasis cannot be established
pN0	No lymph node metastasis
pN1	<2 unilateral inguinal metastases, no ENE
pN2	>3 unilateral inguinal metastases or bilateral metastases
pN3	ENE of lymph node metastases or pelvic lymph node metastases

Total Number of Lymph Nodes Removed

Total number of lymph nodes removed may serve as an index of the quality of surgical care for penile cancer and was shown by Johnson, et al., in a population-based study to be associated with enhanced 5 year survival when eight or more lymph nodes were removed, compared with having fewer than eight nodes removed

BOX 37-1 Minimal Diagnostic Criteria for Carcinoma of the Penis

PRIMARY TUMOR (T)

Clinical examination

Incisional-excisional biopsy of lesion (or complete resection) and histologic examination for grade, anatomic structure invaded, and presence of vascular invasion

REGIONAL AND JUXTAREGIONAL LYMPH NODES (N)

Clinical examination

CT, if inguinal adenopathy is palpable*

CT/PET may be considered for bulky inguinal adenopathy†

Superficial inguinal node dissection or dynamic sentinel node biopsy (as indicated for high grade, vascular invasion, or invasive histologic pattern)

Aspiration cytology (as indicated)

DISTANT METASTASES (M)

Clinical examination

Biochemical determinations (liver functions, calcium)

CT scan of the chest, abdomen, pelvis; bone scintigraphy; or CT/PET scan (as indicated)

TABLE 37-2 Treatment of the Primary Penile Tumor

STAGE	TREATMENT
Tis (glans)	Laser therapy, glans resurfacing; alternative: topical therapy
Ta, Tis (foreskin, shaft skin)	Surgical excision to achieve negative margin; alternatives: laser therapy, topical therapy (Tis only)
Ta, T1 grade 1-3 (glans)	Therapy based on size and position of lesion as well as potential side effects, excision, glans resurfacing procedures, glansectomy, radiotherapy (not indicated for Ta)
Ta, Tl grade 1-3 (foreskin, shaft)	Complete surgical excision to achieve negative margin
T2 (glans) without gross cavernosum involvement	Total glansectomy with or without corpora cavernosa transection to achieve negative surgical margins, partial penectomy, radiotherapy
T2 (corporeal invasion), T3	Partial or total penectomy
T4 (adjacent structures)	Consider neoadjuvant chemotherapy with surgical consolidation for responding patients if baseline resectability is a concern
Local disease recurrence after conservative therapy	Complete surgical excision to achieve negative surgical margins; may require partial or total penectomy; select patients with superficial low-grade recurrences may be candidates for repeat penile-conserving procedure
Radiotherapy	Select patients with T1-T2 tumors involving glans, coronal sulcus <4 cm

Historical teaching proposes a 2-cm macroscopic excision margin from the tumour edge.

Organ sparing surgical techniques have been developed to preserve penile tissue, through localized excision and penile reconstruction.

However, oncological control is paramount in these patients. A 5 mm margin is required for G1 and G2 lesions whereas 10 mm margin is adequate for G3 tumors.

Minimum penile stump length for directing penile stream and intercourse should be atleast 2.5 cm.

Techniques to lengthen the penile stump after partial penectomy:

1. Division of suspensory ligaments of the penis
2. Mobilization of corpora proximally from pubic arch
3. V-Y plasty at the penopubic junction
4. Z-plasty at the penoscrotal junction

PRINCIPLES OF SURGERY

Penectomy

- Partial penectomy should be considered the standard for high-grade primary penile tumors, provided that a functional penile stump can be preserved and negative margins are obtained. If a partial penectomy is not possible, a total penectomy should be performed.
- Partial or total penectomy when invasion into the corpora cavernosum is necessary to achieve a negative margin.
- Intraoperative frozen sections are recommended to determine negative margins.

Surgical Management of Inguinal and Pelvic Lymph Nodes

Standard or modified ILND or DSNB is indicated in patients with penile cancer in the absence of palpable inguinal adenopathy if high-risk features for nodal metastasis are seen in the primary penile tumor:

Lymphovascular invasion

≥pT1G3 or ≥T2, any grade

>50% poorly differentiated

DSNB is only recommended if the treating physician has experience with this modality.

If positive lymph nodes are found on DSNB, ILND is recommended.

PLND should be considered at the time or following ILND in patients with ≥2 positive inguinal nodes on the ipsilateral ILND site or in the presence of extranodal extension on final pathological review.

A bilateral PLND should be considered either at the time or following ILND in patients with ≥4 positive inguinal nodes (in total among both sides).1

Organ Preservation

Surgical amputation of the primary tumor remains the oncologic gold standard for rapid definitive treatment of the penile primary tumor; local recurrence rates range from 0% to 8%.

Patients with penile primary tumors exhibiting favorable histologic features (stages Tis, Ta, T1; grade 1 and grade 2 tumors) are at a lower risk for metastases.

These patients are also best suited for organ-sparing or glans sparing procedures.

Circumcision and Limited Excision Strategies

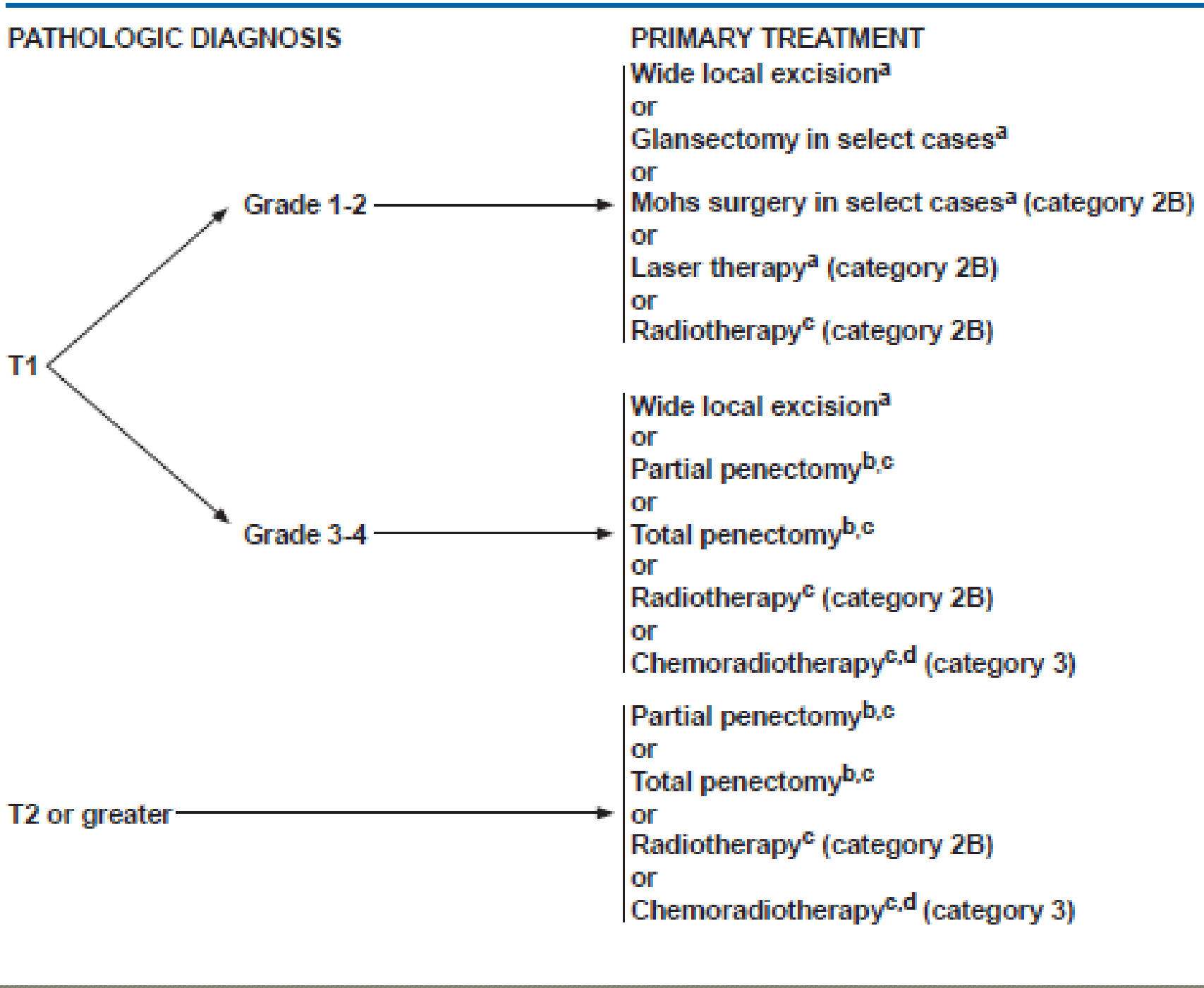
- *Mohs Micrographic Surgery*
- *Laser Ablation*

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 exhibiting adverse features for cure by organ preservation strategies. These are consistently associated with tumors of size 4 cm or more, grade 3 lesions, and those invading deeply into the glans urethra or corpora cavernosa.

Local recurrence rates overall after organ preservation are higher than with traditional amputation; however, when

local recurrences are detected and treated, early survival does not appear be adversely affected.


PATHOLOGIC DIAGNOSIS
PRIMARY TREATMENT
T1
Grade 1-2
Wide local excision[a]
or
Glansectomy in select cases[a]
or
Mohs surgery in select cases[a] (category 2B)
or
Laser therapy[a] (category 2B)
or
Radiotherapy[c] (category 2B)
Grade 3-4
Wide local excision[a]
or
Partial penectomy[b,c]
or
Total penectomy[b,c]
or
Radiotherapy[c] (category 2B)
or
Chemoradiotherapy[c,d] (category 3)
T2 or greater
Partial penectomy[b,c]
or
Total penectomy[b,c]
or
Radiotherapy[c] (category 2B)
or
Chemoradiotherapy[c,d] (category 3)

TREATMENT OF THE INGUINAL NODES

The presence and the extent of metastasis to the inguinal region are the most important prognostic factors for survival in patients with squamous penile cancer.

Contemporary Indications for Inguinal Lymphadenectomy:

Prognostic Significance of the Presence and Extent of Metastatic Disease

Patients proved to have no evidence of inguinal metastases on the basis of histologic examination of the inguinal nodes or repeated normal examination findings over time; the average 5-year survival rate was 73%.

In patients with resected inguinal metastases the 5-year survival averaged 60%.

Patients with minimal nodal metastases (usually two or less) exhibited 5-year survivals that ranged from 72% to 88% compared with 0% to 50% when a greater degree of nodal involvement was present.

Finally, pelvic lymph node involvement has been a particularly ominous finding with respect to long-term survival; the combined results of several small series reveal an average 5-year survival of 14% when pelvic nodal metastases are present.

Taken together, these data suggest that the pathologic criteria associated with long-term survival after attempted curative surgical resection of inguinal metastases (i.e., 80% 5-year survival) include minimal nodal disease (up to two involved nodes in most series), unilateral involvement, no evidence of ENE of cancer, and absence of pelvic nodal metastases.

Presence of Palpable Adenopathy as a Selection Factor for Inguinal Dissection

It is advantageous to find and to treat nodal metastasis at the earliest possible opportunity.
The presence of palpable adenopathy is associated with proven nodal metastasis in about 43% of cases
on average (range 8% to 64%). In the remainder, lymph node enlargement is secondary to inflammation.
Historically a course of antibiotics was recommended for patients with suspicious nodes to potentially discern metastasis from cancer. However, several authors have raised the issue that this causes a significant delay and could affect survival. Should the fine-needle aspiration result be negative, depending on clinical suspicion, close observation, repeat aspiration, or excisional biopsy is performed.

Evolving Indications for Lymphadenectomy in Patients without Palpable Adenopathy

Various study reveal an improvement in survival for patients undergoing early therapeutic versus delayed therapeutic dissection.

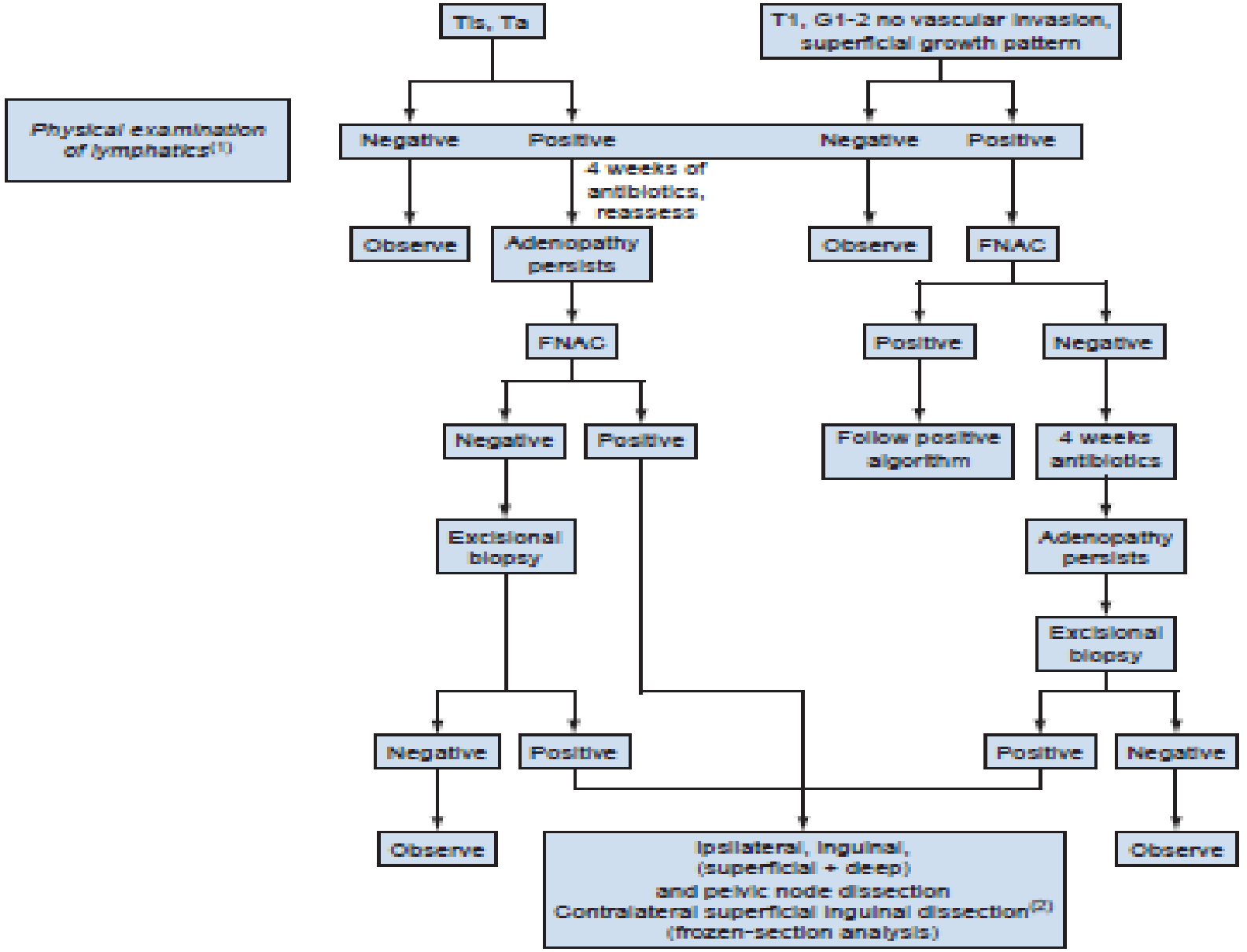
Furthermore, five of the six series show that delayed therapeutic

dissection can rarely salvage patients who experience

Superficial and Modified Complete Inguinal Dissection.

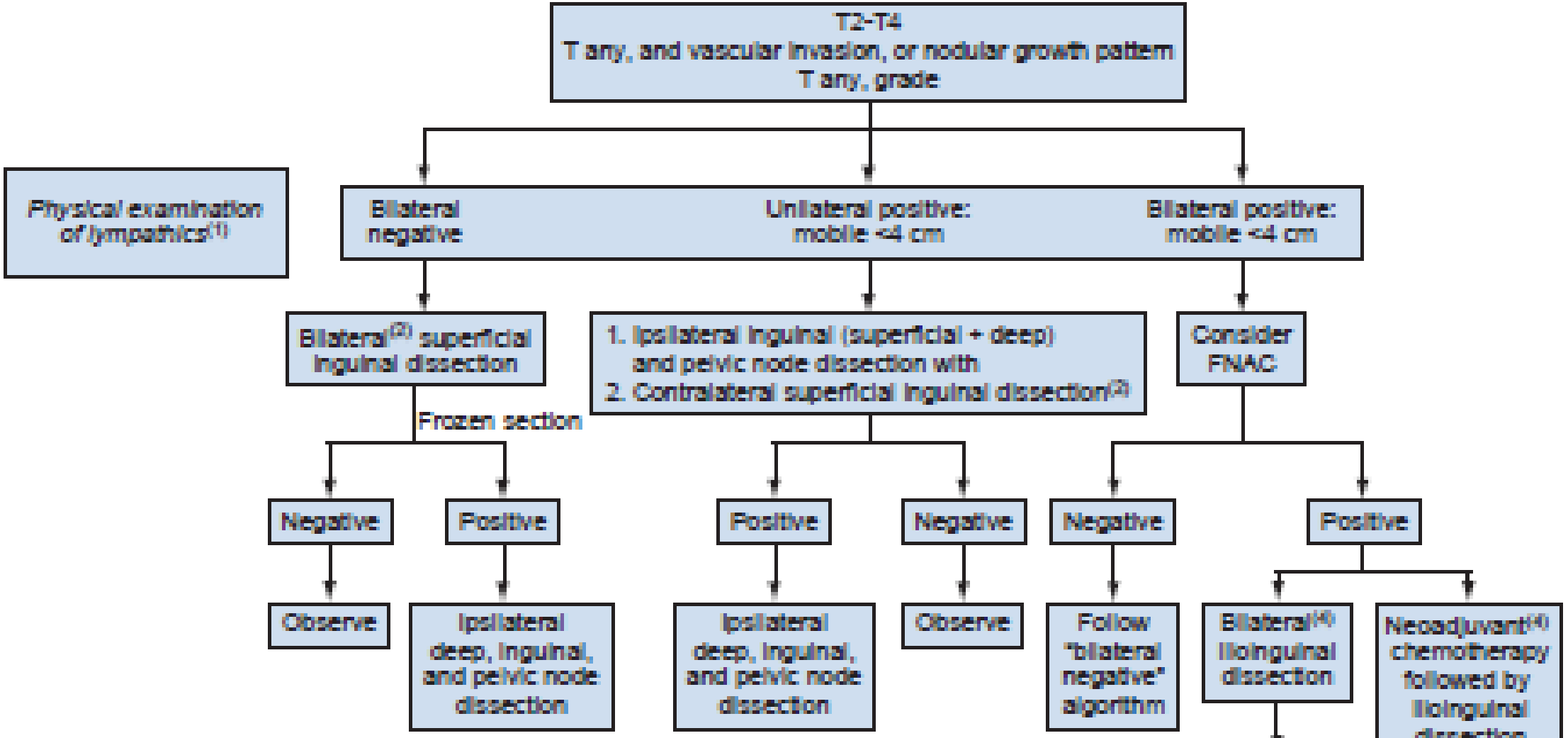
Both superficial inguinal and modified complete dissections have been proposed as staging tools for the patient without palpable inguinal lymphadenopathy. Superficial node dissection involves removal of those nodes superficial to the fascia lata. A complete IILND (removal of those nodes deep to the fascia lata contained within the femoral triangle as well as the pelvic nodes) is then performed if the superficial nodes are positive at surgery by frozen-section analysis. The rationale for superficial dissection is that two series have shown no positive nodes deep to the fascia lata unless superficial nodes were also positive.

Thus, for patients undergoing ILND for curative intent (i.e., in whom preoperative studies reveal no pelvic adenopathy), PLND should routinely be considered in patients with two or more positive inguinal lymph nodes or when extracapsular nodal extension is present. PLND in this setting serves as an effective staging tool for identifying those patients at increased risk for pelvic metastases in whom adjunctive therapy should be considered.



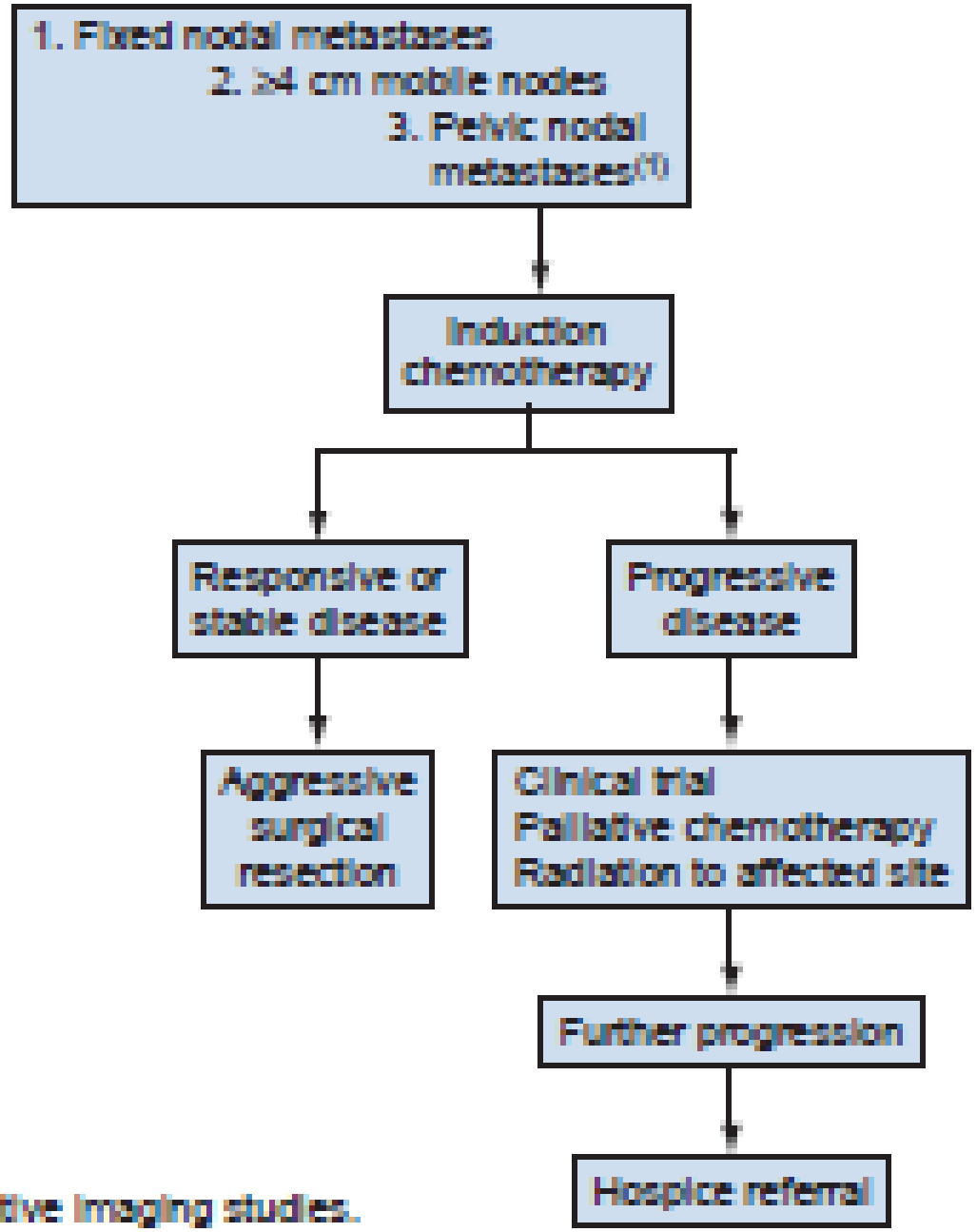
A (1) Includes physical examination and/or imaging studies.
(2) Complete modified dissection and dynamic sentinel node biopsy (experienced centers) acceptable.

Figure 37–4. **Management of regional disease. A, Low-risk patients.**



(1) Includes physical examination and/or imaging studies.
(2) Complete modified dissection and dynamic sentinel node biopsy (experienced centers) acceptable.
(3) Consider if >2 positive lymph nodes, or bilateral metastases, extranodal extension of cancer, or positive pelvic lymph nodes.
(4) Either approach is acceptable.

B



C (1) Subsequent to preoperative imaging studies.

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