Lymphatic Metastases from Pelvic Tumors: Anatomic Classification, Characterization, and Staging

The spread of pelvic tumors to lymph nodes is an important means of tumor dissemination. Nodal metastases have important management and prognostic impact. Pelvic tumors usually metastasize first to regional lymph nodes, which are specific groups of nodes for each tumor, and are classified according to the TNM system as N-stage disease. If a pelvic tumor spreads to a lymph node outside of the defined regional nodes, this is considered M-stage disease, which usually results in upstaging of the disease to overall stage IV cancer and may potentially affect the patient’s treatment options. Knowledge of the regional nodal spread of each tumor is essential in formulating effective search strategies for cross-sectional imaging studies performed for staging. Also important is correct description of the nomenclature of nodal metastases to facilitate proper staging. In this review, the patterns of regional nodal spread and N-stage classification are presented for carcinomas of the anus, bladder, cervix, endometrium, ovary, penis, prostate, rectum, testis, vagina, and vulva. Pelvic lymph node anatomy and nomenclature are reviewed with schematic illustrations and clinical examples from patients with pelvic tumors.

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The diagnosis of pelvic tumor lymphatic metastases represents an important goal and challenge of modern imaging. Nodal metastasis is an important mechanism of tumor dissemination (in addition to hematogenous and direct local-regional spread). Metastasis to lymph nodes has an important impact on the overall stage of each pelvic tumor, on how these patients are treated and on the prognosis for patients with pelvic neoplasia. Depending on anatomic location and tumor origin, the pathways of nodal metastasis and the nodal, or N, stage vary substantially among tumors. In the evaluation of cross-sectional imaging studies for nodal metastases, it is important to be aware of the potential sites of metastasis, the relative likelihood of metastasis to a given node group depending on the specific tumor, and how nodal metastasis affects staging and management. The purposes of this article are to illustrate the anatomic location and the nomenclature of pelvic lymph node groups and to review the patterns of nodal spread from individual pelvic tumors with a description of the effect of the location and number of nodal metastases on staging and management.

### Principles of Nodal Metastasis

To better understand the concept of nodal metastasis from any tumor, including a pelvic tumor, it is worth considering the mechanism of tumor dissemination via the lymphatic system. The lymphatic system represents a complex network that functions by collecting extravasated fluid, macromolecules, and cells of the immune system and then returning them to the blood circulation. This drainage network is lined by endothelial cells and is interspaced by lymph nodes. The network begins in the tissues as a series of blind-ending capillaries that drain into collecting vessels. These collecting vessels return lymph to the systemic blood circulation via the thoracic duct. This system of lymphatic drainage is important in immune mediation because it channels lymphocytes and antigen-presenting cells to lymph nodes. However, this system also functions as an important pathway for tumor dissemination.

There are some unique features of the lymphatic system that facilitate its role in tumor dissemination. Lymphatics are optimally suited to the entry and transport of cells, which facilitates the movement of leukocytes. This feature also assists in the entry of tumor cells into the lymphatic circulation. There are at least four potential reasons for this. First, lymph vessels are larger in caliber than small capillaries. Second, the physical movement of a tumor cell into a lymphatic may be easier than movement into a capillary because lymphatics lack a basement membrane and have fewer intercellular junctions. Third, the flow velocities in lymphatics are an order of magnitude slower than flow in the capillaries of the systemic circulation. Fourth, lymph is similar to interstitial fluid in terms of constituents and chemistry, and this promotes cell viability. Tumor cells are, therefore, subjected to weaker shear forces and lower serum toxicity in the lymphatics than in the hematogenous circulation.

To facilitate the process of tumor metastasis to lymph nodes, growth of the local lymphatic network leading to high lymphatic density can be an important process. There are a number of lymphangiogenic growth factors, the overexpression of which may play a role in the development of a suitable milieu for the migration of tumor cells into the lymphatic system. Of particular importance are the vascular endothelial growth factor (VEGF) family of glycoproteins, which play a role in lymphatic and vascular proliferation. This family includes subtypes A, B, C, and D, as well as VEGF receptors. For example, overexpression of VEGF-C in colorectal cancer significantly correlates with lymphatic vessel invasion, lymphatic vessel density, and lymph node metastases.

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### Essentials

- Metastasis to lymph nodes from pelvic tumors is an important means of tumor dissemination.
- Each pelvic tumor drains to regional lymph nodes, the extent of which is described by the N stage in the TNM system, while metastases outside of the regional nodes are considered M-stage disease.
- The pathway of regional nodal spread and N-stage classification vary considerably among pelvic tumors.
- Knowledge of pelvic nodal anatomy and nomenclature is essential in reviewing staging cross-sectional imaging studies.

### Nodal Anatomy of the Pelvis

An understanding of the location of lymph node groups in the pelvis is essential for formulating an effective treatment plan. The pelvic nodal basin comprises four major lymph node subgroups: iliac, presacral, obturator, and hypogastric nodes. The iliac nodes are located along the iliac vessels and are divided into external and internal iliac nodes. The presacral nodes are located in the retroperitoneal space along the sacral promontory and are divided into superior and inferior presacral nodes. The obturator nodes are located in the obturator fossa and are divided into internal and external obturator nodes. The hypogastric nodes are located in the presacral space and are divided into middle and lateral hypogastric nodes. These nodes play a critical role in the spread of pelvic tumors and are important for staging and treatment planning.

Abbreviations:

- EBRT = external-beam radiation therapy
- FDG = fluorodeoxyglucose

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External Iliac Lymph Nodes

These nodes (Fig 2) are in proximity to the external iliac artery and vein, and the relationship of the nodes to the vessels determines the nomenclature of the subgroups of the external iliac nodes. These nodes are found caudal to the bifurcation of the common iliac vessels and cranial to the inguinal ligament (12). The lateral group is situated lateral to the external iliac artery. The middle subdivision is located medial to the external iliac artery and lateral to the accompanying vein. The medial subgroup applies to nodes in a somewhat variable position, but the nodes are medial to both external iliac vessels. In some cases the medial external iliac lymph node group describes a node group posteromedial to the external iliac vessels. In the latter case, these nodes can be in proximity to the obturator internus muscle and are, therefore, called by some the obturator nodes. Although the subject of some debate, obturator nodes are generally considered to be a part of the medial external iliac node group (12).

Internal Iliac Lymph Nodes

These nodes (Fig 3) are close to the internal iliac vessels, and there are many subdivisions, generally named according to the adjacent vessel. The internal iliac group of nodes is more posterior in the pelvis than are the external iliac nodes. This group includes the lateral sacral nodes, which are close to the paired lateral sacral arteries. Presacral nodes are immediately anterior to the sacrum and posterior to the mesorectal fascia. The anterior internal iliac subdivision is the most anterior of the internal iliac nodes; it is located anteriorly at the origin of the proximal branches of the anterior division of the internal iliac arteries. The term hypogastric nodes is used in a variable way, with some authors using it to describe the most cephalic of the internal iliac nodes (11,13), while others use this term for the entire internal iliac group (9,10).

Inguinal Lymph Nodes

These nodes (Fig 4) are located inferior to the level of the inguinal ligament, and

Figure 1: Common iliac lymph nodes. (a) Axial contrast material–enhanced computed tomographic (CT) image and (b) volume-rendered reformation of contrast-enhanced CT image show locations of named subgroups of common iliac lymph nodes: 1 = lateral, 2 = medial, 3 = middle. The relationship of these node locations to common iliac artery (a) and vein (v) can be seen.

Figure 2: External iliac lymph nodes. (a) Axial contrast-enhanced CT image and (b) volume-rendered reformation of contrast-enhanced CT image show location of named subgroups of external iliac lymph nodes: 1 = lateral, 2 = middle, 3 = medial (including obturator). The relationship of these node locations to external iliac artery (a) and vein (v) can be seen.
inferior to the external iliac node group. They can be subdivided into superficial and deep inguinal nodes (8,10,12). The superficial subgroup lies anterior to the inguinal ligament, the superficial femoral vessels, and the saphenous veins. The deep inguinal lymph nodes are within the femoral sheath and are usually located medial to the common femoral vein.

**Perivisceral Nodes**

In addition to the major node groups described above, there are also nodes immediately adjacent to the pelvic viscera (8). These include the perirectal nodes, which are located in the mesorectal fat and drain along superior hemorrhoidal vessels and then into inferior mesenteric vessels nodes. Perivisceral nodes also include the perivesical (around the bladder) nodes and the periprostatic nodes.

**Criteria for Diagnosis of Nodal Metastasis**

CT and magnetic resonance (MR) imaging are the most commonly used imaging techniques for staging in patients with pelvic malignancies, although other techniques may be used in specific scenarios (eg, endorectal or endoanal ultrasonography in patients with rectal or anal carcinoma). In this section, we will discuss the CT and MR imaging findings that may help predict metastatic involvement of lymph nodes in these patients.

Once a lymph node is visualized in the setting of a patient with a pelvic malignancy, there are a number of potentially useful features to determine if it is involved with tumor or not. However, the sensitivity and specificity of these features on cross-sectional images are modest.

**Size**

There is a fundamental problem with relying on size as a sole criterion for the diagnosis of nodal metastases. The difficulty is the wide variation in size of nonmetastatic lymph nodes, which can substantially overlap with the size of metastatic nodes. In an attempt to establish a normal range for lymph node size, Vinnicombe et al (13) evaluated a group of healthy volunteers with CT with and without bipedal lymphangiography. In that study, the 95th percentiles for normal nodes’ short-axis diameter were 7 mm for internal iliac nodes, 8 mm for obturator nodes, and 10 mm for external iliac nodes. Using MR imaging, Grubnic et al (14) found that the 95th percentile sizes are 6 mm for pelvic nodes and 5 mm for retroperitoneal nodes. To analyze the accuracy of malignant node diagnosis on the basis of size, Hilton et al (15) assessed retroperitoneal nodes in patients with testicular nonseminomatous germ cell cancer. With a criterion of a short-axis diameter larger than 10 mm, the sensitivity for detection of a malignant node was only 37%, but the specificity was 100%. If a criterion of larger than 4 mm was used, then the sensitivity and specificity were 93% and 38%, respectively. In a similar evaluation of size criteria for diagnosis of nodal metastases, Oyen et al (16) found that, on CT images in patients with prostate cancer, a criterion of larger than 6 mm resulted in sensitivity and specificity of
78% and 97%, respectively. Using a threshold of 5-mm short-axis diameter for metastasis (from a variety of pelvic tumors), Fukuda et al (17), demonstrated a sensitivity and specificity, respectively, of 85.7% and 77.8% on a per-patient basis and 54.5% and 84.9% on a hemipelvis basis.

As a result of the suboptimal sensitivity and specificity profile of size criteria, there is a lack of consensus regarding the normal limit for size in the diagnosis of pelvic tumor nodal metastases. In addition, size criteria may be different for different cancers (9). Koh et al (9) recommend the use of a size threshold of 8 mm (short-axis diameter) for pelvic nodes and 10 mm for abdominal retroperitoneal nodes. In the case of testicular cancer, however, an 8-mm retroperitoneal abdominal node is considered “suspicious.” The need for specific size criteria for different types of cancer is illustrated, for example, by the lymph node metastases in rectal cancer: Almost 60% of the metastatic inguinal nodes of approximately 10 mm. This highlights both the limitations of using size criteria alone for nodal staging and the importance of knowledge of regional nodal drainage pathways.

**Shape**

The shape of lymph nodes can also be a helpful diagnostic feature. A normal lymph node has a fatty hilum and is an oblong kidney-bean–shaped structure. It ordinarily has a smooth outline except for small vessels at the hilum of the node. Loss of this normal morphology may occur in the presence of metastatic disease. In a study of patients with gastric cancer, Fukuya et al (21) found that nodes with a higher short-axis-to-long-axis ratio (more round than oblong) were more likely to be malignant. In that study, the mean short-axis-to-long-axis ratio of malignant nodes was 0.81, compared with 0.57 for benign nodes. In addition to the loss of normal elongated shape, the smoothness of the margin of a lymph node should also be studied. In patients with rectal cancer, for example, Brown et al (18) demonstrated that nodes with an irregular border were more likely to be involved by tumor.

**Internal Architecture**

In addition to the finding of an irregular outline in abnormal nodes, Brown et al (18) also found that a greater number of malignant nodes exhibit signal intensity heterogeneity on T2-weighted MR images, as compared with benign nodes (18). The finding of preservation of the normal fatty hilum indicates a more likely benign node (9). On CT images, central necrosis in a node, although not specific, can be seen with metastatic involvement (22).

**Recommended Approach**

Despite the multiple attempts to provide morphologic and size criteria to differentiate benign from malignant lymph nodes on cross-sectional imaging studies, none of these alone has demonstrated sufficient diagnostic accuracy because of the substantial overlap of the imaging findings (15–18). Given the limited accuracy of any of these features considered alone, it seems prudent to use a combination of size, shape, and internal architecture criteria together. Furthermore, the size criterion should be modified on the basis of the location of the lymph node and the type of primary tumor. For example, if a node is larger than 8 mm in short axis diameter in the pelvis or larger than 10 mm in the abdomen, it should be considered suspicious for metastasis. In the case of testicular cancer, the size threshold can be lowered to 8 mm for abdominal retroperitoneal nodes. If the shape is round or irregular, the node is more likely metastatic. If there is signal

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**Table 1**

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Regional Nodes of Pelvic Tumors</th>
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<tbody>
<tr>
<td>Nodes</td>
<td>Anus</td>
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<tr>
<td>Perivesical</td>
<td>Regional</td>
</tr>
<tr>
<td>Inguinal</td>
<td>Regional</td>
</tr>
<tr>
<td>Internal iliac</td>
<td>Regional</td>
</tr>
<tr>
<td>External iliac</td>
<td>Non</td>
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<tr>
<td>Common iliac</td>
<td>Non</td>
</tr>
<tr>
<td>Paraortic</td>
<td>Non</td>
</tr>
</tbody>
</table>

Source.—Reference 24.

Note.—Non = nonregional.

* Regional only in setting of previous scrotal or inguinal surgery.
intensity heterogeneity on T2-weighted MR images or central necrosis on CT images, this is additional potential evidence for metastasis.

Nodal Metastasis of Pelvic Tumors—Effect on Staging

The current U.S. and international standard cancer staging system defines the extent of primary tumor (T stage), the extent of nodal metastases (N stage), and the presence of distant metastases (M stage). This is referred to as the TNM staging system. The TNM system is in constant evolution and is updated by the International Union against Cancer (23), with a view to maintaining a global, clinically relevant classification system. Details of the TNM staging of pelvic tumors can be found in the most recent American Joint Committee on Cancer text (24). The N stage depends on criteria that vary from tumor to tumor, including nodal size, number, unilateral versus bilateral, and location of nodal metastases. In the staging of nodal metastases, nodal spread is considered regional or nonregional (24). The regional lymph node groups are defined for each tumor (summarized in Table 1). Regional nodal metastases are described by the N stage, whereas nonregional lymph node metastases constitute distant disease, conferring M stage (usually M1) disease. This has a direct impact on overall tumor stage, since M1 disease, in the case of pelvic tumors, upstages the patient to stage IV (of IV) cancer and thus carries with it the potential to influence prognosis and clinical management.

For example, a positive common iliac lymph node in a patient with cervical cancer is defined as N1-stage disease because it represents a regional node for this tumor. On the other hand, metastasis to the same common iliac node group for some other pelvic tumors, such as bladder cancer, is not considered to be regional nodal spread; in this case, the common iliac node constitutes M1-stage disease and overall stage IV cancer. Similarly, paraaortic nodal metastasis is a regional metastasis for endometrial cancer, carrying a staging impact of N1 and overall stage III (at least) disease. Nodal metastasis to the same paraaortic location in cervical cancer represents a nonregional nodal metastasis and therefore M1 and overall stage IV disease. Hence, knowledge of the regional and nonregional nodes for each tumor is essential for proper staging purposes.

Pelvic Tumors: Patterns of Nodal Metastasis

In this section, the common sites for nodal metastasis from different pelvic tumors will be described, as will characteristics of nodal metastasis that are specific to the particular tumor. The tumor types are each illustrated with selected clinical examples demonstrating nodal anatomy and nodal metastasis staging. The regional

<p>| N-Stage Classification for Anal Cancer |</p>
<table>
<thead>
<tr>
<th>Stage</th>
<th>Findings</th>
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<tbody>
<tr>
<td>NX</td>
<td>Regional nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional nodal metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in perirectal lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in unilateral internal iliac and/or inguinal lymph nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in perirectal and inguinal nodes or bilateral internal iliac or inguinal lymph nodes</td>
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</table>

Source.—Reference 24.
Lymphatic Metastases from Pelvic Tumors

REVIEW: Lymphatic Metastases from Pelvic Tumors

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nodes for each tumor are outlined in Table 1.

Anal Carcinoma

Metastatic spread to regional lymph nodes represents the most common mode of tumor spread from cancer of the anal canal and margin (25). Nodal metastasis is more likely in cases of larger tumor size or a poorly differentiated anal tumor (26). Metastasis most commonly occurs to the perirectal nodes, with inguinal nodal spread being the second most common location of nodal metastasis (25,27). In the presence of nodal metastasis from anal cancer, the site of spread can be treated with radiation therapy, and the use of a higher radiation dose to the primary tumor is also advocated (28). Figure 5a–5c illustrates a case of perirectal and inguinal nodal metastases. Figure 5d, however, depicts external iliac nodal metastasis, a nonregional node, constituting M1 stage disease. Table 2 outlines the N-stage classification system for anal cancer.

Bladder Carcinoma

Nodal metastasis from bladder cancer most commonly occurs in the obturator and internal iliac nodes (29). If these nodes are free of tumor, nodal metastasis to more cranial node groups is extremely unlikely (29). Higher N stage correlates with higher T stage of the primary lesion (30,31). The chance of nodal metastasis above the aortic bifurcation (nonregional nodal metastasis) also increases progressively with higher T-stage tumors.

The depiction of node-positive disease can alter the treatment pathway from surgery to chemotherapy or combined chemoradiation (28,32), and the N stage has a substantial impact on 5-year survival in these patients (30,33).

The prognosis declines with greater number of nodal metastases, with greater size of nodal metastases, and with capsular penetration of the nodes involved by tumor (34,35). Recent evidence suggests that the lymph node density (ratio of involved to uninvolved nodes removed at pelvic lymphadenectomy) is a better predictor of disease-specific survival than is N-stage determination (36). Figure 6 illustrates perivesical, regional, and nonregional metastatic lymph nodes from bladder cancer. Table 3 outlines the N-stage classification system for bladder cancer.

Cervical Carcinoma

Nodal metastasis from cervical cancer most commonly occurs in the obturator nodes, internal iliac nodes, or external iliac nodes; in the absence of metastasis to these sites, metastasis to more cranial sites such as paraaortic nodes is rare (37,38). Pelvic nodal metastasis correlates with primary tumor T stage in cervical cancer, and paraaortic nodal spread only occurs when pelvic nodes are also involved (37). Nodal metastases correlate with the presence of parametrial invasion by the primary tumor (39).

The surgical removal of involved nodes improves survival in these patients (40). If there is pelvic or paraaortic nodal metastasis, patients undergo retroperitoneal lymph node dissection, extended-field radiation therapy plus chemotherapy, and, possibly, brachytherapy. Additional staging with positron emission tomography...
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Fig. 7: Cervical cancer on axial contrast-enhanced CT images. (a) Right obturator (arrow) and right parametrial (arrowhead) nodes are enlarged. These are regional nodes for cervical cancer, compatible with N1 stage. (b) Left middle common iliac node (arrow) is enlarged. This node resides in the lumbosacral fossa, with psoas muscle lateral and common iliac vessels anterior to it. It is a regional lymph node for cervical cancer, representing N1 stage. (c) Left paraaortic (black arrow), interaortocaval (arrowhead), and paracaval (white arrow) lymph nodes are enlarged. These are not regional nodes for cervical cancer and thus are compatible with M1 stage disease.

Table 3

<table>
<thead>
<tr>
<th>N-Stage Classification for Bladder Cancer</th>
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<tr>
<td>Stage</td>
</tr>
<tr>
<td>NX</td>
</tr>
<tr>
<td>N0</td>
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<tr>
<td>N1</td>
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<tr>
<td>N2</td>
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<td>N3</td>
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Source.—Reference 24.

PET is often recommended in cases with pelvic or paraaortic nodal spread to assess for further disease dissemination (28). Figure 7 depicts perivisceral, regional, and nonregional metastatic lymph nodes from cervical cancer. Table 4 outlines the N-stage classification system for cervical cancer.

Endometrial Carcinoma

Paraaortic lymph nodes are considered regional nodes for endometrial cancer (24) (in addition to pelvic nodes; see Table 1). This partly reflects the pattern of spread in this tumor. While metastatic involvement of paraaortic nodes is not characteristic of other pelvic tumors, such as cervical and bladder cancer, in the absence of metastases to pelvic nodes endometrial cancer metastases can occur in isolation to paraaortic nodes, particularly to left-sided paraaortic nodes (41). Pelvic nodal metastases, however, are more common than paraaortic disease (42). Node-positive endometrial cancer is more common in tumors of higher T stage (42) and in endometrial cancer of higher grade (43).

In patients with early T-stage (stage I–II) cancer, the number of metastatic pelvic lymph nodes has important prognostic implications (44). In patients with pelvic and/or paraaortic nodal metastasis (Stage IIIC disease), adjuvant chemotherapy and tumor-directed radiation therapy are recommended (28). If nodal recurrence occurs, then radiation therapy can be used with or without chemotherapy. Table 4 outlines the N-stage classification system for endometrial cancer.

Ovarian Carcinoma

Ovarian tumors commonly spread to paraaortic lymph nodes in addition to pelvic lymph nodes (45). Nodal metastases are common, particularly in higher T-stage (stage III–IV) tumors (46,47), with an incidence of 35%–78%. In early-stage ovarian cancer (unilateral, clinical stage I), metastases to paraaortic and pelvic lymph nodes can also occur, and when present in pelvic nodes, these metastases can be ipsilateral, contralateral, or bilateral (48). As is the case for many other tumors, survival is adversely affected by nodal spread of disease (49,50).

Initial surgical management of ovarian epithelial cancer consists of total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic and paraaortic lymphadenectomy. Nodal metastasis results in upstaging to overall stage IIIA, which is commonly treated with chemotherapy. Additional chemotherapy is also considered after remission in patients with stage III disease (28). Figure 8 is an example of paraaortic (regional) nodal spread from ovarian cancer. Table 4 outlines the N-stage classification system for ovarian cancer.

Penile Carcinoma

In patients with penile cancer, nodal metastasis most commonly occurs at the inguinal lymph nodes (51). At the time of presentation, up to 96% of patients with penile cancer will have palpable inguinal lymph nodes, and 45% will have nodal metastases (52).
Predictors of lymph node metastasis include pathologic stage of the primary tumor, lymphatic embolization (tumor emboli within peritumoral lymphatics), and histologic grade (53).

It should be noted that inguinal lymphadenopathy is often a manifestation of reactive enlargement due to co-morbid infection or inflammation (52). The clinical decision for inguinal lymphadenectomy is made after 2–6 weeks of antibiotic therapy. If the enlarged nodes remain palpable after antibiotic treatment for this time, inguinal lymphadenectomy is performed. If inguinal lymphadenectomy shows metastatic disease, complete pelvic lymphadenectomy is considered (54), although this is controversial (55).

While the prognosis is much worse for node-positive penile cancer (56,57), early resection of nodal metastases can improve survival (58). Prognosis is adversely affected by a greater number of metastatic nodes, bilateral disease, deep pelvic nodal metastases, and extranodal extension (51).

For stage IV disease, including disease with nonregional lymph node metastases, palliative chemotherapy or radiation therapy is advocated (54). The propensity for nonmetastatic enlarged lymph nodes in patients with penile cancer is illustrated in Figure 9a, a case in which enlarged external iliac nodes were resected but proved to be benign at histologic examination. Figure 9b demonstrates regional metastatic nodal disease from penile cancer. Table 5 outlines the N-stage classification system for penile cancer.

**Prostate Carcinoma**

Nodal metastasis occurs in approximately 9% of patients with prostate cancer (59). Metastasis most commonly involves the internal iliac, external iliac, or obturator nodes (59). In patients with unilateral cancer, prostate nodal metastases tend to be ipsilateral (59). Therapeutic options for low to intermediate T stage (T1–T2c) and low to intermediate Gleason score (score, 2–7) include expectant management, external-beam radiation therapy (EBRT), brachytherapy, and radical prostatectomy. Patients with a high risk for nodal metastases (on the basis of nomograms) are candidates for pelvic nodal irradiation with or without adjuvant androgen-deprivation therapy (luteinizing hormone–releasing hormone agonists or orchiectomy) (28).

In surgically treated patients, the decision to perform pelvic lymphadenectomy is also based on the nonogram-derived probability of nodal metastasis (60). If nodal metastasis is found, then adjuvant androgen-deprivation therapy...
**Figure 10:** Prostate cancer. (a) Axial T2-weighted MR image (5300/160; flip angle, 90°) shows mild enlargement, rounded shape, and heterogeneous signal intensity of right obturator node (arrow) adjacent to right obturator externus. This is compatible with N1 disease. (b) Axial T2-weighted MR image (6050/155; flip angle, 90°) performed with endorectal and phased-array surface coils shows enlarged right anterior internal iliac lymph node with heterogeneous signal intensity (arrow). This represents N1 disease. (c) Axial contrast-enhanced CT image shows enlarged paraaortic (arrow) and retrocaval (arrowhead) nodes. These are nonregional nodes for prostate cancer and therefore represent M1 disease.

**Figure 11:** Rectal cancer. (a) Axial T2-weighted MR image (5117/94; flip angle, 90°) shows enlarged left perirectal node (arrow) with heterogeneous signal intensity. This is compatible with N1 stage. (b) Coronal T2-weighted MR image (5000/103; flip angle, 90°) shows at least four enlarged perirectal lymph nodes (arrowheads), which constitute N2 stage. Rectal tumor (T) and a Foley catheter (arrow) are noted in the rectum. (c) Axial contrast-enhanced CT image shows enlarged heterogeneous paraaortic lymph node (arrow). This nonregional nodal metastasis represents M1 stage rectal cancer.

...is considered (28). For patients with higher T stage (T3a or greater) or Gleason score (score, 8–10), treatment options are usually androgen-deprivation therapy and EBRT, with radical prostatectomy considered only in selected patients (small-volume tumors with no fixation). When radical prostatectomy is performed for T3 disease, pelvic lymph node dissection is typical; if nodal metastases are detected, adjuvant androgen-deprivation therapy is considered. Figure 10 shows cases of regional and nonregional metastatic lymph nodes from prostate cancer. Table 4 outlines the N-stage classification system for prostate cancer.

**Rectal Carcinoma**

Nodal metastasis most commonly occurs with initial spread to mesorectal lymph nodes (61). Involved mesorectal lymph nodes are usually at the same level as or proximal to the rectal tumor, with metastasis to mesorectal nodes distal to the tumor accounting for only 2% of malignant nodes (62). Extramesorectal nodes are most commonly found along the middle rectal artery; the internal iliac chain; and the obturator, median sacral, and, less...
commonly, external or common iliac nodes (63).

For rectal cancer, paraaortic nodes are nonregional, and spread to these nodes constitutes M1 (stage IV) disease (24). Inguinal nodes also represent a nonregional site of nodal metastasis in these patients. This is associated with a very poor prognosis and is generally indicative of diffuse disease (64). Inguinal metastases are more common in cancers localized in the lower third of the rectum. Patients with inguinal metastases from rectal cancer have a very poor 5-year survival (64). Patients with T1–T2 rectal tumors can be treated with resection alone. If there are nodal metastases (or if the tumor is T3), however, neoadjuvant chemo- and radiation therapy are recommended (28). Figure 11 shows cases of regional and nonregional metastatic lymph nodes from rectal cancer. Table 6 outlines the N-stage classification system for rectal cancer.

Testicular Carcinoma

The spread of testicular cancer is most commonly by means of lymphatic metastasis. The regional metastatic lymph nodes for testicular cancer are the paraaortic lymph nodes, with lymphatic drainage following the gonadal vessels to the retroperitoneum (24). Figure 12a shows paraaortic (regional) nodal metastases from testicular cancer. It is important to note, however, that when patients have had inguinal or scrotal surgery, the lymphatic drainage is altered. Klein et al (65) reported on 22 patients with inguinal nodal metastases from testicular cancer, 21 of whom had a history of scrotal or inguinal surgery. In patients with a history of scrotal or inguinal surgery prior to presentation with a testicular tumor, inguinal external iliac and intrapelvic nodes are considered regional (24). After resection, inguinal and iliac lymph nodes can also form a site of disease relapse in these patients (66) (Fig 12b). It should be noted that in assigning an N stage to patients with testicular cancer, the maximum node size is an important descriptor (rather than the maximum short-axis diameter), and this should be reported on the staging imaging studies. Table 7 outlines the N-stage classification system for testicular cancer.

A large series of patients with testicular cancer who had undergone retroperitoneal node dissection (67) was used to determine the relative frequency of nodal metastasis to specific sites based on the side of testicular neoplasm. In that study, the paraaortic nodes were the most common site of spread. There was also a laterality of distribution of metastases, with nodal metastasis more commonly occurring to the paraaortic nodes on the same side as the tumor. For left-sided tumors, the nodes to the left of and in front of the aorta (left paraaortic and preaortic nodes, respectively) are considered ipsilateral. In 80% of cases, left-sided tumors spread to ipsilateral paraaortic nodes only (and to both ipsilateral and contralateral nodes in 20%). Metastasis to contralateral nodes in the absence of ipsilateral metastases is rare. Metastasis of right-sided tumors to paracaval (to the right of the inferior vena cava), precaval (anterior to the inferior vena cava), interaortocaval, and preaortic nodes is considered ipsilateral. Right-sided tumors spread to ipsilateral nodes alone in 83% of cases and to both ipsilateral and contralateral nodes in 13%. Isolated metastasis to contralateral nodes alone occurs in a small minority of right-sided tumors. When common or external iliac node metastases occur, they usually do so on the same side as the primary tumor.

The importance of nodal metastasis is integral to the management of testicular cancer (60). In the case of both seminomas and nonseminomatous germ cell tumors, the primary lesion is treated with radical inguinal orchectomy. N stage subdivides overall stage II disease into IIA, IIB, and IIC on the basis of the presence of N1, N2, and N3 disease, respectively. In patients with seminomas, stage IIA and IIB disease, including that in ipsilateral iliac nodes, can be treated with infraadiaphragmatic EBRT. For stage IIC (nodes > 5 cm) and III seminomas, systemic chemotherapy is advocated, with further management dependent on treatment response (28).

Table 6

<table>
<thead>
<tr>
<th>Stage</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in one to three regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in four or more regional lymph nodes</td>
</tr>
</tbody>
</table>

Source.—Reference 24.
For stage II or IIIB nonseminomatous germ cell tumors, treatment options include chemotherapy followed by retroperitoneal lymph node dissection. Stage IIC (nodes $\geq 5$ cm) and III (including nonregional nodal metastasis) nonseminomatous germ cell tumors are primarily treated with chemotherapy, with entry into clinical trials considered for stage IIIC disease (28).

For nonseminomatous germ cell tumors, evaluation of residual retroperitoneal nodal size after first-line chemotherapy is especially important. In these patients, a residual node measuring larger than 1 cm in maximum transverse diameter should be resected, since these nodes will contain mature teratoma in 50% of cases and vital cancer in 35% (68). In addition to absolute nodal size after chemotherapy, the relative reduction in size compared with that on pretherapy images also helps to predict the likelihood of teratoma in these residual retroperitoneal nodes (69).

**Vaginal Carcinoma**

The regional drainage of vaginal cancer is dependent on the anatomic level of the primary tumor. The upper two-thirds of the vagina drain primarily to deep pelvic nodes, including the internal and external iliac chain nodes and the obturator nodes (24). The lower one-third drains into the inguinal and femoral nodes. Al-Kurdi and Monaghan (70) studied 99 patients with a primary vaginal neoplasm and the distribution of nodal metastasis with respect to the anatomic level of the vaginal tumor. In that study, tumors in the upper one-third of the vagina metastasized to deep pelvic nodes, whereas tumors from the lower one-third metastasized to both deep pelvic and inguinal nodes, as did tumors that involved all parts of the vagina. Figure 13 shows a case of external iliac (regional) nodal metastases. Table 4 outlines the N-stage classification system for vaginal cancer.

Nodal metastasis affects the management of vaginal cancer (68). Stage I–II vaginal tumors are treated with EBRT targeted to the primary lesion, as well as to the expected lymphatic drainage sites of the tumor (inguinal and/or pelvic lymph nodes). EBRT can be used alone or as an adjuvant therapy after vaginectomy and pelvic and/or inguinal lymphadenectomy, depending on patient factors. For stage III or IVA tumors, including those with N1 disease, radiation therapy, including node-directed EBRT, is standard.

**Vulvar Carcinoma**

In patients with vulvar cancer, nodal spread occurs to regional inguinal and femoral lymph nodes, while metastasis to deep pelvic nodes such as the internal or external iliac nodes are considered as distant metastases (24). Nodal status markedly affects overall staging. Unilateral regional nodal spread constitutes N1 disease (overall stage II), whereas bilateral regional nodal spread represents N2 disease (overall stage IV). Table 8 outlines the N-stage classification system for vulvar cancer.

Figure 14 illustrates bilateral inguinal nodal metastases. The prognostic effect of bilateral metastases is considerable, with the median survival associated with stage III and IV vulvar cancer of 20 and 8 months, respectively, whereas the median survival associated with stage II vulvar cancer is 128 months (71). Bafna et al (72) found that although bilateral inguinal nodal metastases carried a poor prognosis, unilateral disease can have a good prognosis unless multiple nodes are involved. Paladin et al (73) found that the penetration of tumor through the lymph node capsule and the maximum size of the lesion within the node correlated with poorer prognosis.
For early-stage vulvar carcinoma (stage I or II), radical vulvectomy is performed with femoral and inguinal nodal dissection (60). In light of the morbidly of inguinal lymph node dissection, sentinel node identification with technetium 99m sulfur colloid has been suggested as a viable approach (74). In stage III or IV cancer, radical vulvectomy is supplemented by radiation therapy, including irradiation of involved nodal sites.

**Future Directions**

The suboptimal accuracy of current cross-sectional imaging techniques in the diagnosis of nodal metastasis from pelvic tumors presents an important challenge and opportunity for the development of more accurate diagnostic tests. PET performed with metabolic and targeted compounds and MR imaging performed with injectable nanoparticle contrast agents are two approaches with potential. A better understanding of the molecular basis of the different pelvic tumors may also assist in the development of more specifically targeted imaging agents (75). Moreover, techniques with excellent negative predictive value offer the potential to prevent the morbidity of lymph node dissection, while those with strong positive predictive value should allow for the most appropriate treatment while facilitating clinical trials and outcome assessments.

**PET with Metabolic and Targeted Compounds**

The implementation of fluorine 18 fluorodeoxyglucose (FDG) PET has been greatly enhanced by the use of combined PET/CT by providing accurately coregistered anatomic and functional images. This has facilitated the localization of tissues with high FDG uptake, such as tumors (76). The relatively poor spatial resolution and the potential for inaccurate results in the pelvis because of FDG residues in the bladder and ureters are limiting features (77). An additional limitation is in the detection of tumors, such as prostate cancer, that do not have a marked elevation in glucose metabolism. Because of this, FDG PET appears to be of limited utility in the evaluation of lymph node metastasis from prostate cancer (78,79). Alternative radiotracers for prostate cancer, such as carbon 11 (11C)-labeled acetate or 11C-labeled choline may play a future role (80–85).

In other pelvic cancers, mixed accuracy has been found with FDG PET in the evaluation of lymph node metastasis. Studies in uterine and cervical cancer (86–89), for example, have shown high specificity (approaching 100%), but the technique is limited due to lower sensitivity for nodal metastasis from uterine cancers (87,88) (sensitivity, 53%–60%) and cervical cancer (86,89) (sensitivity, 58%–91%). In particular, FDG PET is insensitive to metastatic lymph nodes of smaller size, with a cutoff of 5 mm identified in the evaluation of metastases from cervical cancer (89).

**MR Imaging with Nanoparticle Contrast Agents**

Ultrasmall superparamagnetic iron oxide (USPIO) contrast agents can be used to detect lymph node metastasis with MR imaging on the basis of the cellular constituents of lymph nodes rather than size or morphology. USPIOs are incorporated into cellular elements of the normal reticuloendothelial system, including macrophages in lymph nodes (90). The superparamagnetic effect of USPIOs leads to low signal intensity in normal lymph nodes on T2- and T2*-weighted MR images. When the normal reticuloendothelial elements of nodes are replaced by tumor cells, the USPIOs can no longer concentrate in these regions, and signal intensity will not be altered (91). False-negative results can occur with microscopic tumor deposits in otherwise normal nodes (92). Reactive nodes frequently show low signal intensity at the center of the node on T2*-weighted images (93).

A study reported in 2005, that included patients with endometrial or cervical cancer (94), compared MR images analyzed with size criteria for metastasis versus MR images obtained with USPIOs. MR imaging with USPIOs had sensitivity and specificity of 91%–100% and 87%–94%, respectively, on a per patient basis; the sensitivity and specificity of unenhanced MR imaging were 27% and 94%, respectively.

A multicenter trial assessed the efficacy of MR imaging with USPIOs in detection of nodal metastases from prostate cancer (95) and yielded a sensitivity and specificity, respectively, of 82% and 93%, compared with a sensitivity and specificity of 34% and 97% for CT. In that same report, the negative predictive value was 96%, which led the authors to conclude that a negative USPIO-enhanced MR findings could preclude lymph node dissection in patients with prostate cancer with intermediate to high risk of lymph node metastasis (95).

**Figure 14**

**Vulvar cancer.** Axial T2-weighted single-shot fast spin-echo MR images (a, flip angle, 90°) in one patient show marked enlargement of (a) left and (b) right superficial inguinal lymph nodes (arrow). Both nodes have central high signal intensity compatible with necrosis. Since these are bilateral inguinal metastatic nodes, this is N2 stage vulvar cancer.
High levels of accuracy in diagnosis of nodal metastasis have also been found with this technique in patients with testicular (96), bladder (97), or penile cancer. A recent meta-analysis of the diagnostic performance of MR imaging with nanoparticles in the detection of metastatic lymph node involvement by all tumors (98) demonstrated overall sensitivity and specificity of 88% and 90%, respectively.

Summary

The spread of pelvic tumors to lymph nodes is an important means of tumor dissemination and substantially affects prognosis and management. Knowledge of the nodal anatomy of the pelvis is essential in interpretation of cross-sectional images, from any modality, that are used to stage these tumors. It is also important to be aware of the different regional nodes for each type of tumor and the N-stage categorization for each tumor. Routine cross-sectional imaging studies have less-than-optimal diagnostic test performance, but improvements are likely to be delivered by functional imaging modalities such as PET and USPIO-enhanced MR imaging, as well as by molecular imaging strategies.

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