Tracking Down the Lymphatic Drainage Network of Female Reproductive Organs: Depicting Pathways of Nodal Lymphatic Spread of Ovarian, Endometrial, Cervical and Vaginal Cancer

Poster No.: C-2271
Congress: ECR 2014
Type: Educational Exhibit
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Keywords: Cancer, Education, MR, CT, Genital / Reproductive system female
DOI: 10.1594/ecr2014/C-2271

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Learning objectives

Understanding the patterns of normal lymphatic drainage of female reproductive organs is an essential tool in depicting the pathways of lymphatic disease spread and planning effective search strategies in imaging studies performed for staging gynecologic cancer.

Review lymphatic vessels anatomy and correlate it with the pattern of nodal metastases of ovarian, endometrial, cervical and vaginal cancers.
Background

Gynecologic cancer contributes significantly to women mortality and morbidity. Endometrial cancer is the most frequently occurring female genital malignancy, followed by ovarian and cervical cancers; as for primary vaginal malignancies they are rare, accounting only for 1%-2% of the cases. They are all more common in postmenopausal women, except for cervical cancer, with a peak incidence in the 25-29 year age group.

The spread of tumors to lymph nodes is an important mechanism of disease dissemination, in addition to hematogenous and direct local-regional spread. The subperitoneal space provides the pathways for the vascular and lymphatic vessels of pelvic organs and, therefore, a pathway for nodal disease spread. Enlarged pelvic, abdominal or inguinal nodes usually indicate tumor involvement. An abnormal short-axis > 10 mm for abdominal and pelvic nodes or > 10-15 mm for inguinal nodes is often used as a computed tomography (CT) criterion for malignant lymph nodes; however, size alone is a poor discriminator, as microscopic metastases can exist in a normal size node and enlarged nodes can be reactive. Other findings suggestive of node metastasis are loss of fatty hilum, loss of oblong kidney-bean-shaped structure or presence of central necrosis. Magnetic resonance imaging (MRI) can further characterize nodes that are equivocal on CT. Although there are conflicting reports in literature, the introduction of diffusion-weighted MR imaging (DW-MRI) and the finding of high intensity signal on DW-MRI high b-value for malignant nodes, as well as a similar diffusion restriction to the primary tumor, may be helpful. Given the limited accuracy of any of these features alone, it seems prudent to combine them together in order to provide an accurate clinical staging, which has not only prognostic value, but also great management impact.

There are two staging systems for gynecologic malignancies, the TNM (tumor, node, metastasis) system and the more commonly used developed by the International Federation of Obstetrics and Gynecology (FIGO). Gynecologic tumors usually metastasize first to regional lymph nodes, which include specific groups of nodes for each tumor, classified as N-stage disease in TNM. When dissemination occurs to a distant lymph node, outside the defined regional nodes, it is considered M-stage disease, which usually results in upstaging of the disease to overall stage IV cancer in FIGO staging system.
Findings and procedure details

1. OVARY

Normal Lymphatic Drainage

The ovary has three pathways of lymphatic drainage. The main lymphatics follow the ovarian vessels, along the infundibulopelvic ligaments, to the paraaortic nodes at the level of the renal pedicle. Lymph vessels also pass through the broad ligament and parametrium to drain to pelvic lymph nodes, as well as along the round ligament to the inguinal nodes. Furthermore, it is reported that after the menopause the flow of lymph is reduced and it drains mainly to the paraaortic nodes. (Fig. 1 on page 7)

OVARIAN CANCER

Lymphatic Disease Spread

Lymphatic spread of ovarian cancer commonly follows the pathway of ovarian veins, skipping pelvic nodes, to involve paraaortic nodes at the renal pedicle; these are the most frequently found regional adenopathies. Retroperitoneal nodal spread may be present even in cases with little or no apparent intraperitoneal involvement. In addition to paraaortic nodes, ipsilateral or contralateral pelvic nodes - including perivisceral nodes, obturator, internal and external iliac, lateral sacral and common iliac nodes - as well as inguinal nodes are also considered regional. (Fig. 2 on page 7)

2. UTERUS

Normal Lymphatic Drainage

Vessels from the body and fundus accompany those of the ovaries to the paraaortic chain, with some passing to the external iliac nodes.

From the cervix, vessels pass laterally in the parametrium to the external iliac nodes, posterolaterally to the internal iliac nodes and posteriorly in the sacrogenital fold to the rectal and sacral nodes; some may reach the obturator or gluteal nodes. (Fig. 3 on page 8)

ENDOMETRIAL CANCER
Lymphatic Disease Spread

Pelvic lymph nodes, including perivisceral, obturator, internal and external iliac, sacral and common iliac nodes, are the most common regional nodes involved in endometrial cancer. Besides the former, paraaortic nodes are also considered regional. Endometrial malignancies can give isolated paraaortic nodal metastases, without occurring pelvic nodal invasion. Although pelvic and paraaortic nodes are both regional, their involvement is considered separately in both TNM and FIGO staging systems, reflecting prognostic data that have suggested a worse outcome when the latter are involved. As for inguinal nodes, they are considered non-regional. (Fig. 4 on page 9)

Depth of myometrial invasion, depicted by MR imaging, correlates with the presence of lymph node metastases and overall patient survival.

CERVICAL CANCER

Lymphatic Disease Spread

Nodal spread of cervical cancer most commonly occurs to the obturator, internal and external iliac, sacral and common iliac nodes. Rarely, in the absence of metastases to these sites, can more cranial locations, as paraaortic nodes, be affected, as opposed to endometrial malignancy. Inguinal and paraaortic nodes involvement affects adversely the prognosis, as these are not considered regional. (Fig. 5 on page 11)

Primary tumor T-stage, as well as parametrial invasion by the primary tumor correlates with the presence of nodal metastasis.

3. VAGINA

Normal Lymphatic Drainage

The drainage of vaginal lymphatic vessels is dependent on the anatomic level. It can be divided into three groups, but the regions drained are not sharply demarcated. Upper vessels go along the uterine artery to the internal and external iliac nodes; intermediate vessels accompany the vaginal artery to the internal iliac nodes; lower vaginal vessels pass to the superficial and deep inguinal nodes and some efferents may pass to the internal iliac nodes. Posterior wall lymphatics communicate with rectal lymphatics and may drain to the sacral, inferior gluteal and rectal nodes. (Fig. 6 on page 12)

VAGINAL CANCER
Lymphatic Disease Spread

The regional drainage of vaginal cancer includes the deep pelvic nodes, such as obturator, internal and external iliac nodes, for lesions of the upper two-thirds of the vagina and inguinal nodes for lesions of the lower one-third. Malignancies involving all parts of the vagina may spread to both deep pelvic and inguinal nodal groups. (Fig. 7 on page 13)
Fig. 1: Schematic drawing illustrating the Normal Lymphatic Drainage of the Ovary. The ovary has three pathways of lymphatic drainage, that drain to the paraaortic, the pelvic and the inguinal lymph nodes. The paraaortic chain is the main lymphatic pathway.

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**Fig. 2:** Lymphatic Disease Spread in Ovarian Cancer. A) Schematic drawing. In addition to paraaortic nodes, pelvic nodes (including perivisceral nodes, obturator, internal and external iliac, lateral sacral and common iliac nodes) as well as inguinal nodes are all considered regional (R) for ovarian cancer. B) Axial contrast-enhanced CT (B1-3, B6), axial T2-weighted MR (B4, B7) and DW-MR with high b-value (B5, B8) images of a patient with ovarian serous adenocarcinoma. Image B1 shows a small, but metastatic left paraaortic node (arrow), at the level of the renal pedicle. Image B2 shows enlarged bilateral common iliac (arrows), with nodal metastases. Images B3-8 show enlarged right external iliac nodes (small arrows) and right inguinal nodes (large arrows) with diffusion restriction. All the former nodes revealed to be nodal metastases after histopathology evaluation. C) Axial contrast-enhanced CT of a patient with ovarian carcinoma and enlarged left paraaortic node, at the level of the renal pedicle (arrow); ultra-sound-guided biopsy of a left enlarged supraclavicular node revealed nodal invasion. D) T2-weighted MR coronal reconstruction of a patient with ovarian carcinoma and enlarged bilateral nodes along the common iliac (small arrows) and internal iliac chains (large arrows).

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Fig. 3: Schematic drawing illustrating the Normal Lymphatic Drainage of the Uterus. The body and fundus drain to the paraaortic chain, with some passing to the external iliac nodes. The cervix drains to the external iliac nodes, the internal iliac nodes and the rectal and sacral nodes; some of the lymphatics may reach the obturator or gluteal nodes.

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Fig. 4: Lymphatic Disease Spread in Endometrial Cancer. A) Schematic drawing. Paraaortic and pelvic lymph nodes (including perivesical, obturator, internal and external iliac, sacral and common iliac nodes) are considered regional (R) for endometrial cancer. Inguinal nodes are considered non-regional (NR). B) Axial non contrast-enhanced CT (B1-2), axial T2-weighted MR (B3), ADC map (B4) and axial DW-MR with high b-value (B5) images of a patient with endometrial adenocarcinoma. Image B1 shows an enlarged paraaortic node (arrow). Images B3-5 shows an enlarged right external iliac node (arrow), with restriction to diffusion similar to the primary tumor (T); histopathology confirmed that it was a nodal metastasis. C) Axial contrast-enhanced CT (C1), axial T2-weighted MR (C2) and axial gadolinium-enhanced T1-weighted MR (C3) images of a patient with endometrial adenocarcinoma and an enlarged left necrotic obturator node (arrow).
**Fig. 5:** Lymphatic Disease Spread in Cervical Cancer. A) Schematic drawing. Pelvic nodes (including obturator, internal and external iliac, sacral and common iliac nodes) are regional (R) for cervical cancer. Inguinal and paraaortic nodes are considered non-regional (NR). B) Axial contrast-enhanced CT axial of a patient with cervical squamous cell carcinoma, showing (B1) enlarged paraaortic node (arrow), (B2) enlarged left internal (large arrow) and external iliac nodes (small arrow). C) Axial contrast-enhanced CT (C1), axial T2-weighted MR (C2), ADC map (C3) and DW-MR with high b-value (C4) images of a patient with cervical squamous cell carcinoma with enlarged heterogenous bilateral
external iliac nodes (arrow), with both necrosis and a solid component showing diffusion restriction similar to the primary tumor (T).

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**Fig. 6:** Schematic drawing illustrating the Normal Lymphatic Drainage of the Vagina. Upper lymphatic vaginal vessels drain to the internal and external iliac nodes, intermediate vessels to the internal iliac nodes and lower vessels drain mainly to the inguinal nodes. Posterior wall lymphatics may drain to the sacral, inferior gluteal and rectal nodes.
Fig. 7: Lymphatic Disease Spread in Vaginal Cancer. A) Schematic drawing. The regional (R) drainage of vaginal cancer includes the deep pelvic nodes, such as obturator, internal and external iliac nodes, for lesions of the upper two-thirds of the vagina and inguinal nodes for lesions of the lower one-third. Paraaortic nodes are non-regional (NR). B) Axial T2-weighted MR (B1, B7), ADC map (B2, B6), DW-MR with high b-value (B3, B5) and axial contrast-enhanced CT (B4) images of a patient with vaginal squamous cell carcinoma with a suspicious small right inguinal node (arrow), showing diffusion restriction similar to the primary tumor (T).

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Identification of regional and non-regional nodal metastasis is one of the most important factors in accurate clinical staging. Perivisceral, external, internal and common iliac nodes are considered regional lymph nodes, exception made for common iliac nodes in vaginal cancer. In the particular case of paraaortic nodes, they are considered regional lymph nodes for both endometrial and ovarian cancer, but not for cervical, vaginal or most pelvic cancers. As for inguinal nodes they are regarded as regional in ovarian and vaginal cancer. Tumor spread to a lymph node outside the defined regional nodes has an impact on prognosis, usually resulting in an upstaging of the disease and therefore affecting treatment options.

The diagnosis of lymphatic metastases represents a challenge for modern imaging, but also an important goal, as it can adversely affect patient survival. Radiologists need to be familiar with pathways of lymphatic tumor spread to provide helpful staging information and ensure that the proper therapy is administered.
References


