Sentinel Lymph Node Mapping for Endometrial Cancer

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Endometrial Cancer

• Most common gynecologic malignancy in US
  – estimated 52,630 new cases in 2014
  – estimated 8,590 deaths in 2014

• Median age at diagnosis is 62

• Most (67.9%) are diagnosed at the local stage with the 5-year survival 95.1%

Endometrial Cancer

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Endometrial Cancer

SEER 18 2004–2010, All Races, Females by SEER Summary Stage 2000

Endometrial Cancer

- 10-15% of patients will have metastatic nodal disease

- 15% deemed to have Grade 1 tumors preoperatively on office biopsy or D&C will have higher-grade disease on final pathology

- *Important to stage and subsequently treat these patients appropriately*
Staging of Endometrial Cancer

Surgically staged according to the joint 2010 International Federation of Gynecology and Obstetrics (FIGO)
Stage I Endometrial Cancer

Stage IA Endometrial Cancer
- Uterus
- Cervix
- Endometrium
- Cancer
- Myometrium
- Vagina
- Fallopian tube
- Ovary

Stage IB Endometrial Cancer
- Uterus
- Cervix
- Vagina
- Cancer

Stage IA and stage IB endometrial cancer. In stage IA, cancer is in the endometrium only or less than halfway through the myometrium (the muscle layer of the uterus). In stage IB, cancer has spread halfway or more into the myometrium.
Stage II Endometrial Cancer

Stage II endometrial cancer. Cancer has spread into connective tissue of the cervix, but has not spread outside the uterus.
Stage III Endometrial Cancer

**IIIA**
Stage IIIA endometrial cancer. Cancer has spread to the outer layer of the uterus and/or to the fallopian tubes, ovaries, or ligaments of the uterus.

**IIIB**
Stage IIIB endometrial cancer. Cancer has spread to the vagina and/or to the parametrium (connective tissue and fat around the uterus and cervix).

**IIIC**
Stage IIIC endometrial cancer. Cancer has spread to lymph nodes in the pelvis and/or around the aorta (the largest artery in the body, which carries blood away from the heart).
Stage IV Endometrial Cancer

Stage IVA Endometrial Cancer

- Small intestine
- Large intestine (part of the bowel)
- Endometrium
- Uterus
- Bladder
- Cancer
- Cervix

Stage IVA endometrial cancer. Cancer has spread into the bladder and/or bowel.
Treatment

Most patients undergo surgical treatment with a total hysterectomy, BSO, and pelvic washings

- the *standard of treatment* includes a complete or selective pelvic and para-aortic lymphadenectomy for staging disease

- proper staging provides information on the actual extent of the disease rather than on perceived risks based on uterine factors, such as grade, histology, and depth of myometrial invasion
Nodal Assessment

• One of most important prognostic factors for endometrial carcinoma is the presence of extrauterine disease, particularly pelvic and paraaortic lymph node metastases

• The rate of nodal spread varies with tumor stage and grade
High Risk of Nodal Disease

- Serous or clear cell, or high-grade histology
- Myometrial invasion greater than 50%
- Large tumor (> 2 cm in diameter or filling the endometrial cavity)
Nodal Dissection

• One value of staging relates the ability to describe the extent of the disease and to define comparable patient populations for whom prognosis and therapy are similar.

• Most controversial is the assertion that surgical staging has a therapeutic benefit independent of the node status.
Nodal Dissection

• In contemporary management, this information results in less use of radiation, and substitution of vaginal cuff brachytherapy for pelvic radiation.
Nodal Dissection - NONE

- Most patients present with low risk features
  - **GOG-33** – study of 621 patients
    - 75% had grade 1 to 2 tumors
    - 59% had inner 1/3rd or less myometrial invasion
    - 9% had positive lymph nodes

Nodal Dissection - NONE

• Most patients present with low risk features
  – PORTEC trial –
    • evaluated stage IC, grade 1; stages IB and IC, grade 2; or stage IB, grade 3 who underwent hysterectomy without LND and compared observation to postoperative radiation

    • comparable 5-year survival rates (85% observation, 81% pelvic radiation)

Nodal Dissection - NONE

- Most patients present with low risk features
  - ASTEC trial – randomized multicenter study of more than 1400 patients comparing LND to no nodal assessment

  - No therapeutic benefit to lymphadenectomy in early stage endometrial cancer

Nodal Dissection - ROUTINE

• Rationale includes –
  – the inaccuracy of preoperative or intraoperative assessments predicting risk for nodal disease
  – the potential for therapeutic benefit
    • earlier, retrospective studies comparing multiple-site pelvic lymph node sampling versus no node sampling did report significant survival advantage
  – lack of significant morbidity associated with procedure
  – postoperative adjuvant therapy is best made with the most complete information

Nodal Dissection - SELECTIVE

• Surgical staging is the most accurate way to determine the extent of disease spread
  – palpation of pelvic lymph nodes is not sufficiently accurate

• Some studies show rates of nodal assessment to be as low as 30%
  – patients subjected to unnecessary adjuvant therapy and its associated side effects
Sentinel Lymph Node Mapping

• Logic of SLN mapping lies in targeting the correct nodes that are most likely to harbor disease

• Goal of sampling is to obtain a representative biopsy
Sentinel Lymph Node Mapping

- Meta-analysis of 26 studies including 1101 SLN procedures found sensitivity of 93 percent for detection of lymph node metastases in women with endometrial cancer

SLN Mapping

- Internal iliac and obturator region (59%)
- External iliac region (30%)
- Common iliac region (8%)
- Para-aortic region (3%)
Para-aortic SLN

• 2009 study, 847 of 1942 patients underwent both pelvic and para-aortic node removal

• Only 12 (1.6%) of 734 patients who had negative pelvic nodes had isolated positive para-aortic nodes

SLN Mapping Techniques

• A radioactive tracer or colored dye are used to visualize colored nodes

• Considered positive if they contain:
  – macrometastasis (tumor clusters > 2 mm)
  – micrometastasis (tumor clusters 0.2-2.0 mm)
  – isolated tumor cells (single tumor cells or tumor clusters < 0.2 mm)
SLN Mapping Techniques

• Cervical injection
  – 2-sided or 4 quadrant option
  – 4 mL used in a combined superficial (1-3 mm) and deep (1-2 cm) cervical injection
Fluorescent SLN Mapping

• Indocyanine green is injected and near-infrared (NIR) fluorescent imaging used to visualize and carry out dissection

Pathology

• Key component to SLN procedures

• Initial examination is performed using hematoxylin and eosin (H&E) staining
  – if negative, 2 adjacent 5-mcg sections are cut, 50 mcg apart
  – at each level, one side is stained with H&E and the other with immunohistochemistry using the anticytokeratin AE1:AE3 for a total of four slides per block
  – with this immunohistochemistry ultrastaging, an additional 3-4% of micrometastases to SLNs can be detected
SLN Mapping Algorithm

• The algorithm decreases false-negative rate of 14.9% to 1.9%
  – takes into account grossly enlarged suspicious nodes and includes a site-specific lymphadenectomy for the nonmapping hemipelvis

• The algorithm has a sensitivity of 98.1% and a negative predictive value of 99.8%
  – 1 out of 421 cases had isolated positive right para-aortic lymph node not detected by algorithm

Pitfalls

• Some, but not all of the positive nodes, are removed
  – does every microscopically positive node need to be removed?
  – is there therapeutic role in removing normal-appearing lymph nodes?
References


Pathologic factors of prognostic significance

• FIGO stage – often the single strongest predictor of outcome

• Histologic cell type
  – endometrioid adenocarcinoma has good prognosis
  – serous carcinoma is aggressive, with survival rates varying from 40% to 60%
  – clear cell carcinoma is highly aggressive, with 5-year survival rates of 30% to 75%
Pathologic factors of prognostic significance

• Grade – histological differentiation has long been considered one of most sensitive indicators of tumor spread
  – 50% of grade 3 lesions have greater than one-half myometrial invasion, with pelvic and para-aortic lymph node involvement approaching 30% and 20%, respectively

• myometrial invasion –

• vascular space invasion –
Pathologic factors of prognostic significance

- adnexal involvement –
  - 6% of clinical stage I and occult stage II patients have spread to adnexa
  - of these, 32% have pelvic node metastases

- peritoneal cytology

- pelvic and para-aortic lymph nodes -