Grossing in Endometrial Cancer: What to Do, What to Say

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Endometrial Cancer

Grossing in Endometrial Cancer: What to Do, What to Say

• Gross examination of a hysterectomy for endometrial cancer
  ▪ Prophylactic hysterectomy for Lynch syndrome cases
• Handling of lymph nodes and omentum
• Other issues:
  ▪ The relevance of tumor size
  ▪ Sentinel lymph node mapping
  ▪ Margins

Hysterectomy for Endometrial Carcinoma

Gross Examination

• Document structures received
• Radical hysterectomy (i.e., right and left parametria and vaginal cuff) just in cases with either tumor extension into the cervix or tumor arising in the LUS
• Obtain measurements

Hysterectomy for Endometrial Carcinoma

Gross Examination

• Ink anterior/posterior serosal surfaces (optional)
  ▪ Useful for orientation and to document serosal involvement
• Ink parametrial and vaginal cuff margins in cases of radical hysterectomies (mandatory)
• Open the uterus along the lateral walls, 3 and 9 o’clock, immediately upon receipt

Hysterectomy for Endometrial Carcinoma

Weight the Specimen

• Uterine weight will determine the CPT code to be used for reimbursement

<table>
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<tr>
<th>CPT code</th>
<th>Surgery</th>
<th>Medicare Physician Fee Schedule, Houston, TX region</th>
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<tr>
<td>58570</td>
<td>TH uterus 250 g or less</td>
<td>$804.61</td>
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<td>58571</td>
<td>TH w/t/o 250 g or less</td>
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<td>58573</td>
<td>TH w/t/o uterus over 250 g</td>
<td>$1,259.08</td>
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Endometrial Cancer

- Identify the tumor and measure it
- Cross section the uterine wall (left to right)
- Vertical sections of the lower uterine segment and cervix

Endometrial Cancer

- Examine ovaries and fallopian tubes and document findings
- Obtain tumor samples for tumor bank and/or investigational purposes
- Fix the specimen (within 1 hour of receipt in pathology) or proceed to submit sections for microscopic examination

How Many Sections to Submit for Microscopic Examination?

- Tumor
  - 1 section per cm considering the tumor largest dimension
  - Tumor/non-tumor interface should be sampled if possible
  - At least 1 full thickness section to document the deepest extent of myometrial invasion
  - Additional sections might be needed in cases difficult to assess on gross examination

- If no tumor is seen macroscopically or in cases of endometrial hyperplasia
  - To submit the entire endometrium and adjacent myometrium in sequence (fundus to LUS)
  - Leave the sections of residual myometrium in a sequential order in the formalin filled container in case that we need to submit more myometrial tissue to determine depth of invasion

- Non neoplastic endometrium
  - At least one representative section
- Endometrial polyps
  - In toto
- LUS/upper cervix
  - At least two sections, ant and post, vertical sections
- Cx
  - At least two sections, ant and post, vertical sections
  - Consideration to additional sampling may be given to cases of high grade carcinoma or when the tumor approaches the cervix
### How Many Sections to Submit for Microscopic Examination?

#### Fallopian Tubes
- In cases of serous carcinoma or carcinosarcoma to submit in toto using the SEE-FIM protocol
- Although representative sections including the fimbrial end are routinely submitted in other histotypes, some studies recommend to use the SEE-FIM protocol in all cases of endometrial carcinoma (Kulac I, et al. 2013, Koc N, et al. 2016)
- 1.6% of grossly normal fallopian tubes harbor microscopic carcinoma (Fadare O, Khabele D, 2013)

#### Ovaries
- To submit in toto in cases of serous carcinoma
- Representative sections, after careful examination, are routinely submitted
- Some authors recommend entire submission of the ovaries regardless of histotype (Silverberg 2007)
- 2.7% of normal ovaries harbor microscopic carcinoma (Fadare O, Khabele D, 2013)

#### Omentum
- Part of the staging in serous and clear cell carcinoma and carcinosarcomas
- No standard sampling recommendations
- Grossly positive, 1 or 2 sections
- Grossly negative
  - 1 section per 2 or 3 cm of maximum omental dimension (Usubütün et al., 2007)
  - 4 to 6 blocks
- ICCR recommendation for omental sampling used for ovarian, fallopian tube and peritoneal cancer; should be adopted for endometrial cancer (McCluggage WC., et al. 2015)
- Practical and economical reasons

#### Lymph Nodes
- Carefully dissect lymph nodes from adipose tissue
- Leave a small amount of adipose tissue around larger lymph nodes
- Depending on size (>3 mm) they can be bisected or sliced in neat, parallel slices of 2-3 mm thickness –slicing should be perpendicular to the longest axis
- All lymph node tissue is submitted for microscopic examination in properly identified cassettes

#### Prophylactic Hysterectomy in Lynch Syndrome
- Women with Lynch syndrome are at an increased risk of developing endometrial carcinoma and less frequently ovarian carcinoma
- Prophylactic hysterectomy and bilateral salpingo-oophorectomy is considered a cost-effective measure that reduces the risk of gynecological cancer in Lynch syndrome patients
  - It is included in the NCCN guidelines for postmenopausal women and in those who have completed childbearing
  - Usually no gross abnormalities are detected in these cases
Prophylactic Hysterectomy in Lynch Syndrome

- A cohort of 25 cases from MSKCC
  - Hysterectomy and BSO, 18 cases
  - Hysterectomy, 2 cases
  - Hysterectomy, BSO and colectomy, 5 cases
  - Endometrium, fallopian tubes and ovaries submitted in toto (SEE-FIM protocol)
    - 3 cases with atypical endometrial hyperplasia
    - 2 cases with FIGO grade 1 endometrioid adenocarcinoma in a background of atypical hyperplasia
    - 1 of 23 oophorectomies showed an ovarian carcinoma, mixed endometrioid and clear cell carcinoma, associated with endometriosis
    - Fallopian tubes showed no significant pathology

Karamzin Y, et al. 2013

Prophylactic Hysterectomy in Lynch Syndrome

- A cohort of 25 cases from Ontario
  - Hysterectomy and BSO, 23 cases
  - Hysterectomy and USO, 1 case
  - Hysterectomy, 1 case
  - 2 cases with endometrioid carcinoma, one FIGO grade 1 and one FIGO grade 2 – one in the background of atypical hyperplasia
  - 6 cases with atypical hyperplasia
  - No ovarian, tubal or cervical carcinomas were identified

* Over half of cases with endometrium submitted in toto, over half of cases with sampling of LUS, ovaries in toto in 68% and fallopian tubes in toto in 60% of cases


Prophylactic Hysterectomy in Lynch Syndrome

- 39 cases from MGH, Portuguese Oncology Institute-Porto and Centro Hospitalar S. João
  - Hysterectomy and BSO, 33 cases
  - Hysterectomy and USO, 1 case
  - Hysterectomy, 2 cases
  - Hysterectomy, BSO and colectomy, 3 cases
  - Total inclusion of the endometrium in 61.5% of cases, LUS was sampled in 79.5% of cases
  - Ovaries and fallopian tubes submitted in toto in 23.1% (SEE-FIM protocol)


Prophylactic Hysterectomy in Lynch Syndrome

- Three cases of endometrial endometrioid adenocarcinoma
  - Two FIGO grade 1 tumors
    - One was a microscopic finding in a background of non atypical hyperplasia
    - The other was 1.3 cm
  - The third tumor measured 4.5 cm, with an epicenter in the LUS and FIGO grade 2
  - 7 cases with hyperplasia (atypical and non atypical)
  - No ovarian or fallopian tube tumors


Prophylactic Hysterectomy in Lynch Syndrome

- At the present time, there is no definitive evidence to make recommendations about how to submit the adnexal structures
  - Proposal presented by Downes MR, et al. in 2014 which recommends the processing of the ovaries and fallopian tubes in toto using the SEE-FIM protocol has gained traction among clinicians
    - It will allow us to study more cases and obtain data to make definitive recommendations in the future

Does Tumor Size Matter?

- Tumor size ($\leq 2$ cm), endometrioid adenocarcinoma FIGO grade 1 or 2, and $\leq 50\%$ myometrial invasion: no metastasis (Mariani A, et al. 2000)
- Tumor size became part of the Mayo algorithm to triage low grade endometrioid carcinoma cases for staging (institutional consensus at Mayo Clinic in 2004)

Does Tumor Size Matter?

Multivariate analysis Variable results
- Tumor size ($\geq 2$ cm) is not an independent predictor of LN mt and extrauterine disease (Eucher ED, et al 2013)
- Tumor size ($\geq 3.5$ cm) is an independent predictor of LN mt and RFS in patients with low-risk EC, but not in women with intermediate/high-risk EC (Canlorbe G, et al. 2016)
- ESMO
  - Low risk, FIGO stage IA, FIGO grade 1 or 2 EndCa
  - Intermediate risk, FIGO stage IA, FIGO grade 3 EndCa or FIGO stage IB, FIGO grade 1 or 2 EndCa
  - High risk, FIGO stage IB, FIGO grade 3 EndCa, and any other high grade endometrial carcinoma

It is easy to obtain the size of a small, polypoid tumor

Issues with Tumor Size

- FIGO grade 2
- FIGO grade 2 in atypical hyperplasia

Other Issues with Tumor Size

- Large plaque-like tumor with superficial myometrial invasion versus a relatively small, but deeply invasive tumor
- More than one tumor

Intraoperative Assessment

Conventional Approach
- No Staging
  - FIGO grade 1 or 2 endometrial endometrioid adenocarcinoma
  - Invasion $< 50\%$ myometrial thickness
- Staging
  - All other cases
Endometrial Cancer

Intraoperative Assessment

Paradigm-shift
- Tumor size in the Mayo Clinic algorithm
  - Grade 1 or 2 endometrioid adenocarcinoma
    - Tumor size ≤ 2 cm and myometrial invasion ≤ 50%
    - LN mt < 0.3%
    - Tumor size > 2 cm and myometrial invasion ≤ 50%
    - LN mt 10% (pelvic)
    - Dissection of pelvic lymph nodes ONLY

NCCN Guidelines 2015
- Sentinel lymph node mapping may be considered in selected patients
- Expertise of the surgeon and attention to the technical detail is critical
- The use of SLN mapping in high-risk histologies should be taken with caution
- To be used in cases with no mt detected on imaging studies or exploration

NCCN Guidelines 2015
- The radiolabeled colloid most commonly injected into the cervix is technetium-99m; colored dyes include (isosulfan blue 1%, methylene blue 1%, and patent blue 2.5% sodium)
- Indocyanine green (ICG) has recently emerged as a useful dye that requires a near infra-red camera for localization
  - It provides a very high SLN detection rate
- Low volume metastasis to SLN detected only by enhanced pathologic ultrastaging is another potential value to staging with SLN

NCCN Guidelines 2015
- Key points to successful SLN mapping is the adherence to the SLN algorithm
  - This requires the performance of a side-specific nodal dissection in cases of failed mapping and removal of any suspicious or grossly enlarged lymph node
Endometrial Cancer

Emergent Approach
Proposal for Low Grade Endometrial Ca

- If bilateral SLN detected, no additional staging
- If unilateral SLN detected, frozen section
  - If no invasion: no additional staging
  - Grades 1/2, ≤2 cm and ≤50% MI: no additional staging
  - Grades 1/2, >2 cm, >50% MI: side specific pelvic LND and PA nodes

Proposal for High Grade Endometrial Ca

- If bilateral SLN detected, no additional staging
- If unilateral SLN detected: side specific pelvic LN and PA nodes
- If no SLN detected: bilateral pelvic and PA nodes

SLN for Routine Processing

- MDACC Method
  - SLN positive, no further work up
  - SLN negative
    - 1 H&E level + 2 unstained at 250 microns into the block
    - H&E stained level +, no further work up
    - H&E stained level -, Keratin cocktail IHC

- MSKCC Method
  - SLN positive, no further work up
  - SLN negative
    - 2 H&E levels with 1 unstained slide per level 50 microns apart
    - H&E stained level +, no further work up
    - H&E stained level -, Keratin cocktail IHC

Grossing SLN

- Lymph nodes sectioned perpendicular to long axis at 2.0 mm intervals
- Entire lymph node submitted for routine processing
SLN report

- Mt should be reported as
  - Isolated tumor cells < 0.2 mm
  - Micrometastasis 0.2 to 2.0 mm
  - Macrometastasis > 2.0 mm

Margins

CAP synoptic report
Margins (Note G)
- Cannot be assessed
- Uninvolved by invasive carcinoma
  - Distance of invasive carcinoma from closest margin mm
    Specify margin
- Involved by invasive carcinoma
  - Specify margin(s)

CAP protocol for endometrial cancer
G. Margins
The paracervical soft tissue is the only true margin in total hysterectomy specimens, and reporting the status of this margin is usually not performed; conversely, reporting the status of the vaginal and parametrial margins in a radical hysterectomy is optional.

Serosal involvement = FIGO stage IIIA disease, but this SHOULD NOT BE REPORTED AS A MARGIN

Involvement of Cervical Stroma by Endometrial Carcinoma (FIGO Stage II)
To report:
- Depth of invasion into the stroma/full thickness of cervical wall
- Ectocervical or vaginal cuff margin status

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