Role of PET/CT in Gynecologic Malignancies

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Objectives

Role of PET/CT in
- Cervical cancer
- Endometrial cancer
- Ovarian cancer
- Vulvar cancer
Cervical Cancer
Cervical cancer

- Cervical cancer worldwide
  - 3rd most common cancer in women
  - ~ 300,000 deaths annually

US

- Screening Pap smears (precancerous lesions)
- HPV prevention vaccines

Despite a marked decrease in the incidence of cervical cancer, those women who develop the disease have nearly a 40% chance of dying from their disease.

NCHS, Centers for Disease Control and Prevention, 2017
Cervical cancer

Most common histologic types:
- Squamous cell – 69%
- Adenocarcinoma - 25%
- Other histologies – 5%

Human papillomavirus (HPV) - central to the development of cervical cancer (99.7% of cervical cancers) – 70% subtypes HPV-16 and HPV-18
Cervical Cancer – staging

Clinical staging - International Federation of Gynecology and Obstetrics (FIGO) system (2009)
- physical examination, cystoscopy, proctoscopy, colposcopy, and biopsy, chest radiograph, IVP

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage IB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 cm, confined to cervix, no vaginal, parametrial invasion</td>
<td></td>
</tr>
<tr>
<td>Early stage cervical cancer</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage IB2</th>
<th>Stage IIA</th>
<th>Stage IIB</th>
<th>Stage IIIA</th>
<th>Stage IIIB</th>
<th>Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4 cm Upper 1/3 vaginal Parametrial Lower 1/3 vagina Pelvic sidewall/ Hydronephrosis Bladder/rectum invasion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advanced-stage cervical cancer</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Illustrations services, UTSW
Cervical Cancer – staging

Limitations of FIGO clinical staging

- Subjective and user dependent
- Parametrial, sidewall and lymph node metastases
- Understaging – 34 - 36.2%
- Clinical staging x surgical findings:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>~90%</td>
</tr>
<tr>
<td>Stage IB1</td>
<td></td>
</tr>
<tr>
<td>Stage IB2</td>
<td>66-83%</td>
</tr>
<tr>
<td>Stage IIA</td>
<td></td>
</tr>
<tr>
<td>Stage IIB</td>
<td></td>
</tr>
<tr>
<td>Stage IIIA</td>
<td></td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>~90%</td>
</tr>
<tr>
<td>Stage IV</td>
<td></td>
</tr>
</tbody>
</table>
Cervical Cancer – staging

Role of imaging studies – treatment planning

Stage I
- Early stage cervical cancer
  - <4 cm, confined to cervix, no vaginal, parametrial invasion

Stage IB1
- Advanced-stage cervical cancer
  - >4 cm
  - Upper 1/3 vaginal
  - Parametrial

Stage IB2
- Stage IIA
- Stage IIB
- Stage IIIA
- Stage IIIB
- Stage IVA
- Advanced-stage cervical cancer
  - lower 1/3 vagina
  - Pelvic sidewall/Hydronephrosis
  - Bladder/rectum invasion

Stage IVB
- Full dose chemo ± radiation

Surgery

Chemo/radiation

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Medical Center
Radiology
Cervical Cancer – staging

Role of imaging studies – treatment planning

Stage I
- <4cm, confined to cervix, no vaginal, parametrial invasion

Early stage cervical cancer

Stage IB1
- >4 cm upper 1/3 vaginal
- Parametrial

Stage IB2
- >4 cm lower 1/3 vagina
- Pelvic sidewall/ hydronephrosis
- Bladder/rectum invasion

Stage IIA
- Advanced-stage cervical cancer

Stage IIB
- Pelvic sidewall/ hydronephrosis

Stage IIIA
- Bladder/rectum invasion

Stage IIIB
- Optional
- Pelvic MRI
- Uncertain clinical staging
- Radiation planning

Stage IVA
- PET/CT
- Evaluate extent of disease

Stage IVB
- CT abdomen and pelvis
- If uncertain tumor size/local spread on clinical examination
- Pelvic MRI
- If suspicious lymph node on CT
- PET/CT

UT Southwestern Medical Center Radiology
Cervical cancer – role of PET/CT

1) Initial staging
   I. Local staging
   II. Lymph nodes
   III. Distant metastatic disease

2) Therapy planning

3) Response to treatment

4) Recurrence

5) Prognosis
1) Initial staging
   I. Local staging
   ‡ PET/CT – describe size, location, SUV
   ‡ MRI is better for local staging

FIGO Stage IVA - suspected invasion of the bladder
Cervical cancer – initial staging

1) Initial staging
   I. Local staging

FIGO Stage IIB – parametrial invasion
MRI in cervical cancer – local staging

**Tumor size**

- 4 cm

**Local invasion**

- **Vaginal**
  - Upper (IIA) x lower (IIIA)
  - 3rd of vagina

- **Parametrial**

**Stage**

- **Stage IIB**
  - Surgery (IB1) x chemoradiation (IB2)

- **Stage III**
- **Stage IV**

**Pelvic sidewall**

- Bladder/rectum
Cervical cancer – lymphadenopathy

1) Initial staging

II. Lymphadenopathy
   - Impacts radiotherapy field
   - Worse prognosis

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>31-79%</td>
<td>63-97%</td>
</tr>
<tr>
<td>PET or PET/CT</td>
<td>72-81%</td>
<td>69-100%</td>
</tr>
</tbody>
</table>

J Clin Oncol. 2005;23:9329–9337
Gynecol Oncol. 2007;106:29–34.
Gynecol Oncol 2016 ; 142(3): 413–41
Cervical cancer - lymphadenopathy

6 mm lymph node
FDG avid

CT criteria for positive lymph node

8 mm
10 mm
Cervical cancer - lymphadenopathy

60 y/o, Stage IB

Metastatic paraaortic lymphadenopathy
Non-malignant uptake in the pelvis

Premenopausal women

Endometrial uptake:
- Ovulation
- Menstrual phase

Ovarian uptake:
- Ovulation
- Early luteal phase
- Normal follicles and corpus luteum

Fibroid uptake

Abdom Radiol (NY) 2018 Mar 8
1) Initial staging

III. Distant metastases

- Supraclavicular lymph nodes
- Mediastinal lymph nodes
- Lung
- Bone
- Peritoneum
- Omentum
- Adrenal gland
- Liver
Cervical cancer - lymphadenopathy

58 y/o, Stage IVA

Metastatic mediastinal lymphadenopathy

Full dose chemo ± radiation
Cervical cancer – radiation planning

2) Therapy planning

- PET/CT guided intense modulated radiation therapy (IMRT)
  - Better overall survival
  - Less bladder and bowel complications

Cervical cancer – radiation planning

2) Therapy planning

- PET/CT results
  - Change management in 18% of study by
    - Extension of radiation field to include the paraaortic area
    - Change to the total administered dose to the involved nodes in the pelvic area

3) Response to treatment

- PET/CT performed after treatment is predictive of survival
- PET/CT after completion of therapy (mean 3 months)
  - at 5 years
    - If no uptake – 80% survival
    - Persistent uptake in cervix or lymph nodes – 32% survival
    - New sites of uptake – 0% survival
Cervical cancer – response to treatment

34 y/o, stage IIB

Initial PET/CT

3 months post treatment PET/CT
Cervical cancer - recurrence

4) Recurrence
   - Local recurrence
   - Nodal – pelvic, para-aortic, supraclavicular nodes
   - Lung
   - Peritoneum
   - Adrenal glands
   - Intestines
   - Skin
Cervical cancer - recurrence

4) Recurrence

- PET/CT for recurrence detection:
  - sensitivity of 96.1%, specificity of 84.4% and accuracy of 91.7%
  - FDG avid recurrence in 85% of the asymptomatic patients with recurrence

PET is a good post therapy imaging modality for detection of recurrence of cervical cancer, even in asymptomatic patients, guides treatment plan and may have favorable impact in prognosis and survival
Cervical cancer - recurrence

56 y/o, stage IIIB

Initial scan

Post treatment

1 year after treatment
5) Prognosis

- PET parameters
  - Maximum SUV
  - Mean SUV
  - Metabolic tumor volume (MTV)
  - Total lesion glycolysis (TLG)
Cervical cancer - prognosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Journal</th>
<th>Date</th>
<th>number of patients</th>
<th>FIGO stage</th>
<th>Locations</th>
<th>parameters</th>
<th>Primary endpoint</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chung</td>
<td>Preoperative FDG PET/CT maximum SUV predicts recurrence of uterine cervical uterine</td>
<td>Eur Journ Nucl Med Molec Imaging</td>
<td>2010</td>
<td>75</td>
<td>IB to IIA</td>
<td>primary tumour</td>
<td>SUV max, clinical parameters</td>
<td>recurrence</td>
<td>preop SUV max (p = 0.014), parametral involv (p = 0.04) associated with recurrence</td>
</tr>
<tr>
<td>Yilmaz</td>
<td>FDG PET/CT in cervical cancer: relationship between primary tumor FDG uptake and metastatic potential</td>
<td>Nucl Med Commun</td>
<td>2010</td>
<td>43</td>
<td>N/a</td>
<td>primary tumour</td>
<td>SUV max</td>
<td>clinical staging, local extension, lymph node mets and distant mets</td>
<td>significant difference high vs low SUV lymph node metastasis rate between the two groups (P &lt; 0.05)</td>
</tr>
<tr>
<td>Chung</td>
<td>Prognostic value of metabolic tumor volume measured by FDG PET/CT in patients with cervical cancer</td>
<td>Gynecol Oncology</td>
<td>2011</td>
<td>63</td>
<td>IB to IIA</td>
<td>primary tumour</td>
<td>MTV</td>
<td>DFS</td>
<td>MTV &gt;=23.4 mL (p = 0.037) and age</td>
</tr>
<tr>
<td>Pan</td>
<td>The SUVmax and serum squamous cell carcinoma antigen (SCC ag) function as prognostic biomarkers in patients with primary cervical cancer</td>
<td>J cancers res clin oncol</td>
<td>2012</td>
<td>82</td>
<td>N/a</td>
<td>primary tumour</td>
<td>MTV, TLG, SUVmax, SUVmean</td>
<td>Presence of LN metastases and relapse after primary treatment</td>
<td>MTV and TLG were significantly higher (p = 0.0006 and p = 0.03) in pN1 patients in comparison to pN0 patients</td>
</tr>
<tr>
<td>Crivellaro</td>
<td>18F-FDG PET/CT can predict nodal metastases but not recurrence in early-stage uterine cervical cancer</td>
<td>Gynecol Oncol</td>
<td>2012</td>
<td>69</td>
<td>IB1 and IIA</td>
<td>primary tumour</td>
<td>MTV, TLG, SUVmax, SUVmean</td>
<td>recurrence, DFS, OS</td>
<td>TLG (cutoff, 7600; hazard ratio, 2.981; P &lt; 0.05) to predict recurrence</td>
</tr>
<tr>
<td>Yoo</td>
<td>Prognostic significance of volume-based metabolic parameters in uterine cervical cancer determined using 18F-fluorodeoxyglucose positron emission tomography</td>
<td>Int J Gynecol Cancer</td>
<td>2012</td>
<td>73</td>
<td>N/a</td>
<td>N/a</td>
<td>MTV, TLG, SUVmax, SUVmean</td>
<td>recurrence, DFS, OS</td>
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<tr>
<td>Onal</td>
<td>Prognostic value of pretreatment 18F-fluorodeoxyglucose uptake in patients with cervical cancer treated with definitive chemoradiotherapy.</td>
<td>Int J Gynecol Cancer</td>
<td>2013</td>
<td>149</td>
<td>N/a</td>
<td>primary tumour</td>
<td>N/a</td>
<td>DFS, OS</td>
<td></td>
</tr>
<tr>
<td>Micco</td>
<td>Combined pre treatment MRI and 8F FDG PET/CT parameters as prognostic biomarkers in patients with cervical cancer</td>
<td>Eur Jornal of Radiology</td>
<td>2014</td>
<td>49</td>
<td>IB-VB</td>
<td>primary tumour</td>
<td>MTV, TLG, SUVmax</td>
<td>DFS, OS</td>
<td>MTV (p = 0.014/0.026) predictor of both DFS/OS (p = 0.024) predictor of DFS</td>
</tr>
<tr>
<td>Chong</td>
<td>Comparison of the Prognostic Value of F-18 Pet Metabolic Parameters of Primary Tumors and Regional Lymph Nodes in Patients with Locally Advanced Cervical Cancer Who Are Treated with Concurrent Chemoradiotherapy.</td>
<td>PloS One</td>
<td>2015</td>
<td>56</td>
<td>N/a</td>
<td>primary tumour and metastatic lymph nodes</td>
<td>MTV, TLG, SUVmax</td>
<td>DFS</td>
<td>The metabolic parameters of the primary tumors were not associated with DFS.</td>
</tr>
<tr>
<td>Hong</td>
<td>Prognostic value of total lesion glycolysis measured by 18F FDG PET/CT in patients with locally advanced cervical cancer</td>
<td>Nuclear Medicine Communications</td>
<td>2016</td>
<td>56</td>
<td>IIIB to IVA</td>
<td>primary tumour</td>
<td>SUV max, SUVmean, MTV, TLG</td>
<td>recurrence free survAval</td>
<td></td>
</tr>
<tr>
<td>Hong</td>
<td>Prognostic Value of the Sum of Metabolic Tumor Volume of Primary Tumor and Lymph Nodes Using 18F-FDG PET/CT in Patients With Cervical Cancer</td>
<td>Medicine</td>
<td>2016</td>
<td>56</td>
<td>IIIB to IVA</td>
<td>primary tumour, pelvic and parametral lymph nodes</td>
<td>MTV, TLG, SUVmax (sum)</td>
<td>recurrence free survAval</td>
<td></td>
</tr>
<tr>
<td>Herrera</td>
<td>18F FDG PET/CT metabolic parameters as useful prognostic factors in cervical cancer patients treated with chemoradiation</td>
<td>Radiation Oncology</td>
<td>2016</td>
<td>38</td>
<td>IB1 to IVA</td>
<td>primary tumour</td>
<td>SUV, MTV, TLG</td>
<td>overall survAval, disease free survAval, loco-regional control</td>
<td>pre treatment TLG cutoff (&gt;=562 OS and DFS p = 0.03 and p = 0.05)</td>
</tr>
<tr>
<td>Chung</td>
<td>Prognostic value of preoperative intratumoral FDG uptake heterogeneity in early-stage uterine cervical cancer.</td>
<td>J Gynec Oncol</td>
<td>2016</td>
<td>85</td>
<td>IB-IVA</td>
<td>N/a</td>
<td>MTV, TLG, SUVmax, uptake heterogeneity</td>
<td>recurrence</td>
<td>recurrence TLG (p = 0.001), MTV (p = 0.001), SUV (p = 0.004), het (p = 0.005) predictive of recurrence</td>
</tr>
<tr>
<td>Leseur</td>
<td>Pre- and post-treatment 18F-FDG PET/CT parameters to predict treatment response and survival in cervical cancer</td>
<td>Radiother Oncol</td>
<td>2016</td>
<td>53</td>
<td>Locally advanced</td>
<td>primary tumour</td>
<td>MTV, TLG, SUVmax</td>
<td>DFS and OS</td>
<td>MTV1 (53.65% Amax) in PET1 and TLG2 (32% SUVmax) in PET2 for DFS. MTV1 (53%) was the most significant OS predictor.</td>
</tr>
<tr>
<td>Sun</td>
<td>The Volume-metabolic Combined Parameters from (18F)FDG PET/CT May Help Predict the Outcomes of Cervical Carcinoma</td>
<td>Acad Radiol</td>
<td>2016</td>
<td>91</td>
<td>N/a</td>
<td>primary tumour and whole body uptake</td>
<td>cervical metabolic tumor volume (CMTV), cervical total lesion glycolysis (CTLG), whole-body metabolic tumor volume (WB MTV), whole-body total lesions glycolysis (WB-TLG)</td>
<td>DFS and OS</td>
<td>CMTV and FIGO stage significant for OS (P &lt; 0.05 for all), CMTV remains as prognostic factor for OS regardless of patients’ FIGO stage (P &lt; 0.05). CMTV, MTV, WB-MTV, and WB-TLG were independent prognostic factors for OS (P &lt; 0.05 for all).</td>
</tr>
<tr>
<td>Khili</td>
<td>Use of Metabolic Parameters as Prognostic Factors During Concomitant Chemoradiotherapy for Locally Advanced Cervical Cancer.</td>
<td>Am J Clin Oncol</td>
<td>2017</td>
<td>34</td>
<td>IB2 to IVA</td>
<td>primary tumour</td>
<td>MTV, TLG, SUVmax and SUV between the 2 studies (DSU Amax)</td>
<td>OS and PFS</td>
<td>SUV Amax (4.6, DSU Amax = 40%, MTV = 5.6 mL, and TLG &gt;= 21.6 mL were significantly associated with OS and DFS</td>
</tr>
</tbody>
</table>

**Results:**
- SUVmax predicts worse prognostic value.
- SUV max predicts worse prognostic value.
- SUVmax, MTV, TLG > 215.02 predictor for DFS.
- FIGO stage and TLG > 215.02 predictor for DFS.
- FIGO stage (HR = 4.87, 95%CI: 1.38-17.18, P = 0.014) and MTVS > 59.01 cm(3) (HR = 7.37, 95% CI: 1.54-35.16, P = 0.012) predictive factors for DFS.
- FIGO stage (HR = 4.87, 95%CI: 1.38-17.18, P = 0.014) and MTVS > 59.01 cm(3) (HR = 7.37, 95% CI: 1.54-35.16, P = 0.012) predictive factors for DFS.
Cervical cancer - prognosis

5) Prognosis

- Maximum SUV of primary cervical cancer is predictive of disease outcome

- Metabolic tumor volume (MTV) and total lesion glycolysis (TLG), volume-based metabolic parameters, are also predictive of outcome

- Lymph node status on PET/CT is significant independent prognostic factor
Cervical cancer - SUMMARY

1) Initial staging:
   - Lymphadenopathy
   - Distant metastases

2) Therapy planning
   - Radiation field and dose (IMRT)

3) Response to treatment
   - Status of disease in post treatment PET correlates with survival

4) Recurrence
   - High accuracy for detection of recurrence
   - Tailor treatment

5) Prognosis
   - SUVmax, MTV, TLG
Question 1

In regards to cervical cancer:

a) Incidence has been recently increasing
b) Majority of cancers are adenocarcinoma
c) PET/CT and MRI play a central role in treatment planning
d) Main role of PET/CT is in local staging
Comments to question #1:

a) Incorrect. Incidence has been decreasing due to screening and HPV prevention vaccines

b) Incorrect. Majority of cancers are squamous cell carcinomas

c) Correct. Both imaging modalities have complementary role in cervical cancer

d) Incorrect. PET/CT is important for lymph node and metastatic staging. MRI is the best study for local staging.

Reference:
For the treatment of cervical cancer:

a) All tumors, regardless of stage, are treated with surgery

b) The locally advanced cancers (≥1B2) are treated with surgery followed by radiation

c) The early stage tumors (< 1B2) are treated with radiation only

d) Imaging studies (PET/CT and MRI) have a central role in treatment planning of patients with cervical cancer
Comments to question #2

a) Incorrect. Treatment of cervical cancer will vary depending on the stage

b) Incorrect. The locally advanced cancers (≥1B2) are treated with chemoradiation

c) Incorrect. The early stage tumors (< 1B2) are treated with surgery

d) Correct. Imaging studies (PET/CT and MRI) have a central role in treatment planning of patients with cervical cancer

Reference:
Endometrial Cancer
## Endometrial cancer

- Most common gynecologic malignancy in developed countries
- Adenocarcinoma of the endometrium - most common histologic type
- Associated with obesity – adipose tissue converts ovarian androgens into estrogens, which induce endometrial proliferation

### Two histologic categories:

<table>
<thead>
<tr>
<th>Type I tumors</th>
<th>Type II tumors</th>
</tr>
</thead>
</table>
| Endometrioid tumors (grade 1 or 2) | Endometrioid tumors (grade 3)  
• tumors of non-endometrioid histology: serous, clear cell, mucinous, squamous, transitional cell, mesonephric, and undifferentiated |
| 80% of endometrial carcinomas | 20% of endometrial carcinomas |
| Favorable prognosis, estrogen-responsive | High-grade, poor prognosis, not clearly associated with estrogen stimulation |
| May be preceded by an intraepithelial neoplasm (atypical and/or complex endometrial hyperplasia) | Precursor lesion is rarely identified |
Endometrial cancer - staging

Surgical staging - International Federation of Gynecology and Obstetrics (FIGO) system
- Hysterectomy, bilateral salpingooophorectomy, lymph node dissection, peritoneal washing, omental biopsies

Role of imaging
- MRI
  - Early stage disease – minimally invasive surgery without lymphadenectomy
  - Advanced stage disease - surgical planning
- PET/CT – pelvic / periaortic lymphadenopathy and distant metastases

Oncol 2015;117(3):559–81
Endometrial cancer – role of PET/CT

1) Initial staging
   I. Local staging - MRI
   II. Lymph nodes
   III. Distant metastatic disease

2) Response to treatment/recurrence
Endometrial cancer – local staging (MRI)

**Depth of myometrial invasion**

- **Stage IA**
  - <50% myometrial invasion

- **Stage IB**
  - >50% myometrial invasion

- Depth of myometrial invasion – presence of lymph node metastases and overall survival
- Intact junctional zone excludes myometrium invasion
- Overestimation in the corneal regions

Low risk:
- <50% myometrial invasion
- Endometrioid
- Grades 1 or 2

NO lymphadenectomy
Endometrial cancer – local staging (MRI)

Cervical stroma invasion

Stage II

- Hysterectomy
- Bilateral salpingo-oophorectomy
- Lymphadenectomy
- Radical hysterectomy if parametrial invasion

Better surgical planning

Serosa/ adnexal/ Vaginal/ lymphadenopathy

Stage III

- Maximum surgical debulking
- Imaging – location of implants

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Endometrial cancer

Approach to lymph nodes – controversial (particularly in women with early stage disease)

High risk of nodal disease (regardless of stage):
- Serous, clear cell, or high-grade histology
- Myometrium invasion greater than 50%
- Large tumor (>2 cm in diameter or filling the endometrial cavity)

<table>
<thead>
<tr>
<th>Histologic grade</th>
<th>n</th>
<th>Pelvic lymph nodes involved</th>
<th>Para-aortic lymph nodes involved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>None</td>
<td>Inner third</td>
</tr>
<tr>
<td>1</td>
<td>180</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>288</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>153</td>
<td>0</td>
<td>9</td>
</tr>
</tbody>
</table>

Total extrafascial hysterectomy + bilateral salpingo-oophorectomy with pelvic and paraaortic lymph node dissection

Adapted from Creasman WT, Morrow CP, Bundy BN, et al, Cancer 1987; 60(8 Suppl):2035
**Endometrial cancer - lymphadenopathy**

1) Initial staging

II. Lymphadenopathy

**PET/CT x CT performance for metastatic lymphadenopathy**

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>54%</td>
<td>85%</td>
</tr>
<tr>
<td>PET/CT</td>
<td>63%</td>
<td>83%</td>
</tr>
</tbody>
</table>

No solid evidence in literature to replace surgical staging for lymph node involvement by tumor
PET/CT endometrial cancer - lymphadenopathy

52 y/o with endometrioid grade 1, < 50% myometrial invasion
Endometrial cancer - distant metastases

1) Initial staging

III. Distant metastases

- Prevalence: 11.8% (high grade tumors) – initial staging

- Location:
  - Peritoneum, lungs, supraclavicular / thoracic / inguinal lymph nodes, bone, pleura

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPP</th>
</tr>
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<tbody>
<tr>
<td>64.6%</td>
<td>98.6%</td>
<td>86.1%</td>
<td>95.4%</td>
</tr>
</tbody>
</table>

Radiology. 2017 Nov 29:170963
Endometrial cancer

2) Response to treatment/recurrence

- 5 year survival rate of 90% - value of tumor response evaluation is questionable
- Unlikely to be cost-effective, as the probability of recurrence is low
- Potential role in mapping the extent of disease in patients with recurrence

PET/CT endometrial cancer - recurrence

29 y/o recurrent endometrioid grade 1, 4 years before, no adjuvant treatment, now with hematuria
Endometrial cancer – Summary

1) Initial staging
   I. Local staging
      § MRI – depth of myometrial invasion, cervical involvement
   II. Lymph nodes
      § PET/CT better than CT
   III. Distant metastatic disease
      § incidence of 11.8% in unsuspected cases (high grade)

2) Response to treatment/recurrence
   § No established role for imaging in the follow up of asymptomatic patients
   § May be useful to map sites of disease in patients with suspected recurrence
Question 3

In regards to endometrial cancer:

a) MRI is the study of choice to determine the percentage of myometrial invasion

b) Obesity is a protective factor for endometrial cancer development

c) All patients undergo pelvic lymphadenectomy regardless of tumor stage

d) PET/CT has similar performance as CT alone for detection of distant metastases
Comments to question #3:

a) Correct. MRI is the study of choice for local staging in patients with endometrial carcinoma

b) Incorrect. Obesity is a risk factor for endometrial adenocarcinoma

c) Incorrect. Lymphadenectomy is reserved for high risk endometrial cancers

d) Incorrect. PET/CT has better sensitivity than CT alone for detection of distant metastases in endometrial cancer.

References:

Ovarian Cancer
Ovarian cancer

- Second most common gynecologic malignancy
- 5th leading cause of cancer death among women in the US
- High likelihood of recurrence (50%–75% of patients) despite aggressive treatment strategies
- Cytoreductive surgery, followed by chemotherapy, is the mainstay of primary treatment for high-grade early- and advanced-stage disease
- Follow up: combination of serum CA-125 assay, physical examination, and anatomic imaging
- FIGO: surgically staged
Ovarian Cancer

High grade serous epithelial ovarian, fallopian tubal, and peritoneal carcinomas are considered a single clinical entity due to their shared clinical behavior and treatment.

Epithelial ovarian carcinoma (EOC)

Five main histologic types:
- High grade serous
- Endometrioid
- Clear cell
- Mucinous
- Low grade serous
Ovarian cancer Ca-125

- Ovarian cancer–associated antigen CA-125 - part of the mucin family glycoproteins
- In patients with elevated CA-125 levels that normalize after chemotherapy, two consecutive measurements of elevated CA-125 levels are indicative of recurrent epithelial ovarian cancer
- CA-125 is neither specific for ovarian cancer nor sensitive for small volume disease
- Approximately 20% of all ovarian cancers are negative for CA-125 expression
- Despite high positive predictive values (>95%) associated with CA-125, its negative predictive value is low, at 50%–60%
- Therefore, CA-125 is useful when levels are elevated, but normal values do not exclude the possibility of recurrence
Ovarian cancer – role of PET/CT

1) Initial staging
2) Response to treatment
3) Recurrence
Ovarian cancer

1) Initial staging

- Surgically staged
- FDG PET/CT better to identify extent of disease compared to CT – potentially improving surgical debulking

AJR AM J Roentgenol. 2004 Jan;182(1):227-33
Abdom Radiol (2018)
Ovarian cancer

2) Response to treatment

- High accuracy to detect response to treatment
- Predictive of overall survival

J Clin Oncol 23:7445–7453
Ovarian cancer – recurrence

With appropriate surgical selection criteria, secondary cytoreduction surgery may substantially prolong survival in patients with recurrent ovarian cancer.
3) Recurrence

- Sensitivity of 80%–100%
- Specificity of 42% to 100%
- CA-125 and PET/CT had the highest pooled specificity (93%) and sensitivity (91%)
- Treatment for suspected recurrent ovarian cancer may be altered on the basis of PET/CT findings in as many as 40%–60% of patients
- Combined PET and contrast-enhanced CT - change in strategy in approximately 40%–44% of patients compared with contrast-enhanced CT findings alone (12%)

FDG PET/CT indicated in patients with rising CA-125 levels, and negative/equivocal CT or MR imaging for detection of recurrent ovarian cancer
Ovarian cancer – Case

59 y/o with clear cell carcinoma of ovary
Ovarian cancer – PET/CT

False-negative FDG PET/CT:
- Small lesions (less than 6-10 mm)
- Cystic or necrotic lesions
- Mucinous lesions
- Low-grade tumors

False-positives / pitfalls:
- Focal retained activity in the urinary system
- FDG uptake within atherosclerotic plaque
- Misalignment due to bowel peristalsis, bladder filling, or diverticulitis
Cervical cancer - pitfall

Ureter
Ovarian cancer – patterns of spread

- Ovarian cancer usually spreads to:
  - local lymph nodes
  - implants on the peritoneum
  - less frequently, hematogenously

- Common sites of implantation:
  - pelvis
  - right hemidiaphragm
  - liver
  - right paracolic gutter
  - bowel
  - omentum
  - transdiaphragmatic spread to the pleura
Ovarian cancer – Case

poorly differentiated papillary serous adenocarcinoma
Summary PET/CT in ovarian cancer:

- Most useful for evaluation of patients with rising serum CA-125 levels with negative or inconclusive CT or MR imaging
- There is also a role to evaluate response to treatment
- Also able to depict disease recurrence in the absence of elevated CA-125 levels
- May fail to depict diffuse peritoneal disease and cystic, necrotic, or mucinous lesions
In regards to ovarian cancer:

a) PET/CT has central role in initial staging

b) Main indication for PET/CT in ovarian cancer is rising Ca-125 with equivocal / negative anatomical imaging.

c) Virtually all ovarian cancers are positive for Ca-125

d) Mucinous and low grade ovarian cancer are usually positive on PET/CT
Comments to question #4

a) Incorrect. There is no established role for PET/CT in initial staging for patients with ovarian cancer

b) Correct. Main indication for PET/CT in ovarian cancer is rising Ca-125 with equivocal / negative anatomical imaging.

c) Incorrect. Approximately 20% of the ovarian cancers are negative for Ca-125

d) Incorrect. Mucinous and low grade ovarian cancer are usually negative on PET/CT

Reference:
Vulvar cancer

**Vulvar carcinoma** is uncommon - 5–8% of all gynecologic malignancies (75% SCC)

**Associated with** human papillomavirus (HPV) 16 or 18 infection, although the association is not as strong as the association between HPV and cervical or vaginal cancer

**Nodal involvement** – stage IIIA

**Treatment:**

- **Stage I-II:** surgery – local excision or radical vulvectomy and lymphadenectomy
- **Sentinel lymph node** (stage IB or II)
- **Stage III-IV:** chemoradiation followed or not by surgery
Vulvar cancer

Distribution of stage at diagnosis:
- 59% - confined to primary
- 30% - spread to regional organs and lymph nodes
- 6% - distant metastases

5 year survival 72%
Vulvar cancer

Regional lymphatic drainage from the vulva

- primarily occurs through the superficial inguinal nodes, although the deep inguinal nodes can also be involved

1- Superficial inguinal nodes (85%): anterior to inguinal ligament, femoral vessels and saphenous vein

2- Deep inguinal nodes (deep femoral nodes) (15%): medially along the common femoral vein – drain to external iliac lymph nodes
Vulvar cancer – role of PET/CT

1) Initial staging
- Symptoms that suggest metastases (ie, bowel and bladder dysfunction)
- Tumors ≥4 cm in diameter - For women with smaller tumors and who are surgical candidates, imaging if there is node-positive disease on sentinel node biopsy
- Clinically palpable inguinofemoral nodes
  - Sensitivity of 53-95.2%
  - Specificity of 75-90%

2) Detection of recurrence
- Groin lymph nodes
- Distant metastatic disease

Cohn et al. Gynecol Oncol 2002 Apr;85(1):179-84
Crivellaro et al. Medicine (Baltimore). 2017 Sep;96(38):e7943
Vulvar cancer

58 y/o with squamous cell carcinoma of the vulva
Vulvar cancer - Summary

Summary PET/CT in vulvar cancer:

- Detection of metastatic inguinal lymph nodes and distant metastasis in initial staging
- Also plays a role in detecting recurrent metastatic disease after treatment completion
Question 5

In regards to vulvar cancer

a) Vulvar carcinoma is the second most common gynecologic malignancy

b) Vulvar cancer is not associated with HPV infection

c) Majority is metastatic at diagnosis

d) Usually, the first site of metastatic disease in to the superficial inguinal lymph nodes
Comments to question #5

a) Incorrect. Vulvar carcinoma is uncommon – 5-8% of gynecologic malignancies

b) Incorrect. Associated with human papillomavirus (HPV) 16 or 18 infection, although the association is not as strong as the association between HPV and cervical or vaginal cancer

c) Incorrect. Only 6% has distant metastasis at the initial diagnosis.

d) Correct. Usually, the first site of metastatic disease in to the superficial inguinal lymph nodes

Reference:
Thank you!

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