Staging and Treatment for GYN Cancers

2016-2017 FCDS Educational Webcast Series
Rescheduled from 1/19/2017

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CDC & Florida DOH

“We acknowledge the Centers for Disease Control and Prevention, for its support of the Florida Cancer Data System, and the printing and distribution of the materials for the 2016-2017 FCDS Webcast Series under cooperative agreement DP003872-03 awarded to the Florida Department of Health. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention”.

Florida Department of Health

FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2016-2017 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.
Presentation Outline

- AJCC TNM Staging – NPCR Quick Reference
- Overview Major GYN Cancer Characteristics
- Anatomy of the Female Reproductive System
- GYN Cancer Staging – FIGO and AJCC TNM 7th ed.
- Site Specific Factors for GYN Cancers
- NCCN/FIGO Treatment Guidelines
- Text Documentation
- Questions

Manual Ordering Information

- COST: $64.95
- ISBN: 978-0-387-88440-0

- Required - Florida Mandate
  - FCDS will not purchase
  - Facility may purchase
  - Individual may purchase

- Also Required to Purchase 8th Edition in 2016-2017

- https://cancertaging.org
- http://springer.com
- 1-800-SPRINGER

Chapter Outline and Contents

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<td>b. Clinically significant</td>
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<tr>
<td>Grade</td>
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<td>Histopathologic Type</td>
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<td>Bibliography</td>
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</tr>
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<td>Staging Form</td>
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</table>

AJCC Cancer Staging Manual, 7th ed. – Chapter 1, Table 1.10, p.14

TNM Staging – Points in Time

**Timing for Clinical Stage** - Date of Diagnosis up to the 1st treatment... in the Absence of Disease Progression or within first 4 months after Diagnosis

**Timing for Pathologic Stage** - Date of Diagnosis through definitive surgery... in the Absence of Disease Progression or within first 4 months after Diagnosis

**Timing for Post-Treatment Stage (Pathologic - yp)** - Pathologic Stage following treatment with neoadjuvant therapy(s) and definitive surgery (can include progression after neo-TX)

**Timing for Post-Treatment Stage (Clinical - yc)** - Clinical Stage following treatment with neoadjuvant therapy(s) and before definitive surgery or no definitive surgery (can include progression after neo-TX)

Source: NPCR AJCC TNM 7th ed. Quick Reference
Clinical Stage – Pretreatment

Clinical Stage (Pre-TX Stage) is the extent of disease defined by diagnostic study before information is available from surgical resection or initiation of neoadjuvant therapy, or within 4 months after date of diagnosis, whichever is shorter.

- Patient Medical History
- Physical Examination
- Diagnostic Imaging Studies
- Endoscopy
- Biopsy of primary tumor
- Biopsy of single node or sentinel nodes
- Biopsy of metastatic sites
- Exploratory Surgery
- Other relevant lab tests, biomarker tests, or examinations

Source: NPCR AJCC TNM 7th ed. Quick Reference

Lymph Node Bx or Resection

A lymph node biopsy can be either clinical or pathologic. If the only assessment of the primary tumor is a clinical (cT) assessment, then a biopsy of a single lymph node or of a sentinel lymph node can also be included in the clinical (cN) stage. In this situation, there would have been no evaluation of the primary tumor that qualifies for the pT. This allows for the assignment of a clinical stage when a pathological stage is not applicable.

Generally a resection of the primary tumor that qualifies for the pT is required in order to assign the pN. If there is a resection that qualifies for the pathologic assessment of T(pT), then any microscopic evidence of regional node involvement is classified as pN. MUST have at least ONE node microscopically examined to assign a pN. This can be a FNA, biopsy or excision of a node as long as there is microscopic confirmation.

Source: NPCR AJCC TNM 7th ed. Quick Reference
Pathologic Stage

Pathologic Stage includes any information obtained about the extent of cancer through completion of definitive surgery as part of the first course of treatment or identified within 4 months after the date of diagnosis, whichever is longer, as long as there is no systemic or radiation therapy initiated or the cancer has not clearly progressed during that time frame.

Must meet chapter-specific criteria for surgical resection to assign

Includes all of the clinical stage information from clinical stage, plus

- Observations at time of surgical resection from operative report
- Pathologic Examination of surgically resected primary specimen
- Pathologic Examination of surgically resected regional lymph nodes
- Pathologic Examination of biopsy or resection of metastasis

Source: NPCR AJCC TNM 7th ed. Quick Reference

Pathologic Stage

Pathologic stage classification starts at moment of DIAGNOSIS.

Pathologic stage is defined by the same diagnostic studies used for clinical staging supplemented by findings from surgical resections and histologic examination of the surgically removed tissues.

Pathologic stage includes three equal pieces of information:

- All of the clinical classification information not disproven by the intra-operative or pathology findings.
- PLUS includes the operative findings during the resection not submitted to or disproven on pathology.
- PLUS includes the pathology report findings of the resected specimen.

Source: NPCR AJCC TNM 7th ed. Quick Reference
Pathologic Stage

If a biopsied tumor is not resected for any reason (e.g., when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

- To use the highest T and highest N to assign the pathologic stage, you have to have both microscopic confirmation of the highest T for a pT AND microscopic confirmation of the highest N for a pN.

- **IMPORTANT:** pT blank and pN3 is not enough for a pathologic stage so the pN will be used for the clinical stage.

Source: NPCR AJCC TNM 7th ed. Quick Reference

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Post-Treatment Stage

Documents measured response to initial (neoadjuvant) therapy(s)

- Complete Response
- Partial Response
- No Response
- Progression

May be clinical measurement only – yc

- Based on post-treatment imaging, physical examination, biopsy

More often it is post-treatment pathologic stage – yp

- Based on post-treatment surgical resection of primary site and regional nodes
- Must meet chapter-specific criteria for surgical resection

What about pre-treatment that consisted of less than 1 month of endocrine therapy – hormone therapy (prostate, breast, thyroid)?

**This is Not Neoadjuvant Tx…even though it begins before surgery**

Source: NPCR AJCC TNM 7th ed. Quick Reference
Presentation Outline

- Cervix, Vagina, Vulva – In Situ and HPV-Related Neoplasms
  - Reporting Requirements - CIN III, VAIN III, VIN III, AIN III and SIN III
- Cervix, Vagina, Vulva – Invasive Cancers (SCC, melanoma)
  - Corpus Uteri – Epithelial (adenocarcinoma)
  - Corpus Uteri – Mesenchymal (pure sarcoma)
  - Corpus Uteri – Mixed Tumors (adeno-sarcoma)
- Ovary/Fallopian Tube – Epithelial and Stromal Tumors
- Ovary/Fallopian Tube – Borderline Malignancy
- Ovary/Fallopian Tube – Germ Cell Tumors
- Female Primary Peritoneal Malignancy
Female Reproductive System

Source: http://teachmeanatomy.info

Female Reproductive System

Source: http://www.anatomypic.com
Female Reproductive System

Source: http://www.cea1.com/femaleanatomy

Female Reproductive System

Source: http://www.novartis.com
Female Reproductive System

Overview – Cervix, Vagina, Vulva

- Causes & Risk Factors
- Signs and Symptoms
- PAP and HPV Testing
- WHO Classification
- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors - stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines

Source: http://www.cancer.org
Causes and Risk Factors

Environmental
- HPV Infection
- Chlamydia Co-Infection
- HIV Immunosuppression
- Do Not Get Screened
- Oral Contraceptive Use
- Smoking Cigarettes

Genetic
- 80% in women > 50yrs
- Personal History
- DES Exposure
- Family History

Cervical Cancer Screening

April 2014 the FDA Approved the First HPV DNA Test for Primary Cervical Cancer Screening for women age 25+ that examines 14 high-risk strains of HPV

Test developed by Roche called “cobas”

Clinical Trials suggest “cobas” is better for screening than pap test because it can identify women at risk for pre-cancerous lesions earlier than pap smear

May eventually replace pap smear
Signs and Symptoms

- Tumor Mass
- Wart-like bump
- Abnormal color
- Abnormal texture
- Itching or Burning
- Unusual vaginal discharge
- Bleeding between periods
- Bleeding after menopause
- Bleeding or pain during sex

http://www.inovio.com

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Signs and Symptoms

<table>
<thead>
<tr>
<th>Gynecologic Cancer Symptoms</th>
<th>Cervical Cancer</th>
<th>Ovarian Cancer</th>
<th>Uterine Cancer</th>
<th>Vaginal Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal vaginal bleeding or discharge</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Pelvic pain or pressure</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Abdominal or back pain</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Bleeding</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Changes in bowel habits</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Itching or burning of the vulva</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Changes in incontinence or skin, such as a rash, sore, or wart</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

http://www.cdc.gov/cancer/gynecologic/images/GYN_Symptoms
>6 Million Women in U.S. have HPV Infection – at risk
>33% of Women Eligible for Screen are NOT Screened
Routine Screening detects most cancers pre-invasive
PAP and HPV DNA Screening are for “Prevention”
PAP Screening detects >90% of cancers
HPV DNA Screening may replace PAP Screen
Annual PAP No Longer Routine
Post-Menopausal Risk
Other GYN cancers and HPV – vulva, vagina, anus

Source: American Cancer Society

HPV > Neoplasia > Cancer

HPV Vaccine for Prevention of HPV not Treatment

Source: http://www.clinicalepigeneticsjournal.com/1868-7083-4-13-1.jpg
Other Characteristics

- **Reportable** Non-invasive carcinoma
  - Anus - AIN III
  - Vulva - VIN III
  - Vaginal - VAIN III

- **Not Reportable** Non-invasive carcinoma
  - Cervix - CIS (carcinoma in-situ)
  - Cervix - CIN III

WHO Histologic Classification

- Squamous cell carcinoma
- Adenocarcinoma
- Adenosquamous carcinoma
- Malignant Melanoma
Overview – Corpus Uteri

- Causes & Risk Factors
- Signs and Symptoms
- WHO Classification
- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors - stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines

Causes and Risk Factors

**Environmental**
- Oral Contraceptive Use
- Obesity and Diabetes
- Early age at menarche
- Late menopause
- Null parity – NO Children
- Hormone Manipulation
  - Estrogen Replacement
  - Tamoxifen Therapy
- Recurrent Bladder Infections
- History of Radiation Therapy

**Genetic**
- Older age (>55 years)
- Race – Uterine Sarcoma
- Retinoblastoma Gene
- Lynch syndrome

Signs and Symptoms

- Unusual vaginal discharge
- Bleeding between periods
- Bleeding after menopause
- Bleeding or pain during sex
- Pelvic pain
- Pain during intercourse
- Pain or difficulty when emptying the bladder

Source: American Cancer Society

WHO Histologic Classification

- Carcinoma and Carcinosarcoma
  - 8000-8790, 8980-8981, 9700-9701

- Adenosarcoma
  - 8380

- Sarcoma (pure sarcoma)
  - 8890-8898, 8930-8931
Other Characteristics

- ICD-O-3 term “stromal endometriosis” [8931/3] - This Condition IS Reportable

![Diagram of common locations for endometriosis implants](http://fertilitydocs.com/gif/endodiag.gif)

Source: http://fertilitydocs.com/gif/endodiag.gif

Overview – Ovary, Fallopian Tube & Primary Peritoneal Neoplasms

- Causes & Risk Factors
- Signs and Symptoms
- WHO Classification

- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors - stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines
Causes and Risk Factors

Environmental
- Hormone manipulation
  - Estrogen Replacement
  - Fertility Drug – Clomid
- Obesity
- Oophorectomy reduces risk of ovarian and fallopian tube cancer but may increase risk for primary peritoneal cancer after prophylactic salpingo-oophorectomy

Genetic
- Age > 40
- Family history
- BRCA1 and BRCA2
- Lynch syndrome
- HNPCC syndrome (hereditary non-polyposis colorectal cancer)
- Fallopian Tube-NCCN-suggested that these cancer may be the origin of some ovarian and primary peritoneal cancers

Source: 2014 Cancer Facts & Figures - American Cancer Society

Signs and Symptoms
- Pelvic mass detected on abdominal/pelvic exam
- Ascites – malignant fluid in the peritoneal cavity
  - Causes abdominal distention and bloating
- Pelvic or abdominal pain
- Difficulty eating or feeling full quickly – early satiety
- Urinary symptoms (urgency or frequency) without other obvious source of malignancy

http://www.cdc.gov/cancer/gynecologic/images/GYN_Symptoms
WHO Histologic Classification

- **Ovarian Epithelial**
  - Serous cystadenocarcinoma
  - Mucinous cystadenocarcinoma
  - Endometrioid adenocarcinoma
  - Clear cell cystadenocarcinoma

- **Ovarian Germ Cell Tumors**
  - Dysgerminoma
  - Embryonal carcinoma
  - Choriocarcinoma
  - Teratoma – malignant reportable

- **Borderline Malignant Neoplasm**

Source: http://www.clearityfoundation.org/images
Germ Cell & Sex Cord Stromal Tumor

Source: http://www.nccn.org/ovary

Other Characteristics

Borderline Neoplasm of Ovary

- 1973 – 1989 Not Reportable ICD-O
- 2001 – Not Reportable ICD-O-3
- ??? ??? ICD-O-4
Other Characteristics

- Epithelial Neoplasms - Ovary/Peritoneum
  - Bulky Disease at First Presentation
  - Common Sites for Seeding
    - Peritoneum
    - Diaphragm
    - Liver Surface
  - Pulmonary Involvement Common
  - Pleural Involvement Common
  - Elevated CA-125 Common

Other Characteristics

- Historical Assessment

- Classified as Ovarian in Origin
  - Serous Tumors with Ovarian Involvement
  - Mucinous Tumors with Ovarian Involvement

- Current Evaluation Criteria - evolving

- Improvements in Imaging and IHC/FISH expected to reduce misclassification
Other Characteristics

- Serous Tumors forming 6mm mass in ovary should be considered ovarian primaries.

- Serous Tumors forming multiple small ovarian masses should be considered peritoneal if the disease is mainly extra-ovarian.

- Mucinous neoplasms metastatic to ovary are often misclassified as ovarian primaries.

Staging GYN Cancers

Federation Internationale de Gynecologie et d'Obstetrique (FIGO)
FIGO and AJCC TNM 7th ed.

FIGO and AJCC TNM criteria for stage are nearly identical

<table>
<thead>
<tr>
<th>FIGO</th>
<th>TNM</th>
<th>CS Ext</th>
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<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>IA2</td>
<td>IA2</td>
<td>112</td>
</tr>
<tr>
<td>IB</td>
<td>2B</td>
<td>220</td>
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<td>IBc</td>
<td>3C</td>
<td>330</td>
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<tr>
<td>IBc1</td>
<td>3C1</td>
<td>331</td>
</tr>
<tr>
<td>IVA</td>
<td>4A</td>
<td>410</td>
</tr>
</tbody>
</table>

SS2000 has not been updated to current FIGO criteria

Use the FIGO stage stated in the medical record

When both FIGO Stage (or AJCC Stage) and TNM detail are available, record the more specific T, N, M Category Code with detail in preference to a statement of FIGO stage.

AJCC TNM Chapter & Name

- Chapter 33 – Vulva
- Chapter 34 – Vagina
- Chapter 35 – Cervix Uteri
- Chapter 36 – Corpus Uteri
- Chapter 37 – Ovary AND Primary Peritoneal Carcinoma
- Chapter 38 – Fallopian Tube
- Chapter 39 – Gestational Trophoblastic Tumors
### FIGO and AJCC TNM

#### Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>FIGO</th>
<th>TNM</th>
<th>FIGO</th>
<th>TNM</th>
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<td>IB</td>
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</table>

**Notes:**
- FIGO: folders of tumor, nodes, and metastasis.
- TNM: tumor, nodes, and metastasis.

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### TNM – FIGO – CS Data Collection

#### Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>FIGO</th>
<th>TNM</th>
<th>FIGO</th>
<th>TNM</th>
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</table>

**Notes:**
- FIGO: folders of tumor, nodes, and metastasis.
- TNM: tumor, nodes, and metastasis.

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**Note:** For histologic grade and histopathologic type, see AJCC staging manual.
SS2000 last updated in 2000
SS2000 is NOT consistent with 2010 FIGO Stage

Therefore, FIGO Stage noted in SS2000 may not meet same criteria as FIGO 2010

DO NOT USE 2010 FIGO to assign SS2000
DO Apply SS2000 Anatomic Stage Criteria as Described in the SS2000 Manual
### Uterine Carcinoma – FIGO/AJCC TNM

#### Staging-Endometrial Carcinoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>FIGO Categories</th>
<th>FIGO Stages</th>
<th>Surgical Pathologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2a</td>
<td>IA</td>
<td>Ia</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td></td>
<td>IB</td>
<td>Ib</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td></td>
<td>IIA</td>
<td>IIa</td>
<td>Carcinoma is at the serosa in any dimension</td>
</tr>
<tr>
<td></td>
<td>IIB</td>
<td>IIb</td>
<td>Carcinoma invades one-half of the myometrium</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>III</td>
<td>Carcinoma invades more than one-half of the myometrium</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>IV</td>
<td>Carcinoma invades the serosa and/or vagina</td>
</tr>
</tbody>
</table>

#### Regional Lymph Nodes (N)

<table>
<thead>
<tr>
<th>FIGO Categories</th>
<th>FIGO Stages</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
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<tr>
<td>N1</td>
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<tr>
<td>N2</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td></td>
</tr>
</tbody>
</table>

**Surgical-Pathologic Findings**

- Regional lymph nodes cannot be assessed
- No regional lymph node metastasis
- Regional lymph node metastasis in para-aortic lymph nodes, with or without positive pelvic lymph nodes
- Regional lymph node metastasis in para-aortic lymph nodes, with or without positive pelvic lymph nodes

### Uterine Sarcoma – FIGO/AJCC TNM

#### Staging-Uterine Sarcoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>FIGO Categories</th>
<th>FIGO Stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2a</td>
<td>IA</td>
<td>Ia</td>
<td>Primary tumor cannot be assessed</td>
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<td></td>
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<td>III</td>
<td>Carcinoma invades more than one-half of the myometrium</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>IV</td>
<td>Carcinoma invades the serosa and/or vagina</td>
</tr>
</tbody>
</table>

**Leiomyosarcoma and Endometrial Stromal Sarcoma**

- T2a: Localized disease to the uterus, within the pelvis
- T2b: Tumor invades other pelvic structures (not including the abdomen)
- T2c: Tumor invades other pelvic structures (including the abdomen) and/or distant metastases

**Regional Lymph Nodes (N)**

<table>
<thead>
<tr>
<th>FIGO Categories</th>
<th>FIGO Stages</th>
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<tbody>
<tr>
<td>N0</td>
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<tr>
<td>N1</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td></td>
</tr>
</tbody>
</table>

**Definition**

- Regional lymph node cannot be assessed
- No regional lymph node metastasis
- Regional lymph node metastasis in para-aortic lymph nodes
- Regional lymph node metastasis in para-aortic lymph nodes, with or without positive pelvic lymph nodes

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Staging Ovary – FIGO/AJCC TNM

FCDS Required GYN Site Specific Factors

<table>
<thead>
<tr>
<th>Schema Name</th>
<th>2014 FCDS Required</th>
<th>Additional CoC Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adnexa</td>
<td>Uterine</td>
<td>Other</td>
</tr>
<tr>
<td>Cervix</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Corpus</td>
<td>Adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>Corpus</td>
<td>Carcinoma</td>
<td></td>
</tr>
<tr>
<td>Corpus</td>
<td>Sarcoma</td>
<td></td>
</tr>
<tr>
<td>Fallopian Tube</td>
<td>None</td>
<td>1,4,5,6,7</td>
</tr>
<tr>
<td>Genital</td>
<td>Female</td>
<td>Other</td>
</tr>
<tr>
<td>Merkel Cell</td>
<td>Vulva</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>None</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>Female</td>
<td>Genital</td>
</tr>
<tr>
<td>P slighta</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Vagina</td>
<td>None</td>
<td>1,2,3,4,5,6,7</td>
</tr>
<tr>
<td>Vulva</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>
NCCN/FIGO Treatment Guidelines
Cervix, Vulva, Vagina

Choosing the Most Appropriate Type of Surgery Based on Clinical Stage

Any Histology

NCCN Guidelines – Cervical Cancer – Version 1.2017
Surgery
Cervix, Vulva, Vagina

PRINCIPLES OF SURGERY: SURGICAL STAGING

- Vulvar cancer is staged using the American Joint Committee on Cancer (AJCC) and the International Federation of Gynecology and Obstetrics (FIGO) staging systems. (Table 31.1)

- Staging involves complete surgical resection of the primary vulvar tumor(s) with at least 1-cm margins and either a unilateral or bilateral inguinal lymphadenectomy, or an SN biopsy in select patients. Inguinal lymphadenectomy removes the LNs superficial to the inguinal ligament, within the proximal femoral triangle, and deep to the cribriform fascia.

- ILN status is the most important determinant of survival. (2) Historically, an en bloc surgical resection of the vulvar tumor and complete bilateral inguinal lymphadenectomy (resection of superficial inguinal and deep femoral nodes) were performed, but this approach was associated with significant morality. (3)

- The current standard involves resection of the vulvar tumor and LNs through separate incisions. (4)

- The choice of vulvar tumor resection technique depends on the size and extent of the primary lesion and may include radical local excisions and modified radical vulvectomy.

- There are no prospective trials comparing the resection techniques above. Retrospective data suggest there is no difference in recurrence outcomes between radical local excisions compared with radical vulvectomy.

- For a primary vulvar tumor that is <4 cm, located 2 cm or more from the vulvar midline and in the setting of clinically negative inguinal lymph nodes, a unilateral inguinofemoral lymphadenectomy or SN biopsy is appropriate (see Principles of Surgery: Inguinal and Femoral Lymph Node Biopsies). (5)

- For a primary vulvar tumor located within 2 cm from or crossing the vulvar midline, a bilateral inguinofemoral lymphadenectomy or SN biopsy is recommended.

- Note: patients are not candidates for lymphadenectomy including those with stage IA disease due to a <5% risk of lymphatic metastases. (6)

- For patients with stage IB-IIA disease, inguinal lymphadenectomy is recommended due to a risk of >10% of lymphatic metastases. (7)

- A negative unilateral lymphadenectomy is associated with a <5% risk of contralateral metastases. (8)

- In the setting of positive LN disease after unilateral lymphadenectomy, contralateral lymphadenectomy is recommended. Any nodes that are grossly enlarged or suspicious for metastases during the unilateral lymphadenectomy should be evaluated by frozen section pathology intraoperatively in order to tailor the extent and bilaterality of the LN dissection.

- Those with locally advanced disease may benefit from en bloc radiation with concurrent platinum-based chemotherapy if a complete response is not achieved, surgical resection of the residual disease is recommended in patients with resectable disease who are appropriate surgical candidates. (9)

- The management of bulky (inguinal) LNs in the setting of an unresectable or T3 primary vulvar lesion is uncertain. It is reasonable to consider either 1) primary chemoradiative surgery of the bulky LNs followed by platinum-based chemoradiation to the bilateral groin and primary vulvar tumor, or 2) platinum-based chemoradiation to the bilateral groins and primary vulvar tumor alone. (10)

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Surgery
Cervix, Vulva, Vagina

TABLE 1: Resection of Cervical Cancer as Primary Therapy

<table>
<thead>
<tr>
<th>Comparison of Hysterectomy Types</th>
<th>Comparison of Trachelectomy Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple/Endovaginal Hysterectomy Type 1</td>
<td>Radical Hysterectomy Type C*</td>
</tr>
<tr>
<td>Modified/Radical Hysterectomy Type I</td>
<td>Radical Hysterectomy Type C**</td>
</tr>
<tr>
<td>Radical Hysterectomy Type C***</td>
<td>Simple Trachelectomy</td>
</tr>
<tr>
<td>Simple Trachelectomy</td>
<td>Radical Trachelectomy**</td>
</tr>
</tbody>
</table>

- Indication: Stage IA-1
- Intention: Cautery for incontinence
- Uterus: Removed
- Ovaries: Optional removal
- Cervix: Removed
- Vaginal margin: None
- Cervix: Not mobilized
- Cardinal ligaments: Resected at uterine and cervical border
- Uterosacral ligaments: Divided at cervical border
- Bowel: Mobilized to base of cervix
- Rectum: Not mobilized
- Surgical approach: Lateral parametrical or anterior parametrical

Radiation Therapy
Cervix, Vulva, Vagina

- External radiation therapy with high-energy beam
- Intracavitary radiation therapy
  - Low-dose brachytherapy
  - High-dose brachytherapy
- Interstitial radiation therapy
  - Needles containing radioactive material are placed directly into the cancer and surrounding tissue(s)
- Combinations of above

http://radonc.ucla.edu/Gyn-CTDosimetry

Chemo and Immuno Therapy
Cervix, Vulva, Vagina

**Early Stage** Chemotherapy/Immunotherapy Options
Fluorouracil (5FU) - Topical Chemotherapy applied directly to skin
Imiquimod  - Topical Immunotherapy applied directly to effected skin

<table>
<thead>
<tr>
<th>First line combination therapy</th>
<th>Possible first line single agent therapy</th>
<th>Second line therapy*(Agents listed are category 2B unless otherwise noted)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Cisplatin/paclitaxel/Bevacizumab</em> (category 1)</td>
<td><em>Cisplatin (preferred as a single agent)</em></td>
<td><em>Bevacizumab</em></td>
</tr>
<tr>
<td><em>Cisplatin/paclitaxel (category 1)</em></td>
<td><em>Paclitaxel</em></td>
<td><em>Alumum-based paclitaxel</em></td>
</tr>
<tr>
<td><em>Topotecan/paclitaxel/Bevacizumab</em> (category 1)</td>
<td></td>
<td><em>Docetaxel</em></td>
</tr>
<tr>
<td><em>Cisplatin/paclitaxel</em></td>
<td></td>
<td><em>5-FU (5-fluorouracil)</em></td>
</tr>
<tr>
<td><em>Topotecan/paclitaxel</em></td>
<td></td>
<td><em>Gemcitabine</em></td>
</tr>
<tr>
<td><em>Cisplatin/gemcitabine (category 3)</em></td>
<td></td>
<td><em>Budriside</em></td>
</tr>
</tbody>
</table>

**Targeted Therapies** - Cetuximab, Erlotinib or Pazopanib + or - Chemo

NCCN Guidelines - Cervical Cancer - Version 1.2017
NCCN/FIGO Treatment Guidelines
Corpus Uteri – Endometrium

Uterine Neoplasm Histology Groupings

NCCN Guidelines - Uterine Neoplasms - Version 1.2017
Endometrial Carcinoma
Primary Treatment

NCCN Guidelines - Uterine Neoplasms - Version 1.2017

Endometrial Carcinoma
Primary Surgery

NCCN Guidelines - Uterine Neoplasms - Version 1.2017
Endometrial Carcinoma Primary Surgery & Surgical Staging

**Principles of Surgical Staging for Endometrial Cancer**

- Total hysterectomy, bilateral salpingo-oophorectomy (HBOO), and lymph node assessment is the primary treatment of apparent uterine-confined endometrial carcinoma, unless patients desire (and are candidates for) fertility sparing options (see HBOO). Select patients with metastatic endometrial carcinoma are also candidates for hysterectomy [see Hysterectomy and Pathologic Evaluation (HBOO)].
- Endometrial carcinoma should be removed set bloc to optimize outcomes; intraperitoneal morcellation or tumor fragmentation should be avoided.
- HBOO and lymph node assessment may be performed by any surgical route (e.g., laparoscopic, robotic, vaginal, abdominal), although the standard in those with apparent uterine-confined disease is to perform the procedure via a minimally invasive approach. Randomized trials, a Cochrane Database Systematic Review, and population-based surgical studies support that minimally invasive techniques are preferred in this setting due to a lower rate of surgical site infection, transfusion, venous thromboembolism, decreased hospital stay and lower cost of care, without compromise in oncologic outcome.1-13
- The lymph node assessment includes evaluation of the nodal basins that drain the uterus, and often comprises a pelvic nodal dissection with or without aortic nodal dissection. This continues to be an important aspect of surgical staging in women with uterine-confined endometrial carcinoma, as the procedure provides important prognostic information that may alter treatment decisions.
- Pelvic lymph nodes from the external iliac, internal iliac, obturator, and common iliac nodes are frequently removed for staging purposes.
- Para-aortic nodal evaluation from the infrarenal to the infrarenal regions may also be utilized for staging in women with high-risk tumors such as deeply invasive lesions, high-grade histology, and tumors of serous carcinoma, clear cell carcinoma, or carcinosarcoma.
- Sentinel lymph node (SLN) mapping may be considered in select patients (see pages 2-4 of HBOO).14
- Excision of suspicious or enlarged lymph nodes in the pelvic or aortic regions is important to exclude nodal metastases.
- Some patients may not be candidates for lymph node dissection.
- Visual evaluation of the peritoneal, diaphragmatic, and serosal surfaces with biopsy of any suspicious lesions is important to exclude extraintestinal disease.
- Some patients may not be candidates for lymph node dissection.
- While pelvic lymph node dissection does not impact staging, FIGO and AJCC nonetheless recommend that surgeons continue to obtain this during the HBOO.
- Omental biopsy is commonly performed in those with serous carcinoma, clear cell carcinoma, or carcinosarcoma, which should be undertaken with particular caution.

NCCN Guidelines - Uterine Neoplasms - Version 1.2017

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Endometrial Carcinoma Primary Surgery & Surgical Staging

**Principles of Sentinel Lymph Node (SLN) Mapping for Endometrial Cancer Staging**

- The role of SLN mapping in endometrial carcinomas is under evaluation. Prospective and retrospective studies demonstrate that compared to systemic lymphadenectomy, SLN mapping with ultrastaging may increase the detection of lymph node metastasis with low false-negative rates in women with apparent uterine-confined disease.15-22 To date, no randomized trials evaluating this technique in endometrial carcinomas have been conducted. If SLN mapping is considered, the expertise of the surgeon and attention to technical detail is critical. The use of SLN mapping in high-risk histologies (serous carcinoma, clear cell carcinoma, or carcinosarcoma) should be undertaken with particular caution.

- SLN mapping can be considered for the surgical staging of apparent uterine-confined malignancy. If there is no metastasis demonstrated by imaging studies or in obvious extraintestinal disease at exploration.
- A cervical injection with dye has emerged as a useful and validated technique for identification of lymph nodes that are at high risk for metastasis (i.e., SLN in patients with early-stage endometrial cancer.23-25)
- The combination of a superficial (1-3 mm) and deep (1-2 cm) cervical injection leads to dye delivery to the main layers of lymphatic channel origins in the cervix and corpus, namely the superficial subserosal, intermediate stromal, and deep submucosal lymphatic sites of origin (Figure 1 on ENDO C-3 of 5).
- Injection into the uterine cervix provides excellent dye penetration to the region of the uterine vessels and main uterine lymphatic trunks that course in the parametria and appear in the broad ligament leading to pelvic and occasionally parametrical sentinel nodes.
- The uterine body lymphatic trunks commonly cross over the obliterated umbilical artery with the most common location of pelvic SLN being medial to the external iliac, ventral to the hypogastic, or in the superior part of the obturator region (Figure 2 on ENDO C-3 of 5).
- A less common location is usually seen when the lymphatic trunks do not cross over the obliterated umbilical and move cephalad following the mesorectum; in these cases, the SLN is usually seen in the common iliac presacral region (Figure 3 on ENDO C-3 of 5).
- The radiolabeled colloid most commonly injected into the cervix is technetium-99m (99mTc) labeled oxine dyes are available in a variety of forms (Iosufin Blue 1% and Methylene Blue 1%, Patent Blue 2.5% sodium).
- Inert blue green (IG) recently emerged as a useful imaging dye that requires near infrared camera for localization, provides a very high SLN detection rate, and is commonly used in many practices at the present time.17
- Low volume nodal metastasis to SLN detected only by enhanced pathologic ultrastaging is another potential value to staging with SLN.16-22
- Key points to a successful SLN mapping is the adherence to the SLN algorithm, which requires the performance of a side-specific nodal dissection in cases of failed mapping and removal of any suspicious or grossly enlarged nodes regardless of mapping (Figure 4 on ENDO C-4 of 5).17-22
Endometrial Carcinoma Primary Surgery & Surgical Staging

PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED

Figure 4: The SLN algorithm for surgical staging of endometrial cancer

1. Peritoneal & serosal evaluation & washings
2. Retropertitoneal evaluation
   - Excision of all mapped SLN with histostaging
   - Any suspicious nodes must be removed regardless of mapping
3. If there is no mapping on a hemi-pelvis, a site-specific LND is performed
   - Para-aortic LND: done at attending discretion

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Endometrial Carcinoma Post-Surgical Adjuvant TX

All staging in guideline is based on updated 2019 FIGO staging. (See St. 1)

<table>
<thead>
<tr>
<th>Adverse Risk Factors</th>
<th>Histologic Grade/Aduajvant Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G1</td>
</tr>
<tr>
<td>Adverse risk factors not present</td>
<td>Observe</td>
</tr>
<tr>
<td>Adverse risk factors present</td>
<td>Observe or Vaginal brachytherapy</td>
</tr>
<tr>
<td>Adverse risk factors not present</td>
<td>Observe or Vaginal brachytherapy</td>
</tr>
<tr>
<td>Adverse risk factors present</td>
<td>Observe or Vaginal brachytherapy</td>
</tr>
<tr>
<td>Adverse risk factors not present</td>
<td>Observe or Vaginal brachytherapy</td>
</tr>
<tr>
<td>Adverse risk factors present</td>
<td>Observe or Vaginal brachytherapy and/or EBT</td>
</tr>
<tr>
<td>Adverse risk factors present</td>
<td>Observe or Vaginal brachytherapy and/or EBT</td>
</tr>
<tr>
<td>Adverse risk factors present</td>
<td>Observe or Vaginal brachytherapy and/or EBT</td>
</tr>
</tbody>
</table>

*The degree of surgical staging to assess disease status depends on intraoperative findings. Multidisciplinary expertise is recommended.

NCCN Guidelines - Uterine Neoplasms - Version 1.2017
Endometrial Carcinoma
Post-Surgical Adjuvant TX

Treatment for Carcinosarcoma, Serous, or Clear Cell AdenoCA

Endometrial Carcinoma Radiation Therapy

**PRINCIPLES OF RADIATION THERAPY FOR UTERINE NEOPLASMS**

- RT is directed at sites of known or suspected tumor involvement, and may include external beam RT (EBRT) and/or brachytherapy. Diagnostic imaging is often used to assess locoregional extent and to rule out distant metastases before administration of RT. In general, EBRT is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered: 1) to an intact uterus, either preoperatively or definitively; or 2) more commonly, to the vagina after hysterectomy. For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.
- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, pararectal, upper vaginal/para-vascular tissue, and para-vascular lymph nodes (in patients with cervical involvement). Extended-field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended-field depends on the clinical situation but should at least lie to the level of the renal vessels. External-beam doses for microscopic disease should be 45 to 50 Gy. Multiple conformal fields based on CT treatment planning should be utilized.
- Initiate brachytherapy as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery. Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IB disease, in general, a total dose of 75 to 80 Gy low-dose-rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the size of EBRT.
- The target for vaginal brachytherapy after hysterectomy should be limited to the upper two-thirds of the vagina.
- For high-dose-rate brachytherapy, when used as a boost to EBRT, doses of 4 to 6 Gy x 2 to 3 fractions prescribed to the vaginal mucosa are commonly used.
- For high-dose-rate vaginal brachytherapy alone, commonly used regimens include 7 Gy x 3 prescribed at a depth of 0.5 cm from the vaginal surface or 6 Gy x 5 fractions prescribed to the vaginal surface.
- Evidence supports the use of combined-modality radiation and chemotherapy as adjuvant treatment for patients with extrarectal disease.6
- Palliative EBRT should be individualized to disease extent and patient performance status. Various dose/fractionation schemes can be considered. A common approach is 30 Gy in 10 fractions.

Endometrial Carcinoma Systemic Therapies

**SYSTEMIC THERAPY FOR RECURRENT, METASTATIC, OR HIGH-RISK DISEASE**

**CHEMOTHERAPY REGIMENS**

- Multi-agent chemotherapy regimens preferred, if tolerated
  - Carboplatin/paclitaxel6
  - Carboplatin/doxorubicin6
  - Carboplatin/doxorubicin/paclitaxel6,6
  - Carboplatin/doxorubicin/paclitaxel6,6
  - Single agents
    - Carboplatin
    - Paclitaxel
    - Doxorubicin
    - Liposomal doxorubicin
  - Docetaxel
  - Bevacizumab8
  - Tamoxifen6
  - Raltitrexed
  - Topotecan
  - Ridaforolimus
  - Vemurafenib
  - Temsirolimus
  - Dasatinib
  - Bortezomib for carcinomasoma
  - Cisplatin
  - Rofosfamide for carcinomasoma
  - Ixabepilone
  - Vinorelbine
  - Epirubicin
  - Trastuzumab
  - ErbB2

**HORMONE THERAPY**

- Megestrol/progestin (alternating)
- Progestational agents
- Aromatase inhibitors
- Tamoxifen
Uterine Sarcoma
Primary Treatment

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Uterine Sarcoma
Post Clinical & Surgical Evaluation

NCCN Guidelines – Uterine Neoplasms Version 1.2017
Uterine Sarcoma
Post Clinical & Surgical Evaluation

PATHOLOGIC FINDINGS/HISTOLOGIC GRADE

- High-grade ESS
- IRIS
- MLS

ADDITIONAL THERAPY

Stage I
- Observe or
- Consider systemic therapy (category Z)

Stage II, III
- Consider systemic therapy and/or
- Consider EBRT

Stage IV
- Systemic therapy and/or
- EBRT
- Palliative EBRT

Srv Surveillance (IITASII-4)

NCCN Guidelines - Uterine Neoplasms Version 1.2017

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Uterine Sarcoma – Radiation

PRINCIPLES OF RADIATION THERAPY FOR UTERINE NEOPLASMS

- RT is directed at areas of known or suspected tumor involvement, and may include external beam RT (EBRT) and/or brachytherapy. Diagnostic imaging is often used to assess locoregional extent and to rule out distant metastases before administration of RT. In general, EBRT is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered: (1) to an intact uterus, either preoperatively or definitively; or (2) more commonly, to the vagina after hysterectomy. For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.
- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, parametria, upper vagina, para-ovarian tissues, and para-aortic lymph nodes (in patients with cervical involvement). Extended-field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation but should at least be to the level of the renal vessels. External beam doses for microscopic disease should be 45 to 50 Gy. Multiple conformal fields based on CTV treatment planning should be utilized.
- Initiate brachytherapy as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery. Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IIIb disease, in general, a total dose of 75 to 80 Gy low-dose-rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 6.5 cm from the vaginal surface; the dose depends on the use of EBRT.
- The target for vaginal brachytherapy after hysterectomy should be the upper two-thirds of the vagina.
- For high-dose-rate brachytherapy, when used as a boost to EBRT, doses of 4 to 8 Gy x 2 to 3 fractions prescribed to the vaginal mucosa are commonly used.
- For high-dose-rate vaginal brachytherapy alone, commonly used regimens include 7 Gy x 3 prescribed at a depth of 6.5 cm from the vaginal surface or 6 Gy x 5 fractions prescribed to the vaginal surface.
- Evidence supports the use of combined modality radiation and chemotherapy as adjuvant treatment for patients with extracervical disease.
- Palliative EBRT should be individualized to disease extent and patient performance status. Various dose/fractionation schemes can be considered. A common approach is 36 Gy in 12 fractions.

NCCN Guidelines - Uterine Neoplasms Version 1.2017

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Uterine Sarcoma - Chemotherapy

SYSTEMIC THERAPY FOR UTERINE SARCOMA
(Clinical trials strongly recommended)

Combination regimens:
- Docetaxel/gemcitabine
  (preferred for leiomyosarcoma)
- Doxorubicin/ifosfamide
- Doxorubicin/carboplatin
- Gemcitabine/docetaxel
- Gemcitabine/vinorelbine

Single-agent options:
- Docetaxel
- Doxorubicin
- Epirubicin
- Eribulin (category 2B)
- Gemcitabine
- Ifosfamide
- Liposomal doxorubicin
- Paclitaxel
- Temozolomide
- Trabectedin
- Vinorelbine (category 2B)
- Doxetaxel (category 3)

HORMONE THERAPY
(For Low-grade ESS or Hormone Receptor Positive (ER/PR) utMS): 
- Medroxyprogesterone acetate 
  (category 2B for ER/PR positive utMS) 
- Megestrol acetate 
  (category 2B for ER/PR positive utMS) 
- Aromatase Inhibitors 
- GnRH analogs 
  (category 2B for low-grade ESS and ER/PR positive utMS)

NCCN Guidelines - Uterine Neoplasms - Version 1.2017

NCCN/FIGO Treatment Guidelines
Ovary / Fallopian Tube / Primary Peritoneum

CANCER
IT'S PERSONAL
THE RIGHT PATIENT, THE RIGHT TREATMENT.
Ovary, Fallopian Tube & Primary Peritoneum Surgery

PRINCIPLES OF SURGERY(1-44)1

Newly diagnosed invasive epithelial ovarian cancer apparently confined to an ovary or to the pelvis

In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all pelvic disease and to evaluate for occult disease in the upper abdomen or retroperitoneum.

• On entering the abdomen, aspiration of ascites or peritoneal lavage should be performed for peritoneal cytologic examinations.
• All peritoneal surfaces should be visualized, and any peritoneal surface or adhesions suspicious for harboring metastasis should be selectively excised or biopsied. In the absence of any suspicious areas, random peritoneal biopsies should be taken from the pelvis, pericolic gutters, and undersurfaces of the diaphragm (diaphragm scraping for Pap test is an acceptable alternative).
• EK0 and hysterectomy should be performed with every effort to keep an encapsulated mass intact during removal.
• For selected patients desiring to preserve fertility, UKC may be considered.
• Omentectomy should be performed.
• Para-aortic lymph node dissection should be performed by stripping the nodal tissue from the ureter and the aorta bilaterally to at least the level of the inferior mesenteric artery and preferably to the level of the renal vessels.
• The preferred method of dissecting pelvic lymph nodes is bilateral removal of lymph nodes overlying and anterior to the common iliac vessels, overlying and medial to the external iliac vessels, overlying and medial to the hypogastric vessels, and from the obturator fossa at a minimum anastomosis to the obturator nerve.2

Newly diagnosed invasive epithelial ovarian cancer involving the pelvis and upper abdomen

In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all abdominal, pelvic, and retroperitoneal disease. Residual disease >1 cm defines optimal cytoreduction; however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes.3
• Resection of omentum (if present) should be performed for peritoneal cytologic examinations. All involved omentum should be removed.
• Suspicious and/or enlarged nodes should be resected, if possible.
• Those patients with tumors outside the pelvis 5 cm (proposed stage III) should have bilateral pelvic and para-aortic lymph node dissection as previously described.
• Procedures that may be considered for optimal surgical cytoreduction include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cytoresection and/or omentectomy, partial hysterectomy, partial omentectomy, bowel resection, and/or formal pelvic lymphadenectomy.
• Select patients with low-volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for IP therapy. In these patients, consideration should be given to placement of IP catheter with initial surgery.


Ovary, Fallopian Tube, & Primary Peritoneum Surgery

PRINCIPLES OF SURGERY(1-44)1

Interval cytoreduction after neoadjuvant chemotherapy of invasive epithelial ovarian cancer

As with a primary cytoreduction procedure, every effort should be made to achieve maximum cytoreduction during an interval cytoreduction procedure. Maximal effort should be made to remove all gross disease in the abdomen, pelvis, and retroperitoneum.

• Interval cytoreductive surgery should be performed after 4 cycles of neoadjuvant chemotherapy for women with a response to chemotherapy or stable disease. Alternate timing of surgery has not been prospectively evaluated but may be considered based on individual patient-centered factors.
• All peritoneal surfaces should be visualized, and any peritoneal surface or adhesions suspicious for harboring metastasis should be selectively excised or biopsied.
• An omentectomy should be performed.
• Suspicious and/or enlarged nodes should be resected, if possible. Removal of lymph nodes noted to have potential metastasis at the time of initial diagnosis should be considered, even if not currently suspicious or enlarged.
• Procedures that may be considered for optimal surgical cytoreduction include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cytoresection and/or omentectomy, partial hysterectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.

Risk-Reducing Salpingo-oophorectomy (RRO) Protocol
• Perform operative laparoscopy.
• Survey upper abdomen, bowel surfaces, omentum, appendix (if present), and pelvic organs.
• Expose any abnormal peritoneal findings.
• Obtain pelvic washing for cytology (50 cc normal saline instilled and aspirated immediately).
• Perform total EK0, removing 2 cm of prosthetic omentum resection of IP ligament, all tube up to the cornu, and all peritoneum surrounding the ovaries and tubes, especially peritoneum underlying areas of adhesion between tubes and ovaries and the pelvic sidewall.6
• Engage in minimal instrument handling of the tubes and ovaries to avoid traumatic distention of endosalpinx.
• Both ovaries and tubes should be placed in an endobag for retrieval from the pelvis.
• Both ovaries and tubes should be processed according to SEE-FIM protocol.7
• If occult malignancy or STC is identified, perform referral to gynecologic oncologist.
• The prevention benefits of salpingo-oophorectomy alone are not yet proven. If considered, the Fallopian tube from the fimbria to its insertion into the uterine should be removed. In addition, the Fallopian tube should be processed and assessed as described above. The concern for risk-reducing salpingo-oophorectomy alone is that women are still at risk for developing ovarian cancer. In addition, in premenopausal women, oophorectomy reduces the risk of developing breast cancer by 50%. See NCCN Guidelines for Genetic/Familial High Risk Assessment: Breast and Ovarian.

Ovary, Fallopian Tube, & Primary Peritoneum Surgery

**Primary Surgery**
- Radical pelvic dissection
- Bowel resection
- Diaphragm or other peritoneal surface stripping
- Omentectomy
- Splenectomy
- Partial hepatectomy
- Cholecystectomy
- Partial cystectomy
- Ureteroenocystomy
- Distal pancreatectomy

**Ancillary/Palliative Surgery**
- Paracentesis
- Thoracentesis/pleurodesis
- Ureretal stents
- Nephrostomy
- Surgical relief or intestinal obstruction
- Gastroscopy tube
- Vascular access device
- Indwelling peritoneal or pleural catheter
- Intestinal stents
- Video-assisted thoracoscopy

Ovary, Fallopian Tube & Primary Peritoneum Treatment by FIGO Stage & Grade


Ovary, Fallopian Tube & Primary Peritoneum Primary/Adjuvant Chemotherapy

Ovary, Fallopian Tube & Primary Peritoneum Primary/Adjuvant Chemotherapy

PRINCIPLES OF SYSTEMIC THERAPY (3 of 7)

Ovarian/Fallopian Tube/Primary Peritoneal/Carcinosarcoma/Clear Cell/Endometroid/Ovarian/Borderline Epithelial/Grade 1 (Low-Grade) Serous/Endometrioid

Stage II/II:

- IP Regimen
  - Paclitaxel 135 mg/m² IV continuous infusion over 3 or 24 hour Day 1; cisplatin 75–100 mg/m²; Day 2 after IV pacitaxel; paclitaxel 60 mg/m²
  - IP Day 8; Repeat every 3 weeks x 6 cycles. (category 1)

- IV Regimen
  - Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)
  - Paclitaxel 60 mg/m² IV over 1 hour followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)
  - Paclitaxel 60–75 mg/m² IV over 1 hour followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)
  - Bevacizumab-containing regimens per NCCN and GOG.218
  - Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour, and bevacizumab 7.5 mg/kg IV over 30–90 minutes Day 1. Repeat every 3 weeks x 6 cycles. Continue bevacizumab for up to 12 additional cycles. (category 2C)
  - Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. Starting Day 1 of cycle 2, give bevacizumab 15 mg/kg IV over 30–90 minutes every 3 weeks for up to 22 cycles. (category 2B)

- Additional options for the following less common histopathologies:
  - Carcinosarcoma (BRMM)
    - Carboplatin/cisplatin
    - Paclitaxel/Ifosfamide (category 2B)

- Miscellaneous tumors
  - 5-FU/docetaxel/cisplatin
  - Cisplatin/cisplatin

- Borderline epithelial carcinomas and grade 1 (low-grade) serous/endometrioid
- Hormone therapy (Aromatase inhibitors [e.g., anastrozole, letrozole], leuprolide acetate, tamoxifen) (category 2B)

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Ovary, Fallopian Tube & Primary Peritoneum Chemotherapy for Recurrence

PRINCIPLES OF SYSTEMIC THERAPY (5 of 7)

Acceptable Recurrence Therapies for Epithelial Ovarian/Fallopian Tube/Primary Peritoneum Cancer

Preferred Agents
- Platinum Sensitive Disease
  - Carboplatin
  - Carboplatin/paclitaxel
  - Carboplatin/paclitaxel/bevacizumab
  - Carboplatin/Cisplatin (category 1)
  - Carboplatin/paclitaxel/Bevacizumab
  - Carboplatin (category 1)
- Non-Platinum Sensitive Disease
  - Paclitaxel
  - Paclitaxel/Cisplatin
  - Paclitaxel/Cisplatin/Bevacizumab
  - Paclitaxel/Cisplatin/Bevacizumab/Aromatase inhibitors

- Hormonal Therapy
- Targeted Therapy
- Radiation Therapy

Other Potentially Active Agents
- Afatinib
- Cephalostatin
- Cyclophosphamide
- Doxorubicin
- Ifosfamide
- Intravenous
- Metopitant
- Oxaliplatin
- Paclitaxel
- Paclitaxel, albumin bound (nab-paclitaxel)
- Pentazocine
- Venetoclax
- Aromatase inhibitors
- Leuprolide acetate
- Tamoxifen
- Pazopanib
- Palbociclib

Germ Cell & Sex Cord Stromal Tumor

Surgery followed by Chemotherapy

PRINCIPLES OF SYSTEMIC THERAPY (4 of 7)

Malignant Germ Cell Tumors
- BEP (bleomycin, etoposide, cisplatin)
- Bleomycin 30 units weekly
- Etoposide 100 mg/m² daily for days 1-5, cisplatin 20 mg/m² daily for days 1-5
- Repeat every 21 days for 3 cycles for good risk (category 2B), or 4 cycles for poor risk.
- Etoposide/carboplatin:
  - For select patients with stage III-IV resected dysgerminoma for whom minimizing toxicity is critical, 3 cycles of etoposide/carboplatin can be used.
  - Carboplatin 400 mg/m² on day 1 plus etoposide 120 mg/m² on days 1, 2, and 3 every 4 weeks for 3 cycles.

Malignant Sex Cord Stromal Tumors
- BEP (category 2B)
- Paclitaxel/carboplatin (category 2B)

Text Documentation - Ovary

Additional Resources

- FIGO Staging Classifications for GYN Cancers, FIGO, 2012
- 2013 WHO Classification of Tumours of Female Reproductive Organs, World Health Organization, Lyon, France, 2013
- NCI Physician Data Query for Healthcare Professionals
- CDC Information about GYN Cancers
- American Cancer Society
- SEER Training for Cancer Registry Professionals
- NCRA Informational Abstracts (Text Documentation)
- NCCN Evidence Based Treatment Guidelines, NCCN, 2017
Questions

Be brave. Ask questions. Get the facts about gynecologic cancer.

http://www.cdc.gov/cancer/gynecologic