Gynecologic Cancer Surveillance and Survivorship: Informing Practice and Policy

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Northside Cancer Institute
Our Learning Objectives

• Review survival rates, risks and patterns of gynecologic cancer recurrence
• Discuss current surveillance guidelines and practice
• Understand new Society of Gynecologic Oncology surveillance recommendations
• Discuss how best to implement surveillance and survivorship plans for gynecologic cancer survivors
## Cancer Statistics – 2012

<table>
<thead>
<tr>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>29% Breast</td>
<td>26% Lung and bronchus</td>
</tr>
<tr>
<td>14% Lung and bronchus</td>
<td>14% Breast</td>
</tr>
<tr>
<td>9% Colon and rectum</td>
<td>9% Colon and rectum</td>
</tr>
<tr>
<td>6% Uterine corpus</td>
<td>7% Pancreas</td>
</tr>
<tr>
<td>5% Thyroid</td>
<td>6% Ovary</td>
</tr>
<tr>
<td>4% Melanoma</td>
<td>4% Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>4% Non-Hodgkin</td>
<td>3% Uterine corpus</td>
</tr>
<tr>
<td>3% Kidney</td>
<td>2% Liver</td>
</tr>
<tr>
<td>3% Ovary</td>
<td>2% Brain</td>
</tr>
<tr>
<td>3% Pancreas</td>
<td></td>
</tr>
</tbody>
</table>

(Siegel R et al., *CA Cancer J Clin* 2012; 62(1):10-29)
Estimated New Gynecologic Cancers: 2012

(Uterus 47,130) (Vulva 4,490)
(Ovary 22,280) (Vagina & Other 2,680)
(Cervix 12,170)

(Siegel R et al., CA Cancer J Clin 2012; 62(1):10-29)
Estimated Gynecologic Cancer Deaths: 2012

- Ovary: 15,500
- Uterus: 8,010
- Cervix: 4,220
- Vulva: 950
- Vagina & Other: 840

(Siegel R et al., CA Cancer J Clin 2012; 62(1):10-29)
Ovarian Cancer: Histologic Distribution

- Epithelial: 90%
- Germ Cell: 5%
- Stromal: 5%
Ovarian Cancer:
Temporal Trends in Survival 1975-2005

[Graph showing survival months from 1975 to 2005 with key dates and treatments]
# Ovarian Cancer: Survival by Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent</th>
<th>5-year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>24%</td>
<td>90%</td>
</tr>
<tr>
<td>II</td>
<td>6%</td>
<td>80%</td>
</tr>
<tr>
<td>III</td>
<td>55%</td>
<td>15-50%</td>
</tr>
<tr>
<td>IV</td>
<td>15%</td>
<td>5-15%</td>
</tr>
</tbody>
</table>
Ovarian Cancer: Recurrence

- Recurrence rates remain high: 25% - 80%
- Recurrence pattern: 26-50% within the pelvis

Ovarian Cancer: Current Guidelines

- NCCN guidelines:
  - PE + tumor marker assessment every 2-4 months for the first 2 years; then 6-month intervals for the next 3 years
  - Radiographic imaging as clinically indicated
# Ovarian Cancer: Radiologic Surveillance

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>40–93%</td>
<td>50–98%</td>
<td>Lymph nodes</td>
<td>&lt;1 cm peritoneal, omental, bowel metastases</td>
</tr>
<tr>
<td>MRI</td>
<td>62–91%</td>
<td>40–100%</td>
<td>Upper abdomen, lower pelvis, carcinomatosis</td>
<td>&lt;1–2 cm Lymph nodes</td>
</tr>
<tr>
<td>PET/CT</td>
<td>73–88%</td>
<td>40–75%</td>
<td>Rising CA-125, lymph nodes, inconclusive CT</td>
<td>&lt;1 cm</td>
</tr>
</tbody>
</table>

- **CT**: Computed Tomography
- **MRI**: Magnetic Resonance Imaging
- **PET/CT**: Positron Emission Tomography/Computed Tomography

Sensitivity and specificity values are approximate ranges.
Ovarian Cancer: CA-125

• Correlates with disease status in most cases

• MRC OV05/EORTC 55955:
  – RCT of 1442 women with EOC in complete remission
  – If CA-125 >2x ULN, randomized to early treatment or delayed treatment (not until clinical or symptomatic relapse)
  – 529 women randomized: 265 early, 264 delayed

(Rustin GJ et al. Lancet 2010;376:1155-1163)
Ovarian Cancer: CA-125

• Results
  – No difference in overall survival (HR = 0.98)

• Conclusions
  – Value of routine CA-125 measurement not proven

• Takeaway
  – Provocative, but not likely to be uniformly adopted

(Rustin GJ et al. Lancet 2010;376:1155-1163)
Epithelial Ovarian Cancer

- Months 0-24: PE q 3 months
- Months 24-36: PE q 4-6 months
- Years 3-5: PE q 6 months
- Years >5: PE yearly
- CT/PET if recurrence suspected
- CA-125 if recurrence suspected
Low Malignant Potential Tumors

- Overall quite good prognosis
- Recurrences tend to occur late
  - 70% after 5 years
  - 30% after 10 years
- <5% progress to invasive cancers
Low Malignant Potential Tumors

- NCCN guidelines:
  - PE + CA-125 q 3-6 months
  - Pelvic ultrasound scans for those with fertility-sparing surgery
  - Hysterectomy/BSO once fertility is completed
Low Malignant Potential Tumors

- Surveillance similar to that used for epithelial ovarian cancer
- Prompt attention to symptoms or PE abnormalities because of good salvage rates for recurrent disease
Germ Cell Tumors

- Helpful tumor markers:
  - AFP: yolk sac tumors, embryonal carcinomas, polyembryomas, immature teratomas
  - hCG: choriocarcinomas, embryonal carcinomas, polyembryomas
  - LDH: dysgerminomas
Sex Cord Stromal Tumors

- Serum tumor markers include:
  - estradiol, inhibin, MIS, testosterone
- Median time to recurrence for granulosa cell tumors: 4-6 years
- 30-45% recurrences in the pelvis
Current Germ Cell/Stromal Tumor
NCCN Guidelines

• PE + tumor markers every 2-4 months for 2 years

• In patients without elevated tumor markers, radiologic assessment in the first 2 years can be helpful
Germ Cell Tumors

- Months 0-24: PE + tumor markers q 2-4 months
- Months 24-36: PE alone yearly
- Years 3-5: PE yearly
- Years >5: PE yearly
- CT if recurrence suspected
Sex Cord Stromal Tumors

- Months 0-24: PE + tumor markers q 2-4 months
- Months 24-36: PE + markers q 4-6 months
- Years 3-5: PE + markers q 6 months
- Years >5: PE + markers q 6 months
- CT if recurrence suspected
Endometriatral Cancer
Endometrial Cancer

- Recurrence rates:
  - early stage disease: 2-15%
  - advanced/aggressive histology: 50%
- > 70% recurrences occur within 3 years

<table>
<thead>
<tr>
<th>Stage</th>
<th>Distribution (%)</th>
<th>5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confined to uterus</td>
<td>69%</td>
<td>95.5%</td>
</tr>
<tr>
<td>Regional spread (lymph nodes)</td>
<td>19%</td>
<td>67.5%</td>
</tr>
<tr>
<td>Distant</td>
<td>8%</td>
<td>17.1%</td>
</tr>
<tr>
<td>Unknown (unstaged)</td>
<td>4%</td>
<td>55.5%</td>
</tr>
</tbody>
</table>
Endometrial Cancer
NCCN Guidelines

- PE q 3-6 months for 2 years, then every 6 months or annually
- Vaginal cytologic evaluation q 6 months for 2 years and then annually
Endometrial Cancer: Recurrence Detection

- Sensitivity/detection rate:
  - symptoms: 41-83%
  - PE: 35-68%
  - PE and symptoms: >80%
  - vaginal cytology: 0-7%
  - CXR: 0-20%
  - CA-125: negligible to 15%
  - CT scan: 5-21%
  - PET scan: 83-100% (limited data)
Endometrial Cancer

- Months 0-12: PE q 3-6 months*
- Months 12-24: PE q 3-6-12 months*
- Years 2-5: PE q 6-12 months*
- Years >5: PE yearly
- Pap not indicated; CT if recurrence suspected

* Depending on risk profile: low, intermediate, or high
Cervical Cancer
# Cervical Cancer Stage Distribution and Survival

<table>
<thead>
<tr>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distribution of Patients</th>
<th>Five-year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>62%</td>
<td>85%</td>
</tr>
<tr>
<td>18%</td>
<td>60%</td>
</tr>
<tr>
<td>11%</td>
<td>35%</td>
</tr>
<tr>
<td>9%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Cervical Cancer
NCCN Guidelines

- PE + Pap every 3-6 months for the first 2 years, then every 6 months for the next 3 years
- Optional annual chest radiographs
Cervical Cancer: Detection Rates

- PE accounts for the highest rate of asymptomatic detection: 29-75%
- Pap: 0-17%
- Chest radiographs: 20-47%
- PET-CT useful in recurrent setting:
  - Sensitivity 86%
  - Specificity 87%
  - Ongoing investigation as surveillance tool
Vulvar Cancer: Context

- Lymph node status is the single most important prognostic factor
- 5-year survival:
  - Negative LNs >80%
  - Positive LNs 13-50%
Vulvar Cancer

• No NCCN guidelines to inform

• Recurrence rate in the first 2 years:
  – Negative LNs: 17.5%
  – Positive LNs: 44.2%

• Nearly 1 in 10 patients had a late (>5 years) reoccurrence of disease (same site or 2nd primary)

• >95% of late relapses were local

• Cornerstone of surveillance: PE of vulva and groin
Vaginal Cancer

- Paucity of information to guide post-treatment surveillance
- Surveillance relies primarily on PE and symptom assessment for vaginal, cervical, vulvar and perianal neoplasia
# Oncology

**Posttreatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations**

Ritu Salani, MD, MBA; Floor J. Backes, MD; Michael Fung Kee Fung, MB, BS; Christine H. Holschneider, MD; Lynn P. Parker, MD; Robert E. Bristow, MD, MBA; Barbara A. Goff, MD

## Cervical, vulvar, and vaginal cancer surveillance recommendations

<table>
<thead>
<tr>
<th>Variable</th>
<th>Months</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-12</td>
<td>12-24</td>
</tr>
<tr>
<td>Review of symptoms and physical examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk (early stage, treated with surgery alone, no adjuvant therapy)</td>
<td>Every 6 mo</td>
<td>Every 6 mo</td>
</tr>
<tr>
<td>High risk (advanced stage, treated with primary chemotherapy/radiation therapy or surgery plus adjuvant therapy)</td>
<td>Every 3 mo</td>
<td>Every 3 mo</td>
</tr>
<tr>
<td>Papanicolaou test/cytologic evidence</td>
<td>Yearly&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yearly&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Routine radiographic imaging (chest x-ray, positron emission tomography/computed tomography, magnetic resonance imaging)</td>
<td>Insufficient data to support routine use</td>
<td>Insufficient data to support routine use</td>
</tr>
<tr>
<td>Recurrence suspected</td>
<td>Computed tomography and/or positron emission tomography scan</td>
<td>Computed tomography and/or positron emission tomography scan</td>
</tr>
</tbody>
</table>

<sup>a</sup> May be followed by a generalist or gynecologic oncologist; <sup>b</sup> Insufficient evidence for cancer recurrence but may have value in the detection of other lower genital tract neoplasia.
Post Treatment ...
Survivorship

... broadens the definition of comprehensive cancer control to include activities beyond palliation ...
... and prompts a different way of looking at the continuum of cancer control, suggesting a link between survivorship activities and prevention – and a circular rather than linear model for comprehensive approaches to cancer control.
Traditional

Prevention  Palliation
Not-so-traditional

screening
prevention
genetic testing
genetic counseling
education

diagnosis and treatment
survivorship
education
palliation
impact on family history

prevention lifestyle changes
Survivors’ Health Behaviors

- 15.1% of survivors are current smokers
- 27.5% of survivors are obese (BMI $\geq 30$ kg/m$^2$)

(Behavioral Risk Factor Surveillance System, U.S., 2009; MMWR 1/20/2012)
31.3% of cancer survivors versus 24.2% of the general population reported no leisure-time physical activity during the past 30 days.

(Behavioral Risk Factor Surveillance System, U.S., 2009; MMWR 1/20/2012)
% with Limitations:
Survivors versus General Population

Collaborative Care

• Shared role of the primary care provider/geriatrician with the cancer specialist in providing cancer care

• Complex co-morbid issues:
  – Cognitive impairment
  – Cardiovascular disease
  – Obesity/diabetes
  – Functional decline
  – Osteoporosis
  – Poor quality of life
Methods of Delivering Survivorship Care

Roles and Responsibilities*

Oncologist:
- Cancer therapy
- Keep primary care physician informed
- Guidance in long-term survivorship care
- Transition of patient to primary care physician at appropriate time
- Availability for questions, consults, referrals

Primary care physician:
- Ensure physical and emotional health needs of the survivor are addressed
- Assume responsibility for aspects of care of the chronic disease that are feasible in the primary care setting
- Refer for problems and/or periodic evaluations
- Consult in areas of uncertainty

Communication Points
a. Cancer diagnosis, stage and/or TNM classification, planned therapeutic approach, brief overview of chemotherapy, radiation therapy, and/or surgery
b. Survivorship Care Plan: summary of cancer and cancer therapy, a list of potential late effects, up-to-date recommendations for monitoring for recurrence and late effects, contact information
c. Continued update with changes in surveillance recommendations and new information regarding potential late effects.

*Adapted with permission from From Cancer Patient to Cancer Survivor: Lost in Transition.¹

(Oeffinger KC, McCabe MS JCO 2006;24:5117-5124)
Barriers to Appropriate Care

• Lack of ….
  – coordination among health-care providers
  – standardized follow-up medical care
  – knowledge among cancer survivors about appropriate follow-up
  – adequate health insurance coverage
Selected Recommendations from the President’s Cancer Panel & IOM Reports

- When treatment ends, all survivors should receive a summary record that includes important disease characteristics and treatments received.

- In addition, they should be provided with a follow-up care plan incorporating available evidence-based standards of care.
# Endometrial Cancer Treatment Summary

The treatment summary provides a brief record of major aspects of cancer adjuvant treatment. This is not a complete patient history or comprehensive record of intended therapies.

## Patient Information

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Medical Record #:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient DOB: (MM/DD/YYYY)</td>
<td>Patient Phone:</td>
</tr>
<tr>
<td>Support Contact Name:</td>
<td>Relationship:</td>
</tr>
<tr>
<td>Support Contact Phone:</td>
<td></td>
</tr>
</tbody>
</table>

## Background Information

<table>
<thead>
<tr>
<th>Age at Diagnosis:</th>
<th>Family History:</th>
<th>Genetic Testing:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Comorbid Conditions:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Onset of Menopause: [ ] Yes – Age of Onset: ______ [ ] No

## Surgery / Biopsy Information

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Date</th>
<th>Surgeon</th>
<th>Tumor Type</th>
<th>Histology</th>
<th>Grade</th>
</tr>
</thead>
</table>

(MM/DD/YYYY)  
(MM/DD/YYYY)

# Lymph Nodes Removed:     # Lymph Nodes Positive:

## Staging

<table>
<thead>
<tr>
<th>Tumor Type:</th>
<th>Tumor Size:</th>
<th>Depth of Invasion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>AJCC Staging: T:</td>
<td>N:</td>
<td>Stage Group:</td>
</tr>
<tr>
<td>FIGO Staging:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Clinical Trial Information

Treatment on Clinical Trial: [ ] Yes   [ ] No   [ ] Declined or Not Eligible

Name of Clinical Trial(s):  
Start Date: (MM/DD/YYYY)

## Chemotherapy Treatment / Targeted Therapy Summary

<table>
<thead>
<tr>
<th>Height: in</th>
<th>Pre-Treatment Weight: lbs</th>
<th>Post-Treatment Weight: lbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Last Menstrual Period: (MM/DD/YYYY)</td>
<td>Date of Last Menstrual Period: (MM/DD/YYYY)</td>
<td></td>
</tr>
</tbody>
</table>

Chemotherapy Start Date: (MM/DD/YYYY)  
Chemotherapy End Date: (MM/DD/YYYY)

<table>
<thead>
<tr>
<th>Chemotherapy Drug Name</th>
<th>Route</th>
<th>Dose/m²</th>
<th>Schedule</th>
<th>Dose Reduction Needed</th>
<th># of Cycles Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reason for Stopping Treatment: [ ] Completion  
[ ] Toxicity  [ ] Progression  [ ] Other:

Bisphosphonates: [ ] No  [ ] Yes  Duration:

Hormonal Therapy: [ ] No  [ ] Yes  Type:
Endometrial Cancer Treatment Summary

The treatment summary provides a brief record of major aspects of cancer adjuvant treatment. This is not a complete patient history or comprehensive record of intended therapies.

### Radiation Therapy Summary

<table>
<thead>
<tr>
<th>Location</th>
<th>Mode</th>
<th>Tumor Dose Total</th>
<th>Dates of Rx From</th>
<th>To</th>
<th># of Fractions</th>
<th>Elapsed Days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### Side Effects & Toxicities Experienced During Treatment

- **Side Effects Experienced:**
  - Fibrosis
  - Cardiac Symptoms
  - Cognitive
  - Fatigue
  - Hair Loss
  - Menopause Symptoms
  - Nausea/Vomiting
  - Neuropathy
  - Weight Gain
  - Other: ______
  - N/A

- **Serious Toxicities Experienced During Treatment (list all):**

- **Hospitalization for Toxicity During Treatment:** Yes  No

- **Neurotoxicity that Impairs Activity of Daily Living:** Yes  No

### Care Provider Contact Information

- **Provider: GYN Oncologist**
  - Name:
  - Contact Information:

- **Provider: Radiation Oncologist**
  - Name:
  - Contact Information:

- **Provider: Nurse Practitioner**
  - Name:
  - Contact Information:

- **Provider: Nurse Navigator**
  - Name:
  - Contact Information:

- **Provider: Primary Care Physician or OB/GYN**
  - Name:
  - Contact Information:
Case of Ms. G

• 56 year old woman with recurrent metastatic cervical cancer and elevated blood pressure.
• No prior history of hypertension.
• BP on exam 190/95, no associated symptoms, normal ECG.
• Currently receiving topotecan and bevacizumab.
"I'm sure if I moved to a fresh water environment, my hypertension would abate."
VEGF Inhibitors and Cardiotoxicity

(Izzedine H Ann Oncol 2009;5:807-815)
Anti-HTN Agents and Angiogenic Inhibitors: Caution

(Izzedine H Ann Oncol 2009;5:807-815)
Ms. G’s Model of Care

(Izzedine H Ann Oncol 2009;5:807-815)
Providing Care to the Cancer Survivor

“The older cancer patient/survivor may present an exceptional opportunity to target primary, secondary, and tertiary prevention strategies, capable of effecting beneficial outcomes for a broad spectrum of diseases and conditions that not only include cancer, but cardiovascular disease, osteoporosis, functional decline (cognitive decline, psychological wellbeing and overall quality of life)”.