GYNECOLOGIC CANCERS IN THE ELDERLY

Erin E. Stevens, MD, FACOG
Gynecologic Oncology
Billings Clinic Cancer Center
What is the most common gynecologic malignancy in the United States?

1. Cervical Cancer
2. Uterine Cancer
3. Ovarian Cancer
4. Vaginal Cancer
5. Vulvar Cancer
PRE-TEST QUESTIONS

• What is the most fatal gynecologic malignancy in the United States?
  1. Cervical Cancer
  2. Uterine Cancer
  3. Ovarian Cancer
  4. Vaginal Cancer
  5. Vulvar Cancer
GYNECOLOGIC CANCER STATISTICS
GYNECOLOGIC CANCERS - 2013

- **Uterine Corpus Cancer**
  - New Cases: 49,560
  - Deaths: 8,190

- **Ovarian Cancer**
  - New Cases: 22,240
  - Deaths: 14,030

- **Cervical Cancer**
  - New Cases: 12,340
  - Deaths: 4,030

ACS: Cancer Facts & Figures (2013)
• **Uterine Corpus Cancer**
  - New Cases: 63,230
  - Deaths: 11,350

• **Ovarian Cancer**
  - New Cases: 22,240
  - Deaths: 14,070

• **Cervical Cancer**
  - New Cases: 13,240
  - Deaths: 4,170

ACS: Cancer Facts & Figures (2013)
CERVICAL CANCER
QUESTION #1

- My scope of practice:

1. I don’t do paps or pelvic exams
2. I do paps but refer out abnormals
3. I do paps and colposcopy
4. I do paps, colposcopy, LEEPs
5. I do paps, colposcopies, LEEPs, CKCs, hysterectomies
### 2012 Screening Recommendations

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommended Screening</th>
<th>Key Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; Age 21</td>
<td>No Screening</td>
<td>No Screening</td>
</tr>
<tr>
<td>Age 21-29</td>
<td>Cytology Alone Q3 years</td>
<td>HPV Reflex Testing ONLY</td>
</tr>
<tr>
<td>Age 30-65</td>
<td>HPV and Cytology Co-Testing Q5 years or Cytology Q3 Years</td>
<td>HPV Routine Testing; Genotype Testing For HPV 16/18</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>No Screening Following Adequate Negative Screening</td>
<td>If History of CIN2+ Continue x 20 years</td>
</tr>
<tr>
<td>After Hysterectomy</td>
<td>No Screening Unless History of CIN2+</td>
<td>If History of CIN2+ Continue x 20 years</td>
</tr>
<tr>
<td>After HPV Vaccination</td>
<td>Age Specific</td>
<td>Same as Unvaccinated Women</td>
</tr>
</tbody>
</table>

WHAT IS “ADEQUATE SCREENING?”

- 3 consecutive negative cytology (done q3 years)
- 2 consecutive negative co-tests (done q5 years)
- No history of CIN2+ within the last 20 years
BUT SHOULD BE STOP?

- US Census Bureau by 2030, 20% of women will be older than 65
- Rate of hysterectomy have declined 13% from 1965 to 2002
- Older women diagnosed with cervical cancer
  - NCDB: 18.9% diagnosed after age 65
  - SEER: 19.7% diagnosed after age 65

Dilley, et al. SGO 2018 Annual Meeting
Cervical cancer rates uncorrected for hysterectomy may underestimate risk.

QUESTION #3

What do you do if you see this?

1. Nothing
2. Pap
3. Biopsy
4. Run from the room and refer the patient to someone else
CERVICAL CANCER

• If you diagnose cervical cancer (and this step requires biopsy)
  • Refer the patient to gyn oncology
  • Staging is still done clinically with rectovaginal exam
  • Imaging will depend on stage
    • PET/CT
    • MRI
    • Often not CXR/IVP anymore
TREATMENT FOR CERVICAL CANCER

- Curative
  - Radical hysterectomy with lymph node dissection
  - Radiation therapy with chemosensitization
- Palliative
  - Quad shot radiation therapy
  - Chemotherapy
UTERINE CANCER
ENDOMETRIOID ADENOCARCINOMA

- **Risk Factors**
  - Hypertension
  - Obesity
  - Nulliparity
  - Diabetes Mellitus
  - Anovulation
  - Unopposed Estrogen
Probability of Having Uterine Cancer

- 0-49 years: 0.3%
- 50-59 years: 0.6%
- 60-69 years: 1%
- 70+ years: 1.3%

Probability of Dying of Uterine Cancer

- 0-49 years: <0.1%
- 50-59 years: 0.1%
- 60-69 years: 0.2%
- 70+ years: 0.5%

https://cancerstatisticscenter.cancer.org
FIGURE

Association of uterine malignancy and BMI in overweight and obese women who underwent hysterectomy

Proportion of cases with uterine cancer

BMI, body mass index.

The American Institute for Cancer Research estimates that 59% of U.S. endometrial cancer cases, or about 3 in 5, could be prevented by being at a healthy weight and being physically active.\(^2\)
<table>
<thead>
<tr>
<th>Factors Influencing Risk</th>
<th>Estimated Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older age</td>
<td>2-3</td>
</tr>
<tr>
<td>Residency in North America or Northern Europe</td>
<td>3-18</td>
</tr>
<tr>
<td>Higher level of education or income</td>
<td>1.5-2</td>
</tr>
<tr>
<td>White race</td>
<td>2</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>3</td>
</tr>
<tr>
<td>History of infertility</td>
<td>2-3</td>
</tr>
<tr>
<td>Menstrual irregularities</td>
<td>1.5</td>
</tr>
<tr>
<td>Late age at natural menopause</td>
<td>2-3</td>
</tr>
<tr>
<td>Early age at menarche</td>
<td>1.5-2</td>
</tr>
<tr>
<td>Long-term use of high dosages of menopausal estrogens</td>
<td>10-20</td>
</tr>
<tr>
<td>Long-term use of high dosages of combination oral contraceptives</td>
<td>0.3-0.5</td>
</tr>
<tr>
<td>High cumulative doses of tamoxifen</td>
<td>3-7</td>
</tr>
<tr>
<td>Obesity</td>
<td>2-5</td>
</tr>
<tr>
<td>Stein-Leventhal disease or estrogen-producing tumor</td>
<td>&gt;5</td>
</tr>
<tr>
<td>History of diabetes, hypertension, gallbladder disease, or thyroid disease</td>
<td>1.3-3</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Relative risks depend on the study and referent group employed.

TREATMENT FOR UTERINE CANCER

- Surgery
  - Hysterectomy, BSO, lymph node dissection
  - Curative in ~50%
- Radiation therapy
  - Curative and adjuvant treatment
- Chemotherapy
- Hormonal management
  - Mirena IUD, Provera, Megace/Tamoxifen
WHAT DO THEY DIE OF?

Early stage, low grade
7.2% die of uterine cancer
42.1% die of heart disease

Ward, KK et al 2012 Gyn Onc
OVARIAN MASSES & CA 125

What are you actually supposed to worry about?
QUESTION #6

Pelvic ultrasound reads “complex adnexal mass concerning for neoplasm.” What do you do?

1. Take it out
2. Watch it with repeat ultrasound
3. Refer to general gynecology
4. Refer to gyn oncology
“A new, often uncontrolled growth of abnormal tissue; tumor”

- Therefore, it may be a cancer
- But it may not be a cancer
  - (odds are, it probably isn’t a cancer)
ADNEXAL MASSES: HOW COMMON?

• Annually in the US
  • Millions and millions of adnexal masses
  • Only 22,000 ovarian cancers diagnosed yearly
• Premenopausal (~90 million aged 13-50)
  • Incidence: 13 million (14%)
  • Prevalence: 27 million (30%)
• Postmenopausal (~30 million aged >50)
  • Incidence: 1.5 million (5%)
  • Prevalence: 5 million (16%)

Holcomb (2011) Assessment of the Pelvic Mass Patient with ROMA
US Census Bureau (2008)
University of Kentucky Ovarian Cancer Screening Program (2009)
ADNEXAL MASS: SYMPTOMS

- Bloating
- Pelvic Pain
- Abdominal Pain
- Trouble Eating
- Early Satiety
- Urinary Urgency
- Urinary Frequency

Symptoms are present almost daily for a period of at least one month.

ACS (2007) Ovarian Cancer Has Early Symptoms
A patient is seeing you for an annual exam and wants a CA125 because her friend has ovarian cancer. What do you do?

1. Order the test
2. Do not order the test
LIMITATIONS OF CA-125

- **Not a screening test!**
  - Not approved to evaluate ovarian masses
  - Approved for monitoring treatment response of patients with ovarian cancer to chemotherapy
- Elevated in only 50% of early ovarian cancers
  - Poorly expressed in mucinous, clear cell, undifferentiated and sarcomatoid cancers
- Not (as) helpful in premenopausal women
QUESTION #8

- That same asymptomatic patient gets a CA125 checked and it’s 40. Now what?
  
  1 – CT scan chest, abdomen, pelvis
  2 – Pelvic ultrasound
  3 – Repeat test in 4-6 weeks
  4 – Do nothing
**ELEVATED CA-125: GYNECOLOGIC**

- **Benign**
  - Adenomyosis
  - Benign neoplasm
  - Endometriosis
  - Functional cysts
  - Leiomyomata
  - Meigs' syndrome
  - Menstruation
  - Pregnancy
  - Ovarian Hyperstimulation
  - Pelvic Inflammation

- **Malignant**
  - Epithelial Ovarian Cancer
  - Fallopian Tube Cancer
  - Primary Peritoneal Cancer
  - Adenocarcinoma of Cervix
  - Some Germ Cell Tumors
  - Sertoli-Leydig Tumors
ELEVATED CA-125: NON-GYNECOLOGIC

- Cirrhosis
- Colitis
- Heart Failure
- Diabetes
- Diverticulitis
- Liver Disease
- Lupus
- Mesothelioma

- Pericarditis
- Polyarteritis nodosa
- Postoperative period
- Prior Radiation
- Renal Disease
- Sarcoid
- Tuberculosis
- Pleural Effusion
- Ascites
LOW RISK WOMEN

- TVS and tumor markers alone or in combination are **ineffective** for screening
  - Because of the low prevalence
    - 1/2500 women/year
  - To create a test with
    - 100% sensitivity & 99% specificity
  - PPV would be only 4.8%
    - 20/21 women operated on would not have cancer
OVARIAN CANCER
Table S1. Age-specific Probability of Developing Ovarian Cancer for US Women*

<table>
<thead>
<tr>
<th>Current age</th>
<th>10-year probability:</th>
<th>or 1 in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.1%</td>
<td>870</td>
</tr>
<tr>
<td>50</td>
<td>0.2%</td>
<td>474</td>
</tr>
<tr>
<td>60</td>
<td>0.3%</td>
<td>327</td>
</tr>
<tr>
<td>70</td>
<td>0.4%</td>
<td>265</td>
</tr>
<tr>
<td>80</td>
<td>0.4%</td>
<td>283</td>
</tr>
<tr>
<td><strong>Lifetime risk</strong></td>
<td><strong>1.3%</strong></td>
<td><strong>78</strong></td>
</tr>
</tbody>
</table>

*Among those who are cancer-free. Based on cases diagnosed 2012-2014. Percentages and “1 in” numbers may not be numerically equivalent due to rounding.


©2018, American Cancer Society, Inc., Surveillance Research
Figure S4. Epithelial Ovarian Cancer Incidence Rates* by Age and Race, US, 2010-2014

*Age adjusted to the 2000 US standard population. Persons of Hispanic origin may be of any race. Asians/Pacific Islanders include those of Hispanic and non-Hispanic origin. American Indians and Alaska Natives are not shown due to <25 cases reported for several age groups.

## Staging & Survival Predictions

<table>
<thead>
<tr>
<th>Stage</th>
<th>5 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>II</td>
<td>60-80%</td>
</tr>
<tr>
<td>III</td>
<td>30-50%</td>
</tr>
<tr>
<td>IV</td>
<td>&lt;30%</td>
</tr>
</tbody>
</table>
# Ovarian Cancer Stats

<table>
<thead>
<tr>
<th>Stage</th>
<th>5 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>II</td>
<td>60-80%</td>
</tr>
<tr>
<td>III</td>
<td>30-50%</td>
</tr>
<tr>
<td>IV</td>
<td>&lt;30%</td>
</tr>
</tbody>
</table>

75% new cases
Figure S5. Age-adjusted Ovarian Cancer Mortality Rates* by Age Group and Race/Ethnicity, 1975-2015

*Per 100,000, age adjusted to the 2000 US standard population. Note: American Indians and Alaska Natives not pictured due to <25 deaths in some years. Rates for Hispanics exclude data from Louisiana, New Hampshire, and Oklahoma due to missing data on Hispanic ethnicity for some years.

Treatment options for advanced stage ovarian cancer

Option # 1

Primary debulking surgery

Surgery
Chemotherapy x 6

Option # 2

Neoadjuvant chemotherapy followed by surgery

Surgery
Chemotherapy x 3
Surgery
Chemotherapy x 3
FAGOTTI SCORE

• Diagnostic laparoscopy for assessment of disease
• Goal of surgery: “No visible cancer” (R0 resection)
• 4 or more areas = neoadjuvant chemotherapy
NEoadjuvant Chemotherapy vs Debulking Surgery

A Intention-to-Treat Analysis

<table>
<thead>
<tr>
<th></th>
<th>PDS</th>
<th>NACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Events</td>
<td>253</td>
<td>245</td>
</tr>
<tr>
<td>No. of Patients at Risk</td>
<td>336</td>
<td>334</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>189</th>
<th>195</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>62</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
FRAILTY INDEX

- Functional age, not chronologic
- Index of 30 variables
- Combination of need for assistance with ADLs and chronic medical problems
- Generally, 4-5 variables qualifies a person as frail
Fig. 1. Patients with frailty (deficit index ≥0.15) had a median OS of 26.5 months versus 44.9 m for the non-frail patients (deficit index <0.15), (p < 0.001).
WHAT SHOULD WE CONSIDER?

- Stage IV disease
- Age >80
- Age 75-79 AND
  - ECOG > 1 (ASA 3-4) or
  - Complex surgery likely
- Frail
- Albumin <3.5
TREATMENT CONSIDERATIONS IN ELDERLY PATIENTS
SURGERY

- Anesthesia risks
- Physiologic reserve
- Extent of surgery
- Frailty
- Postoperative complications/mortality
CHEMOTHERAPY

• Backbone of treatment: platinum/taxane based
• Single agent vs doublet
• Weekly (MITO 7) vs q3 weeks
GOALS OF CARE
ANY QUESTIONS?

A world with less cancer is a world with more birthdays.

THE OFFICIAL SPONSOR OF BIRTHDAYS.

American Cancer Society