Screening for Cancer in Women: Updates & Current Trends

CAROLYNN YOUNG, MD, FACOG
ROCKVILLE GYNECOLOGY
ROCKVILLE, MARYLAND
Disclosures

- Clinical study with Phenogen Sciences
  - Evaluating BrevagenPlus
Case Study

- A 49 year old woman presents for an annual exam
  - Normal menstrual cycles
  - Sexually active, monogamous, partner--vasectomy
  - Good energy, normal appetite, denies pelvic pain
  - No family history of cancer
Case Study

- 49 year old woman
  - Normal mammogram six month ago
  - Negative pap, negative HPV last year
  - Normal physical exam including breast and pelvic exam

- What additional cancer screening is necessary?
Cancers in Women

- Uterine: 280 cases/100,000
- Ovarian: 12/100,000
- Cervical: 8.1/100,000
- Vulvar: 2.4/100,000
- Vaginal: 0.01/100,000

- Breast: 12,500 cases/100,000 (1 in 8)
Two Groups of Cancers in Women

- Not hereditary:
  - Vaginal
  - Vulvar
  - Cervical

- Hereditary component:
  - Uterine
  - Ovarian
  - Breast
Vaginal Cancer

- Usually associated with HPV
- Melanoma can occur
- Presents as abnormal bleeding or discharge or palpable mass
- 20% asymptomatic at diagnosis
Vulvar Cancer

- Most associated with HPV infection
- Melanoma
- Pelvic exam every 1-2 years
- Abnormal areas should be biopsied
Cervical Cancer

- Average age of diagnosis in US: 48 years
- Incidence
  - 0.1/100,000 under 20
  - 1.5/100,000 ages 20-24
  - 11-16/100,000 ages 30-85
Risk Factors for Cervical Cancer

- High-risk HPV
- Ever smoker
- New sex partners
- Oral contraceptive use
- Immunocompromised state
- In-utero diethylstilbestrol exposure
Cervical Cancer Screening

- Ages 21-29: Pap every 3 years
- Ages 30+: Pap & HPV every 3-5 years
- Discontinue screening at 65-70... IF
  - Not at increased risk
  - Adequate prior screening
    - 2 neg Pap/HPV or 3 neg pap smears within the last 10 yrs
    - Most recent within the last 5 years
  - No history of high-grade cervical dysplasia
Special Situations

- Completed HPV vaccine series ➔ no change in screening

- Hysterectomy for benign disease
  - Cervix removed ➔ no further screening
  - Cervix intact ➔ routine screening
Importance of Family History

- Family history of cancer:
  - Breast
  - Ovarian
  - Uterine
  - Colon
Genetic Testing: Identifying High Risk Patients

- BRCA mutation carriers—lifetime cancer risks: Up to
  - 87% breast
  - 44% ovarian
- Lynch syndrome
  - 82% colon
  - 72% uterine
  - 12% ovarian
BRCA mutation: Who to Screen?

- **Personal or Family History:**
  - Breast cancer: <50, male breast cancer, 2 primary breast cancers, triple negative breast cancer
  - Ashkenazi Jewish ancestry & breast or ovarian cancer (any age)
BRCA mutation: Who to Screen?

- 3 or more breast/ovarian/pancreatic/prostate cancers (same side of family)
- Ovarian cancer (or tubal/peritoneal cancer)
- Previously identified BRCA mutation in the family
Lynch Syndrome: When to Screen?

- Colon or uterine cancer <50
- 3+ Lynch-related cancers on same side of family
  - Colon
  - Uterus
  - Ovary
  - Stomach
  - Small bowel
  - Hepatobiliary
  - Kidney/ureter
  - Brain
Family History Questionnaire for Common Hereditary Cancer Syndromes

This is a screening tool for the common features of hereditary cancer syndromes. Based on the family history information you provide here, you MAY be appropriate for genetic testing and your provider may be able to change your medical management to improve your care.

*Instructions: Please circle yes to those that apply to you and/or your family.*

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer before age 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian Cancer at any age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast Cancer in both breasts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both Breast AND Ovarian Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Breast Cancers on the same side of the family (diagnosed at any age)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Breast Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Triple Negative” Breast Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family members who have tested positive for the BRCA gene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine Cancer before age 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal Cancer before age 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both Uterine and Colorectal Cancer, one diagnosed before age 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 or more of the following cancers on the same side of the family:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine, Colorectal, Ovarian, Stomach, Kidney/Urinary Tract, Brain, or Small Bowel</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Do you have Ashkenazi Jewish Ancestry with Breast Cancer in the family (diagnosed at any age)?

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have YOU been personally diagnosed with Uterine Cancer at Any age?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient Signature: ____________________________ Date: ____________

Patient Name Printed: ____________________________

For Office Use Only

Patient is a candidate for genetic testing: Yes No

Genetic testing information provided: Yes No

Genetic testing completed: Yes No

Provider Signature: ____________________________
Panel Testing

- Screens for multiple genetic mutations
  - BRCA
  - Lynch
  - CHEK2
  - PALB2
  - TP53
Uterine Cancer

- 3% of the General Population

Symptoms
- Abnormal bleeding
- Postmenopausal bleeding
- Pelvic pain
Uterine Cancer

- Risk factors
  - Family history of uterine cancer
  - Prolonged anovulation
  - Obesity
  - Hypertension
  - Diabetes
  - Tamoxifen Use (postmenopause)
  - Lynch syndrome (27-71% lifetime risk)
Uterine Cancer Screening

- Routine screening is not recommended

- Screen for Lynch syndrome based on family/personal history

- If + for Lynch syndrome → hysterectomy/BSO recommended
Evaluation of Abnormal/Postmenopausal Bleeding

- Women 45+, or younger with risk factors
- Bleeding <21 days apart, or lasting > 7 days

- Ultrasound
- Endometrial biopsy
- Hysteroscopy D&C
Ovarian Cancer Screening

- 1 in 70 (1.6%)
- Leading cause of cancer death from GYN malignancies
- Early detection → improved survival
  - 5 year survival
  - Stage 1: 90%
  - Stage 4: 25%
- 75% of ovarian cancers are detected at stage 2+
Ovarian Cancer Risk Factors

- Age
- Family history of ovarian cancer
- BRCA 1 or 2 mutation
- Lynch syndrome
- Uninterrupted menstrual cycles (ex. infertility)
- HRT
- Endometriosis
Ovarian Cancer Symptoms

- Pelvic pain
- Bloating
- Urinary frequency
- Early satiety

- Must have symptoms for 2+ weeks
- Must be a change from baseline
Ovarian Cancer Screening

- Routine screening ➔
  - not recommended unless high-risk

- 1st degree relative with ovarian cancer:
  - 5% lifetime risk ➔
  - screening is not recommended
Ovarian Cancer Screening

- High risk patients:
  - BRCA mutation or Lynch syndrome
  - Pelvic exam, ultrasound & CA125 every 6 months
  - Start at:
    - Age 30
    - 5-10 years prior to earliest family member
  - Removal of tubes/ovaries recommended
    - at age 40 or when childbearing is completed
CA-125

- Abnormal if >35 in postmenopausal woman
- Concerning if >200 in premenopausal woman
- Multiple benign processes elevate CA125
- Needs to be interpreted with a pelvic ultrasound
Breast Cancer Screening

- 1 in 8 women will develop breast cancer (12%)
- Up to 85% do not have a family history of breast cancer
Breast Cancer Risk Factors

- Age
- Family History of breast cancer
- Early menarche
- Nulliparity or pregnancy after age 30
- Late menopause (>55)
- Sedentary lifestyle
- Being overweight or obese after menopause
- Alcohol consumption
- Having dense breasts
- Using combination hormone therapy
- Atypical hyperplasia on breast biopsy
- Radiation therapy to the chest
- Diethylstilbestrol exposure in-utero
Breast Cancer Relative Risks

- BRCA mutation: 7
- Increased Breast Density: 4.5
- Chest Wall Radiation: 4
- Atypical hyperplasia: 3.5
- Early Menarche: 1.7
- Nulliparity: 1.7
- Family History: 1.3
- Hormone Replacement Therapy: 1.3
- Postmenopausal Obesity: 1.2
- Late Menopause: 1.2
Alcohol consumption & Breast Cancer

- Increased risk of breast cancer with 3+ drinks/week
- 2013 Meta-analysis:
  - 10% increased risk for every 10 g alcohol per day
- Nurses’ Health Study:
  - 2-fold higher risk if >1 drink per day & used HRT for >5 years

GOOD NEWS!

- Folic acid supplementation of 300mcg daily may attenuate the increased risk
Breast Cancer Screening Options

- SBE does not decrease breast cancer mortality
  - Increases patient anxiety
  - Increases the number of benign breast biopsies
  - Replaced with “Breast Self-Awareness”

- CBE: Low sensitivity
  - Detects 5% of breast cancers that are not detectable on mammogram
Breast Cancer Screening Options

- Mammography: 90% sensitive
  - Lower if breast tissue is dense
- Breast MRI
- Whole breast US
Mammogram recommendations in Average-Risk Women 40-49 years

- ACS: age 40-44 ➔ individual decision
  - 45-49 ➔ annually
- ACOG: annual mammogram & CBE
- ACP: discuss R vs. B; every 2 years
- USPTF: individual decision; every 2 years
Mammogram Recommendations: 50-74 yrs (average risk)

- ACS: Annual
- ACOG: Annual
- ACP: Biennial
- USPTF: Biennial
Mammogram Recommendations: 75+

- ACS: annual mammogram if life expectancy >10 yrs
- ACOG: discuss R vs. B
- ACP: not recommended
- USPTF: insufficient evidence
Mammography: The Risks

Radiation exposure:
- 1 cancer is caused from radiation for every 60-180 breast cancer deaths prevented
- Callbacks/additional imaging
- Additional biopsies
Mammogram Risks

- “False Positive” diagnosis:
  - 30% of DCIS will regress
  - We don’t know which 30%!
  - 70% will progress to invasive cancer
Tomosynthesis (3D Mammogram)

- Higher cancer detection rate in women with dense breasts
- Lower call-back rate
- Data based on retrospective studies
- Increased radiation dose
  - Not in newer techniques
Breast Cancer Screening Options: MRI

- For high-risk women:
  - BRCA mutation
  - 20-25%+ lifetime risk of breast cancer
  - Radiation to chest (ages 10-30)
  - Other genetic mutations
  - High sensitivity; High false-positive
BRCA Mutation Carriers: Breast Cancer Screening

- Self-breast awareness starting at 18
- CBE q 6 months starting at 25
- Annual mammogram starting at 25-30
- Annual breast MRI starting at 25
Case Study

- A 49 year old woman presents to your office for an annual exam
  - Her menstrual cycles are normal
  - Sexually active, monogamous, partner had a vasectomy
  - Good energy, normal appetite, denies pelvic pain
  - No family history of cancer
Case Study

- Normal mammogram six month ago
- Negative pap smear with a negative HPV last year
- Normal physical exam including a breast and pelvic exam
- What additional cancer screening is necessary?  NOTHING!!!
Cancer Screening in Women: Summary

- Evaluate Family History: Identify candidates for BRCA & Lynch testing
- Breast Cancer:
  - Annual CBE
  - Consider Annual mammogram starting at 40:
    - 15% lower mortality if annual starting at 40
- Uterine Cancer
  - Evaluate abnormal bleeding in premenopausal women, or any postmenopausal bleeding
Cancer Screening in Women: Summary

- Ovarian Cancer
  - Symptoms; check ultrasound
- Cervical Cancer
  - Pap q 3 years 21-29
  - Pap & HPV q 3 years ages 30-65
- Vulvar/Vaginal Cancer: Clinical exam; evaluate concerns
References: Cervical Cancer Screening


References: Uterine Cancer Screening


References: Ovarian Cancer Screening

Ovarian cancer: changes in patterns at diagnosis and relative survival over the last three decades.
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Symptoms of ovarian cancer.
Olson SH, Mignone L, Nakraseive C, Caputo TA, Barakat RR, Harlap S


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References: Breast Cancer Screening


