Follow-Up of Women after Treatment for Gynecologic Malignancies

Ritu Salani, MD
Associate Professor
Gynecologic Oncology

Disclosures
- Advisory board/Consultant
  - Genentech
  - Clovis
  - AstraZeneca

Objectives
- Review cancer survivorship care and guidelines for patients with ovarian cancer
- Discuss the rationale for current examination practices and surveillance testing
- Provide an overview of symptom management for common issues in the survivorship period
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Cancer cases in 2019

- New cases: 891,480
- Gynecologic cancers 97,140

Breast 268,600
Colorectal 67,100
Uterus 61,880
Ovary 22,530
Cervix 13,170
Other gyn cancers 11,420

10.9%

Siegel, R. Cancer Statistics, 2019

Cancer survivorship

Survivorship begins at the time of cancer diagnosis
- Maybe even when symptoms develop
- Over 8 million women living with or a history of cancer
  - Over 1.2 million are gynecologic cancer survivors!

Estimated to increase by ~25% over the next ten years
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Cancer survivorship

- Over 8 million women who are cancer survivors
  - ~1.2 million are gynecologic cancer survivors
- Continued growth expected

Cancer care overview

Start here

Treatment with intent to cure

Diagnosis and staging

Progression on treatment

Recurrence/second cancer

Death

Essential components of survivorship care

DETECTION/SURVEILLANCE of recurrent cancers, new cancers, and late effects of cancer and its treatment

PREVENTION of recurrent and new cancers and other late effects

INTERVENTION for the long-term and late effects of cancer and its treatment

COORDINATION among providers to ensure that all survivors’ health needs are met
Cancer surveillance visits

- Assessment of late and long term effects
- Genetic risk assessment
- Promotion of healthy lifestyle
- Screening for secondary malignancies
- Evaluation for early detection of recurrence

Gynecologic cancer surveillance

- No standard practice
  - Significant variation
  - Optimal interval unknown
  - Unclear impact on survival or detection of recurrence
  - Low value care
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History of surveillance
- Survey of gynecologic oncologist
- Surveillance practice in 1992
  - All stages and cancer types

Surveillance
- Most common methods of detection
  - Patient symptoms
  - Physical examination
  - Imaging

Surveillance: Physical examinations

Current Recommendations
- Review of symptoms and physical examination
- Bimanual pelvic and rectovaginal
- 26%–50% of recurrences occur within the pelvis

Gaps and Limitations
- Reproducibility is low and may not detect other common sites of recurrence
  - Such as retroperitoneal lymph nodes, upper abdominal organs, or lungs
- Physical examination alone may not be sufficient in certain patients
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Surveillance goals

- Impact Survival Outcomes: Both monitoring for disease recurrence and treatment should translate to decreased mortality.
- Balance Benefits and Pitfalls for Patients: Disease monitoring may result in negative psychological impact on patients.
- Remain Cost-Effective: Effective surveillance plans should aim to reduce excessive costs and unnecessary use of resources for conducting surveillance testing.
- Ensure Clinical Effectiveness: Adherence to recommended guidelines should minimize unnecessary testing while providing optimal surveillance.

Surveillance: Guidelines

- Increase Clinical Detection: Routine clinical examination and diagnostic testing can play a key role in detecting recurrence.
- Decrease Morbidity: Continual monitoring for disease recurrence and follow-up treatment can decrease morbidity.
- Use Cost-Effective Practices: Cost-effective practices and follow-up plans are essential for effective detection of recurrence.
- Improve Survival Outcomes: Thorough examination and educating survivors is the most effective method for detection of recurrence.

Cervix cancer

- 13,170 new cases
- 4,250 deaths
  - ~50% in stage I
  - Incidence decreasing
- Recurrences often occur within 3 years
  - Advanced disease with earlier and higher recurrence rates
## Cervix cancer recurrence

- **Symptoms (74%)**
  - Vaginal bleeding/discharge
  - Abdominopelvic pain
  - Lymphedema or leg pain/sciatica
  - Systemic symptoms
- **Physical exam 29-75%**
  - Speculum and bimanual pelvic exam

Salani R. Gynecol Oncol 2017;146:3.

## Cervix cancer: Cytology

- **Abnormal cervical/vaginal cytology (0-17%)**
  - Cancer on cytology is rarely an isolated finding
  - Most often low grade changes
    - Series of 61 women, 5.6% abnormal Pap rate
    - 1 case required intervention (VAIN II)
    - Led to unnecessary interventions
  - Abnormal cytology with prior radiation therapy (up to 34%)
    - Benign or mild changes in absence of other findings


## Cervix cancer: Cytology recommendations

- Limit use to no more than once/year
  - Reserve colposcopy for high grade changes
- Consider elimination in certain groups
  - After radiation therapy
  - Unclear role after trachelectomy
- Continue to evaluate for lower genital tract disease
  - Visual inspection
- Significance of HPV clearance?

Salani R. Gynecol Oncol 2017;146:3-15.
Cervix cancer: Imaging

- Chest x-rays and CT scans: Low rates of detection
  - No benefit for survival outcomes
- PET CT scans: Sensitivity 86% and specificity 87%
  - Prognostic significance
    - Post treatment in high risk patients
    - Additional studies are warranted
  - Role in asymptomatic patients is unclear
  - Best use when recurrence suspected

Cervix cancer: Recommendations

Endometrial cancer

- Estimated new cases 61,880
- Estimated deaths 12,160
  - Incidence increasing
    - ~70% in early stage
- 95% recur within 3 years
  - Higher risk with advanced stage and type II histology
Endometrial cancer recurrence

- Approximately 90% of recurrences detected by...
- Symptoms
  - Vaginal bleeding
  - Pelvic pain
- Physical examination
  - Speculum exam
  - Bimanual exam

References available upon request

Endometrial cancer: Cytology

<table>
<thead>
<tr>
<th>Author</th>
<th>Study size</th>
<th>Recurrence rate (%)</th>
<th>Cytology alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berchuck 1995</td>
<td>354</td>
<td>44 (12%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Agboola 1997</td>
<td>4280</td>
<td>496 (11.6%)</td>
<td>2 (0.04%)</td>
</tr>
<tr>
<td>Gadducci 2000</td>
<td>131</td>
<td>24 (18%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Monroe 2001</td>
<td>390</td>
<td>27 (6.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Bristow 2006</td>
<td>717</td>
<td>36 (5.0%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Salani 2011</td>
<td>154</td>
<td>4 (2.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Novetsky 2013</td>
<td>433</td>
<td>51 (11.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Lee 2016</td>
<td>389</td>
<td>14 (3.6%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Endometrial cancer: Imaging

- Evaluations of different modalities
  - Ultrasound, CT scans, MRI, PET/CT scans
- Recurrence rates:
  - Early stage: 3% low risk and 14% in high risk
  - Advanced stage: ~50%
- Detection of asymptomatic recurrence is low
- Recommend avoiding routine imaging
Impact on practice
- Database evaluation of surveillance exams
  - 17,638 stage I and II endometrial cancer patients
- Cytology rates consistent: 2011 performed in 66.9% of cases
- CT scans (abdominal/pelvis): 11.7% in 1992 to 24.8% in 2011

Endometrial cancer: Wasted costs
- Mean cost per patient
  - Cytology $63
  - CT scan $750

Just one of Pap test and one CT scan in every uterine cancer patient... $49.6 million dollars!!!

Endometrial cancer: Recommendations

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Ovarian cancer

- Estimated new cases 22,530
- Estimated deaths 13,980
  - Incidence and death rate are decreasing
- ~75% are diagnosed in advanced stages
- Recurrence is common
  - Early and advanced stages

Ovarian cancer recurrence

- Symptoms (49%)
  - Abdominal bloating
  - Abdominopelvic pain
  - Nausea/vomiting
  - Satiety
  - Bowel issues
  - Urinary symptoms
- Physical exam (30-50%)
  - Pelvic disease in 25-50%
  - Abdominal distension
  - Limitations
    - Nodal assessment
    - Upper abdominal disease

Ovarian cancer: CA 125 levels

- Glycoprotein discovered in 1981
- Potential applications
  - Assess adnexal mass risk for ovarian cancer
  - Monitoring response to therapy*
  - Detection for recurrent disease
    - Levels rise months before clinical relapse
- Pitfall: May be elevated in other conditions
Ovarian cancer: CA 125 levels

- European study of 529 ovarian cancer patients
  - Randomized to treatment based on rising CA 125 level versus delayed treatment until symptoms
  - No difference in survival (25.7 vs 27.1 months)
  - Study findings question the role of CA 125
  - European Society recommendation
    - Obtain CA 125 at time of relapse or if requested


Surveillance: CA 125 levels

Current Recommendations

- SGO: Measurement of CA 125 is optimal
- NCCN: After biochemical relapse, recommended options include enrollment in a clinical trial, delaying treatment until symptoms arise, or best supportive care

Gaps and Limitations

- Elevated CA 125 may also be found in other cancers, and monitoring has been associated with significant distress and anxiety
- Early treatment of recurrence may not lead to an improved OS


Ovarian cancer: Imaging

- 412 women
  - 80% recurrence rate
  - Detection method
    - Exam 15%
    - Imaging 27%
    - CA 125 23%
    - CA 125 and imaging 35%
    - Did not report symptoms
  - No survival difference

- 218 recurrent ovarian cancer patients
  - Concordant CA 125 and imaging in 43% only
  - Did not report detection by exam or symptoms
  - No survival difference


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Ovarian cancer: Imaging

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Scans</td>
<td>40%–50%</td>
<td>80%–100%</td>
</tr>
<tr>
<td>MRI Scans</td>
<td>62%–91%</td>
<td>80%–100%</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>40%–65%</td>
<td>90%–100%</td>
</tr>
<tr>
<td>PET/CT Scans</td>
<td>45%–50%</td>
<td>40%–50%</td>
</tr>
</tbody>
</table>

- Best reserved for evaluation of suspected recurrence

Salani R. Gynecol Oncol 2017;146:3; slide from GEMSTONE Oncology.

Recommendations

- Ensure patients know what to expect at each visits
  - Signs/physical findings of recurrence
  - Symptoms of recurrence
  - Review of signs/symptoms of cancer recurrence
  - A physical exam
  - If indicated, a review test results (tumor markers, imaging, etc).
- Ensure patients know what tests are not needed too
- Point of access care
  - Plan if symptoms/signs develop problems between visits

Surveillance

- Ensure patients know what to expect at each visits
  - Signs/physical findings of recurrence
  - Symptoms of recurrence
  - Review of signs/symptoms of cancer recurrence
  - A physical exam
  - If indicated, a review test results (tumor markers, imaging, etc).

Coordination of care

- The following tools can be used in conjunction with information provided by physicians and the patient's cancer care team.

1. **Treatment Summary**
2. **Survivorship Care Plan & Self-Care Plan**
3. **Information Cards**
4. **Survivorship Calendar**

Survivorship care plans

- Provide a summary of treatment and follow up schedule
- Improved coordination of care
  - Primary care physicians reported higher adherence to appropriate screening tests
  - Can help identify the responsible providers for each aspect of care
- Patient and caregiver empowerment
  - Reduces unnecessary anxiety

Long and late term effects
Overview of late and long term effects

Existential/Spiritual
- Sense of purpose/meaning
- Appreciation of life
- Disillusionment
- Loss of faith

Financial
- Financial strain
- Job loss
- Restrictions on care
- Restrictions on insurance

Social
- Changes in relationships
- Disruption to family dynamics
- Social isolation
- Altered intimacy

Psychological
- Depression
- Anxiety
- Uncertainty
- Fear of recurrence
- Cognitive complaints
- Altered body image

Physical/Medical
- Second cancers or recurrence
- Cardiac dysfunction
- Comorbid conditions (diabetes, osteoporosis, etc.)
- Physical symptoms

Side effects of treatment versus recurrence

<table>
<thead>
<tr>
<th>Side effects of treatment</th>
<th>Signs of recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Pain</td>
<td>Persistent pain</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>Bloating/bowel changes</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>Vaginal bleeding</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>Unexplained weight loss</td>
</tr>
<tr>
<td>Scarring</td>
<td>New masses</td>
</tr>
</tbody>
</table>

Physical effects
- All patients have some degree of side effects
- Quality of life
  - Declines during active cancer treatment
  - Remains low for a short period afterwards
  - After 1 year, quality of life tends to be comparable to non-cancer counterparts
Physical effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Definition</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Persistent physical or emotional exhaustion</td>
<td>Rule out other causes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate exercise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Psychological intervention</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Difficulty falling or staying asleep</td>
<td>Cognitive behavioral therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sleep hygiene</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medications</td>
</tr>
<tr>
<td>Pain</td>
<td>Post-operative, musculoskeletal, visceral, neuropathic*</td>
<td>Narcotic/NSAIDS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Palliative surgery</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Nerve damage (often occurring in the hands and feet)</td>
<td>Anti-seizure medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amines acid complex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acupuncture/Biofeedback</td>
</tr>
<tr>
<td>Cognitive deficit</td>
<td>Loss of intellectual function, short-term memory deficits</td>
<td>Stress management</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occupational therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neuropsych evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Psychological interventions</td>
</tr>
</tbody>
</table>

Physical effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Definition</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis</td>
<td>Decreased bone density</td>
<td>Medical bone health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calcium/Vitamin D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bisphosphonates</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>Difficulty with sexual response or desire</td>
<td>Surgical preservation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fertility options</td>
</tr>
<tr>
<td>Menopausal symptoms</td>
<td>Decrease in estrogen, hot flashes</td>
<td>Estrogen therapy</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>Blockage in lymphatic drainage</td>
<td>Compressions stockings</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Surgical options</td>
</tr>
</tbody>
</table>

Resources to manage distress

- Cancer Education:
  - Learning about cancer and its treatment may reduce distress
  - Patient navigator programs are a useful resource

- Social Work & Counseling:
  - Practical problems - illness, food, money, work, school, language, and caregiving
  - Psychosocial problems - wide range

- Mental Health Services:
  - Psychoeducation
  - Medicine
  - Psychotherapy
  - Substance abuse treatment
  - Complementary & integrative therapies
  - Exercise

- Chaplaincy Care:
  - Spirituality and religion are related to better mental health
  - Chaplains provide help for grief, guilt, and hopelessness
Management of stress and distress

- Survivors may be referred to the following specialists, depending on their needs:
  - **Nurses**: Nurses are often the first to detect and screen for distress.
  - **Social Workers**: Social workers provide help for practical and psychosocial problems.
  - **Psychologists**: Psychologists provide in-depth mental health and neurocognitive assessments.
  - **Psychiatrists**: Psychiatrists assess the physical and mental aspects of mental health.
  - **Chaplains**: Chaplains are certified to care for issues like grief, guilt, loss of faith, and spiritual concerns.

Financial effects

- **Increased expenses**
  - From cancer care
  - From indirect needs
- **Decreased income**
  - Days off work
  - Work discrimination

- **Risk of bankruptcy**
  - 2.6 fold higher in cancer survivors

- **Resources**
  - Financial counselors
  - Community support groups
  - Religious groups
  - Cancer awareness programs
  - Caregiver support

Advance directives

- **Used to maintain patient autonomy**
  - Do-not-resuscitate orders
  - Healthcare power of attorney
  - Living will
  - Life-sustaining treatment
- **<1/3 of cancer survivors have advance directives**
  - Though a majority of patients desire a discussion

- **Benefits**
  - Appropriate assignment of a health care decision maker
  - Patient preferences for care being honored
  - Improved patient and family satisfaction
Transition to wellness

Healthy living

- After diagnosis, efforts should be directed to improving general health behaviors
- Opportunity for teachable moments
  - Patients and families are willing
  - Better cancer outcomes and quality of life
- Educational opportunities

Exercise

- Regular physical activity
  - Hasten recovery from treatment
  - May improve progression free and overall survival
  - Improves fatigue, depression and quality of life
- The American Cancer Society recommends
  - 150 minutes of moderate activity/week
  - Limit sedentary behavior
  - Ensure safety when starting new exercises
  - Know limitations
## Nutrition and weight

- Two-thirds of the population are overweight
  - Cancer risks increase with weight
- The American Cancer Society guidelines
  - Limit processed meats and red meat
  - Eat 2.5 cups of vegetables and fruit each day
  - Choose whole grains when possible
  - Monitor portion sizes
  - Limit alcohol intake

## Routine cancer screening

- Survivors are at risk for secondary malignancies
  - Continue recommended screening
  - Treatment doesn’t protect from developing other cancers and actually might increase the risk!
- Reduce possible risk factors
- Advocate healthy behaviors

<table>
<thead>
<tr>
<th>Cancer screening</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>Mammograms every 1-2 years beginning at age 40-50</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>Annual fecal hemoccult/ColoGuard</td>
</tr>
<tr>
<td></td>
<td>Colonoscopy every 10 years beginning at age 45</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>Every 3-5 years (if indicated)</td>
</tr>
</tbody>
</table>

## Management of medical co-morbidities

- A majority of survivors have at ≥ 1 medical condition
  - During treatment, patients tend to receive less care for other medical issues
  - Survivors report a lack of education of management
- Cancer and medical co-morbidities have a negative impact on one another
- Coordinating care and health promotion of other medical problems is essential
- Make sure patients have a primary care physician and keep appointments
Tobacco cessation

- Associated with multiple cancers and serious health problems
  - Higher risk of complications from therapy
  - Increased risk of recurrence and second malignancies
  - Negative effect on survival
- Over 10% of cancer survivors continue to smoke
  - ~30% of gynecologic cancer survivors continue to smoke
- Patient education
- Counseling
- Supportive measures

Genetic predisposition

- Contributes to ~10% of gynecologic malignancies
  - BRCA1/BRCA2
  - Lynch syndrome
- Know your family history
  - Types of cancers
  - Age of diagnosis
- Identification of high risk patients
  - Prevention
  - Early detection of secondary malignancies
  - Education
  - Testing for family members

The future
Conclusions

- Survivorship is an essential component of cancer care
- Multifaceted surveillance strategies are required to ensure early detection of recurrent disease
  - Ensure patients know what to expect
- Many patients experience late and long term effects of cancer or cancer treatment
  - Identify management strategies
- Promotion of wellness can improve overall health outcomes

Thank You!
Ritu.Salani@osumc.edu