Gynecologic Cancer Surveillance: Guidelines for the General Practitioner

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Objectives

* Review post-treatment surveillance recommendations for patients with endometrial, ovarian, cervical, vaginal, and vulvar cancers
* Discuss rationale for use (or non-use) of laboratory and radiologic testing in surveillance
* Identify survivorship issues for patients and providers

AJOG: June 2011

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

Gynecologic Malignancies

Cancer Site	Estimated New Cases	Estimated Deaths
Cervix	12,990	4,120
Ovary	22,280	14,240
Uterus	60,050	10,470
Vulva	5,950	1,110
Vaginal/Other	4,620	950

In 2016, it was estimated that 105,890 women would be diagnosed with a gynecologic cancer and some 30,890 will die from the disease.

ACS: Cancer Facts & Figures (2016)

Estimated Cancer Deaths (2015)

Women
277,280

26%	Lung & bronchus
15%	Breast
9%	Colon & rectum
7%	Pancreas
5%	Ovary
4%	Leukemia
4%	Uterine corpus
3%	Non-Hodgkin lymphoma
3%	Liver & intrahepatic bile duct
2%	Brain & other nervous system
23%	All other sites

* Gynecologic cancers are ***3 times*** more fatal than breast cancer

ACS: Cancer Facts & Figures (2015)

Role of Surveillance

* Clinical detection
* Cost-effective practices
* Decrease morbidity
* Impact survival outcomes

* *Should be directed at detecting recurrences that are amenable to curative or significant palliative treatment*

Role of Surveillance

* "The role of surveillance is based on the concept that detection of recurrence in the asymptomatic stage results in better therapeutic options and outcomes." (Salani 2011)

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How Good Are We?

TABLE 1

Sensitivity/detection rate of the methods that were used to detect recurrence in patients at routine visits after treatment

	Type of cancer, %		
Method of detection	**Endometrial**	**Ovarian**	**Cervical**
Symptoms	41-83	—	46-95
Physical examination	35-68	15-78	29-75
Cytologic evidence	0-7	—	0-17
Chest radiograph	0-20	—	20-47
Cancer antigen 125 level	15	62-74	—
Computed tomography scan	0-20	40-93	0-45[a]
Positron emission test–computed tomography scan	100[a]	45-100	86

[a] Limited data.

Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.

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Surveillance Guidelines

Endometrial Cancer

Endometrial Cancer

TABLE 2
Endometrial cancer surveillance recommendations

	Months			Years	
Variable	**0-12**	**12-24**	**24-36**	**3-5**	**>5**
Review of symptoms and physical examination					
Low risk (stage IA grade 1 or 2)	Every 6 mo	Yearly	Yearly[a]	Yearly[a]	Yearly[a]
Intermediate risk (stage IB-II)	Every 3 mo	Every 6 mo	Every 6 mo[b]	Every 6 mo[b]	Yearly[a]
High risk (stage III/IV, serous or clear cell)	Every 3 mo	Every 3 mo	Every 6 mo	Every 6 mo	Yearly[a]
Papanicolaou test/cytologic evidence	Not indicated	Not indicated	Not indicated	Not indicated	Not indicated
Cancer antigen 125	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Radiographic imaging (chest x-ray, positron emission tomography/ computed tomography, magnetic resonance imaging)	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography and/or positron emission tomography scan ± cancer antigen 125	Computed tomography and/or positron emission tomography scan ± cancer antigen 125	Computed tomography and/or positron emission tomography scan ± cancer antigen 125	Computed tomography and/or positron emission tomography scan ± cancer antigen 125	Computed tomography and/or positron emission tomography scan ± cancer antigen 125

[a] May be followed by a generalist or gynecologic oncologist; [b] Consider alternating visits with a generalist and gynecologic oncologist.

Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.

Endometrial: Physical

* Physical Examination
  * Detection rate: 35-68%
  * Speculum exam
  * Bimanual exam
  * Rectovaginal exam

  * Only physical exam has shown utility in detection of endometrial cancer recurrence (Sartori 2010)

Endometrial: Symptoms

* Number one symptom: Vaginal bleeding
  * Often indicative of local occurrence
  * Can be salvaged with radiation therapy

Endometrial: Symptoms

* Symptoms
  * Detection rate: 41-83%
  * Distant recurrence: 70%
* Other Symptoms
  * Abdominal/pelvic pain
  * Lethargy
  * Weight loss
  * Headaches
  * Coughing

Endometrial: Physical/Symptoms

* Combination Physical & Symptoms
  * Detection rate > 80%

Endometrial: Cytology

* Detection rate: 0-6.8%
* Cytologic abnormalities
  * 25% of recurrences
  * Only 6.8% were asymptomatic
* Routine use: $27,000 per case detected
* Not recommended

Endometrial: CA125

* Detection rate: 15%
* Should not be used routinely, especially in low risk patients
* May be appropriate:
  * Advanced disease
  * Serous histology
  * Pretreatment elevation (50% will have this)

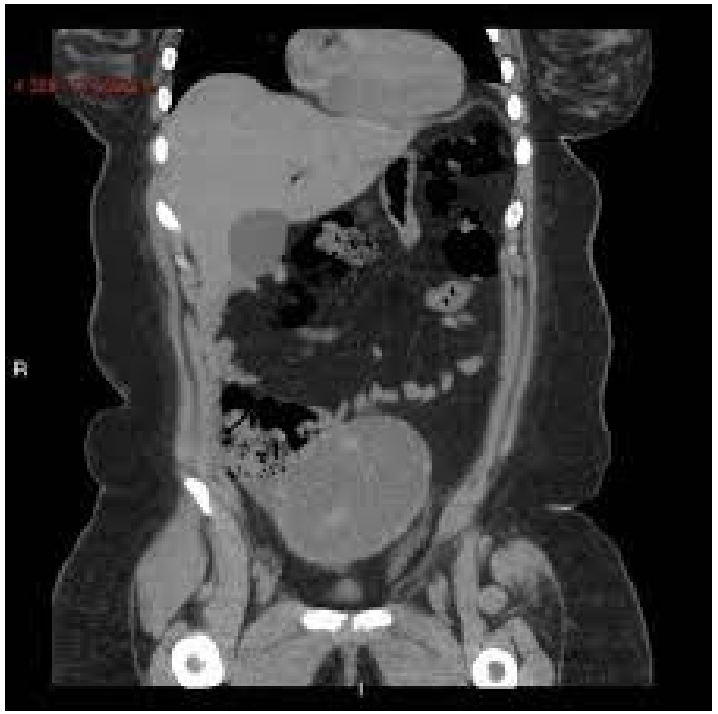
Endometrial: Routine Imaging

* Annual chest radiographs
  * Detection rate: 0-20%
  * Low cost, but low yield
  * Not recommended
* Routine CT scans
  * Detection rate: 5-21%
  * Improves to 50% when symptomatic
* PET/CT
  * Helpful with suspected recurrence (84-100%)

Endometrial: Recurrence Suspected

* CT Scan – chest/abdomen/pelvis
* PET/CT
* CA 125

* *Take home message: Save imaging for those who are symptomatic.*



Endometrial: Conclusions

* Most patients are low risk for recurrence
* More than half of recurrences will be detected based on symptoms alone
* Cytology and routine imaging are not indicated

* With the exception of local disease, recurrent endometrial cancer is associated with poor prognosis – ***regardless of the time of detection.***

Surveillance Guidelines

Ovarian Cancer

Ovarian Cancer: Epithelial

TABLE 3
Ovarian cancer surveillance recommendations

	Months			Years	
Variable	**0-12**	**12-24**	**24-36**	**3-5**	**>5**
Review of symptoms and physical examination	Every 3 mo	Every 3 mo	Every 4-6 mo	Every 6 mo	Yearly[a]
Papanicolaou test/ cytologic evidence	Not indicated	Not indicated	Not indicated	Not indicated	Not indicated
Cancer antigen 125	Optional	Optional	Optional	Optional	Optional
Radiographic imaging (chest x-ray, positron emission tomography/ computed tomography, magnetic resonance imaging)	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan
	Cancer antigen 125	Cancer antigen 125	Cancer antigen 125	Cancer antigen 125	Cancer antigen 125

[a] May be followed by a generalist or gynecologic oncologist.

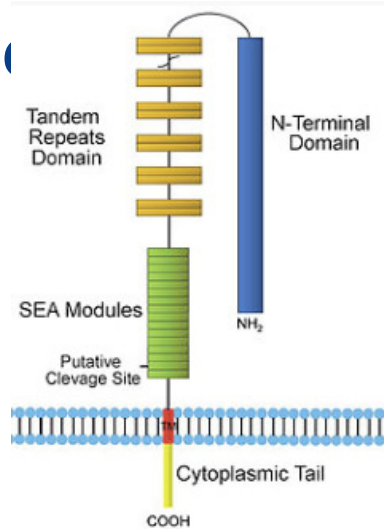
Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.

Ovarian: Physical

* Detection rate: 15-78%
* Physical exam
  * Abdominal exam
  * Bimanual examination
  * Rectovaginal examination

Ovarian: CA125

* Double upper limit of normal on two occasions at least one week apart (GCIG Criteria)
* Often elevated 2-5 months prior t relapse
  * Sensitivity: 62-94%
  * Specificity: 91-100%



Ovarian: CA125

* European Organization for Research & Treatment of Cancer (Rustin 2009)
  * 527 patients with recurrent disease
  * Treatment for elevated CA125 vs when symptomatic
  * **Overall survival outcomes DID NOT DIFFER**

Ovarian Cancer: 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

Ovarian: Cytology

* Not indicated for ovarian cancer surveillance
* Follow ASCCP guidelines for pre-existing dysplasia

Ovarian: Routine Imaging

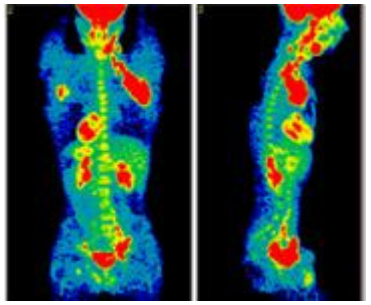
* Benefits of Routine Imaging
  * Diagnose asymptomatic recurrence
  * Higher rate of optimal secondary cytoreductive surgery
  * *May* benefit overall survival

* Insufficient data to support routine use

Ovarian: Routine Imaging

* CT scans
  * Sensitivity: 40-93%
  * Specificity: 50-98%
  * Lack the ability to detect small volume disease
* MRI
  * Sensitivity: 62-91%
  * Specificity: 40-100%
  * Cost prohibitive

Ovarian: Routine Imaging



* PET/CT
  * Sensitivity: 45-100%
  * Specificity: 40-100%
  * Diagnostic accuracy: 95%
  * Slightly more sensitive for CT scans for detection of recurrent disease, especially with normal CA125 but clinical suspicion of disease

Ovarian: Recurrence Suspected

* Recurrence rates
  * 25% in early stage disease
  * >80% with advanced disease
* 26-50% of recurrences occur in the pelvis

* *Second line therapies are rarely curative and often only result in short term progression free survival intervals.*

Ovarian Cancer: Nonepithelial

TABLE 4
Nonepithelial ovarian cancer (germ cell and sex-cord stromal tumors) surveillance recommendations

	Months			Years	
Variable	**0-12**	**12-24**	**24-36**	**3-5**	**>5**
Review of symptoms and physical examination					
Germ cell tumors	Every 2-4 mo	Every 2-4 mo	Yearly	Yearly	Yearly
Sex-cord stromal tumors	Every 2-4 mo	Every 2-4 mo	Every 6 mo	Every 6 mo	Every 6 mo
Serum tumor markers					
Germ cell tumors	Every 2-4 mo	Every 2-4 mo	Not indicated	Not indicated	Not indicated
Sex-cord stromal tumors	Every 2-4 mo	Every 2-4 mo	Every 6 mo	Every 6 mo	Every 6 mo
Radiographic imaging (chest x-ray, computed tomography, magnetic resonance imaging)					
Germ cell tumors	Not indicated unless tumor marker normal at initial presentation	Not indicated unless tumor marker normal at initial presentation	Not indicated	Not indicated	Not indicated
Sex-cord stromal tumors	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography scan	Computed tomography scan	Computed tomography scan	Computed tomography scan	Computed tomography scan
	Tumor markers	Tumor markers	Tumor markers	Tumor markers	Tumor markers

Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.

Surveillance Guidelines

Cervical & Vaginal Cancer

Cervical, Vaginal, Vulvar Cancer

TABLE 5
Cervical, vulvar, and vaginal cancer surveillance recommendations

	Months			Years	
Variable	**0-12**	**12-24**	**24-36**	**3-5**	**>5**
Review of symptoms and physical examination					
Low risk (early stage, treated with surgery alone, no adjuvant therapy)	Every 6 mo	Every 6 mo	Yearly[a]	Yearly[a]	Yearly[a]
High risk (advanced stage, treated with primary chemotherapy/ radiation therapy or surgery plus adjuvant therapy)	Every 3 mo	Every 3 mo	Every 6 mo	Every 6 mo	Yearly[a]
Papanicolaou test/cytologic evidence	Yearly[b]	Yearly[b]	Yearly[b]	Yearly[b]	Yearly[b]
Routine radiographic imaging (chest x-ray, positron emission tomography/computed tomography, magnetic resonance imaging)	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan

[a] May be followed by a generalist or gynecologic oncologist; [b] Insufficient evidence for cancer recurrence but may have value in the detection of other lower genital tract neoplasia.

Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.

Cervical: Physical

* 29-75% recurrence diagnosed during routine physical
  * Speculum exam
  * Bimanual exam
  * Rectovaginal exam

* Physical exam accounts for highest detection rate compared to cytology or imaging

Cervical: Symptoms

* 46-95% present with symptoms despite surveillance
  * Abdominal/pelvic pain
  * Leg pain
  * Lymphedema
  * Vaginal bleeding/discharge
  * Urinary symptoms
  * Cough
  * Weight loss

Cervical: Cytology

* Detection rates: 0-17%
* Role of cytology limited after RT
* Recommend yearly or eliminate altogether

* If routine use, no colposcopy unless HGSIL

Cervical: Routine Imaging

* Chest X-Ray
  * Detection rate: 20-47%
  * Distant failure often not salvagable
  * Little evidence to support use
* CT scan & MRI
  * Rates of detection low

* Insufficient data to support routine use

Cervical: Routine Imaging

* PET/CT
  * Asymptomatic
    * Looking for locoregional recurrence
    * Amenable to curative treatment
  * Symptomatic
    * Sensitivity: 86%
    * Specificity: 87%
  * Still cost prohibitive for routine use at this time

Cervical: Recurrence Suspected

* 75% of recurrences will occur in first 2-3 years
* Survival rates
  * Asymptomatic: 8-53 months
  * Symptomatic: 8-38 months

* Locoregional recurrence is amenable to treatment that can result in cure or long term survival

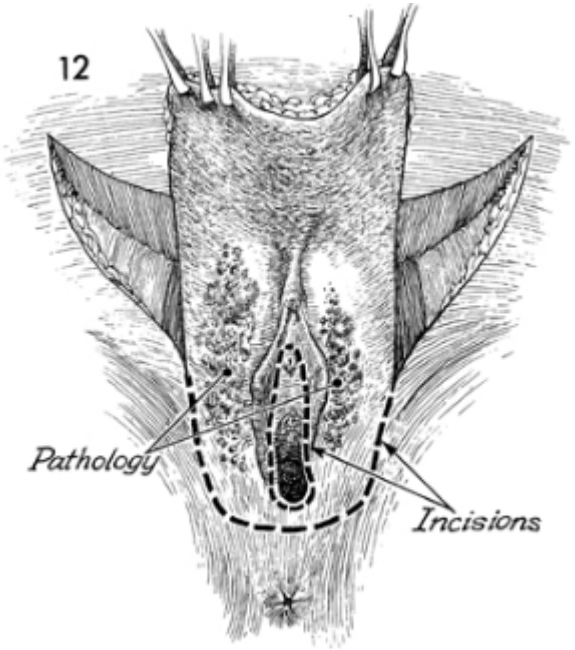
Surveillance Guidelines

Vulvar Cancer

Vulvar Carcinoma

* 4% of gynecologic malignancies

* Standard surgical managemen
  * Radical local excision
  * Inguinofemoral lymphadenect
* Preoperative chemoradiation
  * Unresectable disease
* Sentinel lymph node detection



Atlasofpelvicsurgery.com

Cervical, Vaginal, Vulvar Cancer

TABLE 5
Cervical, vulvar, and vaginal cancer surveillance recommendations

	Months			Years	
Variable	**0-12**	**12-24**	**24-36**	**3-5**	**>5**
Review of symptoms and physical examination					
Low risk (early stage, treated with surgery alone, no adjuvant therapy)	Every 6 mo	Every 6 mo	Yearly[a]	Yearly[a]	Yearly[a]
High risk (advanced stage, treated with primary chemotherapy/ radiation therapy or surgery plus adjuvant therapy)	Every 3 mo	Every 3 mo	Every 6 mo	Every 6 mo	Yearly[a]
Papanicolaou test/cytologic evidence	Yearly[b]	Yearly[b]	Yearly[b]	Yearly[b]	Yearly[b]
Routine radiographic imaging (chest x-ray, positron emission tomography/computed tomography, magnetic resonance imaging)	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan	Computed tomography and/or positron emission tomography scan

[a] May be followed by a generalist or gynecologic oncologist; [b] Insufficient evidence for cancer recurrence but may have value in the detection of other lower genital tract neoplasia.

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Vulvar: Lymph Nodes

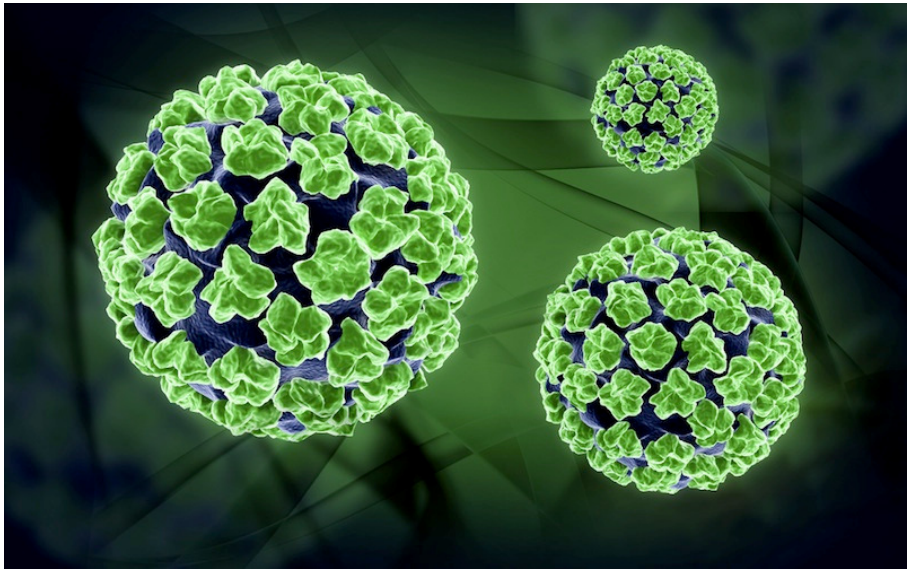
* Negative lymph nodes
  * 17.5% recur in first 2 years
  * 5 year survival of >80%
* Positive lymph nodes
  * 44.2% recur in frist 2 years
  * 5 year survival < 50%
  * As low as 13% if 4 or more nodes are positive
* After 2 years, rates of recurrence are equal

Vulvar: Symptoms

* Burning
* Pruritis
* Lumps
* Ulceration
* Skin changes
* Lymphedema
* Swelling

Vulvar: Physical

* Detailed inspection
* HPV association
  * Cervical
  * Vaginal
  * Anal

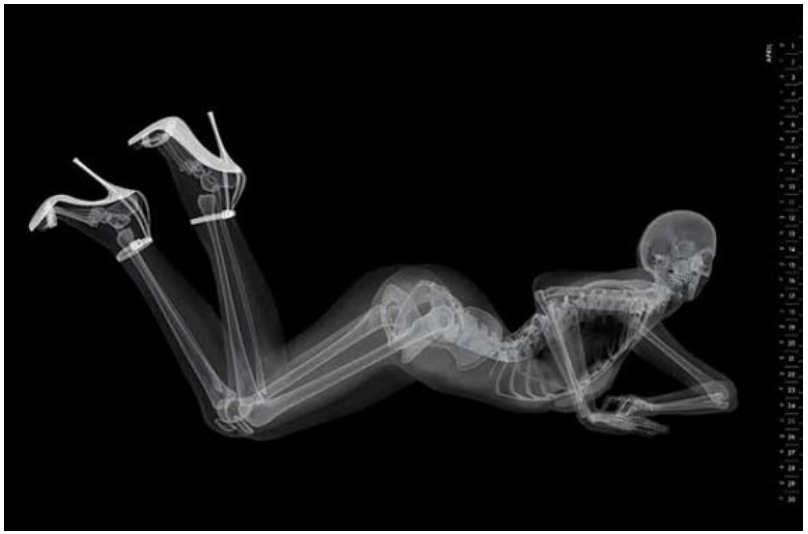


Vulvar: Cytology

* Yearly cytology of cervix if appropriate
  * HPV related disease
* No role of vulvar cytology

Vulvar: Routine Imaging

* Insufficient data to support routine use



This is how I know radiologists need to get out more… it's amazing what you'll find on Google images.

Vulvar: Recurrence Suspected

* Biopsy
* Late recurrence possible
  * More than 1/3 of relapses are >5 years after initial therapy – nearly 1 in 10 patients had a late recurrence
    * 95% are local recurrence
    * 13% also had distant disease

Choosing Wisely & Survivorship

SGO Choosing Wisely

1

Don't screen low risk women with CA-125 or ultrasound for ovarian cancer.

CA-125 and ultrasound in low risk, asymptomatic women have not led to diagnosis of ovarian cancer in earlier stages of disease or reduced ovarian cancer mortality. False positive results of either test can lead to unnecessary procedures, which have risks of complication.

2

Don't perform Pap tests for surveillance of women with a history of endometrial cancer.

Pap testing of the top of the vagina in women treated for endometrial cancer does not improve detection of local recurrence. False positive Pap smears in this group can lead to unnecessary procedures such as colposcopy and biopsy.

3

Don't perform colposcopy in patients treated for cervical cancer with Pap tests of low-grade squamous intraepithelial lesion (LGSIL) or less.

Colposcopy for low-grade abnormalities in this group does not detect recurrence unless there is a visible lesion and is not cost effective.

4

Avoid routine imaging for cancer surveillance in women with gynecologic cancer, specifically ovarian, endometrial, cervical, vulvar and vaginal cancer.

Imaging in the absence of symptoms or rising tumor markers has shown low yield in detecting recurrence or impacting overall survival.

Survivorship

The Society of Gynecologic Oncology has developed a number of resources for cancer survivors to help guide you on next steps after treatment.* Maintaining a healthy lifestyle and routine examinations are key to fighting recurrence. The following tools can be used in conjunction with information provided by your physician or cancer care team. You can also direct your health care provider to these resources so that they may be accurately completed and used. Seek a specialist near you.

Survivorship Toolkit

* Treatment summary
* Survivorship care plan
* Self-Care plan
  * Routine screenings
  * Healthy Living
* Information cards
* Survivorship calendar

sgo.org

Conclusions

* History and physical examination detect the majority of recurrences for gynecologic cancers.
* Routine cytology and imaging should be avoided in the absence of symptoms or physical findings.
* Unfortunately, most recurrences carry a poor prognosis and early detection of these while asymptomatic has minimal, if any, benefit.

Questions?