Uterine Cancer: Risk Evaluation, Diagnosis, and Management for the Family Physician

Heather Paladine, MD, MEd, FAAFP

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Every effort has been made to ensure the accuracy of the data presented here. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.

DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this activity have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will include discussion of unapproved or investigational uses of products or devices as indicated: OCPs and Progesterone contraceptives to prevent uterine cancer, treat abnormal uterine bleeding or hyperplasia. NSAIDs to treat abnormal uterine bleeding.

Heather Paladine, MD, MEd, FAAFP

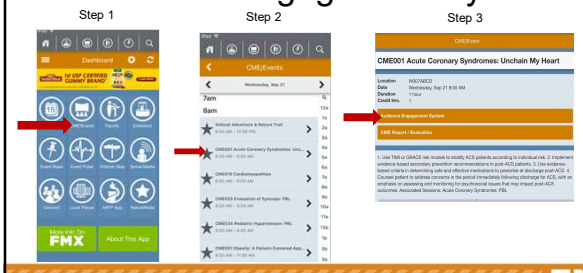
Family Physician; Director/Director of Women's Health, New York Presbyterian-Columbia University Medical Center Residency Program; Assistant Professor of Medicine, Center for Family and Community Medicine, Columbia University Medical Center

Dr. Paladine lives and practices full-spectrum family medicine in Manhattan, New York, where she supervises residents and medical students, and treats a predominantly Latino, low-income patient population. She focuses in women's health, including maternity care and reproductive health. In addition to her work as a physician, Dr. Paladine mentors residents and medical students as a preceptor in clinic and hospital environments and is a member of the board of directors of the New York State Academy of Family Physicians and chair of its Public Health Commission. She believes that the United States needs a health care system based on primary care, and that the public must learn more about family medicine to pave the way.

Learning Objectives

1. Screen for endometrial cancer in accordance with current clinical guidelines.
2. Diagnose endometrial cancer though physical examination and appropriate laboratory and diagnostic studies, as indicated.
3. Develop collaborative treatment plans based on the patient's desire for future fertility and results of the diagnosis.
4. Establish protocols to improve coordination of care with sub-specialists treating cancer patients to improve communication and patient outcomes.

Audience Engagement System



What You Need to Know

- Facts about uterine cancer
- How does uterine cancer present?
- How to diagnose uterine cancer
- Caring for patients after diagnosis
- Risk reduction
- Resources for patients
- Practice recommendations

Uterine Cancer Facts

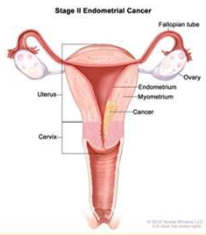
- Endometrial cancer (carcinoma) >95%
- Uterine sarcoma ~3% (pelvic radiation, tamoxifen)
- Rare types: carcinosarcoma, papillary serous carcinoma, clear cell carcinoma

Felix AS, Cook LS, Gaudet MM et al. The etiology of uterine sarcomas: a pooled analysis of the epidemiology of endometrial cancer consortium. British Journal of Cancer (2013) 108, 727–734.

Endometrial Cancer Facts

- Fourth most common cancer among women
- Increasing in the US and other developed countries
- 75% diagnosed in early stage
- Mean age at diagnosis is 60

National Cancer Institute, http://www.cancer.gov/research/progress/snapshots/endometrial
SGO Clinical Practice Endometrial Cancer Working Group, Burke WM, Orr J , Leitao M et al. for the Society of Gynecologic Oncology Clinical Practice Committee. Endometrial cancer: A review and current management strategies: Part I. Gynecologic Oncology 134 (2014) 385–392.



Endometrial Cancer Types

- Type 1: endometrioid, often progresses from hyperplasia
- Type 2
  - poorer prognosis, not related to estrogen
  - serous, mucinoid, squamous, etc.

Setiawan VW, Yang HP, Pike MC, et al. Type I and II Endometrial Cancers: Have They Different Risk Factors? Journal of Clinical Oncology 2013; 31(30): 2607- 2618

AES Question

Which of the following is NOT a risk factor for endometrial cancer?

A. tamoxifen use
B. oral contraceptive use
C. obesity
D. age

Risk Factors & Relative Risk

Unopposed estrogen therapy	2-20
Tamoxifen use	6-8
Lynch syndrome (HNPCC)	6-20
Obesity BMI >=40	7.1
Obesity BMI 35-39	4.5
Obesity BMI 30-34	2.5

Older age	2-3
Late menopause (over 52)	2-3
Early menarche (younger than 12)	1.5-2
Late menarche	0.8
OCP use	0.7
Cigarette smoking	0.6

Setiawan VW, Yang HP, Pike MC, et al. Type I and II Endometrial Cancers: Have They Different Risk Factors? Journal of Clinical Oncology 2013; 31(30): 2607- 2618
SGO Clinical Practice Endometrial Cancer Working Group, Burke WM, Orr J , Leitao M et al. for the Society of Gynecologic Oncology Clinical Practice Committee. Endometrial cancer: A review and current management strategies: Part I. Gynecologic Oncology 134 (2014) 385–392.
ACOG Practice Bulletin. Endometrial Cancer. Obstet Gynecol 2015;125:1006–26.

FMX

SERM risk

- Increased risk with tamoxifen in post-menopausal women only
- No increased risk with raloxifene
- Ospemifene does not seem to have increased risk

FMX

Tamoxifen

- 2-3x increased risk of uterine cancer for post menopausal women
- Risk increases with dose and duration
- No routine screening recommended
- High index of suspicion for any vaginal bleeding or spotting

Tamoxifen and uterine cancer. Committee Opinion No. 601. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014; 123:1394–7.

FMX

AES Question

A 28yo woman with PCOS and obesity has always had irregular periods but usually at least every three months. She now reports no period for six months. Should she have an endometrial biopsy?

A. Yes
B. No

FMX

Which Pre-Menopausal Women Should Have Endometrial Biopsy?

- No general population screening
- ACOG recommendation:
  - Women >45 with abnormal uterine bleeding
  - Women <45 if h/o unopposed estrogen and not responding to medical management
- Women with Lynch syndrome (HNPCC) starting age 35

Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Committee Opinion No. 557. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013; 121: 891-6

FMX

Evaluation of AUB

PALM - structural causes
Polyp
Adenomyosis
Leiomyoma
Malignancy and Hyperplasia

COEIN - non-structural causes
Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

FMX

Treatment of AUB

Acute:
- IV Conjugated equine estrogen
- Oral contraceptives
- Oral medroxyprogesterone acetate
- IV Tranexamic acid

FMX

Treatment of AUB

Long term:
- Oral contraceptives
- Levonorgestrel IUD
- PO or IM progestins
- Tranexamic acid
- NSAIDs

FMX

Endometrial Biopsy Facts

- 68% sensitivity compared with hysterectomy
- 78% sensitivity compared with D&C
- 0-54% rate of sampling failure
- Consider other tests (D&C, sonohysterography, hysteroscopy) if EMB negative and pt is high risk or sx continue

FMX

AES Question

A 52yo woman, post-menopausal for 5 years, has blood-tinged vaginal mucous for 1 month. Which initial test would you do to evaluate her?

A. Pap test
B. Endometrial biopsy
C. Transvaginal ultrasound
D. Hysteroscopy
E. Either B or C

FMX

Common Presentations in Post-Menopausal Women

- Abnormal bleeding or bloody vaginal discharge >90%
- However, the majority of these will not have endometrial cancer
- Pap abnormalities

FMX

Pap Abnormalities Related to Endometrial Cancer

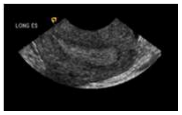
- Endometrial cells present
- Atypical glandular cells (may specify endometrial cells)
- Endometrial adenocarcinoma

Solomon D, Davey D, Kurman R et al. for the Forum Group Members and the Bethesda 2001 Workshop. The 2001 Bethesda System: Terminology for Reporting Results of Cervical Cytology. *JAMA*. 2002;287(16):2114-2119.

FMX

Endometrial Biopsy vs. TVUS

- Either is fine as an initial test for post-menopausal women
- can start with TVUS but will need further eval if endometrial stripe is >4mm
- TVUS is particularly useful if EMB was insufficient



The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. ACOG Committee Opinion No. 440. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:409–11.

FMX

Lynch Syndrome

- Previously called Hereditary Non-Polyposis Colorectal Cancer syndrome (HNPCC)
- Autosomal dominant
- Associated with colon cancer, also commonly ovarian and endometrial cancer at a young age
- Up to 50% lifetime risk of endometrial cancer

Lynch syndrome. Practice Bulletin No. 147. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;124:1042–54.

FMX

Criteria for Genetic Evaluation

- Colon or endometrial cancer before age 50
- Person with endometrial or ovarian cancer AND colon cancer
- Person with endometrial or colon cancer, and a first-degree relative with Lynch syndrome-associated cancer before age 50
- Person with endometrial or colon cancer, and two first-degree relatives with Lynch syndrome-associated cancer at any age
- Can test tumor tissue if available

FMX

Lynch Syndrome - Screening and Risk Reduction

- EMB every 1-2 years, starting age 30-35
- Consider OCP or progestin-based contraception use to reduce risk
- consider TAH/BSO by mid-40s to reduce risk

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment V.2.2015. © National Comprehensive Cancer Network, Inc 2015.

FMX

Hyperplasia

Aka endometrial intraepithelial neoplasia
Can be with or without atypia

- Without atypia: 1-3% chance of progression to cancer
- With atypia: 30-40% chance of progression to cancer

Braun MM et al. Diagnosis and Management of Endometrial Cancer. Am Fam Physician. 2016; 93(6):468-474.

FMX

Hyperplasia Without Atypia

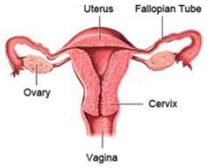
- Treat with levonorgestrel IUD or continuous progestins
- Medroxyprogesterone 10mg daily or norethindrone 5mg tid
- Repeat endometrial biopsy in 6 months

Liegl S. Levonorgestrel-Releasing Intrauterine System vs. Oral Progestins for Treatment of Endometrial Hyperplasia. Am Fam Physician. 2016; 93(11):948-949.

FMX

Hyperplasia With Atypia

Surgical treatment with hysterectomy



FMX

Staging and Treatment

- Generally surgical (TAH/BSO, lymph node dissection, peritoneal cytology)
- Treatment may also include radiation for early/mid-stage cancer and chemotherapy for late stage
- Refer to Gyn-Onc

Endometrial cancer. Practice Bulletin No. 149. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:1006–26.

FMX

Fertility-Sparing Treatments

- Not recommended for most patients
- Should have D&C and consider MRI for staging
- Progesterone therapy
- Follow-up EMB screening every 3 months
- Risk of recurrence is ~50%
- Recommend hysterectomy once childbearing is completed

FMX

Caring for Patients After Diagnosis

- Can consider estrogen for menopausal sx in early-stage disease
- Lower leg swelling affects ⅓ of women and reduces quality of life
- Strongest evidence for exercise and weight reduction, physical therapy may also be helpful

I.J. Rowlands et al. Quality of life of women with lower limb swelling or lymphedema 3–5 years following endometrial cancer. Gynecologic Oncology 2014; 133 (2014) 314–318.
Paskett ED, Dean JA, Oliveri JM, Harrop JP. Cancer-Related Lymphedema Risk Factors, Diagnosis, Treatment, and Impact: A Review. J Clin Oncol 2012; 30:3726-3733
Endometrial cancer. Practice Bulletin No. 149. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:1006–26.

FMX

Endometrial Cancer and Cardiac Risk

- Endometrial cancer is the type of cancer most associated with obesity
- Most women with endometrial cancer will die from cardiovascular disease

Sources: Schmandt RE, Iglesias DA, Co NN, and Lu KH. Understanding obesity and endometrial cancer risk: opportunities for prevention. American Journal of Obstetrics and Gynecology 2011; 205(6): 518-525.
Ward KK, Shah NR, Saenz CC, McHale MT, Alvarez EA, Plaxe SC. Cardiovascular disease is the leading cause of death among endometrial cancer patients. Gynecologic Oncology 2012; 126(2): 176-179.

FMX

Risk Reduction

- OCPs, depo medroxyprogesterone acetate, or levonorgestrel IUD associated with reduced risk
- Maintain healthy body weight
- Physical activity

FMX

Resources for Patients

- www.cancer.gov - National Cancer Institute, overview of uterine cancer
- www.familydoctor.org -patient handouts on endometrial ca evaluation and treatment in English and Spanish
- www.cancer.org - American Cancer Society, information on endometrial cancer, can search for support groups
- http://www.nlm.nih.gov/medlineplus/ - National Library of Medicine, links to patient information from other groups, clinical trials, English and Spanish

FMX

Practice Recommendations

- Post-menopausal women with vaginal bleeding can have either TVUS or EMB as initial evaluation (SORT: B)
- Post-menopausal women with an endometrial thickness of >4mm should be evaluated for endometrial ca (SORT: B)
- Risk reduction for endometrial cancer includes progestin-containing contraception and maintenance of a healthy body weight (SORT: B)

FMX

Questions

FMX

Contact Information

Heather Paladine, MD, FAAFP
hlp222@gmail.com
@paladineh on Twitter

FMX

Billing & Coding

When services performed in conjunction with:

Office Visit 992xx *

*Time-based selection documentation criteria:

- Face-to-face time
- greater than 50% spent counseling/coordinating care

99381-99397 Periodic comprehensive preventive medicine (age-based)

99401-99404 Preventive medicine counseling and/or risk factor reduction interventions (billable in 15 minute increments)

G0101 Cervical or vaginal cancer screening; pelvic and clinical breast examination (Medicare)

Q0091 Screening Papanicolaou smear; obtaining, preparing and conveyance of cervical or vaginal smear to laboratory (Medicare)

FMX

Billing & Coding

Additional tests to confirm or monitor:

58100	Endometrial sampling (biopsy) with or without endocervical sampling (biopsy), without cervical dilation, any method
+58110	Enodmetrial sampling (biopsy) perfomed in conjuction with colposcopy (use with 57420, 574221, 57452-57461)
58120	Dilation and currettage, diagnostic and/or therapeutic (nonobstetrical)
57452	Colposcopy of the cervix including upper/adjacent vagina;
57454	; with biopsy(s) of cervix and endocervical curettage
57455	; with biopsy(s) of the cervix
57456	; with endocervical curettage
57460	; with loop electrode biopsy(s) of the cervix
57461	; with loop electrode conization of the cervix

FMX

Associated Session

- Uterine Cancer: PBL

FMX

Interested in More CME on this topic?
aafp.org/fmx-womens-health

FMX