



Genital Tract Cancers in Females: Endometrial Cancer

Effective Date: June 15, 2014

Scope

This guideline provides recommendations for the screening, diagnosis, and follow-up care of endometrial cancer in females aged ≥ 19 years. Other causes and management of abnormal uterine bleeding (AUB) are outside of the scope of this guideline.

This guideline is part of the BCGuidelines.ca – *Genital Tract Cancers in Females* series. The series includes two other guidelines: *Human Papillomavirus Related Cancers (Cervical, Vaginal & Vulvar)* and *Ovarian, Fallopian Tube and Primary Peritoneal Cancers*. Signs and symptoms for the different female genital tract cancers may overlap (e.g., AUB); and therefore these guidelines may need to be used in conjunction with each other when performing initial diagnostic investigations.

Key Recommendations

- Refer patient with suspected hereditary cancer syndrome to the BC Cancer Agency's (BCCA) Hereditary Cancer Program (HCP).
- Investigate abnormal uterine bleeding (AUB), starting with a history and physical exam.
- Endometrial biopsy and transvaginal ultrasound are the recommended initial diagnostic investigations if other causes of AUB have been ruled out, and if endometrial cancer is suspected.¹
- Routine bloodwork, Papanicolaou smear test (Pap test), and imaging are not needed during follow-up visits post-treatment, unless indicated by symptoms or signs on examination.

Epidemiology^{1,2}

There are 2 major recognized categories of endometrial cancer: type 1 and type 2. Type 1 tumours are much more common (~80% of all cases) and are of lower histological grade. They are associated with estrogen excess and have a more favourable prognosis. Type 2 tumours are much less common and are of higher grade. They are not estrogen-related, and their prognosis is poorer.

Endometrial cancer* represents 3% of all new cancer cases. The median age for diagnosis of endometrial cancer is 62 years, with 74% of cases diagnosed after the age 55. Only 7% are diagnosed before the age of 44, and 26% before the age of 54.³

* Endometrial cancer statistics are based on US populations from 1975-2010.

Risk Factors^{1,2,4}

Hormone-related factors:

- tamoxifen use
- unopposed estrogen replacement therapy
- ovarian estrogen-secreting tumours (i.e., granulosa theca cell tumours)
- anovulatory menstrual cycles (i.e., polycystic ovary syndrome)
- nulliparity and/or infertility
- late menopause
- early menarche
- obesity (body mass index > 30 kg/m²) – which may affect estrogen metabolism
- diabetes – which may affect estrogen metabolism

Others:

- age
- Lynch syndrome (also known as hereditary non-polyposis colorectal cancer [HNPCC]) – personal or family history
- prior pelvic radiation – the only known risk factor for type 2 endometrial cancer

Prevention & Risk Reduction Strategies

- Lifestyle management^{2,5} - physical activity, limiting sedentary behaviour, and weight loss can reduce risk of endometrial cancer.
- Oral contraceptive use^{†,2,6,7} - the use of oral contraceptives may reduce risk.
- Hormone replacement therapy^{†,2,4} - for postmenopausal females with an intact uterus, the use of hormone replacement therapy comprising of both estrogen and progesterone may reduce the risk of endometrial hyperplasia. Unopposed estrogen therapy should be avoided.
- Hysterectomy^{8,9} - a hysterectomy is usually indicated for females with atypical endometrial hyperplasia because of high risk of progressing to cancer. Females who choose to retain their uterus should be managed on an individual basis under the direction of a gynecologist.
- Testing for hereditary cancer gene - those with suspected Lynch syndrome or HNPCC, refer to BCCA's HCP for genetic counselling and possible carrier testing. This includes a personal or family history of colorectal, endometrial, ovarian, gastric, small bowel, hepatobiliary, pancreatic, kidney, ureter, sebaceous gland adenomas, brain tumours; or a history of one or more pathologically confirmed colorectal adenomas ≤ age 40. For more information, refer to *Associated Document: Hereditary Cancer Program Referral Form*.

Screening⁹⁻¹²

There is currently no evidence that mortality is decreased by population-based screening for endometrial cancer, including for high-risk females (e.g., those with Lynch syndrome).

A Pap test (also known as cervical cytology) is not a screening procedure for endometrial cancer.

Diagnosis

Patients with abnormal uterine bleeding (AUB) require investigations. AUB, more specifically anovulatory bleeding and not ovulatory bleeding, is often associated with endometrial hyperplasia and cancer. Anovulatory bleeding is more common near menarche and perimenopause and is often irregular, heavy and prolonged.

† Though oral contraceptives and hormone replacement therapy might reduce one's risk for endometrial cancer, long-term use may increase the risk of other cancers (e.g., cervical, breast).^{1,7}

► Investigations^{1, 9, 13}

A medical history and physical exam will often indicate the cause of AUB and determine the need for further testing.

A medical history includes:

- menses history and relevant symptoms (e.g., bleeding amount, frequency);
- family history (e.g., Lynch syndrome); and
- identifying risk factors (listed above).

A physical exam includes:

- speculum exam (and a Pap test if indicated, but a Pap test is not a diagnostic test for endometrial cancer); and
- pelvic examination.

If clinically indicated, then bloodwork might include:

- complete blood count (when heavy or prolonged bleeding);
- pregnancy test (when pregnancy is possible);
- thyroid function test (when suspicion of thyroid disease); or
- coagulation test (when there is a personal or family history of AUB).

If other causes of AUB have been ruled out, and/or endometrial cancer is suspected, an endometrial biopsy and transvaginal ultrasound are the recommended initial diagnostic investigations.¹

Note that a normal endometrial thickness on ultrasound does not rule out endometrial cancer. Normal endometrium in a premenopausal woman varies in thickness from 4 mm in the follicular phase to 16 mm in the luteal phase of the menstrual cycle.

Those requiring endometrial biopsy include:

- women aged < 40 years with AUB **and** identifiable risk factors (listed above);
- women aged > 40 years with AUB;
- women with significant intermenstrual bleeding; and
- postmenopausal women who develop an unusual vaginal discharge in the absence of an identifiable vaginal cause.

An endometrial biopsy should be performed by either an experienced family physician or a community gynecologist.

For a patient with persistent AUB despite negative biopsy and transvaginal ultrasound results, consider hysteroscopic examination.¹

If high-grade histology or metastatic disease is recognized, then refer to the patient to BCCA's Division of Gynecological Oncology for assessment and management planning by a multidisciplinary team.[‡] The benchmark for an appointment at the BCCA is 2 weeks following referral; urgent cases may be seen sooner upon telephone consultation.

Treatment

Surgery is the mainstay of therapy following a tissue diagnosis. Patients with high-grade (i.e., grade 2 or 3), serous, malignant mixed Müllerian tumor (MMMT), or clear cell histologies should have their surgery performed by a gynecologic oncologist (if possible).

Most patients with low-grade operable endometrial cancer will not need any additional post-surgical therapy.

For patients with high-grade or aggressive histology, or the presence of extra-uterine disease: chemotherapy with or without radiotherapy may be used.

[‡] This multidisciplinary team includes gynecologic oncologists (surgeons), radiation oncologists, medical oncologists, pathologists, radiologists, general practitioners in oncology, nurses, radiation therapists, counsellors and nutritionists.

Follow-up

Once the patient has completed treatment, she will be discharged from the BCCA. Upon discharge, the family physician may be asked to manage the patient's follow-up care.

Follow-up care includes:

- 1) surveillance for recurrence or new cancer;
- 2) monitoring and treating complications and/or side effects from treatment; and
- 3) providing patient support.

Specific recommendations will be provided in the patient's discharge letter. At any time, the patient and/or family physician may consult with the BCCA regarding any follow-up questions or concerns. If recurrent disease is suspected, then re-refer back to the BCCA.

Below are general recommendations for a patient's follow-up visits with her family physician based on the type of therapy.¹⁴

1) When adjuvant treatment is not recommended

The timing of the follow-up visits are:

- Years 1 & 2 = Every 4 - 6 months
 - Years 3, 4 & 5 = Every 6 months
 - Years 5+ = Annually
- Risk of recurrence = low (<5%), most likely to occur within the first 2 years after primary treatment.
 - Site of recurrence = vaginal vault.
 - Counsel about vaginal bleeding.

2) When adjuvant treatment is recommended but is declined

The timing of the follow-up visits are:

- Years 1 & 2 = Every 3 - 4 months
- Years 3, 4 & 5 = Every 6 months
- Years 5+ = Annually

3) Post adjuvant vaginal vault radiation alone

The timing of the follow-up visits are:

- Years 1 & 2 = Every 6 months
 - Years 3+ = Annually
- Risk of recurrence = low (5 - 10%), most likely to occur within the first 2 - 3 years after primary treatment.
 - Site of recurrence = pelvis/vaginal vault, but some will recur distantly.
 - Counsel about vaginal bleeding, pelvic pain, bloating, and increase in abdominal girth.

4) Post adjuvant pelvic radiation +/- chemotherapy

The timing of the follow-up visits are:

- Years 1 & 2 = Every 6 months
 - Years 3+ = Annually
- Risk of recurrence = high, most likely to occur within the first 2 - 3 years after primary treatment.
 - Site of recurrence = distant or locoregional.

A follow-up visit consists of:

- 1) review of any symptoms (e.g., vaginal bleeding or discharge) and of general health concerns; and
- 2) physical exam, including pelvirectal.

Routine bloodwork, Pap test, and imaging are not needed during follow-up visits, unless indicated by symptoms or signs on examination.

► References

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2. BC Cancer Agency. Cancer Management Guidelines - Gynecology – Endometrium – 3.1 Predisposing Factors/Prevention [updated 2011; cited 2014 March].
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12. Vasen HFA, Blanco I, Aktan-Collan K. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): Recommendations by a group of European experts. *Gut.* 2013;62:812-823.
13. Singh S, Best C, Dunn S, et al. Society of Obstetricians and Gynaecologists of Canada. Abnormal uterine bleeding in pre-menopausal women. *J Obstet Gynaecol Can.* 2013;35(5):S1-S28.
14. BC Cancer Agency. Cancer Management Guidelines – Gynecology – Endometrium – 3.6 Follow-up [updated 2013; cited 2014 March].

► Resources

- **BC Cancer Agency**, www.bccancer.bc.ca, which includes many patient resources.
 - o Division of Gynecologic Oncology, telephone 1-800-663-3333 (extensions 2353, 2365, or 2367)
 - o Hereditary Cancer Program, for referrals: telephone 604-877-6000 (extension 672198), www.screeningbc.ca/Hereditary/ForHealthProfessionals/Default.htm
- **HealthlinkBC**, www.healthlinkbc.ca or by telephone (toll free in BC) 8-1-1 or 7-1-1 (for the hearing impaired) for health information, translation services and dieticians.

► Associated Documents

The following documents accompany this guideline:

- BCGuidelines.ca - *Genital Tract Cancers in Females: Human Papillomavirus Related Cancers (Cervical, Vaginal & Vulvar)*
- BCGuidelines.ca - *Genital Tract Cancers in Females: Ovarian, Fallopian Tube and Primary Peritoneal Cancers*
- Hereditary Cancer Program Referral Form

This guideline is based on scientific evidence current as of the Effective Date.

The guideline was developed by the Family Practice Oncology Network and the Guidelines and Protocols Advisory Committee. The guideline was approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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