

## **ENDOMETRIAL CARCINOMA**

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Endometrial carcinoma is the most common gynecologic malignancy in the United States; it accounts for 6 percent of all cancers in women. Fortunately, most cases are diagnosed at an early stage when surgery alone may be adequate for cure. Five-year survival rates for localized, regional, and metastatic disease are 96, 67, and 26 respectively [1].

### **Risk Factors**

#### **Estrogen**

Treatment with estrogen alone increases the risk for endometrial hyperplasia and carcinoma. Endometrial hyperplasia can be demonstrated within one year in 20 to 50 percent of women receiving unopposed estrogen [2]. Furthermore, any factor that increase exposure to estrogen[e.g., hormone replacement therapy, obesity, anovulatory cycles. estrogen-secreting tumor]increases the risk of endometrial cancer, whereas factor that decrease exposure to estrogens or increase progesterone level[e.g. oral contraceptives or smoking ] tend to be protective [3].

#### **Tamoxifen**

Tamoxifen is a competitive inhibitor of estrogen binding to estrogen receptors that also has partial agonist activity (i.e., tamoxifen is a weak estrogen). It is used for adjuvant therapy in women with early stage breast cancer, as treatment for recurrent disease, and for reduction of breast cancer incidence in high-risk women. The site-specific activity of tamoxifen in different tissues is well recognized, suppressing the growth of breast tissue, but stimulating the endometrial lining. Tamoxifen use has been linked to development of endometrial pathology, both benign and malignant [4].

#### **Diabetes and Hypertension**

Women with diabetes mellitus and hypertension are at increased risk for endometrial cancer, at least in part because of co-morbid factors associated with obesity. However, some studies have found independent effects as well [5].

#### **Diet**

A diet containing high amounts of fat (especially animal fat) appears to be a risk factor for endometrial cancer, even after adjusting for caloric intake and body weight [6]. By comparison, two case-control studies showed that plant-based diets high in fiber, legumes (especially soybeans [7]), whole grain foods, vegetables, and fruits appear to reduce the risk of the disease [8].

#### **Other risk factors include:**

Familial predisposition and lack of physical activity.

#### **Pathology**

The most common type of endometrial cancer is endometriod adenocarcinoma (75 to 80 percent). Clear cell and papillary serous carcinomas account for 1 to 5, and 5 to 10 percent of

endometrial cancer cases respectively. Mucinous and squamous cell cancer comprises less than 2 percent of endometrial cancers.

### **Clinical Features**

Ninety percent of patient with endometrial carcinoma have abnormal vaginal bleeding, most commonly postmenopausal bleeding. Occasionally, vaginal bleeding does not occur because of cervical stenosis, particularly in thin, elderly, estrogen-deficient patients. In some patients with cervical stenosis, a hematometria develops, and a small percentage has a purulent vaginal discharge resulting from pyometria.

### **Diagnosis**

#### **Endometrial biopsy**

Endometrial biopsy is the initial diagnostic test to rule out endometrial cancer in women with abnormal uterine bleeding or endometrial cells on Pap smear. Dilatation and Curettage with hysteroscopy and directed biopsy should be considered when the endometrial biopsy is nondiagnostic, but there remains a high suspicion of cancer (e.g., hyperplasia with atypia, presence of necrosis, pyometra, or persistent bleeding).

#### **Transvaginal ultrasonography**

Transvaginal ultrasound can be used to evaluate the endometrium by measuring the endometrial wall thickness. In postmenopausal women, an endometrial thickness of less than 4 to 5 mm is associated with a low risk of endometrial disease [9-10]; a thicker lining should be further evaluated by office biopsy, hysteroscopy with directed biopsy, or D&C. Cancer becomes increasingly more frequent relative to benign disease as the endometrial thickness approaches 20 mm, which was the mean endometrial thickness in 759 women with endometrial cancer [10].

### **Management**

The cornerstone of treatment for endometrial cancer is total abdominal hysterectomy and bilateral salpingo-oophorectomy, and this operation should be performed in all cases whenever feasible. In addition, many patients require some type of adjuvant radiation therapy to help prevent vaginal vault recurrence and to sterilize occult disease in lymph nodes. Chemotherapy in endometrial cancer is only of palliative value [11].

### **Screening**

#### **General population**

Screening for endometrial cancer is generally not warranted in asymptomatic women. Many cases are diagnosed at an early stage since the malignancy commonly causes abnormal vaginal bleeding. Moreover, adequate inexpensive, noninvasive screening tests are not currently available. Although endometrial cancer occasionally is diagnosed after endometrial or glandular cells are discovered on Pap smear, the sensitivity of the Pap smear for detection of endometrial cancer is low and not sufficient to recommend it as a screening tool. Endometrial biopsy is more sensitive, but is relatively uncomfortable; equivocal tests may lead to additional unnecessary evaluation [12].

#### **Women at risk of Hereditary Nonpolyposis Colorectal Cancer (HNPCC)**

Women who are at risk of HNPCC are also at high risk (40 to 60 percent) of developing endometrial cancer. In fact, the risk of developing endometrial cancer may be slightly higher than the risk of developing colon cancer and endometrial cancer may be the first manifestation of malignancy [13]. These women also have a 12 percent lifetime risk of developing ovarian cancer [14].

Because of the high risk for development of endometrial cancer in women with or at risk of HNPCC, the American Cancer Society recommends that annual screening by endometrial biopsy be initiated by age 35 [15]. These recommendations cover the following:

- Women who are known to carry HNPCC-associated mutations
- Women who have a family member known to carry this mutation
- Women from families with an autosomal dominant predisposition to colon cancer in the absence of genetic testing.

At present, there are no data regarding the efficacy of this approach, nor is there a consensus on the optimal age (25 to 35) to begin screening. Annual or biennial pelvic ultrasonography has not been shown to be effective for early detection of endometrial cancer in these populations [16]

These women should also be counseled about preventive measures, such as the option of prophylactic hysterectomy at complete childbirth.

### **Patient on Tamoxifen**

The American College of Obstetricians and Gynecologists has developed the following recommendations for monitoring women on tamoxifen [17];1

- Perform an annual gynecologic examination.
- Monitor for symptoms of endometrial hyperplasia or cancer. Women should be educated to report any abnormal vaginal symptoms (e.g., bloody discharge, spotting, staining, leukorrhea).
- Investigate any abnormal vaginal symptoms.
- Limit tamoxifen use to five years duration because benefit beyond this time has not been demonstrated.
- If atypical endometrial hyperplasia develops, the use of tamoxifen should be reassessed and appropriate gynecologic management should be initiated. Hysterectomy should be considered for women with atypical endometrial hyperplasia in whom tamoxifen therapy must be continued.

### **Conclusion**

Endometrial carcinoma is the most common gynecologic malignancy; to date there is no rule for screening program in general population. However, high risk patient for endometrial cancer have to be evaluated and followed up independently.

### **Recommendation and Guidelines for Screening and Prevention of the Endometrial Cancer**

#### **Screening**

The committee members (Authors) agreed that from reviewing all the data currently available regarding the role of screening for the general population of the women for endometrial cancer, it clearly emphasize that there is no role for such screening program in detecting early or pre-invasive changes for those women.

Initiating such screening program using either vaginal ultrasound with or without endometrial sampling will not be cost effective, and its effect on the morbidity and mortality for those women will be extremely low and will not be beneficial for the society.

#### **Early Detection**

As there is no rule for screening for the general population, the committee members agreed that the best approach for such a condition will be the education for the general population and for the primary care physician and family physician regarding the early symptoms and signs of endometrial cancer.

Any women who present with post menopausal or Premenopausal bleeding or abnormal uterine bleeding should be referred immediately to her gynecologist in order for her to do the necessary work-up which must include endometrial sampling at least in order to explore the development of hyperplasia or malignancy.

The committee members agreed that for special sub-group which represent high risk for developing endometrial cancer, like those who have history of breast cancer and they are on Tamoxifen, or those women with chronic anovulation, they should have regular check-up by gynecologist, where they will have ultrasound to evaluate the thickness of the endometrial lining according to gynecologist assessment and their symptoms and the decision for endometrial sampling will be left for the gynecologist according to the patient ultrasound result and her symptoms. Also, these women should be aware to report to their physician when they have abnormal bleeding and endometrial samples or dilation and curratage (D & C) must be done on these patients.

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