Screening and Prevention of Carcinoma Endometrium

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Introduction

Carcinoma endometrium is the most common malignancy of the female genital tract in the developed world and the fourth most common cancer in women after breast, lung, and colorectum. The estimated new cases from endometrial cancer in the United States are 52,630 and deaths are 8,590 [1]. It is the second most common malignancy of the female genital tract in the developing world. The incidence in developing countries and Japan are four to five times lower than the developed world. In India, the rates are as low as 4.3 per 100,000 [2]. In recent years incidence in India is increasing – double the incidence as per recent cancer registry data. Due to increasing magnitude of the problem, screening and steps of prevention are of great importance.

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Screening of Carcinoma Endometrium

Whom to Screen?

The American Cancer Society recommends that at the time of menopause, all women should be told about the risks and symptoms of endometrial cancer. Women should report any unexpected vaginal bleeding, discharge, or spotting.

Women at Low Risk for Endometrial Cancer

At this time, there are no acceptable, reliable, and valid screening tests or examinations to identify endometrial cancer early in women who are at average endometrial cancer risk and have no symptoms.

Women should have regular pelvic exams. A pelvic exam can find some cancers, including some advanced uterine cancers, but it is less effective in finding early endometrial cancers.

The Pap test (or Pap smear), which screens for cervical cancer, can occasionally find some early endometrial cancers, but it is too insensitive and nonspecific for screening for endometrial cancer [3]. In Papanicolaou smears, benign appearing endometrial cells bear no significance in predicting uterine endometrial adenocarcinomas [4].

S. Rajaram et al. (eds.), *Uterine Cancer: Diagnosis and Treatment*,
DOI 10.1007/978-81-322-1892-0_4

Measuring endometrial thickness (ET) with transvaginal ultrasound (TVU) and endometrial sampling with cytological examination have been proposed as possible screening modalities for endometrial cancer. But, there is no evidence that screening by ultrasonography (e.g., endovaginal ultrasound or transvaginal ultrasound) or endometrial sampling (i.e., biopsy) reduces mortality from endometrial cancer. Most cases of endometrial cancer (85 %) are diagnosed in early stage because of symptoms, and survival rates are high. Based on evidence, screening asymptomatic women by measuring endometrial thickness will result in unnecessary additional biopsies because of false-positive test results.

Routine screening of asymptomatic women for endometrial cancer has not been evaluated for its impact on endometrial cancer mortality. Although high-risk groups can be identified, the benefit of screening in reducing endometrial cancer mortality in these high-risk groups has not been evaluated. Using the same cutoffs to define an abnormal ET in asymptomatic women as used in symptomatic women [5, 6] would result in large numbers of false-positive test results and larger numbers of unnecessary referrals for cytological evaluations. Published recommendations for screening certain groups of women at high risk for endometrial carcinoma are based on opinion regarding presumptive benefit [7].

Women at Increased Endometrial Cancer Risk

The American Cancer Society recommends that most women at increased risk should be informed of their risk and be advised to see their doctor whenever there is any abnormal vaginal bleeding. However, there are no guidelines on screening asymptomatic high-risk women and the choice is left to gynecologists. Women at increased risk for carcinoma endometrium include [8] estrogen therapy unopposed by progesterone therapy in a postmenopausal woman with intact uterus, tamoxifen, anovulatory cycles including polycystic ovary syndrome, obesity, high fat diet, diabetes mellitus, hypertension, nulliparity, early menarche, late menopause, hereditary nonpolyposis colorectal cancer (HNPCC) syndrome, atypical endometrial hyperplasia, and pelvic radiation therapy.

Women who have (or may have) hereditary nonpolyposis colon cancer (HNPCC, Lynch syndrome) have a very high risk of endometrial cancer. If colon or endometrial cancer has occurred in several family members, genetic counseling should be offered. The reader is referred to Chap. 3 for complete information on hereditary cancers. Apart from family history other features direct genetic testing and mutational analysis.

The American Cancer Society recommends that women who have (or may have) HNPCC be offered yearly testing for endometrial cancer with endometrial biopsy beginning at age 35. This applies to women known to carry HNPCC-linked gene mutations, women who are likely to carry such a mutation (those with a mutation known to be present in the family), and women from families with colon cancer where genetic testing has not been done.

Modalities of Endometrial Cancer Screening

The methods of screening available are:

1. Measurement of endometrial thickness by ultrasonography
2. Endometrial aspiration biopsy
3. Endometrial curettage

Measurement of Endometrial Thickness and Endometrial Biopsy in Women Without Vaginal Bleeding

Transvaginal sonography (TVS) is a relatively less invasive investigation and is freely available. There is interest in trying to reduce the morbidity from endometrial cancer through early detection, and endovaginal ultrasound as a method to screen women to detect endometrial cancer is a promising option. It measures endometrial thickness that may help determine which women should undergo endometrial biopsy.

Fleischer et al. screened 1,926 asymptomatic postmenopausal women using TVS for endome-

trial disease as part of osteoporosis prevention trial, and 93 of them had endometrial thickness greater than 6 mm. Out of the 1,750 women who underwent biopsy, there were five cases of endometrial abnormality (adenocarcinoma [$n=1$] and atypical hyperplasia [$n=4$]). The negative predictive value was >99 %. One case of adenocarcinoma was detected in the 42 women who had endometrial thickness >6 mm and underwent biopsy. Among this population of asymptomatic postmenopausal women, the estimated sensitivity for TVS with a threshold value of 6 mm was 17 %. The study reveals that despite a high negative predictive value, TVS may not be an effective screening procedure for detection of endometrial abnormality in untreated postmenopausal women who are asymptomatic [9].

Saatli et al. did a retrospective analysis of 530 asymptomatic postmenopausal women who underwent ultrasonographic evaluation with subsequent endometrial sampling if endometrial thickness was above 5 mm. The mean endometrial stripe thickness was 8.7 mm (range: 6–26), and five cases of adenocarcinoma (0.9 %) and 65 (12.2 %) cases of simple/complex atypical hyperplasia were diagnosed [10]. Although TVS can be used to evaluate asymptomatic and occult endometrial pathology, the technique has not been evaluated as a screening method for reducing mortality in asymptomatic women.

Screening endometrial biopsy has also been considered as a way to detect neoplasia early. However, Archer et al. concluded that the yield for neoplasia is so low that screening endometrial biopsy is not justified in asymptomatic perimenopausal and postmenopausal women [11].

Measurement of Endometrial Thickness and Endometrial Biopsy in Women with Vaginal Bleeding

In a study on postmenopausal women with bleeding per vaginum, using a 5-mm threshold to define abnormal endometrial thickening, 96 % of women with cancer had an abnormal TVS result, whereas 92 % of women with endometrial disease (cancer, polyp, or atypical hyperplasia) had an abnormal result. This did not vary by hormone replacement use. However, the number of women with normal histology who had an abnormal TVS result did vary by hormone replacement use. The specificity varied by whether women used hormone therapy or not. Among nonusers, the specificity was 92 % [6].

In another study, women with postmenopausal bleeding underwent transvaginal sonographic measurement of endometrial thickness and curettage and were followed for > or = 10 years. Of the 339 participants, 39 (11.5 %) were diagnosed with endometrial cancer (four had an ET of 5–7 mm and 35 had an ET>8 mm) based on histopathology from curettage. No cancers were detected in women with an ET of less than 4 mm. Using a cutoff point of 4 mm, TVS has 100 % sensitivity and 60 % specificity. Postmenopausal bleeding confers a 64-fold increase risk in endometrial cancer. There was no increased risk of endometrial cancer or atypia in women who did not have recurrent bleeding, whereas women with recurrent bleeding were found to be a high-risk group. No endometrial cancer was missed when endometrial thickness measurement (cutoff value, < or = 4 mm) was used, even if the women were followed up for < or = 10 years concluding that transvaginal sonography is an excellent tool for determining whether further investigation with curettage or endometrial biopsy is necessary in symptomatic women [12]. In this population, 46 % ($N=156$) of the women had an ET greater than 4 mm.

Ultrasonography in Women Using Tamoxifen

Tamoxifen is widely used as part of adjuvant therapy for breast cancer and as chemoprevention for women at increased risk of breast cancer. In addition to the protective effects for breast cancer, the biological and endocrine effects of tamoxifen increase a woman's risk of developing endometrial pathology, including endometrial polyps, endometrial hyperplasia, and endometrial carcinoma.

In a prospective, observational study of 304 women using tamoxifen over 6 years, women underwent annual endovaginal ultrasound screening; women with abnormal ultrasound findings and women who were symptomatic with bleeding

all underwent endometrial biopsy. Thirty-two percent of the ultrasound examinations had associated significant uterine abnormalities identified that required further medical or surgical investigation and treatment. However, most abnormalities (80 %) represented benign polyps for which no treatment was needed. Six cases of primary endometrial cancer were detected, and all cases presented with irregular bleeding. The sensitivity of ultrasound was only 63.3 %, with a specificity of 60.4 %, and had a low positive predictive value for cancer of only 1 % [13].

Routine ultrasound surveillance in asymptomatic women using tamoxifen is not useful because of its low specificity and low positive predictive value. Evaluation of the endometrium in women taking tamoxifen should be limited to women symptomatic with vaginal bleeding.

ACOG Committee Opinion (June 2014) [14] recommends that women taking tamoxifen should be informed about the risks of endometrial proliferation, endometrial hyperplasia, endometrial cancer, and uterine sarcomas. They should be encouraged to promptly report any abnormal vaginal symptoms, including bloody discharge, spotting, staining, or vaginal discharge. Any abnormal vaginal bleeding, bloody vaginal discharge, staining, or spotting should be investigated.

Premenopausal women treated with tamoxifen have no known increased risk of uterine cancer and as such require no additional monitoring beyond routine gynecologic care. Postmenopausal women taking tamoxifen should be closely monitored for symptoms of endometrial hyperplasia or cancer [15, 16].

Correlation is poor between ultrasonographic measurements of endometrial thickness and abnormal pathology in asymptomatic tamoxifen users because of tamoxifen-induced subepithelial stromal hypertrophy [17]. In asymptomatic women using tamoxifen, screening for endometrial cancer with routine transvaginal ultrasonography, endometrial biopsy, or both has not been shown to be effective [13, 18, 19].

Although asymptomatic postmenopausal tamoxifen-treated women should not have routine testing to diagnose endometrial pathology, sonohysterography has improved the accuracy of ultrasonography in excluding or detecting anatomic changes, when necessary [20].

Unless the patient has been identified to be at high risk of endometrial cancer, routine endometrial surveillance has not proved to be effective in increasing the early detection of endometrial cancer in women using tamoxifen. Such surveillance may lead to more invasive and costly diagnostic procedures and, therefore, is not recommended.

There is evidence that suggest the presence of high-risk and low-risk groups for the development of atypical hyperplasias with tamoxifen treatment in postmenopausal women based on the presence or absence of benign endometrial polyps before therapy. Thus, there may be a role for pretreatment screening of postmenopausal women with transvaginal ultrasonography, and sonohysterography when needed, or office hysteroscopy before initiation of tamoxifen therapy [21–24].

Endometrial cancers that occur in tamoxifen-treated women are very similar to those cancers occurring in the general population, with respect to stage, grade, and histology [15, 25, 26]. Prognosis is good and not affected by early detection [27]. To date, there have been no published studies evaluating the effect of endometrial cancer-screening modalities on mortality among women taking tamoxifen for breast cancer treatment or prevention.

Sonohysterography

Sonohysterography is a diagnostic test done in asymptomatic women and distinguishes space occupying endometrial lesions from a thickened endometrium. There are no studies to show that routine screening sonohysterography will confer clinical benefit. Transtubal spill does occur during sonohysterography, but the probability of cancer cell dissemination is low [28].

Endometrial Sampling in Women with Uterine Bleeding

In the setting of abnormal uterine bleeding, endometrial biopsy has gained favor largely as an

alternative to more invasive procedures such as fractional curettage. Several methods of biopsy exist (e.g., Pipelle, Tao Brush, and Uterine Explora Curette) to identify endometrial pathology. Although endometrial biopsy has largely replaced D&C as the first choice in the evaluation of women with bleeding, issues of access to the endometrial cavity and sampling error limit the clinical significance of a negative result. In the Arimidex, Tamoxifen, Alone, or in Combination trial, 36 % of biopsies had insufficient tissue for diagnosis [29].

No studies have evaluated the use of endometrial sampling as routine screening in reducing endometrial cancer mortality.

Hysteroscopy

Hysteroscopy is used in the office setting to directly visualize the uterine cavity. A group of researchers noted that hysteroscopy is not as useful in detecting endometrial cancer as biopsy or D&C [30]. It has not been evaluated as a screening tool [31]. Theoretical risk of tumor spill into the abdominal cavity via the fallopian tube exists in hysteroscopy in cases of endometrial cancer. A study done in Beijing showed that hysteroscopy did not increase the positive peritoneal cytology rate or affect the prognosis of patients with carcinoma endometrium [32].

Although it no role in screening, hysteroscopy may be done in women who have a negative biopsy but continue to bleed or when ultrasonography shows a polyp.

Screening Women on Hormone Replacement Therapy

There is no evidence to suggest that screening women prior to or during estrogen–progestin therapy, also known as hormone therapy, would decrease endometrial cancer mortality [33, 34].

Thus, women on hormone therapy should have a prompt diagnostic work-up for abnormal bleeding. Although women using certain hormone regimens have an increased risk of endometrial cancer, most women who develop cancer will have vaginal bleeding. There is no evidence that screening these women will decrease mortality from endometrial cancer.

Hereditary Nonpolyposis Colorectal Cancer

The lifetime risk of endometrial cancer for women with hereditary nonpolyposis colorectal cancer (HNPCC) and for women who are at high risk for HNPCC is as high as 60 %. These cases are often diagnosed in the fifth decade, 10–20 years earlier than sporadic cases [35–39].

Based on limited evidence, it appears that 5-year survival among HNPCC women diagnosed with endometrial cancer is similar to that of non-hereditary cases in the general population [40]. Because the risk of endometrial cancer is so high among these women, international guidelines suggest gynecologic surveillance including annual transvaginal ultrasound with endometrial biopsy beginning in women aged 25–35 years [7, 41].

The most recent American Cancer Society Cancer Detection Guidelines (updated January 2005) recommend annual screening with endometrial biopsy beginning at age 35 years [42]. Helder-Woolderink et al. screened 75 women above 30 years of age with Lynch Syndrome (LS) or first-degree relatives at 50 % risk of Lynch syndrome annually and concluded that adding standard endometrial sampling to annual TVS has no additional value in the early detection of (pre) malignant endometrial lesions in women with Lynch syndrome [43].

Problems with Screening

Screening of low-risk population leads to huge economic burden. Abnormal ultrasound will warrant further investigation including endometrial biopsy (sampling). Endometrial sampling may result in discomfort, bleeding, infection, and rarely uterine perforation. A study designed to evaluate performance, patient acceptance, and cost-effectiveness of blind biopsy, hysteroscopy with biopsy,

and ultrasound, in 683 women with vaginal bleeding, reported that minor events, including discomfort and distress, occurred in 16 % of women who had hysteroscopy with biopsy and in 10 % of women who had a blind biopsy [44]. Risks associated with false-positive test results include anxiety and additional diagnostic testing and surgery. Endometrial cancers may be missed on endometrial sampling and ultrasound.

Prevention of Carcinoma Endometrium

Most cases of endometrial cancer cannot be prevented, but there are some interventions that may lower the risk of developing this disease. One way to lower endometrial cancer risk is to change modifiable risk factors whenever possible.

Interventions to Reduce the Risk of Carcinoma Endometrium

Oral Contraceptives

Oral contraceptive pills lower the risk of carcinoma endometrium. The relative risk of carcinoma endometrium in ever users of oral contraceptives in comparison with never users is 0.1 (95 % confidence interval 0.0–0.7). The reduction in risk was proportionate to the duration of use [45]. However, compared with never users of oral contraceptives, the relative risks of cervical cancer increased with increasing duration of use [46].

In a meta-analysis of 11 studies, 10 studies found that 4 years of combined oral contraceptive (COC) use was associated with a risk reduction of approximately 56 %; with 8 years use, 67 % reduction in risk; and with 12 years use, 72 % risk reduction. Even though the single-prospective study did not show a duration response, the risk was reduced by 80 % after 9 years of follow-up [44]. A case–control study among postmenopausal women aged 50–74 years in Sweden, which included 709 subjects with incident, histopathologically verified endometrial cancer, and 3,368 controls with an intact uterus confirmed the protective effect of COC. Women who used any type of oral contraceptive had a 30 % risk reduction (odds ratio [OR] = 0.7; 95 % CI, 0.5–0.9) and women who used progestin-only pills had a 60 % risk reduction (OR = 0.4; 95 % CI, 0.2–1.4). Women who used COCs for at least 3 years had a 50 % risk reduction (OR = 0.5; 95 % CI, 0.3–0.7), and those who used COCs for at least 10 years had an 80 % risk reduction (OR = 0.2; 95 % CI, 0.1–0.4). Overall, risk decreased by 10 % per year of COC use and was observed for atypical hyperplasias as well as all grades of invasive endometrial cancer. The protective effect remained for at least 20 years after cessation of use. Subsequent use of hormone replacement did not modify these protective effects [47].

Prevention of Obesity and Increased Physical Activity

Obesity is one of the risk factors for carcinoma endometrium. In obese women serum estrone level is increased due aromatization of androstenedione in adipose tissue into estrogen [48]. There is also a reduction in sex hormone-binding globulin levels in obesity, thus increasing the bioavailable estrogen [49]. Obesity has been associated with several factors known to increase the risk of endometrial cancer, including upper-body or central adiposity, polycystic ovary syndrome, physical inactivity, and a diet high in saturated fat [50]. Hence, steps to reduce obesity will help in primary prevention of carcinoma endometrium. However, the Iowa Women's Health Study found no association between endometrial cancer incidence and intentional weight loss of at least 20 lbs (RR = 0.93; 95 % CI, 0.60–1.44) [51].

Data analyzed from Nurses' Health Study revealed that greater recent physical activity of moderate duration and intensity, such as walking, may reduce endometrial adenocarcinoma risk. This correlation is largely mediated or confounded by body mass index [52].

A recent meta-analysis showed a linear relationship between increase in leisure-time physical activity and decrease in risk of endometrial cancer, within the range of 0–50 h MET (metabolic equivalent of task)/week or 0–15 h/week [53].

In the Netherlands cohort study on diet and cancer, 62,573 postmenopausal women were followed up for 9 years and 226 endometrial cancer case patients were identified. A 46 % reduction

(RR = 0.54; 95 % CI, 0.34–0.85; $P = 0.002$) in risk of endometrial cancer was reported in those women who were physically active 90 min or more per day compared with less than 30 min each day [54]. One case–control study of 822 endometrial cancer cases and 1,111 population controls showed that regular exercise was associated with a 38 % decrease in risk (OR = 0.62; 95 % CI, 0.51–0.76) without a trend for increasing duration or intensity of physical activity [55]. The Breast Cancer Detection Project Follow-up Study used a prospective cohort to assess past-year physical activity of all types and found that recent physical activity is not strongly related to the risk of endometrial cancer and that prolonged exposure and longer follow-up may be necessary [56]. A meta-analysis of five cohort studies, which together comprise 2,663 cases, revealed that excessive sitting time seems to contribute to endometrial cancer risk independently of moderate-to-vigorous-intensity physical activity.

Physical activity is hypothesized to decrease endometrial cancer risk because it reduces serum levels of estradiol and increases levels of sex hormone-binding globulin (SHBG), the binding protein for estradiol [57]. These effects of physical activity may be mediated through prevention of weight gain. In postmenopausal women, adipose tissue is the primary source of estrogen where the aromatization of androgen precursors occurs within this tissue [58]. Consequently, women who maintain a healthy body weight tend to have lower circulating estrogen levels [59].

Encouraging Pregnancy and Breast Feeding

Increasing parity and lactation reduces the risk of breast, endometrial, and ovarian cancers. This is probably due to inhibition of ovulation. The higher the number of full-term pregnancies, the greater the protection. The risk of endometrial cancer is reduced by 30 % for a woman's first birth and by 25 % for each successive birth, and later maternal age at last birth has also been shown to reduce the risk [60]. A case–control study comparing 85 women with carcinoma endometrium and 668 healthy women showed a 58–72 % reduction in risk of endometrial cancer associated with increasing duration of lactation [61]. Hence, encouraging pregnancy and lactation will reduce the risk of endometrial cancer.

Progestins for the Prevention of Prolonged Anovulatory Cycles

Progesterone has been described as the ultimate endometrial cancer suppressor. Estrogen drives endometrial epithelial proliferation. Progesterone inhibits growth and causes cell differentiation. The importance of progesterone as a key inhibitor of carcinogenesis is reflected by the observation that women who ovulate and produce progesterone almost never get endometrial cancer. Cyclical progestins reduce the risk of hyperplasia in women with anovulation [62].

Treatment of Endometrial Hyperplasia

Endometrial hyperplasia can progress to endometrial cancer. A nested case–control study of progression of endometrial hyperplasia (EH) to carcinoma was done with 138 cases, who were diagnosed with EH and then with carcinoma at least 1 year later, and 241 controls. With disordered proliferative endometrium (DPEM) as the referent, atypical hyperplasia significantly increased carcinoma risk with a relative risk of 14 (RR = 14, 95 % CI, 5–38). Progression risks for simple hyperplasia (RR = 2.0, 95 % CI, 0.9–4.5) and complex hyperplasia (RR = 2.8, 95 % CI, 1.0–7.9) were substantially lower and only slightly higher than the progression risk for DPEM [63].

Progestin therapy is very effective in reversing endometrial hyperplasia but is less effective with atypia. For women with atypical complex hyperplasia who no longer desire fertility, hysterectomy is recommended [64].

Avoid Unopposed Exogenous Estrogen

Cochrane database systematic review showed that unopposed estrogen is associated with increased risk of endometrial hyperplasia at all doses and durations of therapy between 1 and 3 years. For women with a uterus, the risk of endometrial hyperplasia with hormone therapy comprising

low-dose estrogen continuously combined with a minimum of 1 mg norethisterone acetate (NETA) or 1.5 mg medroxyprogesterone acetate (MPA) is not significantly different from placebo at 2 years (1 mg NETA: OR 0.04; 95 % confidence interval (CI) 0–2.8; 1.5 mg MPA, no hyperplasia events). The review concluded that hormone therapy for postmenopausal women with an intact uterus should comprise both estrogen and progestogen to reduce the risk of endometrial hyperplasia [65]. Another meta-analysis showed that in women using HRT, those who used progestins continuously (>25 days/months) are at reduced risk relative to nonusers (meta-analysis relative risk, RR, based on observational studies = 0.78, 95 confidence intervals, CI, 0.72–0.86). The reduction in risk is greatest among heavy women. However, women who have ever used progestins sequentially for <10 days each month are at increased risk [meta-analysis results showing on overall RR of 1.76 (1.51–2.05)], while progestins given for 10–24 days/month appear unrelated to risk (RR = 1.07, 0.92–1.24) [66].

Interventions of Unproven or Disproven Effects on Risk

Fruits, Vegetables, and Vitamins

There are case-control studies evaluating the association between dietary factors, particularly fruit and vegetable intake, and endometrial cancer. A systematic review was done which failed to establish an association between fruit intake and endometrial cancer [67, 68].

There is case-control evidence suggesting that regular consumption of soy products reduces the risk of endometrial cancer [69, 70].

A consortium of seven prospective cohort studies examined the association between serum vitamin D levels and the development of endometrial cancer. After controlling for BMI, there was no evidence of an association between circulating vitamin D and risk of endometrial cancer [71]. Multivitamin use has little or no influence on the risk of common cancers, including endometrial cancer, or on total mortality in postmenopausal women [72].

American Cancer Society Recommendations for Prevention of Cancers [73]

Maintain a Healthy Weight Throughout Life

- Avoid excess weight gain at all ages. If currently overweight or obese, losing even a small amount of weight has health benefits and is a good place to start.

Adopt a Physically Active Lifestyle

- Adults: Engage in at least 150 min of moderate intensity activity or 75 min of vigorous-intensity activity each week, preferably spread throughout the week.
- Children and adolescents: Engage in at least 1 h of moderate- or vigorous-intensity activity each day, with vigorous-intensity activity at least 3 days each week.

Consume a Healthy Diet, with an Emphasis on Plant Sources

- Choose foods and beverages in amounts that help maintain a healthy weight.
- Limit consumption of processed meat and red meat.
- Eat at least 2.5 cups of vegetables and fruits each day.
- Choose whole grains in preference to refined grain products.
- If you drink alcoholic beverages, limit consumption.
- Drink no more than one drink per day for women or two per day for men.

Public, Private, and Community Organizations Should Work Collaboratively at National, State, and Local Levels to Implement Policy and Environmental Changes That:

- Increase access to affordable, healthy foods in communities, worksites, and schools, and decrease access to and marketing of foods and beverages of low nutritional value, particularly to youth.

- Provide safe, enjoyable, and accessible environments for physical activity in schools and worksites and for transportation and recreation in communities.

Conclusion

There are no acceptable, reliable, and valid screening tests or examination to diagnose endometrial cancer in asymptomatic women. Universal screening of women using TVS or endometrial sampling is not recommended. Combined oral contraceptive pills, progestins, avoiding unopposed estrogen therapy and lifestyle changes can be used to prevent carcinoma endometrium.

Key Points

1. All women should be told about the risks and symptoms of endometrial cancer at the time of menopause. Menopausal women should be asked to report in case of any unexpected vaginal bleeding, discharge, or spotting.
2. At this time, there are no acceptable, reliable and valid screening tests or exams to identify endometrial cancer early in women who are at average risk for endometrial cancer and have no symptoms.
3. There is no evidence that screening by ultrasonography or endometrial sampling reduces mortality from endometrial cancer as most cases of endometrial cancer (85 %) are diagnosed in early stage because of symptoms, and survival rates are high.
4. Women who have (or may have) hereditary nonpolyposis colon cancer (HNPCC, Lynch syndrome) have a very high risk of endometrial cancer and American Cancer Society recommends that women who have (or may have) HNPCC be offered yearly testing for endometrial cancer with endometrial biopsy beginning at age 35.
5. Routine ultrasound surveillance in asymptomatic women using tamoxifen is not useful because of its low specificity and low positive predictive value. Evaluation of the endometrium in women taking tamoxifen should be limited to women symptomatic with vaginal bleeding.
6. There is no evidence to suggest that screening women prior to or during estrogen-progestin therapy would decrease endometrial cancer mortality.
7. Interventions to reduce the risk of carcinoma endometrium are oral contraceptives, prevention of obesity and increased physical activity, progestins for prevention of prolonged anovulatory cycles, treatment of endometrial hyperplasia and avoiding unopposed exogenous estrogen.

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