Review

A Review of Diagnosis and Therapeutics of Endometrial Carcinomas

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Abstract:
Endometrial cancer (EC) is a cancer of the inner epithelial lining of the uterus which has been increasing worldwide. Being the most common gynecological malignancy, the incidence of endometrial cancer estimated 417,336 worldwide in 2020 as sixth most commonly female cancer. EC is a hormone-sensitive condition that is thought to develop as a result of excessive estrogenic stimulation of the uterine endometrial lining. This estrogenic stimulation causes mitogenic stimulation and, ultimately, malignant transformation of the endometrial glandular epithelium, which is why lower-grade endometrioid ECs are more common. Postmenopausal bleeding (PMB) is a common symptom of EC and accounts for approximately two-thirds of all gynecological visits among perimenopausal and postmenopausal women. Histological examination of endometrial tissue taken with miniature endometrial biopsy instruments is the most common method used to diagnose endometrial cancer. The FIGO staging system has taken into account the extent of myometrial invasion as well as extrauterine disease (uterine serosa, adnexal involvement, peritoneal cytology, intra-abdominal, and lymph nodes). Newly diagnosed EC is treated differently in different regions and treatment centers. Surgery is the main treatment for disease in its early stages. Adjuvant radiotherapy and/or chemotherapy can be used to lower the risk of recurrence, depending on the stage of the disease and other risk factors.

Keywords: Diagnosis, Therapeutics, Endometrial Carcinomas

Submitted: 2 Deceember 2022, Revised: 19 Deceember 2022 , Accepted: 25 Deceember 2022

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Introduction

Endometrial cancer (EC) is a cancer of the inner epithelial lining of the uterus which has been increasing worldwide (1). Being the most common gynecological malignancy, the incidence of endometrial cancer estimated 417,336 worldwide in 2020 as sixth most commonly female cancer (2). Racial, socioeconomic, and geographic disparities also have an impact on the incidence and mortality of EC. Compared to low- and middle-income nations, high-income nations have a higher prevalence of EC (2, 3). Access to high-quality healthcare and the number of oncologists in a given area may be factors that contribute to regional disparities in incidence and mortality (4). When compared to women of lower socioeconomic status, women with higher socioeconomic status were less likely to present with advanced, type II EC and typically had better outcomes due to improved access to healthcare (5).

Endogenous or exogenous estrogen exposure, tamoxifen use, early or late menopause, lower parity, metabolic syndrome, family history, and genetic predisposition are all associated with an increased risk of EC. Conversely, a normal BMI, higher parity, and utilization of oral contraceptives are associated with a lower risk of EC (6). Well-known risk factors for EC include age 55 years and prolonged unopposed estrogen exposure (such as with estrogen replacement therapy, chronic anovulation, and tamoxifen treatment) (7, 8). The increasing rate of obesity is also a well-known risk factor for endometrial carcinomas ranging from 1.5 to 7.1 fold increased risk in different obesity classes (9, 10). Diabetes mellitus is independently associated with an increased risk of EC, according to meta-analyses (11, 12). Carcinogenesis may be exacerbated in diabetics by insulin resistance, hyperinsulinemia, hyperglycemia, inflammation, and disruptions in the IGF-1 pathway (13).

In this study, we have reviewed the diagnostic and therapeutic methods of endometrial carcinomas.

Pathophysiology of endometrial carcinomas

EC is a hormone-sensitive condition that is thought to develop as a result of excessive estrogenic stimulation of the uterine endometrial lining. This estrogenic stimulation causes mitogenic stimulation and, ultimately, malignant transformation of the endometrial glandular epithelium, which is why lower-grade endometrioid ECs are more common. Obesity, hormone therapy like tamoxifen, ovarian cortical hyperplasia (hyperthecosis), polycystic ovarian syndrome, and hormone-producing tumors are all risk factors for hyperestrogenism. Carcinosarcoma, serous, clear cell, undifferentiated carcinoma, and other histological subtypes of EC are less frequently associated with hyperestrogenemia (14).

Diagnosis and symptoms of EC

Postmenopausal bleeding (PMB) is a common symptom of EC and accounts for approximately two-thirds of all gynecological visits among perimenopausal and postmenopausal women. A meta-analysis found that PMB occurred in less than 90% of EC patients; However, only 9% of cases resulted in a diagnosis of EC (15). Further diagnostic endometrial evaluation should be performed on all postmenopausal women who have abnormal uterine bleeding or vaginal bleeding that is associated with risk factors for endometrial cancer or hyperplasia (such as polycystic ovaries, obesity, age over 40, irregular periods, hormone replacement therapy, and tamoxifen use). Histological examination of endometrial tissue taken with miniature endometrial biopsy instruments—typically based on the disposable plastic Pipelle de Cornier prototype—is the most common method used to diagnose endometrial cancer. A

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meta-analysis on the value of Pipelle biopsy for the conclusion of abnormal hyperplasia or endometrial malignant growth determined sensitivity of 81 to 100% and specificity of around 98% (16, 17). Endometrial biopsy estimates the EC more accurately in symptomatic and post-menopausal woman in compare with atypical endometrial hyperplasia (17).

All women who present with PMB should undergo diagnostic testing to rule out EC. Pelvic ultrasonography, endometrial biopsy, or dilatation and curettage, either with or without hysteroscopy, are common diagnostic techniques for PMB (18, 19). Transvaginal ultrasonography should be used to measure endometrial thickness at the thickest point in the sagittal plane; In postmenopausal women with abnormal uterine bleeding, 5 mm is commonly considered to be the normal upper limit for endometrial thickness. This cut-off value has a sensitivity of 96% and a specificity of 61% for EC (20, 21). Patients who already have an endometrial sample that indicates an invasive cancer can skip pelvic ultrasonography. A D&C should be performed when endometrial biopsy histopathological findings are insufficient to confirm the diagnosis; of note, biopsy under hysteroscopy has a higher precision than 'blind' D&C and stays the best quality level for the determination of EC whenever the situation allows (22).

Staging of EC

Staging of endometrial cancer is surgically based (23). The FIGO staging system has taken into account the extent of myometrial invasion as well as extrauterine disease (uterine serosa, adnexal involvement, peritoneal cytology, intra-abdominal, and lymph nodes). Stage I reflect EC that are restricted to the uterine corpus. They are further broken down into stages IA (no myometrial invasion greater than or equal to 50%) and IB (equal to or greater than 50% of myometrial invasion). Stage II tumors are those that invade the cervical stroma but do not spread beyond the uterus. Stage III addresses growth that spread past the uterus yet not external the genuine pelvis. Stages IIIA (invasion of the uterine serosa and/or adnexa), IIIB (parametrium and/or vaginal involvement), and IIIC1 (positive pelvic nodes) and IIIC2 (positive paraaortic lymph nodes) are further subdivided into stages. Tumors in stage IVB with distant metastases and tumors in stage IVA with extension to the bowel or bladder are examples (24). Although the preoperative evaluation of degree can't supplant FIGO organizing, and it doesn't prompt better endurance, it empowers clinicians to tailor treatment. Clinical examination, Pap smear, TVU, and CT of the lungs, liver, and retroperitoneal lymph nodes are useful preoperative assessments. CT is more sensitive than MRI at detecting retroperitoneal lymph nodes (23, 25). In 90% of cases, intraoperative visual estimation of the depth of myometrial invasion is accurate (26, 27). When a pathologist is unavailable during surgery or when time is a constraint, an experienced surgeon can select candidates for lymphadenectomy using a preoperatively known tumor grade and visual estimation of the depth of myometrial invasion.

Due to its excellent soft tissue contrast resolution, magnetic resonance imaging (MRI) is regarded as the most accurate imaging method for preoperative assessment of endometrial cancer. When compared to normal endometrium, EC typically appears hypo- to isointense on T1-weighted images and hyperintense or heterogeneous on T2-weighted images, and it increases after intravenous contrast injection. High signal intensity on DW Images and low signal intensity on the apparent diffusion coefficient maps indicate that EC has restricted diffusion (28).

Using Positron emission tomography (PET) with fluorine is only moderately sensitive in

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diagnosing extrauterine diseases and therefore it is not recommended (29).

Treatment options of EC

Newly diagnosed EC is treated differently in different regions and treatment centers. Surgery is the main treatment for disease in its early stages. Adjuvant radiotherapy and/or chemotherapy can be used to lower the risk of recurrence, depending on the stage of the disease and other risk factors (30). Chemotherapy and endocrine therapy are the only treatment options for metastatic disease (31). Although immunotherapy is not universally available in all jurisdictions, immunotherapy alone or in combination has recently become the standard of care (32).

The primary treatment for women with localized EC is surgery. Women who might benefit from adjuvant treatment are identified and prognosticated using surgical staging. Standard of care is total hysterectomy with bilateral salpingo-oophorectomy (BSO), which can be done openly or minimally invasively. In early-stage EC, minimally invasive techniques have comparable oncological outcomes, a shorter hospital stay, and fewer complications than open laparotomy (33-36). A non-surgical treatment option may be considered for women who wish to preserve their fertility but have low-grade endometrioid EC and no evidence of MMI on imaging (including MRI). With careful monitoring, high-dose oral progestins and/or levonorgestrel-release intrauterine devices (LNG-IUDs) can be used to prevent disease progression (37, 38). Younger women with low-grade, early-stage EC may want to consider ovarian preservation to avoid the menopausal symptoms that come with more extensive surgery. According to one study that used SEER population data, women under the age of 50 with low-grade, early-stage disease may have a better chance of overall survival due to a lower risk of cardiovascular death (39).

Conclusion

Endometrial cancer (EC) is a cancer of the inner epithelial lining of the uterus which has been increasing worldwide. Histological examination of endometrial tissue taken with miniature endometrial biopsy instruments is the most common method used to diagnose endometrial cancer. Newly diagnosed EC is treated differently in different regions and treatment centers. Surgery is the main treatment for disease in its early stages. Adjuvant radiotherapy and/or chemotherapy can be used to lower the risk of recurrence, depending on the stage of the disease and other risk factors.

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