



ENDOMETRIAL CARCINOMA: NARRATIVE REVIEW

Maria Antonia Velásquez López

MD. Universidad Tecnológica de Pereira.

Nathalia Trujillo Ortiz

Fundación Universitaria Autónoma de las Américas

ABSTRACT

Endometrial cancer is the most common gynecological malignancy in developed countries and its incidence has been increasing over recent years. Symptoms include postmenopausal bleeding, abnormal vaginal bleeding, pelvic pain, and dyspareunia. Risk factors include obesity, unopposed estrogen exposure, family history of endometrial or ovarian cancer, and Lynch syndrome. Diagnosis is confirmed through endometrial biopsy, hysteroscopy, or dilation and curettage. Treatment options depend on the stage and grade of the cancer and may include surgery, radiation therapy, chemotherapy, or a combination. This review article summarizes the current state of knowledge on endometrial cancer, including its epidemiology, risk factors, clinical presentation, diagnostic methods, and treatment options. Recent advancements in the field, including emerging biomarkers and targeted therapies, are highlighted. The authors conducted a systematic search of the literature on endometrial cancer, and the results were synthesized and presented using a narrative synthesis approach. The epidemiology of endometrial cancer underscores the importance of preventive measures, including regular gynecological checkups and lifestyle modifications to reduce obesity and improve reproductive health.

KEYWORDS : Endometrial cancer, Risk factors, Histopathology, Hormonal therapy, Prevention

INTRODUCTION

Endometrial cancer is a malignancy that arises from the inner lining of the uterus known as the endometrium. It is the most common gynecologic malignancy in developed countries and its incidence has been increasing in recent years. Endometrial cancer can present with a range of symptoms including postmenopausal bleeding, abnormal vaginal bleeding, pelvic pain, and dyspareunia. The risk factors for developing endometrial cancer include obesity, unopposed estrogen exposure, family history of endometrial or ovarian cancer, and Lynch syndrome. Diagnosis is confirmed through endometrial biopsy, hysteroscopy, or dilation and curettage. Treatment options depend on the stage and grade of the cancer and may include surgery, radiation therapy, chemotherapy, or a combination of these modalities (1).

This review-type article will provide a comprehensive overview of the current state of knowledge on endometrial cancer, including its epidemiology, risk factors, clinical presentation, diagnostic methods, and treatment options. The article will also highlight recent advancements in the field, including emerging biomarkers and targeted therapies. With the increasing incidence of endometrial cancer and the complexity of its management, this article aims to provide a useful resource for healthcare professionals involved in the care of women with endometrial cancer (2).

METHODS

The systematic search of the literature on endometrial cancer was conducted across multiple databases including PubMed, Scopus, and Web of Science, using a predefined search strategy. The search terms included "endometrial cancer", "uterine cancer", "endometrial neoplasms", "endometrial carcinoma", and other relevant keywords, combined using Boolean operators. The search was limited to studies published in English language and between January 2010 and December 2022. Two independent reviewers screened the titles and abstracts of the identified articles for relevance and eligibility. Full-text articles were reviewed for inclusion criteria, which included studies on endometrial cancer epidemiology, risk factors, diagnosis, treatment, and prognosis. Data were extracted from the included studies using a predefined data extraction form. Any discrepancies in study selection, data extraction, or quality assessment were resolved through discussion and consensus (Figure 1). The results of the search

were synthesized and presented using a narrative synthesis approach.

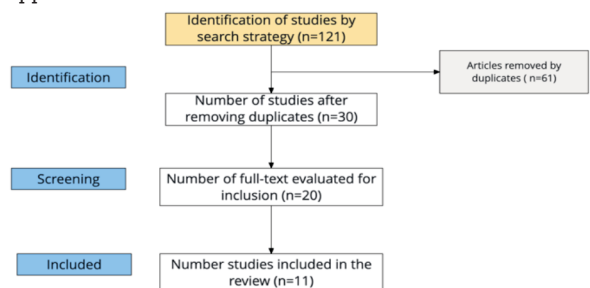


Figure 1. PRISMA

Epidemiology

Endometrial cancer is the most common gynecological malignancy in developed countries, accounting for approximately 4% of all cancers in women. The incidence of endometrial cancer has been increasing over the past few decades, likely due to changes in reproductive patterns and rising rates of obesity. Endometrial cancer typically affects postmenopausal women, with a peak incidence in the sixth and seventh decades of life. There are also notable racial and ethnic disparities in the incidence of endometrial cancer, with higher rates observed among non-Hispanic white women compared to women of other races/ethnicities. Overall, the epidemiology of endometrial cancer underscores the importance of preventive measures, including regular gynecological checkups and lifestyle modifications to reduce obesity and improve reproductive health (3-4).

Histopathology

Endometrial cancer is a heterogeneous disease with several distinct histological subtypes. The most common subtype is endometrioid adenocarcinoma, accounting for approximately 80% of cases. Other subtypes include serous, clear cell, mucinous, and mixed types. Serous carcinoma is associated with a worse prognosis compared to other subtypes and is typically high-grade and characterized by papillary architecture and psammoma bodies. Clear cell carcinoma is also high-grade and characterized by clear cytoplasm and hobnail cells. Mucinous carcinoma is rare and often presents at an advanced stage. Mixed carcinoma, which

includes both endometrioid and non-endometrioid components, is associated with a worse prognosis compared to pure endometrioid carcinoma. Accurate histopathological diagnosis is essential for appropriate treatment planning and prognosis prediction in endometrial cancer (5-6).

Risk factors

Several risk factors are associated with the development of endometrial cancer. The most well-established risk factor is exposure to unopposed estrogen, including endogenous estrogen in conditions such as polycystic ovary syndrome and nulliparity, as well as exogenous estrogen in hormone replacement therapy. Other established risk factors include obesity, diabetes, hypertension, tamoxifen use, and Lynch syndrome. Age is also a significant risk factor, with the incidence of endometrial cancer increasing with age. Women with a family history of endometrial or colorectal cancer are at increased risk, as are those with a history of breast or ovarian cancer.³ An understanding of these risk factors is crucial for identifying women at high risk of endometrial cancer and developing appropriate prevention and screening strategies (7-8).

Diagnosis

The diagnosis of endometrial cancer is typically based on a combination of clinical presentation, imaging, and histopathological examination. Transvaginal ultrasound is the initial imaging modality of choice to evaluate the endometrial thickness and identify any focal abnormalities. Endometrial sampling with biopsy or dilatation and curettage is required for definitive diagnosis and histological characterization of the tumor. In cases where there is suspicion of advanced disease or metastasis, imaging with computed tomography, magnetic resonance imaging, or positron emission tomography may be necessary. Accurate diagnosis is essential for appropriate treatment planning and prognosis prediction in endometrial cancer (1,9).

Treatment

The treatment of endometrial cancer is based on several factors including stage, grade, histologic type, and patient's comorbidities. Surgery remains the primary treatment modality for early-stage endometrial cancer. In the majority of cases, total hysterectomy and bilateral salpingo-oophorectomy are performed, which involves the removal of the uterus, fallopian tubes, and ovaries. The surgical approach can be either abdominal, vaginal or laparoscopic, depending on the patient and surgeon's preference. For women with more advanced stages or those with high-risk features such as deep myometrial invasion or lymph node involvement, the addition of adjuvant treatment such as chemotherapy, radiation therapy or both may be considered. Hormonal therapy with progestins may be used for patients with early-stage or recurrent disease, especially for those with type 1 endometrial cancer (4,10).

Chemotherapy is another treatment option for patients with endometrial cancer, especially for those with advanced or recurrent disease. Commonly used chemotherapy regimens include platinum-based agents such as carboplatin and cisplatin, and taxanes such as paclitaxel and docetaxel. These agents have been shown to improve progression-free survival and overall survival in patients with advanced or recurrent disease. Adjuvant chemotherapy may also be considered in high-risk patients after surgery. Radiation therapy, either external beam or brachytherapy, may be recommended for women with high-risk features, such as positive lymph nodes or close or positive surgical margins. The selection of treatment modalities should be individualized based on the patient's tumor characteristics, overall health status, and patient preference (9,10).

Staging and surgical treatment

The treatment of endometrial cancer is stratified according to the patient's risk of recurrence. In low-risk patients, who have early-stage endometrial cancer with favorable histologic features, surgery alone may be sufficient. However, in patients with high-risk features such as deep myometrial invasion, lymphovascular space invasion, or high-grade histology, adjuvant therapy may be necessary. Adjuvant treatment options include external beam radiation therapy, vaginal brachytherapy, chemotherapy, or a combination of these modalities. Hormonal therapy with progestins may also be used as adjuvant treatment in patients with early-stage disease who are not candidates for surgery or who wish to preserve fertility (7,9).

For high-risk patients, treatment with a combination of chemotherapy and radiation therapy has been shown to improve overall survival compared to radiation therapy alone. In the Gynecologic Oncology Group (GOG) 249 trial, patients with high-risk endometrial cancer were randomized to receive pelvic radiation therapy with or without concurrent chemotherapy with cisplatin and doxorubicin. The addition of chemotherapy resulted in improved progression-free survival and overall survival. Additionally, in patients with recurrent or metastatic disease, chemotherapy is the mainstay of treatment. The use of targeted therapy with drugs such as pembrolizumab, which blocks the PD-1 receptor, has shown promise in patients with advanced or recurrent endometrial cancer (10,11).

CONCLUSION

Endometrial cancer is a major gynecological malignancy that primarily affects postmenopausal women, with a peak incidence in the sixth and seventh decades of life. The incidence of endometrial cancer has been increasing over the past few decades, mainly due to changes in reproductive patterns and rising rates of obesity. Accurate diagnosis is essential for appropriate treatment planning and prognosis prediction in endometrial cancer. The treatment of endometrial cancer is stratified according to the patient's risk of recurrence, and the selection of treatment modalities should be individualized based on the patient's tumor characteristics, overall health status, and patient preference. Preventive measures, including regular gynecological checkups and lifestyle modifications to reduce obesity and improve reproductive health, are crucial in reducing the incidence of endometrial cancer.

REFERENCES

1. Amant F, Mirza MR, Koskas M, et al. Cancer of the corpus uteri. *Int J Gynaecol Obstet.* 2018;143 Suppl 2:37-50. doi:10.1002/ijgo.12629
2. Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. *Ann Oncol.* 2016;27(1):16-41. doi:10.1093/annonc/mdv484
3. Felix AS, Brinton LA. Epidemiology of Endometrial Cancer: Scope of the Problem. *Horm Cancer.* 2010;1(2):63-76. doi:10.1007/s12672-010-0002-8.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424.
5. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer-viewpoint of the IARC Working Group. *N Engl J Med.* 2016;375(8):794-798.
6. Bhaskaran K, Douglas I, Forbes H, et al. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet.* 2014;384(9945):755-765.
7. Howlander N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2017. National Cancer Institute. Accessed February 24, 2023. https://seer.cancer.gov/csr/1975_2017/
8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin.* 2018;68(1):7-30.
9. Colombo N, Preti E, Landoni F, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24 Suppl 6:vi33-8.
10. Abu-Rustum NR, Yashar CM, Bean S, et al. NCCN Guidelines Insights: Uterine Neoplasms, Version 1.2020. *J Natl Compr Canc Netw.* 2019;17(6):660666.
11. Randall ME, Filiaci VL, Muss H, et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. *J Clin Oncol.* 2006;24(1):36-44.