Muğla Sıtkı Koçman Üniversitesi Tıp Dergisi 2025;12(3):221-228
Medical Journal of Mugla Sitki Kocman University 2025;12(3):221-228
Doi: 10.47572/muskutd.1706330

Research Article

The Relationship Between Estrogen, Progesterone and Serum CA-125 Levels and Endometrioid Endometrial Cancer Risk in Postmenopausal Women

Postmenopozal Kadınlarda Östrojen, Progesteron ve CA-125 Düzeyleri ile Endometrioid Endometrial Kanser Riski Arasındaki İlişki

Sema MISIR[1*], Begüm KURT[2], Serap OZER YAMAN[3], Ceylan OZSOY HEPOKUR[1]

[1]Department of Biochemistry, Faculty of Pharmacy, Sivas Cumhuriyet University, Sivas, Turkey.

smisir@cumhuriyet.edu.tr

[2]Department of Gynecology and Obstetrics, Medical Faculty of Sivas Cumhuriyet University, Sivas, Turkey.

[3]Department of Medical Biochemistry, Trabzon Kanuni Health Practice and Research Hospital, Trabzon Faculty of Medicine, University of Health Sciences, Trabzon, Turkey.

*Sorumlu Yazar / Corresponding Author

Received: 26.05.2025
Accepted: 07.11.2025

Abstract
This study aimed to investigate the relationship between serum levels of estrogen (estradiol), progesterone, and serum cancer antigen 125 (CA-125) and the risk of developing endometrioid endometrial cancer (EEC) in postmenopausal women, as well as to evaluate their prognostic significance. A total of 160 postmenopausal women over the age of 50 were included in this retrospective study. Among these, patients with histopathologically confirmed endometrioid endometrial cancer were selected. Serum estradiol, progesterone, and CA-125 levels, obtained within one week before surgery, were analyzed according to disease stage. Correlation analyses between hormone levels and cancer stages were conducted using Pearson's correlation test. The findings demonstrated a positive association between elevated serum CA-125 levels and advanced stages of EEC. Estradiol and progesterone levels were decreased in postmenopausal women, and lower serum levels of progesterone and estradiol were inversely associated with the risk of EEC. A positive correlation was observed between progesterone and estradiol levels, while negative correlations were identified between CA-125 and progesterone and estradiol levels. An increase in serum CA-125 levels was positively correlated with advanced stages of EEC, whereas decreased levels of progesterone and estradiol were inversely related to cancer risk. These findings suggest that further large-scale prospective studies are warranted to validate the prognostic value of these biomarkers.
Keywords: CA-125 Antigen, Endometrial Carcinoma, Estradiol, Progesterone, Prognosis.

Özet
Bu çalışmada, postmenopozal kadınlarda serum östrojen (estradiol), progesteron ve serum kanser antijen 125 (CA-125) düzeyleri ile endometrioid endometrial kanser (EEC) riski arasındaki ilişki ve prognostik değerlerinin belirlenmesi amaçlandı. Bu retrospektif çalışmaya, 50 yaş üstü postmenopozal hasta olmak üzere 160 kişi dahil edildi. Histopatolojik olarak EEC'si doğrulanan hastalardan ameliyattan bir hafta önce belirlenen östrojen, progesteron ve CA-125 seviyeleri evrelere göre değerlendirildi ve korelasyon analizi evrelere göre Pearson testi kullanılarak yapıldı. Bulgularımız serum CA-125 düzeylerindeki yükselmenin ileri evre EEC'lerle pozitif ilişkili olduğu bulundu. Östrojen, progesteron seviyelerinin postmenopozal kadınlarda azaldığı ve postmenopozal progesteron ve östrojen seviyelerinin EEC riskiyle ters orantılı olduğu gözlendi. Progesteron ve östrojen arasında pozitif korelasyon gözlenirken, CA-125 seviyeleri ve progesteron, östrojen arasında negatif korelasyon gözlendi. Serum CA-125 düzeylerindeki yükselmenin ileri evre EEC'lerle pozitif, progesteron ve östrojen seviyelerinin ters orantılı olduğu belirlendi. Bu bulguları doğrulamak için daha geniş prospektif çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: CA-125 Antijeni, Endometrial Karsinom, Östrojen, Progesteron, Prognoz.

Introduction

Endometrial cancer (EC) is recognized as the most prevalent malignancy of the female reproductive system (1) and represents a well-documented cause of morbidity and mortality among postmenopausal women. However, its incidence is increasingly observed in premenopausal women. EC is categorized into two types: Type I and Type II. Type I tumors are classified as stage 1 endometrioid adenocarcinomas, according to the International Federation of Gynecology and Obstetrics (FIGO), and are linked to unopposed estrogen stimulation. In contrast, Type II tumors encompass stage 3 endometrioid, serous, and clear cell carcinomas, which are generally considered estrogen-independent. The incidence of Type I tumors is approximately 60-80%, while Type II tumors account for about 20% of cases (2). The development of EC is influenced by several key risk factors, including advanced age, nulliparity, late menopause, early menarche, a history of infertility, obesity, and exposure to both endogenous and exogenous estrogen due to specific medications (3). Endometrioid type endometrial cancer (EEC) is the most common histological subtype with a good prognosis. Older age, advanced stage, high grade, and lenfovasculer involvement have been associated with poor prognosis and worse survival (4).

Despite advancements in cancer diagnostics in recent years, many diagnostic and prognostic biomarkers are still not utilized in clinical practice to enhance the treatment of EC patients (5). Consequently, it is crucial to identify biomarkers to predict the risk of developing EC, enable early diagnosis, or support prognostic evaluations using non-invasive methods (6). Notably, blood-based biomarkers hold particular significance because they eliminate the need for biopsies, provide minimally invasive tools for predicting prognosis and planning treatment, and are not associated with significant technical challenges in clinical applications (5). The role of serum cancer antigen 125 (CA-125) in diagnosing EC has yielded inconsistent findings. Therefore, its reliability as a marker for EC remains uncertain and subject to debate (3). Identifying additional biomarkers to predict EC prognosis and offer new therapeutic targets is necessary. Determining risk factors for disease recurrence and poor prognosis is critically important. Estrogen plays a pivotal role in the development of EC, and its metabolites have been shown to fluctuate during the disease (6). Unopposed estrogen exposure is considered EC's most significant risk factor (7). Hormonal imbalances induced by estrogen can influence gene expression in cell proliferation and apoptosis, potentially leading to uncontrolled cellular growth and carcinogenesis. Furthermore, estrogen metabolites contribute to oxidative stress, possessing both carcinogenic and anti-carcinogenic properties (6).

The increased use of estrogen-only preparations to alleviate postmenopausal and perimenopausal symptoms in women has coincided with a notable rise in EC incidence. Women undergoing unopposed estrogen therapy face a 3-6 times higher risk of developing endometrial carcinoma (8). Evidence suggests that biomarkers derived from estrogen metabolites through various pathways could be valuable in identifying women at high risk for EC (6).

Progesterone plays a critical role in supporting the secretory proliferation of endometrial tissue. It reduces estradiol receptor concentrations within the endometrium and enhances the metabolism of estradiol into estrone , a less active estrogen, thereby decreasing mitotic activity (2). The imbalance between estrogen and progesterone is known to contribute to the progression of Type 1 EC. Following menopause, ovarian production of estrogen and progesterone ceases, making peripheral conversion the primary source of circulating estrogen (9).

Although hormonal factors are implicated in the development of EC, few epidemiological studies have explored the roles of endogenous estrogens, particularly their metabolites or progesterone. The existing literature contains limited research on the significance of endogenous steroid levels beyond estrogen metabolites (10,11), and to a lesser extent, androstenedione (A4) and testosterone (T) (12-14). These studies have primarily focused on disease risk rather than the biomarker characteristics of these hormones (5). Assessing hormonal levels in premenopausal and perimenopausal women poses challenges due to cyclical variations. In this study, we focused on postmenopausal women, who constitute the majority of EC cases. We propose that the findings will reflect circulating estrogen and progesterone levels and provide additional prognostic insights when combined with preoperative histological tumor evaluations.

This study aims to investigate the relationship between progesterone, estrogen (estradiol) and CA-125 levels with clinicopathological risk

factors in EEC, as well as to assess their prognostic significance.

Material and Method

This retrospective study included patients diagnosed with endometrial cancer at the Department of Obstetrics and Gynecology, Sivas Cumhuriyet University Hospital, between 01.01.2011 and 01.01.2021. Patients were excluded from the analysis if they had concurrent malignancies, incomplete medical records or follow-up data, or had received hormone replacement therapy. The inclusion criteria comprised postmenopausal women with histopathologically confirmed endometrial cancer and available preoperative measurements taken no more than one week prior to surgery of serum CA-125, progesterone, and estradiol levels. Based on these criteria, 160 patients were deemed eligible and included in the study.

CA-125, progesterone, and estradiol levels in serum samples were measured on the autoanalyzer using original reagents. These parameters were examined after daily quality control procedures in the Clinical Biochemistry Laboratory of the Sivas Cumhuriyet University Faculty of Medicine, approved by the Ministry of Health.

EC histologic types and grades were assessed using the International Federation of Obstetricians and Gynecologists' disease staging system (I, II, III, or IV) based on pathology results. Histologic tumor features were summarized from the original pathology reports. Only patients with EEC histology were included in the study, and patients with non-EEC histology were excluded. The diagnosis of EEC was made by histopathologic examination of hematoxylin-eosin stained preparations.

Statistical Analysis

The data were statistically evaluated in the SPSS version 23 software (IBM SPSS Statistics 23, USA) program. The Kolmogorov-Simirnov test was used to determine whether the variables were normally distributed. All variables in each group were determined to be normally distributed. The data were presented using mean and standard deviation (mean ± SD) for normally distributed variables. More than two normally distributed independent variables were compared using the One-Way ANOVA test. Post-hoc analysis for pairwise comparisons was performed using the Tukey test. The "Pearson" test was used for comprehending the correlation between variables that fit the normal distribution. $p<0.05$ was considered statistically significant. We performed a post hoc power analysis to assess the adequacy of the sample size and the reliability of our results. The statistical power was computed utilizing G*Power software (version 3.1) based on the observed effect sizes, sample sizes, and significance level ($\alpha = 0.05$). The computed effect sizes (f) were substantial for CA-125 ($f = 0.57$), estradiol ($f = 0.26$), and progesterone ($f = 0.43$) according to Cohen's criteria. The post hoc power attained for identifying group differences was 99% for CA-125, 85% for estradiol, and 97% for progesterone.

Results

Between 2011 and 2021, a total of 160 cases diagnosed with ECC were included in this study. The patients were classified into three histological grades: minimal (grade 1), mild (grade 2), and moderate (grade 3). The mean ages of the patients in the minimal, mild, and moderate groups were 59.8±7.87, 63.2±7.51, and 60.6±7.33 years, respectively, with no statistically significant differences observed between the groups ($p > 0.05$) (Table 1). Serum levels of CA-125, estradiol, and progesterone were analyzed and presented according to histological grade in Table 1. Statistical analysis revealed a significant correlation between CA-125 levels and tumor grades. The mean CA-125 values were found to be 28.0±8.91(minimal group), 91.0±19.1 (mild group), and 217±40 (moderate group). This increasing trend in CA-125 levels across the grades was statistically significant ($p=0.0001$). CA-125 levels showed statistically significant differences between the moderate group and both the minimal and mild groups ($p= 0.0001$ and 0.025, respectively), while the increase between the minimal and mild groups was not statistically significant ($p=0.223$). Regarding estradiol levels, the mean values were 69.7±15.2 for the minimal group, 63.8±10.2 for the mild group, and 42.9±10.4 for the moderate group. A statistically significant difference was observed between the minimal-moderate and the mild-moderate groups ($p= 0.004$ and 0.012, respectively). Similarly, the mean progesterone levels were 71.8±12.6, 53.8±11.8, and 28.2±9.66 in the minimal, mild, and moderate groups, respectively. Progesterone levels were significantly decreased in the minimal group compared to the mild group ($p= 0.004$). Furthermore, the moderate group showed statistically significant decreases compared to both

the minimal and mild groups (p= 0.0001 and 0.001, respectively.

Furthermore, a strong positive correlation was identified between estradiol and progesterone levels in postmenopausal patients with ECC (r=0.667, p=0.0001), as shown in Figure 1. An negative correlation was observed between CA-125 levels and both estradiol and progesterone concentrations in patients with ECC. The corresponding correlation coefficients are presented in Table 2.

In addition, Figures 2 and 3 demonstrate negative correlations between CA-125 and progesterone and CA-125 and estradiol levels in these patients.

Table 1. Biochemical characteristics of patients with ECC.

Parameters	Minimal (n:80)	Mild (n:42)	Moderate (n:38)	F value	p
Age (year)	59.8±7.87	63.2±7.51	60.6±7.33	2.27	0.107
CA-125 (U/mL)	28.0±8.91	91.0±19.1	217±40.8[a,b]	11.4	0.0001
Estradiol (ng/L)	69.7±15.2	63.8±10.2	42.9±10.4[a,b]	5.24	0.006
Progesterone (ug/L)	71.8±12.6	53.8±11.8[a]	28.2±9.66[a,b]	29.1	0.0001

P values according to One Way Anova test, post hoc Tukey test. Data were expressed as mean ± standard deviation. A significantly different from Minimal, b significantly different from Mild , (P<0.05).

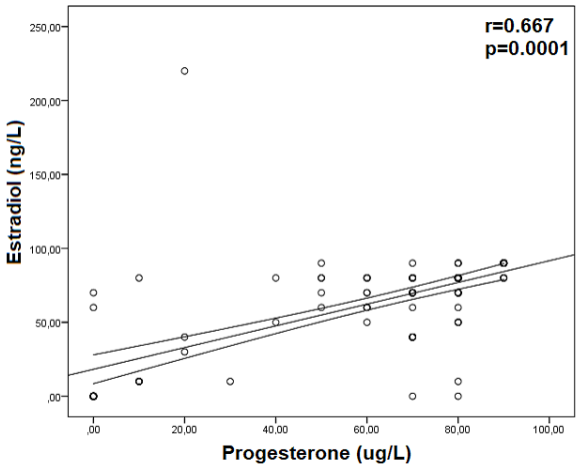

Figure 1. The correlation between Estradiol and Progesterone levels in ECC.

Discussion

Endometrial cancer is recognized as the most common malignancy of the female reproductive system and ranks as the fourth most prevalent cancer among women, following breast, lung, and colorectal cancers (1).Several factors contribute to the development of EC, including advanced age, nulliparity, late onset of menopause, early menarche, a history of infertility, obesity, and prolonged exposure to unopposed estrogen (3).The most common type of EC is EEC, accounting for approximately 75-80% of all cases (15). Due to early detection and the predominance of low-grade endometrioid histology, the prognosis is generally favorable. However, a high-risk disease characterized by non-endometrioid tumors and grade 3 endometrioid carcinoma is associated with a significantly poorer prognosis (5). Early diagnosis enables patients to avoid radical treatments and allows for considering conservative therapeutic options. Identifying biomarkers that can predict the risk of EC development, facilitate early detection, or support prognostic assessment through non-invasive methods is important. By establishing biomarkers specific to endometrial cancer, including its various subtypes, early detection rates can be improved, thereby enhancing the potential for personalized treatment strategies (6). Several prognostic and diagnostic biomarkers have been identified in tumor biopsies; however, to date, only a limited number have been incorporated into clinical practice to enhance the treatment of patients with EC (5).Therefore, monitoring the progression of EEC and accurately predicting patient survival and prognosis remain significant challenges in contemporary medicine (16). Identifying biomarkers in minimally invasive or non-invasive samples such as blood, urine, or saliva that can facilitate and accelerate the detection of EC represents a significant advancement in diagnosing and managing this disease (6).

Table 2. Correlation coefficients of CA-125 levels with Estradiol and Progesterone levels in ECC.

	CA-125 (U/mL)	
	Pearson correlation coefficient	p
Estradiol (ng/L)	-0.287	0.001
Progesterone (ug/L)	-0.279	0.001

p value according to Pearson tests. Statistical significance was set at $p < 0.05$.

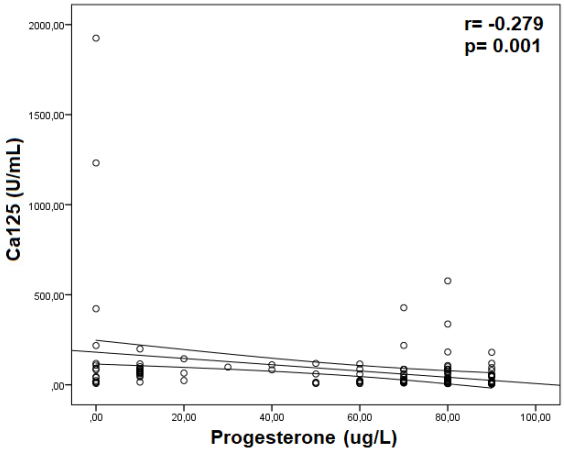

Figure 2. The correlation between CA-125 and Progesterone levels in ECC.

This study aimed to investigate the relationship between CA-125, progesterone, and estradiol levels in EEC and to assess their prognostic significance. These molecular markers may serve as valuable indicators for risk stratification and patient management in endometrioid endometrial carcinoma. Due to cyclical hormonal fluctuations, evaluating hormone levels in premenopausal and perimenopausal women poses challenges. The impact of progesterone and estradiol-related metabolites on cancer risk in postmenopausal women has been infrequently studied. Therefore, our research focused on postmenopausal patients, who constitute the majority of endometrial cancer cases.

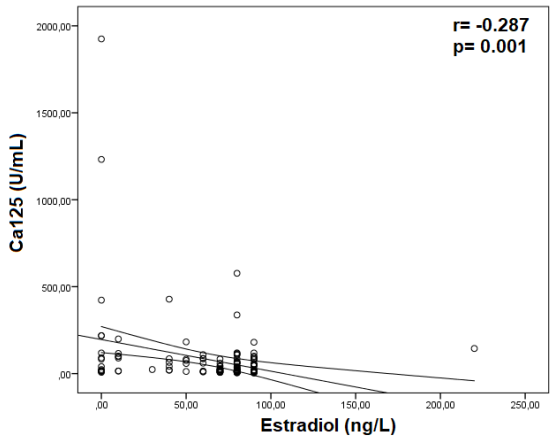

Figure 3. The correlation between CA-125 and Estradiol levels in ECC.

CA-125 is a glycoprotein found at elevated concentrations in various cancers, particularly ovarian, endometrial, colorectal, breast, and lung tumors (17). Although elevated serum CA-125 levels have been associated with advanced-stage EEC, their significance in early-stage EEC remains a subject of ongoing debate (4). Elevated levels of CA-125 can also be observed in various physiological and pathological conditions unrelated to cancer, such as menstruation, pregnancy, endometriosis, and inflammatory diseases of the pleura or peritoneum (17). Therefore, it remains unclear whether serum CA-125 serves as an independent prognostic marker or merely reflects specific clinicopathological characteristics of patients with EC (18). Studies in the literature examining CA-125 and EC have reported that CA-125 levels increase significantly in the advanced stages of the disease (1,3). Another study has reported that preoperative serum CA-125 levels may serve as a biomarker and an independent prognostic factor in patients with early-stage EEC (4). Granberg et al. demonstrated that CA-125 levels in postmenopausal women are lower than in premenopausal women (19). Similarly, Zurawski et al. reported that in over 93% of individuals aged above 60, CA-125 levels were below 20 U/ml (20). The study results indicated that CA-125 levels were elevated in advanced stages of EEC and were significantly correlated with the disease stage (Table 1). Consequently, increased CA-125 levels in patients with advanced EEC may predict a poor prognosis. These findings are consistent with those reported in the literature.

Although it is well-established that hormonal factors have a clear impact on endometrial cancer, relatively few studies have investigated the roles of endogenous estrogen and progesterone. It has been noted that endogenous steroids reflect not only circulating estrogen levels or obesity but also provide additional prognostic information beyond preoperative histological tumor evaluation (5). Since estrogens play a crucial role in maintaining physiological functions across various organs, the decline in estrogen levels following menopause is believed to contribute to the development of numerous conditions commonly observed in postmenopausal and older women (21). Hormonal imbalances induced by estrogen influence gene expression in cell proliferation and apoptosis, potentially leading to uncontrolled cell growth and carcinogenesis (6).

In postmenopausal women, estrone and estradiol are the physiologically most significant estrogens. Although estrone is the most abundant estrogen, research typically focuses on estradiol for investigative purposes (21). According to studies reported in the literature, circulating estrogen levels are elevated in postmenopausal women diagnosed with endometrial cancer compared to healthy postmenopausal individuals

(22,23). A study comparing postmenopausal women with endometrial cancer to healthy postmenopausal controls found significant differences in estrogen levels measured in urine samples. The findings suggest that an imbalance in estrogen metabolites, particularly elevated levels of 4-hydroxy estradiol (4-OHE2), may play a role in endometrial carcinogenesis and could serve as a potential biomarker for assessing estrogen-related EC risk (22).

A study examining the relationship between prediagnostic serum estrogen and estrogen metabolites and the risk of endometrial cancer in postmenopausal women not receiving hormone replacement therapy reported that increased serum levels of catechol estrogens and 16-hydroxy estrone were associated with a higher incidence of endometrial cancer in this population. It reported that the highest risk was associated with unconjugated estradiol levels (11). Naomi et al. reported a positive correlation between estradiol levels and endometrial malignancy in postmenopausal patients (24). In our study, estradiol levels were evaluated about disease stages in patients with EEC. It was observed that estradiol levels declined as the stage of the disease advanced. While some studies have reported elevated estradiol levels, these generally address endometrial cancer as a broader category rather than focusing specifically on EEC. Although estradiol is considered the most influential estrogen in the development of EC, other forms of estrogen and their metabolites may also contribute to the overall risk.

It has been emphasized that maintaining endometrial homeostasis requires a tightly regulated balance between estrogen and progestogen levels. This hormonal equilibrium is essential for preserving the structural and functional integrity of the endometrium (25). It is well established that an imbalance between estrogen and progesterone plays a critical role in the progression of type 1 endometrial cancer (9). Progesterone is a key regulatory hormone in the endometrium, counteracting estrogen-induced proliferation. Inadequate levels of progesterone can result in unopposed estrogenic stimulation, which may lead to the development of endometrial hyperplasia and, eventually, adenocarcinoma (26). Wang et al. demonstrated the potential of combining estrogen receptor (ER) and progesterone receptor (PR) expression with CA-125 levels as a biomarker for predicting lymph node metastasis in endometrial cancer. Their findings suggest that, in addition to CA-125 levels, the evaluation of ER/PR expression may aid in distinguishing between high- and low-risk patients with endometrial cancer about lymph node involvement. This combined biomarker approach could enhance risk stratification and support clinical decision-making in disease management (27). Another study investigated the relationship between postmenopausal levels of pregnenolone and/or progesterone and the risks of endometrial and ovarian cancers. The findings provided epidemiological evidence suggesting that postmenopausal progesterone levels are inversely associated with the risk of endometrial cancer when compared to estradiol levels. Although circulating progesterone concentrations alone were not found to be significantly associated with the risk of either endometrial or ovarian cancer, an elevated progesterone-to-estradiol ratio was reported to be inversely correlated with endometrial cancer risk. These findings underscore the importance of hormonal balance, rather than absolute hormone levels, in influencing carcinogenic risk in postmenopausal women (28). This study observed that progesterone levels declined across the stages of EEC, with a statistically significant difference between the stages. This downward trend may suggest a potential association with poorer prognosis in EEC. When examined in the context of existing research, the findings were consistent with previously published data.

Furthermore, a strong positive correlation was identified between estradiol and progesterone levels, indicating a closely linked hormonal interaction. A deeper understanding of estrogen and progesterone metabolism could provide valuable insights into the underlying mechanisms of endometrioid endometrial cancer. Additionally, an inverse correlation was observed between CA-125 levels and both estradiol and progesterone, further highlighting the complexity of these biochemical relationships.

The results demonstrate that our investigation possessed adequate statistical power (>80%) to identify significant differences across the groups for all three investigated biomarkers. The sample size of 160 postmenopausal women was adequate to produce statistically significant results concerning the associations between serum CA-125, estradiol, and progesterone levels and the risk of endometrioid endometrial cancer. Nevertheless, despite this adequate statistical power, further larger future studies would be beneficial to corroborate these findings, especially to

investigate minor effects that may necessitate a larger sample size for reliable detection.

This retrospective study, conducted on postmenopausal women diagnosed with EEC, has several limitations. It is a single-center retrospective analysis and lacks a control group comprising healthy women. Moreover, certain potentially influential variables, such as body mass index (BMI), could not be obtained, which may have impacted the findings.

Conclusion

In conclusion, it was demonstrated that CA-125 levels in postmenopausal patients with EEC are associated with the stage of the disease and may serve as a clinically valuable marker for preoperative assessment and postoperative surveillance. Additionally, it was observed that estradiol and progesterone levels tend to decrease in patients with advanced-stage disease, indicating a negative correlation. To gain a comprehensive understanding of the complex interplay between EEC and sex hormone metabolism, particularly estradiol and progesterone, further large-scale studies are warranted.

Acknowledgements

None.

Conflict of interest statement

None.

Ethics Committee Approval

This received approval from the Sivas Cumhuriyet University Ethics Committee. The ethical committee approved the study with 2024-11/08 approval on 21.11.2024.

Funding

None

References

1. Zamani N, Gilani MM, Mirmohammadkhani M, et al. The utility of CA-125 and HE4 in patients suffering from endometrial cancer. IJWHRS. 2020;8(1):95-100.
2. Bassette E, Ducie JA. Endometrial Cancer in Reproductive-Aged Females: Etiology and Pathogenesis. Biomedicines. 2024;12(4):886.
3. Gilani MM, Mehr SGD, Mousavi A, et al. The Importance of HE4 and CA 125 in Overall Survival and Recurrence-free Survival of Endometrial Cancer. EEC. 2022;89:89-9.
4. Kurt B, Küçükyıldız İ, Yanık A. The predictive role of CA-125 value in early stage endometrioid endometrial cancer. Cumhuriyet Medical Journal. 2023;45(2):31-37.
5. Forsse D, Tangen IL, Fasmer KE, et al. Blood steroid levels predict survival in endometrial cancer and reflect tumor estrogen signaling. Gynecol. Oncol. 2020;156(2): 400-406.
6. Bukato K, Kostrzewa T, Gammazza AM, et al. Endogenous estrogen metabolites as oxidative stress mediators and endometrial cancer biomarkers. Cell Commun. Sıgnal. 2024; 22(1): 205.
7. Purdie DM, Green AC. Epidemiology of endometrial cancer. Bes Pract. Res. Clin. Obstet. Gynaecol. 2001;15(3):341-354.
8. Brinton LA, Hoover RN. Estrogen replacement therapy and endometrial cancer risk: unresolved issues. Obstetrics & Gynecology. 1993;81(2):265-271.
9. Tian W, Teng F, Zhao J, et al. (2017). Estrogen and insulin synergistically promote type 1 endometrial cancer progression. Cancer Biol. Ther. 2017;18(12):1000-1010.
10. Audet-Walsh E, Lepine J, Gregoire J, et al. Profiling of endogenous estrogens, their precursors, and metabolites in endometrial cancer patients: association with risk and relationship to clinical characteristics. JCEM. 2011;96(2):E330-E339.
11. Brinton LA, Trabert B, Anderson GL, et al. Serum estrogens and estrogen metabolites and endometrial cancer risk among postmenopausal women. Cancer Epidemiol. Biomarkers Prev. 2016;25(7):1081-1089.
12. Lukanova A, Lundin E, Micheli A, et al. Circulating levels of sex steroid hormones and risk of endometrial cancer in postmenopausal women. IJC. 2004;108(3):425-432.
13. Potischman N, Hoover RN, Brinton LA, et al. Case—control study of endogenous steroid hormones and endometrial cancer. JNCI. 1996;88(16):1127-1135.
14. Michels KA, Brinton LA, Wentzensen N, et al. Postmenopausal androgen metabolism and endometrial cancer risk in the women's health initiative observational study. JNCI cancer spectrum. 2019;3(3):pkz029.
15. Erturk A, Korkmaz E, Arslantas Z, et al. Preoperative cancer antigen-125 levels as a predictor of recurrence in early-stage endometrial cancer. RAMB. 2024;70(5): e20231115.
16. Liang C, Chen Y, Chen S, et al. KLRB1 is a novel prognostic biomarker in endometrial cancer and is associated with immune infiltration. Transl. Cancer Res. 2023;12(12):3641.
17. Degez M, Caillon H, Chauviré-Drouard A, et al. Endometrial cancer: A systematic review of HE4, REM and REM-B. Clin. Chim. Acta. 2021;515:27-36.

18. Chao A, Tang YH, Lai CH, et al. Potential of an age-stratified CA125 cut-off value to improve the prognostic classification of patients with endometrial cancer. Gynecol. Oncol. 2013;129(3):500-504.
19. Granberg S, Wikland M, Friberg LG: Tumor marker CA125 level and ovarian volume at different cycle day periods and in postmenopause. Int. J Gynaecol. Obstet. 1990;33:149 -152,
20. Zurawski Jr VR, Sjovall K, Schoenfeld DA, Prospective evaluation of serum CA 125 levels in a normal population, phase I: the specificities of single and serial determinations in testing for ovarian cancer. Gynecol. Oncol. 1990;36(3):299-305.
21. Honma N, Hosoi T, Arai T, et al. Estrogen and cancers of the colorectum, breast, and lung in postmenopausal women. Pathol. Int., 2015;65(9): 451-459.
22. Zhao H, Jiang Y, Liu Y, et al. Endogenous estrogen metabolites as biomarkers for Endometrial Cancer via a Novel Method of Liquid Chromatography-Mass Spectrometry with Hollow Fiber Liquid-Phase Microextraction. Horm Metab Res. 2014;47(02):158-164.
23. Heidari F, Rabizadeh S, Mansournia MA, et al. Inflammatory, oxidative stress and anti-oxidative markers in patients with endometrial carcinoma and diabetes. Cytokine. 2019;120:186-190.
24. Allen NE, Key TJ, Dossus L. Endogenous sex hormones and endometrial cancer risk in women in the European prospective Investigation into Cancer and Nutrition (EPIC). Endocr-Relat Cancer. 2008;15(2):485-497.
25. Gompel A. Progesterone and endometrial cancer. Bes Pract. Res. Clin. Obstet. Gynaecol. 2020;69: 95-107.
26. Kim JJ, Chapman-Davis E. Role of progesterone in endometrial cancer. Semin Reprod. Med. 2010;28(01):81-90.
27. Wang SC, Wu CH, Fu HC, et al. Estrogen/Progesterone Receptor Expression and Cancer Antigen 125 Level as Preoperative Predictors to Estimate Lymph Node Metastasis in Endometrioid Endometrial Cancer. Int. J. Gynecol. Pathol. 2024;43(4):316-325.
28. Trabert B, Geczik AM, Bauer DC. Association of endogenous pregnenolone, progesterone, and related metabolites with risk of endometrial and ovarian cancers in postmenopausal women: the B~ FIT cohort. Cancer Epidemiol. Biomarkers Prev. 2021;30(11):2030-2037.