Original Article

Serum Estradiol and Endometrial Thickness as Complementary Biomarkers in Postmenopausal Bleeding Associated with Endometrial Malignancy: A Retrospective Cross-Sectional Study

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Abstract

Background: Postmenopausal bleeding (PMB) is a clinically important symptom associated with a significant risk of endometrial malignancy. Although transvaginal ultrasonography (TVUS) is widely used for initial evaluation, its limited specificity highlights the need for additional biomarkers to improve diagnostic accuracy. This study aimed to evaluate the association between serum estradiol levels, endometrial thickness, and histopathological characteristics in postmenopausal women with PMB and confirmed endometrial malignancy.

Methods: This retrospective cross-sectional study included 55 postmenopausal women with abnormal uterine bleeding and histopathologically confirmed endometrial cancer. Clinical, demographic, laboratory, hormonal, imaging, and pathological data were extracted from medical records. Serum estradiol levels were categorized as ≤54 pg/mL and >54 pg/mL. Endometrial thickness was assessed by transvaginal ultrasonography and classified as <4 mm or ≥4 mm. Statistical analysis was performed using SPSS version 26, and a p-value <0.05 was considered significant.

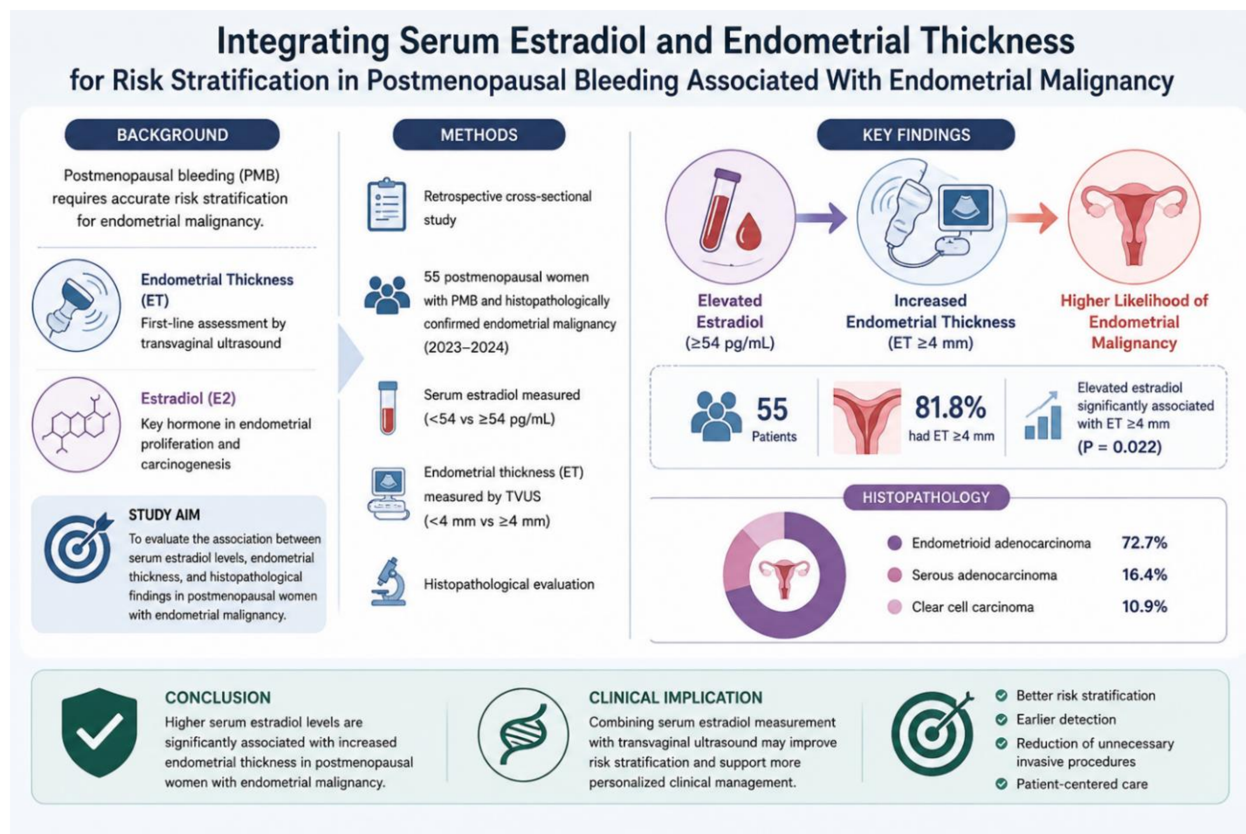
Results: The majority of patients were aged 60–69 years and obese. Most cases were endometrioid adenocarcinoma grade 1. No significant associations were observed between serum estradiol levels and age, BMI, age at menopause, interval between menopause and diagnosis, or histopathological subtype. However, a significant association was found between serum estradiol levels and endometrial thickness (P = 0.022), with all patients in the elevated estradiol group demonstrating an endometrial thickness ≥4 mm.

Conclusion: Serum estradiol levels were significantly associated with endometrial thickness but not with demographic or tumor-related characteristics. These findings suggest that estradiol may serve as a complementary biomarker

alongside ultrasonographic evaluation in the risk stratification of postmenopausal women with abnormal uterine bleeding.

Implications for Patient Care: Combining serum estradiol assessment with transvaginal ultrasonography may improve risk stratification in postmenopausal women with abnormal uterine bleeding. This approach can help identify higher-risk patients for endometrial pathology, guide appropriate use of biopsy, and support conservative management in low-risk cases, enhancing individualized clinical decision-making.

Keywords: Postmenopausal bleeding; Endometrial cancer; Serum estradiol; Endometrial thickness; Transvaginal ultrasonography



Graphical Abstract. Integrating Serum Estradiol and Endometrial Thickness for Risk Stratification in Postmenopausal Bleeding Associated with Endometrial Malignancy. Combined assessment of serum estradiol and endometrial thickness may enhance early detection and clinical risk stratification in postmenopausal bleeding associated with endometrial malignancy.

Introduction

Postmenopausal bleeding (PMB) remains one of the most clinically significant presentations in gynecologic practice, as it is associated with a substantial risk of endometrial carcinoma and premalignant endometrial lesions (1). Endometrial cancer represents the most common gynecologic malignancy in developed countries, and its global incidence continues to rise in parallel with increasing obesity and population

aging (2). Although most cases are ultimately attributable to benign etiologies, the prevalence of endometrial malignancy among women presenting with PMB is sufficiently high to require timely and accurate diagnostic evaluation (1, 3).

Transvaginal ultrasonography (TVUS), particularly the assessment of endometrial thickness (ET), is widely used as the first-line diagnostic modality in the evaluation of PMB (4). Despite its clinical utility and high sensitivity, ET-based triage demonstrates limited specificity, resulting in a considerable number of unnecessary invasive procedures, including endometrial biopsy (5, 6). Moreover, reliance on imaging findings alone may inadequately capture the underlying biological heterogeneity of endometrial pathology (7, 8). Consequently, there is an ongoing need for complementary biomarkers capable of improving diagnostic stratification and supporting more individualized clinical decision-making (9, 10).

Endometrial carcinogenesis is strongly influenced by hormonal exposure, particularly estrogenic stimulation (11, 12). Estradiol, the most biologically active endogenous estrogen, plays a central role in endometrial proliferation through estrogen receptor-mediated signaling pathways (13). Estrogen-driven activation of proliferative and anti-apoptotic pathways has been recognized as a central mechanism in endometrial tumor initiation and progression (11). Persistent or dysregulated estrogen exposure has been implicated in the development of endometrial hyperplasia and carcinoma (14, 15). However, despite the biologically plausible role of estradiol in endometrial carcinogenesis, its translational utility as a clinically actionable biomarker in PMB evaluation remains poorly defined, with existing evidence limited by heterogeneous study populations, variable hormonal assays, and inconsistent diagnostic thresholds (16-18). Importantly, current diagnostic approaches for PMB primarily rely on anatomical and imaging-based parameters without adequately incorporating systemic hormonal status, despite the well-recognized biological role of estrogen in endometrial pathophysiology (3).

This disconnects between biological mechanisms and routine clinical assessment highlights an important unmet need in precision-based gynecologic diagnostics. Integrating hormonal biomarkers into conventional diagnostic pathways may improve patient selection for invasive evaluation and potentially reduce unnecessary procedures in lower-risk patients. Accordingly, the present study aimed to evaluate the association between serum estradiol levels, endometrial thickness, and histopathological characteristics in postmenopausal women with PMB and confirmed endometrial malignancy, with the goal of exploring the potential role of estradiol as a complementary biomarker for diagnostic risk stratification and individualized clinical management.

Methods

Study Design and Setting

This retrospective cross-sectional study was conducted as a medical record review in gynecology outpatient clinics affiliated with Lorestan University of Medical Sciences, Khorramabad, Iran, between 2023 and 2024. Ethical approval was obtained from the Ethics Committee of Lorestan University of Medical Sciences (Approval No: IR.LUMS.REC.1404.156). The study was conducted in accordance with the Declaration of Helsinki. All patient data were anonymized prior to analysis to ensure confidentiality. The reporting of this study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Population

The study population consisted of postmenopausal women presenting with

abnormal uterine bleeding who were subsequently diagnosed with endometrial malignancy based on histopathological examination during the study period. Postmenopausal status was defined as the absence of menstruation for at least 12 consecutive months.

Sampling Method

A census (total population) sampling method was used, and all eligible cases meeting the inclusion criteria within the study period were included. This approach was applied to minimize selection bias and ensure complete inclusion of available eligible medical records.

Data Collection

This study was based on retrospective review of patients' medical records. Data were extracted from hospital files using a standardized data extraction form developed by the researchers. Clinical, demographic, laboratory, hormonal (including serum estradiol levels), imaging, and histopathological data were obtained from existing documented records without any additional patient contact or new laboratory measurements. Data extraction was performed by trained researchers. Records with incomplete or unclear documentation were excluded to ensure data accuracy and consistency.

Study Variables

- ***Independent Variables***

Independent variables included age, body mass index (BMI), age at menopause, and serum estradiol levels. Serum estradiol levels were categorized based on laboratory-specific reference ranges (<54 pg/mL and ≥54 pg/mL), in accordance with assay-dependent variability reported in clinical laboratory practice.

- ***Dependent Variables***

Outcome variables included endometrial thickness and histopathological subtype of endometrial malignancy. Endometrial thickness was categorized as <4 mm or ≥4 mm based on transvaginal ultrasonography findings, using the threshold recommended by the American College of Obstetricians and Gynecologists (ACOG Committee Opinion No. 734) (4).

Ultrasonographic Assessment

Transvaginal ultrasonography (TVUS) was performed as part of routine diagnostic evaluation for postmenopausal bleeding. Endometrial thickness was measured in the sagittal plane at the maximal double-layer thickness of the endometrial echo complex by experienced radiologists or gynecologists, following standardized institutional protocols. To reduce interobserver variability, all measurements were obtained according to routine standardized imaging procedures applied in the participating centers.

Inclusion and Exclusion Criteria

Inclusion criteria were postmenopausal status, presentation with abnormal uterine bleeding, histopathologically confirmed endometrial malignancy, and availability of complete clinical and laboratory records. Exclusion criteria included history of other malignancies, use of hormonal therapy within the previous 6 months, prior gynecologic surgery related to malignancy, hematologic or coagulation disorders, and incomplete medical records. Patients receiving exogenous estrogen therapy were excluded to minimize potential confounding effects on serum estradiol levels and endometrial characteristics.

Statistical Analysis

Statistical analyses were performed using SPSS software version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD), and categorical variables as frequency and percentage. Normality of data distribution was assessed using the Shapiro–Wilk test. Group comparisons for continuous variables were performed using the independent-samples t-test or one-way analysis of variance (ANOVA) for normally distributed

data, and non-parametric tests when appropriate. Associations between categorical variables were analyzed using the chi-square test or Fisher's exact test. A two-sided p-value <0.05 was considered statistically significant. Effect sizes and 95% confidence intervals were reported where applicable to improve interpretation of clinical relevance. Given the retrospective design and exploratory nature of the study, findings were interpreted cautiously and considered hypothesis-generating.

Results

1. Baseline Characteristics of the Study Population

A total of 55 postmenopausal women with abnormal uterine bleeding and histopathologically confirmed endometrial malignancy were included in the study. The majority of patients were aged 60–69 years (40.0%), followed by 50–59 years (25.5%), 40–49 years (23.6%), and 70–79 years (10.9%).

Most patients were obese (54.5%), while 34.5% were overweight, 9.1% had normal weight, and 1.8% were underweight.

More than half of the patients (54.5%) had menopause at ≤49 years. The interval between menopause and cancer diagnosis was ≥9 years in 52.7% of cases. Serum estradiol levels were ≤54 pg/mL in 69.1% of patients. Endometrial thickness was ≥4 mm in 81.8% of cases. Regarding histopathological findings, Grade 1 endometrioid adenocarcinoma was the most common subtype (78.2%), followed by Grade 3 (12.7%), Grade 2 (3.6%), clear cell carcinoma (3.6%), and squamous cell carcinoma (1.8%).

Variable	Category	n	%
Age (years)	40–49	13	23.6
	50–59	14	25.5
	60–69	22	40.0
	70–79	6	10.9
BMI	Underweight	1	1.8
	Normal	5	9.1
	Overweight	19	34.5
	Obese	30	54.5
Age at Menopause	≤49 years	30	54.5
	>49 years	25	45.5
Serum Estradiol Level	≤54 (normal)	38	69.1
	>54 (abnormal)	17	30.9
Interval From Menopause to Diagnosis	<9 years	26	47.3
	≥9 years	29	52.7
Endometrial Thickness	<4 mm	10	18.2
	≥4 mm	45	81.8
Pathological Type	Endometrioid adenocarcinoma (Grade 1)	43	78.2
	Endometrioid adenocarcinoma (Grade 2)	2	3.6
	Endometrioid adenocarcinoma (Grade 3)	7	12.7
	Clear cell carcinoma	2	3.6
	Squamous cell carcinoma	1	1.8

Table 1. Baseline demographic, clinical, and pathological characteristics of postmenopausal women diagnosed with endometrial malignancy and presenting with abnormal uterine bleeding.

2. Association Between Serum Estradiol Levels and Clinical, Demographic, and Pathological Characteristics

The association between serum estradiol levels and clinical, demographic, and pathological variables are presented in Table 2. No statistically significant associations were found between serum estradiol levels and age (P = 0.866), BMI (P = 0.710), age at menopause (P = 0.386), interval between menopause and diagnosis (P = 0.143), or histopathological subtype (P = 0.632). A statistically significant association was observed between serum estradiol levels and endometrial thickness (P = 0.022). All patients with elevated estradiol levels had an endometrial thickness of ≥4 mm, whereas in the normal estradiol group, 73.7% had a thickness ≥4 mm and 26.3% had a thickness <4 mm.

Variable	Category	Estradiol levels		P-value
		Normal (≤54) n (%)	Abnormal (>54) n (%)	
Age (years)	40–49	10 (26.3)	3 (17.6)	0.866
	50–59	10 (26.3)	4 (23.5)	
	60–69	14 (36.8)	8 (47.1)	
	70–79	4 (10.5)	2 (11.8)	
BMI	Underweight	1 (2.6)	0 (0.0)	0.710
	Normal	4 (10.5)	1 (5.9)	
	Overweight	14 (36.8)	5 (29.4)	
	Obese	19 (50.0)	11 (64.7)	
Age at Menopause	≤49 years	19 (50.0)	11 (64.7)	0.386
	>49 years	19 (50.0)	6 (35.3)	
Interval Menopause–Diagnosis	<9 years	15 (39.5)	11 (64.7)	0.143
	≥9 years	23 (60.5)	6 (35.3)	
Pathological Type	Endometrioid G1	28 (73.7)	15 (88.2)	0.632
	Endometrioid G2	2 (5.3)	0 (0.0)	
	Endometrioid G3	5 (13.2)	2 (11.8)	
	Clear cell carcinoma	2 (5.3)	0 (0.0)	
	Squamous cell carcinoma	1 (2.6)	0 (0.0)	
Endometrial Thickness	<4 mm	10 (26.3)	0 (0.0)	0.022
	≥4 mm	28 (73.7)	17 (100.0)	

Table 2. Association between serum estradiol levels and demographic, clinical, and pathological characteristics.

DISCUSSION

In this retrospective cross-sectional study, we evaluated the association between serum

estradiol levels and demographic, clinical, and pathological characteristics in postmenopausal women with endometrial malignancy presenting with abnormal uterine bleeding. The main finding was a significant association between elevated estradiol levels and increased endometrial thickness, while no significant associations were observed with most demographic or histopathological variables. Overall, our findings suggest that serum estradiol may be more closely related to endometrial structural changes than to demographic or tumor-related characteristics in this population. The predominance of patients in the 60–69-year age group is consistent with epidemiological evidence showing that endometrial cancer incidence increases with age due to cumulative hormonal exposure and metabolic alterations. However, no association was observed between age and estradiol levels, supporting the concept that postmenopausal estrogen is mainly driven by peripheral aromatization rather than chronological aging (19, 20). This suggests that postmenopausal estrogen levels are influenced more by metabolic factors than by age itself.

Obesity was highly prevalent in our cohort. Although not statistically significant, higher estradiol levels were more frequent in obese patients. This finding is biologically plausible, as adipose tissue is the main site of estrogen production after menopause via aromatase activity (21, 22). Obesity is a well-established risk factor for endometrial cancer (23). Large epidemiological studies have shown a dose–response relationship between BMI and endometrial cancer risk (24). In our study, the lack of statistical significance may reflect the relatively small sample size and limited statistical power.

No association was found between age at menopause and estradiol levels. Available evidence suggests that reproductive lifespan may have a limited influence on postmenopausal estradiol levels, whereas non-reproductive factors, including metabolic and genetic influences, appear to contribute more substantially to interindividual variability (25, 26). Similarly, the interval between menopause and diagnosis was not significantly associated with estradiol levels. However, shorter intervals were more frequent in the high-estradiol group, suggesting a possible role of sustained estrogen exposure in earlier tumor development (27, 28). This pattern may indicate a potential trend toward earlier disease manifestation in patients with higher estrogen exposure, although this requires confirmation in larger studies. Importantly, a significant association was observed between estradiol levels and endometrial thickness. All patients with elevated estradiol had endometrial thickness ≥4 mm, while thinner endometrium was observed mainly in the normal estradiol group. This supports the proliferative effect of estrogen on the endometrium via receptor-mediated signaling pathways (29). This finding is consistent with clinical guidelines that recommend a 4 mm cutoff in postmenopausal bleeding evaluation due to its high negative predictive value for malignancy (4). From a clinical perspective, estradiol may serve as a complementary biomarker alongside transvaginal ultrasonography in risk stratification of postmenopausal bleeding patients. This combined approach may improve early identification of patients requiring further invasive evaluation such as biopsy. Such an approach could potentially enhance clinical decision-making by improving the identification of patients who may benefit from further invasive diagnostic procedures, such as endometrial biopsy.

Novelty

To our knowledge, this study is among the few to evaluate the combined association of serum estradiol and endometrial thickness in histologically confirmed endometrial malignancy. Unlike previous studies focusing

mainly on BMI or reproductive factors, our work integrates hormonal and imaging parameters, offering a more comprehensive clinical perspective. This integrated approach may provide additional insight into the interplay between systemic hormonal status and structural endometrial changes in postmenopausal women.

Limitations

This study has several limitations. The retrospective design may introduce selection bias. The small sample size reduces statistical power. A single-center setting limits generalizability. Additionally, metabolic and endocrine confounders such as insulin resistance and androgen levels were not assessed. Therefore, residual confounding cannot be excluded.

Future Directions

Future prospective multicenter studies with larger cohorts are needed to validate these findings. Longitudinal studies could clarify temporal hormonal changes in endometrial carcinogenesis. Predictive models integrating hormonal and imaging biomarkers may improve early detection strategies. In addition, incorporating metabolic and endocrine profiles may further enhance risk stratification models.

Conclusion

In conclusion, while serum estradiol levels were not significantly associated with most demographic and pathological variables, a significant relationship was observed with endometrial thickness, highlighting the potential role of estradiol as a biologically and clinically relevant marker in postmenopausal endometrial pathology. These findings suggest that serum estradiol, particularly when interpreted alongside transvaginal ultrasonography, may have potential utility in the clinical evaluation of postmenopausal women with abnormal uterine bleeding.

Implications for Patient Care

This study highlights important clinical considerations for the evaluation and management of postmenopausal women with abnormal uterine bleeding. The observed correlation between elevated serum estradiol levels and increased endometrial thickness suggests that hormonal profiling could serve as a valuable adjunct to transvaginal ultrasonography in routine diagnostic workup. Integrating serum estradiol assessment with imaging findings may enhance early identification of patients at higher risk for clinically significant endometrial pathology, improving diagnostic precision beyond structural evaluation alone.

From a clinical decision-making perspective, this combined approach can support risk stratification strategies. Patients exhibiting both elevated estradiol levels and increased endometrial thickness may represent a subgroup warranting earlier consideration of invasive diagnostic procedures, such as endometrial sampling. Conversely, patients with normal hormonal and ultrasonographic findings may be candidates for conservative management, potentially reducing unnecessary interventions.

Notably, the lack of significant associations between serum estradiol levels and most demographic or histopathological variables indicates that estradiol may act as a marker of endometrial activity rather than a surrogate for baseline patient characteristics. This reinforces its potential utility as a complementary biomarker in personalized risk assessment. In the context of precision medicine, incorporating hormonal biomarkers such as estradiol into diagnostic algorithms may improve individualized care, facilitate earlier detection of clinically relevant endometrial changes, and optimize healthcare resource utilization. These findings provide a rationale for further prospective studies to validate serum estradiol as part of evidence-based protocols for postmenopausal bleeding, ideally within larger, multicenter cohorts.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

All authors contributed to the conception and design of the study, literature search, data interpretation, drafting of the manuscript, and critical revision of the article. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Ethics Statement

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Reference:

1. Clarke MA, Long BJ, Del Mar Morillo A, Arbyn M, Bakkum-Gamez JN, Wentzensen N. Association of Endometrial Cancer Risk With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. JAMA Intern Med. 2018;178(9):1210-22. doi: 10.1001/jamainternmed.2018.2820

2. Kiesel L, Eichbaum C, Baumeier A, Eichbaum M. Obesity Epidemic-The Underestimated Risk of Endometrial Cancer. Cancers (Basel). 2020;12(12). doi: 10.3390/cancers12123860

3. Van Hanegem N, Breijer MC, Khan KS, Clark TJ, Burger MP, Mol BW, Timmermans A. Diagnostic evaluation of the endometrium in postmenopausal bleeding: an evidence-based approach. Maturitas. 2011 Feb 1;68(2):155-64. https://doi.org/10.1016/j.maturitas.2010.11.010

4. Ibrahim AM, Elioba JL, Ali FA, Mohamed MM, Omar AM, Osman AJ, Warsame FD, Ali RA, Emmanuel O, Hakizimana T. The role of transvaginal ultrasonography in evaluating the endometrium of women with postmenopausal bleeding. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2018;14(8):2825.https://dx.doi.org/10.18203/2320-1770.ijrcog20252373

5. Tahmasebi F, Stewart S, Mitra A, Morje M, Sayasneh A. Transvaginal Saline Contrast Sonohystography to Investigate Postmenopausal Bleeding: A Systematic Review. Cureus. 2020;12(8):e10094. doi: 10.7759/cureus.10094

6. Kaur H, Qadri S, Nevill AM, Ewies AAA. The optimal endometrial thickness threshold for prediction of endometrial cancer in postmenopausal women without bleeding remains uncertain–Systematic review and meta-analysis. Journal of Gynecology Obstetrics and Human Reproduction. 2024;53(10):102831. doi: 10.1016/j.jogoh.2024.102831

7. Asselin M-C, O’Connor JP, Boellaard R, Thacker NA, Jackson A. Quantifying heterogeneity in human tumours using MRI and PET. European journal of cancer. 2012;48(4):447-55. https://doi.org/10.1016/j.ejca.2011.12.025

8. Davnall F, Yip CS, Ljungqvist G, Selmi M, Ng F, Sanghera B, et al. Assessment of tumor heterogeneity: an emerging imaging tool for clinical practice? Insights into imaging. 2012;3(6):573-89. https://doi.org/10.1007/s13244-012-0196-6

9. Rižner TL, Romano A. The discovery of biomarkers for endometrial cancer: update over the last years. Expert Review of Molecular Diagnostics. 2025;25(8):425-52. https://doi.org/10.1080/14737159.2025.2505546

10. Njoku K, Barr CE, Crosbie EJ. Current and Emerging Prognostic Biomarkers in Endometrial Cancer. Front Oncol. 2022;12:890908. doi: 10.3389/fonc.2022.890908

11. Shang Y. Molecular mechanisms of oestrogen and SERMs in endometrial carcinogenesis. Nature Reviews Cancer. 2006;6(5):360-8. https://doi.org/10.1038/nrc1879

12. Rodriguez AC, Blanchard Z, Maurer KA, Gertz J. Estrogen signaling in endometrial cancer: a key oncogenic pathway with several open questions. Hormones and Cancer. 2019;10(2):51-63.
https://doi.org/10.1007/s12672-019-0358-9

13. Yu K, Huang ZY, Xu XL, Li J, Fu XW, Deng SL. Estrogen Receptor Function: Impact on the Human Endometrium. Front Endocrinol (Lausanne). 2022;13:827724.
doi: 10.3389/fendo.2022.827724.

14. Ignatov A, Ortmann O. Endocrine Risk Factors of Endometrial Cancer: Polycystic Ovary Syndrome, Oral Contraceptives, Infertility, Tamoxifen. Cancers (Basel). 2020;12(7).doi: 10.3390/cancers12071766

15. Nees LK, Heublein S, Steinmacher S, Juhasz-Böss I, Brucker S, Tempfer CB, et al. Endometrial hyperplasia as a risk factor of endometrial cancer. Archives of Gynecology and Obstetrics. 2022;306(2):407-21. doi: 10.1007/s00404-021-06380-5.

16. Glynne S, Kamal A, Neville A, McColl L, Naji O, Newson L, et al. Endometrial thickness and pathology in postmenopausal women with bleeding on transdermal 17β-estradiol plus body-identical progesterone. Archives of Gynecology and Obstetrics. 2025;312(5):1705-17.
https://doi.org/10.1007/s00404-025-08161-w

17. Büyük E, Gürler A, Erenus M. Relationship between circulating estradiol levels, body mass index, and breakthrough bleeding in postmenopausal women receiving hormone replacement therapy. Menopause. 1998;5(1):24-7.

18. Zeleniuch-Jacquotte A, Akhmedkhanov A, Kato I, Koenig KL, Shore RE, Kim MY, et al. Postmenopausal endogenous oestrogens and risk of endometrial cancer: results of a prospective study. British Journal of Cancer. 2001;84(7):975-81. https://doi.org/10.1054/bjoc.2001.1704

19. Jacobs S, MacNeill F, Lonning P, Dowsett M, Jones A, Powles T. Aromatase activity, serum oestradiol and their correlation with demographic indices. J Steroid Biochem Mol Biol. 1992;41(3-8):769-71.https://doi.org/10.1016/0960-0760(92)90421-E

20. Motlani V, Motlani G, Pamnani S, Sahu A, Acharya N. Endocrine changes in postmenopausal women: a comprehensive view. Cureus. 2023 Dec 29;15(12). doi: 10.7759/cureus.51287

21. Vieira-Potter VJ, Mishra G, Townsend KL. Health of adipose tissue: oestrogen matters. Nature Reviews Endocrinology. 2026;22(2):76-91. https://doi.org/10.1038/s41574-025-01180-2

22. Szymczak J, Milewicz A, Thijssen JHH, Blankenstein MA, Daroszewski J. Concentration of Sex Steroids in Adipose Tissue after Menopause. Steroids. 1998;63(5):319-21. https://doi.org/10.1016/S0039-128X(98)00019-1

23. Schmandt RE, Iglesias DA, Co NN, Lu KH. Understanding obesity and endometrial cancer risk: opportunities for prevention. Am J Obstet Gynecol.2011;205(6):518-25.
https://doi.org/10.1016/j.ajog.2011.05.042

24. Aune D, Navarro Rosenblatt DA, Chan DS, Vingeliene S, Abar L, Vieira AR, et al. Anthropometric factors and endometrial cancer risk: a systematic review and dose-response meta-analysis of prospective studies. Ann Oncol. 2015;26(8):1635-48.
https://doi.org/10.1093/annonc/mdv142

25. Stanczyk FZ, Sriprasert I, Karim R, Hwang-Levine J, Mack WJ, Hodis HN. Concentrations of endogenous sex steroid hormones and SHBG in healthy postmenopausal women. J Steroid Biochem Mol Biol. 2022;223:106080. https://doi.org/10.1016/j.jsbmb.2022.106080

26. Moyer AM, de Andrade M, Weinshilboum RM, Miller VM. Influence of SULT1A1 genetic variation on age at menopause, estrogen levels, and response to hormone therapy in recently postmenopausal white women. Menopause. 2016;23(8):863-9.
doi: 10.1097/GME.0000000000000648
27. Bukato K, Kostrzewa T, Gammazza AM, Gorska-Ponikowska M, Sawicki S. Endogenous estrogen metabolites as oxidative stress mediators and endometrial cancer biomarkers. Cell Commun Signal. 2024;22(1):205. https://doi.org/10.1186/s12964-024-01583-0
28. Cornel KMC, Bongers MY, Kruitwagen RPFM, Romano A. Local estrogen metabolism (intracrinology) in endometrial cancer: A systematic review. Molecular and Cellular Endocrinology. 2019;489:45-65.
29. Koos RD. Minireview: Putting physiology back into estrogens' mechanism of action. Endocrinology. 2011;152(12):4481-8. DOI: 10.1210/en.2011-1449