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Role of metabolic syndrome and obesity in the development of gynecologic neoplasia in postmenopausal women: clinical, hormonal and diagnostic correlates

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Postmenopausal women represent a population with a significantly increased risk of developing gynecological neoplasms. Obesity and metabolic syndrome may contribute to carcinogenesis through complex metabolic and endocrine mechanisms, including insulin resistance, altered sex steroid metabolism, and increased peripheral estrogen production.

Aim – to evaluate the association between obesity, metabolic syndrome components, and hormonal alterations with the development of gynecologic neoplasia in postmenopausal women.

Materials and methods. This study included retrospective and prospective analyses of 306 postmenopausal women with gynecologic tumors. Metabolic syndrome was assessed using biochemical parameters, abdominal circumference, and arterial blood pressure. In the prospectively assessed cohort, anthropometric measurements and hormonal profiles were additionally evaluated. Imaging studies, tumor marker CA-125, and histological verification were performed.

Results. Gynecologic neoplasia distribution was as follows: ovarian cancer (31.7%), endometrial hyperplasia (21.2%), endometrial cancer (16.3%), and uterine leiomyoma (15.4%). Obesity was significantly more prevalent among women with endometrial pathology, reaching 70.0% in endometrial cancer and 63.1% in endometrial hyperplasia. The mean body mass index (BMI) was highest in patients with endometrial cancer (32.7 ± 1.0 kg/m²). A strong association between obesity and endometrial pathology was confirmed. Estrone levels showed a positive correlation with BMI and markers of insulin resistance in the prospectively assessed cohort. Components of metabolic syndrome were significantly more frequent in patients with endometrial hyperplasia and carcinoma compared with other gynecologic tumors.

Conclusion. Obesity and metabolic syndrome are strongly associated with endometrial hyperplasia and endometrial cancer in postmenopausal women. Metabolic and endocrine alterations, particularly hyperinsulinemia and increased estrone bioavailability, create a hormonally permissive environment for endometrial neoplastic transformation. Early metabolic assessment may improve risk stratification and support timely diagnosis.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent from women was obtained for the study. The authors declare no conflict of interest.

Keywords: postmenopause, obesity, metabolic syndrome, endometrial cancer, ovarian cancer.

Роль метаболічного синдрому та ожиріння в розвитку гінекологічних неоплазій у жінок у постменопаузі: клінічні, гормональні та діагностичні кореляти

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Жінки в постменопаузі є популяцією з істотно підвищеним ризиком розвитку гінекологічних неоплазій. Ожиріння та метаболічний синдром сприяють канцерогенезу за допомогою складних метаболічних та ендокринних механізмів, зокрема інсулінорезистентності, порушення метаболізму статевих стероїдів та посиленої периферичної продукції естрогенів.

Мета – оцінити взаємозв'язок між ожирінням, компонентами метаболічного синдрому та гормональними змінами з розвитком гінекологічних неоплазій у жінок у постменопаузі.

Матеріали та методи. У дослідженні було охоплено ретроспективний та проспективний аналізи 306 жінок у постменопаузі з гінекологічними пухлинами. Метаболічний синдром оцінено на підставі біохімічних показників, окружності талії та рівня артеріального тиску. У проспективній групі додатково проводили антропометричні вимірювання та оцінку гормонального профілю. Виконано методи візуалізації, визначення пухлинного маркера СА-125 та гістологічну верифікацію діагнозу.

Результати. Розподіл гінекологічних неоплазій був таким: рак яєчників – 31,7%, гіперплазія ендометрію – 21,2%, рак ендометрію – 16,3%, міома матки – 15,4%. Ожиріння достовірно частіше спостерігалось в жінок із патологією ендометрію, досягаючи 70,0% при раку ендометрію та 63,1% при гіперплазії ендометрію. Середній індекс маси тіла (ІМТ) був максимальним у пацієнток із раком ендометрію ($32,7 \pm 1,0$ кг/м²). Логістичний регресійний аналіз продемонстрував виражену асоціацію між ожирінням та патологією ендометрію. У проспективній групі виявлено позитивну кореляцію рівня естрогену з ІМТ та маркерами інсулінорезистентності. Компоненти метаболічного синдрому значно частіше зустрічалися в пацієнток із гіперплазією та раком ендометрію порівняно з іншими гінекологічними пухлинами.

Висновок. Ожиріння та метаболічний синдром тісно пов'язані з гіперплазією та раком ендометрію в жінок у постменопаузі. Метаболічні та ендокринні порушення, зокрема гіперінсулінемія та підвищення біодоступності естрогену, формують гормонально сприятливе середовище

для неопластичної трансформації ендометрію. Рання оцінка метаболічного статусу може покращити стратифікацію ризику та сприяти своєчасній діагностиці.

Дослідження проведено відповідно до принципів Гельсінської декларації. Для проведення дослідження було отримано інформовану згоду жінок.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: постменопауза, ожиріння, метаболічний синдром, рак ендометрію, рак яєчників.

Introduction

The postmenopausal period, which may span 30-50 years of a woman's life, is marked by profound endocrine transitions that substantially modify metabolic and hormonal regulation. These changes create a biological milieu favorable for the development of gynecologic neoplasia [7]. With global life expectancy increasing, a growing proportion of women remain in the postmenopausal state for extended periods, thereby experiencing long-term exposure to these oncogenic influences [12].

Obesity and metabolic syndrome have emerged as principal modifiable determinants of gynecologic cancer risk. According to the World Health Organization (WHO), the prevalence of obesity in women exceeds 30% globally and continues to rise sharply after the age of 60 [12]. Postmenopausal visceral adiposity intensifies peripheral aromatization of androgens into estrone, the predominant circulating estrogen in this life stage, thereby enhancing estrogen-dependent proliferative signaling [4,5].

Contemporary research highlights several mechanistic pathways linking metabolic syndrome to gynecologic tumorigenesis. Hyperinsulinemia increases insulin-like growth factor 1 (IGF-1) activity, promoting cellular proliferation and reducing apoptosis [10,13]. Insulin resistance decreases hepatic production of sex hormone-binding globulin (SHBG), leading to increased levels of bioavailable estradiol [8]. Enhanced aromatase activity in adipose tissue further elevates estrone concentrations, stimulating estrogen receptor-mediated transcriptional programs associated with tumorigenesis [5,6]. Additionally, adrenal hyperandrogenism, present in approximately 38% of postmenopausal women, provides an additional substrate for peripheral estrogen conversion [7]. Chronic anovulation and relative progesterone deficiency amplify these effects, resulting in prolonged unopposed estrogen exposure [2].

These hormonal and metabolic disturbances generate conditions conducive to the development of endometrial hyperplasia, type I endometrial carcinoma, ovarian epithelial tumors, and continued leiomyoma growth in postmenopausal women. Recent

epidemiologic studies confirm that metabolic syndrome significantly increases the risk of endometrial cancer, with the strongest associations observed among obese postmenopausal women [9,11]. Similar metabolic patterns have been implicated in ovarian carcinogenesis, particularly through inflammatory and IGF-1-mediated pathways [6].

Given the high prevalence of obesity in older women and its profound biological influence on carcinogenic pathways, evaluating the contribution of metabolic syndrome to the development of gynecologic neoplasia is both clinically relevant and timely. This study investigates these associations using data from an extensive cohort of postmenopausal women.

Aim of the study: to investigate the role of metabolic syndrome and obesity in the development of gynecologic neoplasia in postmenopausal women by analyzing clinical, biochemical, hormonal, and imaging findings.

Materials and methods of the study

This study included retrospective and prospective cohorts of postmenopausal women examined and treated at the Oncology Clinic of Azerbaijan Medical University. In total, 306 postmenopausal women with genital tumors of various localizations were included in the study. The mean age of the patients was 60.5 ± 0.4 years, ranging from 46 to 83 years. The mean age at menopause onset was 49.3 ± 0.2 years (45–58 years), while the mean duration of the postmenopausal period was 9.8 ± 0.4 years (range: 2–37 years).

Clinical evaluation, anthropometric assessment (body mass index (BMI) classified according to WHO standards), hormonal testing (estrone, estradiol, testosterone, dehydroepiandrosterone sulfate (DHEA-S), prolactin, follicle-stimulating hormone (FSH), luteinizing hormone (LH)), biochemical profiling (glucose, lipid parameters, insulin levels), tumor marker CA-125, transvaginal ultrasound, and magnetic resonance imaging (MRI) were used. Pre- and postoperative histological confirmation of the diagnosis was obtained. Special attention was given to correlations between metabolic indicators (BMI, insulin resistance, hyperandrogenism) and gynecologic neoplasia.

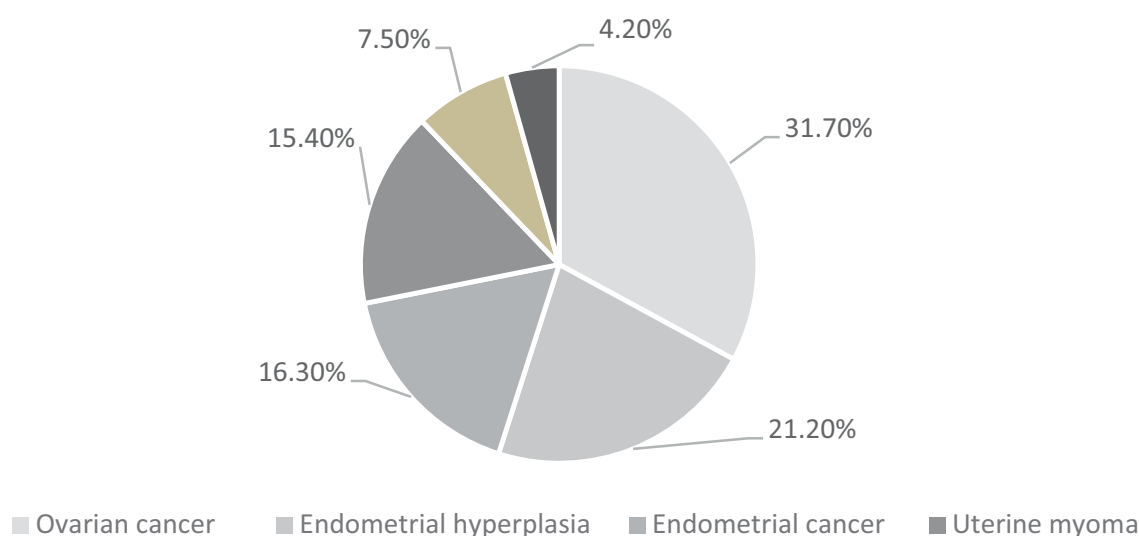


Fig 1. Prevalence of gynecologic pathology in postmenopausal women

Quantitative and qualitative data were analyzed using standard methods of medical statistics. Variational, correlation, analyses of variance (ANOVA), discriminant, and Receiver Operating Characteristic (ROC) analyses were performed. Descriptive statistics included mean (M), standard deviation (SD), standard error of the mean (SEM), 95% confidence interval (95% CI), odds ratio (OR), and minimum and maxi-

um values. Statistical analyses were conducted using Microsoft Excel 2013 and SPSS 26 programs.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of Azerbaijan Medical University. Written informed consent was obtained from all participants prior to enrollment in the study.

Table 1

Hormone indicators in patients with genital neoplasms in the postmenopausal period

Hormones	Genital tumors	M	±m	min	max
Prl	Myoma	671.8	278.6	235.4	1190
	Endometrial hyperplasia	802.9	191.7	42.7	2229
	Endometrial cancer	467.3	85.1	310	602
	Ovarian cancer	560.1	104.6	288.5	908.9
	Benign ovarian tumors	581.6	272.7	161.8	1093
DHEA-S	Myoma	121.2	22.9	11.3	309.7
	Endometrial hyperplasia	121.8	22.5	15.67	545.8
	Endometrial cancer	92.9	24.7	25.4	348.9
	Ovarian cancer	131.6	20.6	40.53	360.7
	Benign ovarian tumors	118.9	18.2	58.68	232.2
E1	Myoma	100.6	11.3	40.23	170.21
	Endometrial hyperplasia	122.2	8.2	40.2	200.9
	Endometrial cancer	116.6	13.7	44.24	191.22
	Ovarian cancer	91.0	13.4	30.9	198.1
	Benign ovarian tumors	102.9	15.1	48.16	180.91

Notes: Prl – prolactin; E1-Estrone, DHEA-S – dehydroepiandrosterone sulfate

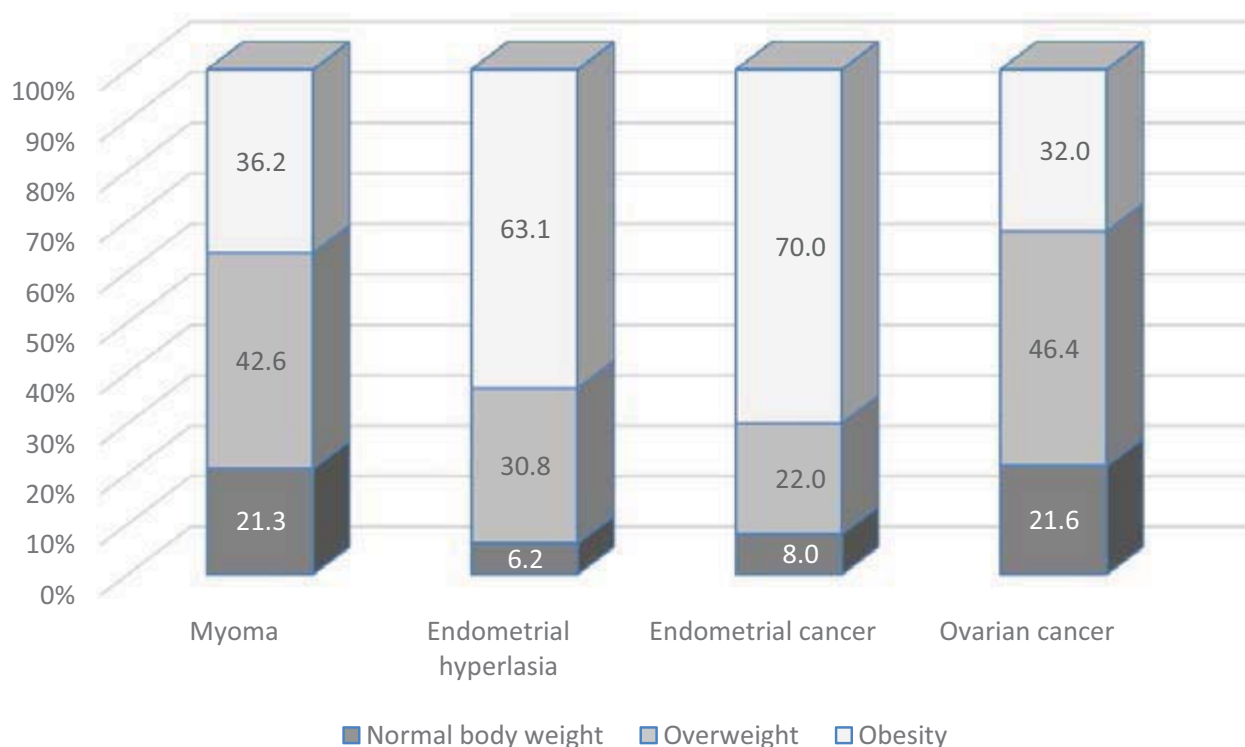


Fig 2. BMI indicators in patients with genital tumors in the postmenopausal period

Results of the study and discussion

Among the examined postmenopausal women, metabolic syndrome and obesity were identified as major contributing factors to gynecologic neoplasia. Obesity was the leading cause of hyperandrogenism in 40.0% of cases. The distribution of gynecologic neoplasia included: ovarian cancer in 97 (31.7%) patients, endometrial hyperplasia in 65 (21.2%), endometrial cancer in 50 (16.3%), leiomyoma in 47 (15.4%), and cervical cancer in 13 (4.2%) of the examined. (Fig 1)

Endometrial thickness averaged 24.9 ± 27 mm in women with endometrial cancer, establishing it as a critical diagnostic marker. A strong association was found between obesity and advanced-stage ovarian cancer; 64 (66.0%) patients were diagnosed at stage III. Hyperinsulinemia and reduced SHBG were common findings, leading to elevated biologically active estrogens. Women with endometrial hyperplasia frequently exhibited insulin resistance, elevated estrone, and low progesterone levels.

These conditions were significantly more frequent in women with obesity, insulin resistance, and metabolic syndrome.

The findings of the present study indicate that excess body weight represents one of the major risk factors for the development of genital neoplasms.

Assessment of the BMI revealed that in patients with ovarian cancer, the mean BMI was 28.7 ± 0.6 kg/m², and obesity of varying severity was observed in 31 (32.0%) of patients. In patients with endometrial cancer, the mean BMI was 32.7 ± 1.0 kg/m², and the prevalence of obesity in this group reached 70.0%.

All the examined patients were divided into groups according to the localization and histological type of the tumors. Mean BMI differed significantly across diagnostic groups (ANOVA, $p < 0.001$). Patients with endometrial cancer demonstrated the highest BMI values (32.7 ± 1.0 kg/m²), followed by women with endometrial hyperplasia (31.9 ± 0.8 kg/m²), compared with ovarian cancer (28.7 ± 0.6 kg/m²) and leiomyoma (29.5 ± 0.9 kg/m²).

Women with obesity had a significantly higher likelihood of developing endometrial hyperplasia and endometrial cancer compared with non-obese patients (OR $\approx$ 3.8–4.0, $p < 0.01$).

In patients with endometrial hyperplasia, the average BMI was 31.9 ± 0.8 kg/m², and obesity was identified in 63.1% of patients. A similar situation was observed in postmenopausal patients with progressive growth of uterine fibroids. The mean BMI was 29.5 ± 0.9 kg/m², ranging from 19 to 44 kg/m², while the prevalence of obesity was 36.2% (Fig. 2).

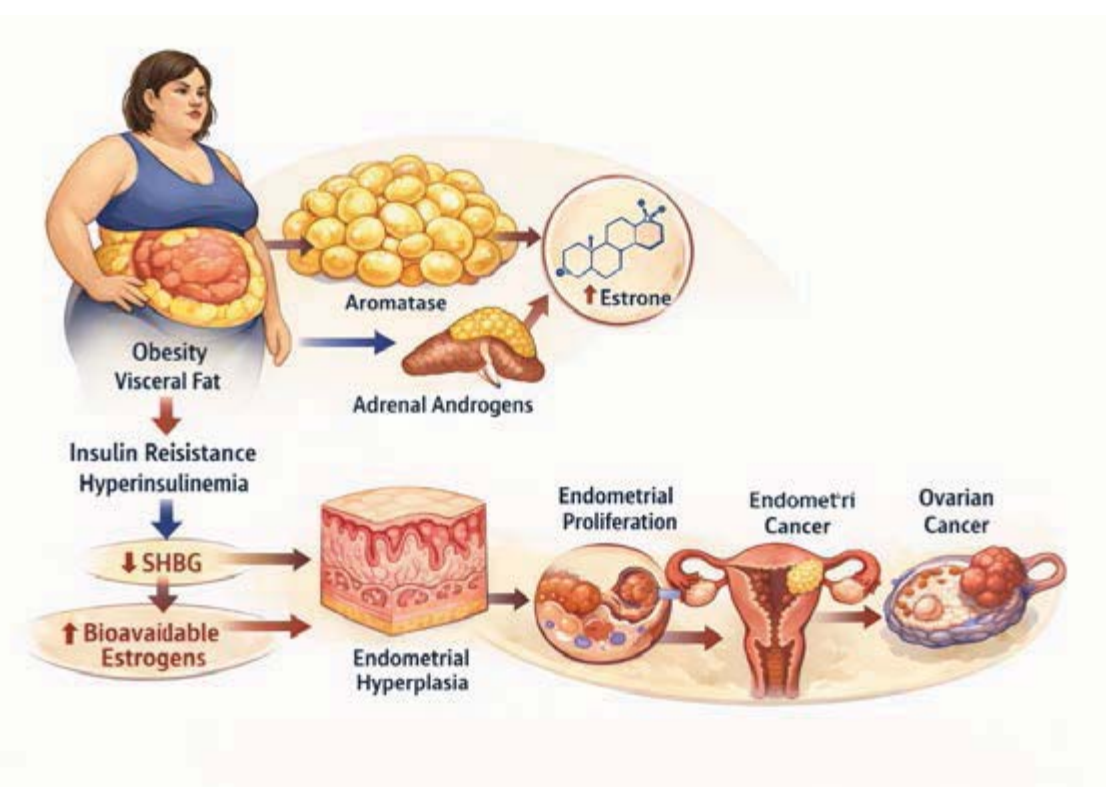


Fig. 3. Pathophysiological links between metabolic syndrome and gynecologic neoplasia in postmenopausal women. Obesity and visceral adiposity promote insulin resistance and hyperinsulinemia, resulting in decreased SHBG levels and increased bioavailability of estrogens. Enhanced aromatase activity in adipose tissue and adrenal androgen excess lead to elevated estrone levels. These metabolic and endocrine alterations stimulate endometrial proliferation and contribute to the development of endometrial hyperplasia, endometrial cancer, and progression of ovarian cancer

Concurrently, patients with endometrial and ovarian cancers exhibited hormonal imbalance manifested by elevated estrone and DHEA-S levels against a background of reduced estradiol and testosterone concentrations, indicating the contribution of dyshormonal changes to the pathogenesis of endometrial neoplasms (Table 1).

Elevated BMI may promote tumorigenesis through obesity-induced endocrine alterations, which create a hormonally permissive environment for endometrial neoplastic transformation.

Correlation analysis revealed a significant positive association between BMI and Estrone levels ($r \approx 0.42$, $p < 0.01$). Reduced SHBG levels were associated with increased bioavailable estrogen fractions, particularly in women with endometrial hyperplasia and carcinoma. (Fig 3)

The findings of this study confirm that metabolic syndrome is a key driver of gynecologic neoplasia in postmenopausal women. The metabolic-endocrine axis, consisting of hyperinsulinemia, estrone dominance, and adrenal androgen excess, creates a sustained proliferative environment that promotes malignant transformation.

Recent literature from 2020 to 2025 supports these findings. A series of updated systematic reviews demonstrated that metabolic syndrome significantly increases the risk of endometrial carcinoma, with pooled ORs ranging from 1.37 to 2.0 [9,11]. B. Park et al. (2022) further noted that this association is strongest in obese postmenopausal women. This reinforces the combined oncogenic effect of adiposity and metabolic dysfunction. These reports align with our observation that endometrial hyperplasia and carcinoma were markedly more prevalent in women exhibiting obesity and insulin resistance.

Additionally, J.P. Fernandes et al. (2022) reported a high prevalence of metabolic syndrome – 61% – among patients with endometrial cancer, particularly among those with elevated inflammatory markers. This finding corresponds to our data showing that chronic low-grade inflammation, insulin resistance, and disrupted sex steroid balance were frequent among women with endometrial pathology [3].

Recent mechanistic analyses also highlight the central role of hyperinsulinemia. B.K. Subedi et al.

(2025) and X. Zhang et al. (2023) demonstrated that elevated insulin suppresses SHBG, thereby enhancing the bioavailability of estrogens and amplifying IGF-1-mediated proliferative signaling [10,13]. I.M. Ordeanu et al. (2025) expanded on this mechanism, emphasizing that hyperinsulinemia dramatically alters the endocrine environment in postmenopausal women [8]. These observations mirror our findings that women with endometrial hyperplasia and carcinoma often exhibit reduced SHBG and increased estrone levels.

From an inflammatory perspective, the concept of «metabolic inflammation» has been increasingly recognized in oncology. A. Da Cunha Junior et al. (2025) demonstrated that obesity-associated cytokines and altered adipokines promote angiogenesis, extracellular matrix remodeling, and epithelial – mesenchymal transition – mechanisms that may accelerate tumor progression. This aligns with our results indicating that metabolic syndrome and obesity were strongly associated with endometrial and ovarian tumor development. B.H. Harris et al. (2022) further emphasized that up to 40% of cancers in high-income countries are now linked to obesity, reinforcing the global relevance of these mechanisms [1,4].

In the context of ovarian cancer, recent reviews have underscored the importance of adipocyte-tumor interactions, showing that insulin resistance, chronic inflammation, and IGF-1 pathways contribute to tumor progression and chemoresistance [6]. Although our study did not assess molecular markers, the predominance of advanced-stage (III) ovarian cancer in metabolically compromised women is consistent with these mechanistic insights.

Collectively, the agreement between our findings and contemporary research supports the modern concept of «metabolically driven gynecologic carcinogenesis». The clustering of obesity, insulin resistance, estrone excess, reduced SHBG, and chronic inflammation in women with gynecologic neoplasia strongly reinforces the need for integrating metabolic assessment into gynecologic oncology practice.

Metabolic syndrome and obesity exert profound influence on the development and progression of gynecologic neoplasia in postmenopausal women. Through mechanisms involving hyperinsulinemia, increased estrone production, chronic inflammation, and hormonal imbalance, metabolic disturbances significantly elevate the risk of endometrial hyperplasia, carcinoma, ovarian cancer, and leiomyoma

growth. Comprehensive metabolic assessment and targeted lifestyle or pharmacological interventions may reduce cancer risk and improve diagnostic accuracy.

This study has several limitations that should be acknowledged. First, the retrospective component of the study did not include a complete hormonal profile or anthropometric measurements such as BMI. Therefore, assessment of metabolic status in these patients was based primarily on biochemical parameters, including fasting blood glucose, lipid profile, abdominal circumference, and arterial blood pressure. Although these parameters are integral components of metabolic syndrome, the absence of detailed hormonal and BMI data limits the ability to fully characterize endocrine and metabolic interactions in the retrospective cohort.

Second, the study was conducted at a single tertiary oncology center, which may limit the generalizability of the findings. Finally, molecular markers of insulin signaling, inflammation, and estrogen receptor activity were not assessed. Future multi-center studies incorporating comprehensive metabolic, hormonal, and molecular profiling are warranted to further elucidate the mechanistic links between metabolic syndrome and gynecologic neoplasia.

Conclusion

Obesity and metabolic syndrome significantly increase the risk of endometrial hyperplasia, endometrial cancer, ovarian cancer, and progression of myoma in postmenopausal women.

According to the results of the study, it was confirmed that:

- 40.0% of women with hyperandrogenism had obesity as the primary cause.
- Hyperinsulinemia reduced SHBG → free estradiol increased.
- Elevated androgens (testosterone, DHEA-S) were common in obese women.
- Combination of obesity + hyperinsulinemia → strongest predictor of endometrial hyperplasia and carcinoma.

Given the high prevalence of metabolic disorders in aging women, early metabolic and hormonal screening is critical for prevention and timely diagnosis of gynecologic neoplasia.

The authors declare no conflict of interest

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