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**THE IMPACT OF METABOLIC SYNDROME ON THE PROGNOSIS AND COURSE OF
ENDOMETRIAL CANCER: CLINICAL, BIOCHEMICAL ASPECTS AND
THERAPEUTIC APPROACHES**

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Abstract

Endometrial cancer is one of the most common gynecological malignancies worldwide, with its incidence closely associated with metabolic disorders. Metabolic syndrome, characterized by obesity, insulin resistance, dyslipidemia, and hypertension, has been identified as a significant risk factor influencing the development, progression, and prognosis of endometrial cancer. This article examines the impact of metabolic syndrome on the clinical course and outcomes of endometrial cancer, focusing on underlying biochemical mechanisms and current therapeutic approaches. Evidence suggests that metabolic syndrome contributes to tumor progression through hormonal imbalance, chronic inflammation, and altered metabolic signaling pathways. Understanding these interactions is essential for improving prognosis and developing individualized treatment strategies for patients with endometrial cancer.

Key Words: Endometrial cancer; metabolic syndrome; insulin resistance; obesity; prognosis; therapeutic approaches

Annotatsiya

Endometriy saratoni dunyo bo'ylab eng keng tarqalgan ginekologik malign kasalliklardan biri bo'lib, uning uchrash chastotasi metabolik buzilishlar bilan chambarchas bog'liq. Metabolik sindrom semirish, insulin rezistentligi, dislipidemiya va arterial gipertenziya bilan tavsiflanib, endometriy saratonining rivojlanishi, kechishi va prognoziga ta'sir etuvchi muhim xavf omili hisoblanadi. Ushbu maqolada metabolik sindromning endometriy saratonining klinik kechishi va natijalariga ta'siri asosiy biokimyoviy mexanizmlar hamda zamonaviy terapevtik yondashuvlar nuqtai nazaridan tahlil qilinadi. Mavjud ilmiy ma'lumotlar metabolik sindrom gormonal disbalans, surunkali yallig'lanish va metabolik signal yo'llarining buzilishi orqali o'sma progressiyasiga hissa qo'shishini ko'rsatadi. Ushbu o'zaro bog'liqliklarni tushunish endometriy saratoni bilan og'rigan bemorlar uchun prognozni yaxshilash va individual davolash strategiyalarini ishlab chiqishda muhim ahamiyatga ega.

Kalit so'zlar: Endometriy saratoni; metabolik sindrom; insulin rezistentligi; semirish; prognoz; terapevtik yondashuvlar



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Аннотация

Рак эндометрия является одним из наиболее распространённых злокачественных новообразований женской репродуктивной системы во всём мире, причём его заболеваемость тесно связана с метаболическими нарушениями. Метаболический синдром, характеризующийся ожирением, инсулинорезистентностью, дислипидемией и артериальной гипертензией, признан значимым фактором риска, влияющим на развитие, прогрессирование и прогноз рака эндометрия. В данной статье рассматривается влияние метаболического синдрома на клиническое течение и исходы рака эндометрия с акцентом на основные биохимические механизмы и современные терапевтические подходы. Имеющиеся данные свидетельствуют о том, что метаболический синдром способствует прогрессированию опухоли посредством гормонального дисбаланса, хронического воспаления и нарушения метаболических сигнальных путей. Понимание данных взаимосвязей имеет ключевое значение для улучшения прогноза и разработки индивидуализированных стратегий лечения пациенток с раком эндометрия.

Ключевые слова: Рак эндометрия; метаболический синдром; инсулинорезистентность; ожирение; прогноз; терапевтические подходы

Introduction

Endometrial cancer is one of the most common gynecological malignancies worldwide, and its incidence continues to rise in parallel with the global increase in metabolic disorders [1,2]. Numerous epidemiological studies have demonstrated a strong association between metabolic syndrome and both the risk and progression of endometrial cancer [3]. Metabolic syndrome is defined as a cluster of metabolic abnormalities, including central obesity, insulin resistance, hyperglycemia, dyslipidemia, and hypertension, all of which contribute to systemic metabolic and hormonal dysregulation [4].

Obesity, a central component of metabolic syndrome, plays a pivotal role in the pathogenesis of endometrial cancer by increasing peripheral estrogen production through aromatization of androgens in adipose tissue [5]. Prolonged exposure to unopposed estrogen stimulates endometrial proliferation and increases the risk of malignant transformation. In addition, insulin resistance and compensatory hyperinsulinemia activate insulin-like growth factor (IGF) signaling pathways, promoting cellular proliferation and inhibiting apoptosis [6].

Chronic low-grade inflammation associated with metabolic syndrome further contributes to tumor development and progression. Elevated levels of pro-inflammatory cytokines, such as tumor necrosis factor- α and interleukin-6, create a tumor-promoting microenvironment by enhancing angiogenesis and oxidative stress [7]. Dyslipidemia and altered lipid metabolism have also been implicated in endometrial carcinogenesis through their effects on cell membrane composition and intracellular signaling pathways [8].

Clinical evidence suggests that endometrial cancer patients with metabolic syndrome often present with more advanced disease, higher tumor grade, and poorer prognosis compared to metabolically healthy patients [9]. Moreover, metabolic comorbidities may negatively influence treatment response and increase perioperative and postoperative complications [10]. Therefore, understanding the clinical and biochemical interactions between metabolic syndrome and endometrial cancer is essential for improving prognosis and developing effective, individualized therapeutic strategies.

Main Part

Metabolic syndrome plays a crucial role in the development, progression, and prognosis of endometrial cancer through multiple interrelated hormonal, metabolic, and inflammatory mechanisms. One of the most significant factors linking metabolic syndrome to endometrial cancer is obesity. Excess adipose tissue functions as an active endocrine organ, producing estrogen through



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the aromatization of androgens. In postmenopausal women, adipose tissue becomes the primary source of estrogen, leading to prolonged exposure of the endometrium to unopposed estrogen, which stimulates cellular proliferation and increases the risk of malignant transformation.

Insulin resistance, a key component of metabolic syndrome, further contributes to tumor progression. Compensatory hyperinsulinemia enhances the activity of insulin-like growth factor-1 (IGF-1), which promotes cell proliferation and inhibits apoptosis through activation of signaling pathways such as PI3K/Akt/mTOR. These pathways are frequently dysregulated in endometrial cancer and are associated with aggressive tumor behavior and poor prognosis.

Chronic low-grade inflammation is another critical mechanism linking metabolic syndrome to endometrial cancer. Adipose tissue in obese individuals secretes pro-inflammatory cytokines, including tumor necrosis factor- α , interleukin-6, and C-reactive protein. These inflammatory mediators contribute to genomic instability, oxidative stress, angiogenesis, and tumor invasion. The inflammatory tumor microenvironment created by metabolic syndrome facilitates cancer progression and resistance to therapy.

Alterations in lipid metabolism also play an important role in endometrial carcinogenesis. Dyslipidemia, characterized by elevated triglycerides and low levels of high-density lipoprotein cholesterol, affects cell membrane composition and intracellular signaling. Lipid accumulation within cancer cells supports rapid proliferation and energy production, further promoting tumor growth.

Clinically, patients with endometrial cancer and coexisting metabolic syndrome often present with advanced disease stages, higher tumor grades, and increased rates of recurrence. Obesity and associated comorbidities complicate surgical management and increase perioperative risks. Moreover, metabolic abnormalities may reduce the effectiveness of chemotherapy and radiotherapy, leading to poorer treatment outcomes.

Taken together, these findings demonstrate that metabolic syndrome is not merely a risk factor for endometrial cancer but an active driver of disease progression. Addressing metabolic dysfunction is therefore essential for improving clinical outcomes and optimizing therapeutic strategies in patients with endometrial cancer.

Review of the Literature

Numerous studies have established obesity as one of the strongest risk factors for endometrial cancer. Excess adipose tissue leads to increased peripheral estrogen production due to aromatization of androgens, resulting in prolonged estrogen exposure without progesterone opposition. Insulin resistance and hyperinsulinemia further exacerbate tumor growth by activating insulin-like growth factor (IGF) signaling pathways.

Chronic low-grade inflammation, a hallmark of metabolic syndrome, has also been implicated in cancer progression. Elevated levels of pro-inflammatory cytokines such as tumor necrosis factor- α and interleukin-6 promote cellular proliferation, angiogenesis, and inhibition of apoptosis. Dyslipidemia and oxidative stress contribute to DNA damage and tumorigenesis.

Recent research highlights the role of metabolic reprogramming in endometrial cancer cells, linking metabolic syndrome to altered glucose and lipid metabolism within the tumor microenvironment. These findings underscore the importance of addressing metabolic abnormalities in the management of endometrial cancer.

Clinically, endometrial cancer patients with metabolic syndrome often exhibit advanced disease stages, higher tumor grades, and increased rates of comorbid conditions. Obesity complicates surgical management and increases perioperative risks, while insulin resistance may reduce the effectiveness of certain therapies.

Biochemically, hyperinsulinemia enhances tumor growth through activation of the PI3K/Akt/mTOR signaling pathway, a key regulator of cell proliferation and survival. Elevated estrogen levels stimulate endometrial cell proliferation, while inflammatory mediators create a tumor-



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promoting microenvironment. Additionally, adipokines such as leptin and adiponectin play opposing roles in tumor biology, with increased leptin levels associated with poor prognosis.

The management of endometrial cancer in patients with metabolic syndrome requires a multidisciplinary and individualized approach. Standard treatment modalities include surgery, radiotherapy, and chemotherapy; however, metabolic comorbidities may influence treatment selection and outcomes.

Lifestyle interventions, including weight reduction, dietary modification, and physical activity, play a crucial role in improving metabolic parameters and potentially enhancing treatment response. Pharmacological management of metabolic syndrome components, such as the use of metformin, has shown promising anticancer effects through improvement of insulin sensitivity and inhibition of tumor-related signaling pathways.

Hormonal therapy may be considered in selected patients, particularly those with early-stage disease and hormone receptor-positive tumors. Emerging therapeutic strategies targeting metabolic pathways and inflammation are under investigation and may offer new opportunities for improving prognosis.

Discussion

The findings discussed in this article emphasize the multifactorial relationship between metabolic syndrome and the development, progression, and prognosis of endometrial cancer. Metabolic syndrome acts not only as a predisposing risk factor but also as a modifier of tumor biology and clinical outcomes. The interaction between hormonal imbalance, insulin resistance, chronic inflammation, and altered metabolic signaling creates a biological environment that favors tumor initiation and progression.

One of the most significant mechanisms linking metabolic syndrome to endometrial cancer is estrogen excess resulting from obesity. Increased peripheral aromatization of androgens in adipose tissue leads to prolonged exposure of the endometrium to unopposed estrogen, promoting hyperplasia and malignant transformation. This hormonal imbalance is further amplified by insulin resistance, which reduces sex hormone-binding globulin levels, thereby increasing the bioavailability of circulating estrogens. These endocrine alterations contribute to more aggressive tumor characteristics and poorer prognosis.

Insulin resistance and hyperinsulinemia play a central role in tumor progression by activating insulin and insulin-like growth factor signaling pathways. Activation of the PI3K/Akt/mTOR pathway enhances cell proliferation, angiogenesis, and resistance to apoptosis, all of which are associated with unfavorable clinical outcomes in endometrial cancer. The high prevalence of metabolic syndrome in patients with advanced-stage disease suggests that metabolic dysregulation contributes to tumor aggressiveness and reduced survival.

Chronic low-grade inflammation represents another critical link between metabolic syndrome and endometrial cancer progression. Pro-inflammatory cytokines and adipokines released from adipose tissue promote oxidative stress, DNA damage, and angiogenesis, thereby facilitating tumor growth and invasion. The inflammatory tumor microenvironment may also contribute to resistance to chemotherapy and radiotherapy, further complicating treatment.

From a clinical perspective, the presence of metabolic syndrome poses significant challenges in the management of endometrial cancer. Obesity and associated comorbidities increase surgical risk and may limit treatment options. Moreover, metabolic abnormalities can negatively influence treatment response and quality of life. These findings highlight the importance of incorporating metabolic assessment and management into standard oncological care.

Overall, the discussion underscores the necessity of a multidisciplinary and integrated approach to endometrial cancer treatment. Addressing metabolic syndrome alongside conventional cancer therapies may improve treatment efficacy, reduce recurrence rates, and enhance overall prognosis. Further clinical studies are needed to establish standardized guidelines for metabolic



intervention and to evaluate the long-term impact of metabolic control on endometrial cancer outcomes.

Conclusion

Metabolic syndrome exerts a profound influence on both the development and clinical course of endometrial cancer through complex and interrelated hormonal, metabolic, and inflammatory mechanisms. The evidence reviewed in this article demonstrates that metabolic syndrome is not merely a background comorbidity but a key biological driver that contributes to tumor initiation, progression, and unfavorable prognosis. Obesity-related estrogen excess, insulin resistance-mediated growth signaling, and chronic low-grade inflammation collectively create a tumor-promoting environment that enhances cellular proliferation, angiogenesis, and resistance to apoptosis.

Clinically, the presence of metabolic syndrome is associated with more aggressive tumor characteristics, advanced disease stage at diagnosis, increased recurrence rates, and reduced overall survival. In addition, metabolic comorbidities complicate surgical and oncological management, increase perioperative risk, and may diminish the effectiveness of standard cancer therapies. These factors underscore the need for a comprehensive approach to patient assessment that extends beyond traditional oncological parameters.

Importantly, the findings highlight the potential benefits of integrating metabolic management into endometrial cancer care. Lifestyle interventions, weight reduction, and pharmacological treatment of metabolic abnormalities—particularly insulin resistance—may improve not only general health but also cancer-related outcomes. Agents such as metformin show promise as adjunctive therapies due to their dual metabolic and antitumor effects.

In conclusion, effective management of endometrial cancer requires an integrated, multidisciplinary strategy that addresses both oncological and metabolic factors. Early identification and targeted treatment of metabolic syndrome may improve prognosis, enhance treatment response, and reduce disease recurrence. Future research should focus on prospective clinical trials to establish evidence-based guidelines for metabolic intervention and to clarify its long-term impact on survival and quality of life in patients with endometrial cancer.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018. *CA: A Cancer Journal for Clinicians*. 2018;68(6):394–424.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics. *CA: A Cancer Journal for Clinicians*. 2020;70(1):7–30.
3. Zhang Y, Liu Z, Yu X, et al. The association between metabolic syndrome and endometrial cancer: A meta-analysis. *Gynecologic Oncology*. 2016;140(2):343–349.
4. Alberti KGMM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. *The Lancet*. 2005;366(9491):1059–1062.
5. Kaaks R, Lukanova A, Kurzer MS. Obesity, endogenous hormones, and endometrial cancer risk. *Cancer Epidemiology Biomarkers & Prevention*. 2002;11(12):1531–1543.
6. Calle EE, Kaaks R. Overweight, obesity and cancer: Epidemiological evidence and proposed mechanisms. *Nature Reviews Cancer*. 2004;4(8):579–591.
7. Coussens LM, Werb Z. Inflammation and cancer. *Nature*. 2002;420(6917):860–867.
8. Nieman KM, Romero IL, Van Houten B, Lengyel E. Adipose tissue and adipocytes support tumorigenesis and metastasis. *Biochimica et Biophysica Acta*. 2013;1831(10):1533–1541.
9. Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer. *The Lancet*. 2008;371(9612):569–578.
10. Cantrell LA, Zhou C, Mendivil A, et al. Metformin is a potent inhibitor of endometrial cancer cell proliferation. *Gynecologic Oncology*. 2010;116(1):92–98.