NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ

QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

apcz.umk.pl/QS Nicolaus Copernicus University in Toruń

BESSMYLNA, Kateryna, CHROBAK, Agata, ŻUKOWSKA, Joanna Katarzyna, KRAVETS, Alesia, ZHUKAVA, Lizaveta, ALANSI, Abdulrahman, WENG, Kai-Chiun, VOLKAVA, Darya, SAKOVICH, Volha, KACYNEL, Ewa and MYŚLICKA, Wiktoria. Obesity and Gynecologic Malignancies: A Narrative Review of Molecular Mechanisms and Clinical Management Challenges. Quality in Sport. 2026;56:72510. https://doi.org/10.12775/QS.2026.56.72510

ARTICLE TIMELINE

Received: 24.05.2026 Revised: 26.05.2026

Accepted: 26.05.2026 Published: 30.05.2026

INDEXING & EVALUATION

MEiN points: 20 Unique ID: 201398

Disciplines: Economics & Finance; Management & Quality Sciences

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines: Economics and Finance (Social Sciences); Management and Quality Sciences (Social Sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

Obesity and Gynecologic Malignancies: A Narrative Review of Molecular Mechanisms and Clinical Management Challenges

Kateryna Bessmylna

https://orcid.org/0009-0009-9220-9162

kateryna.bessmylna@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Agata Chrobak

https://orcid.org/0009-0004-3370-5290

a.chrobakk@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Joanna Katarzyna Żukowska

https://orcid.org/0009-0003-8597-5447

j.zukowska21@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Alesia Kravets

https://orcid.org/0009-0003-2532-4458

alesiakravets.a@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Lizaveta Zhukava

https://orcid.org/0009-0007-8328-2232

zhukavalizaveta@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Abdulrahman Alansi

https://orcid.org/0000-0001-6544-2916

abodialansi@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Kai-Chiun Weng

https://orcid.org/0009-0006-5519-537X

a0939303669@gmail.com

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Darya Volkava
https://orcid.org/0009-0009-2811-146X
darjawolkawa@gmail.com
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Volha Sakovich
https://orcid.org/0009-0009-1768-1512
sakovich.olka@gmail.com
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Ewa Kacynel
https://orcid.org/0009-0002-8290-9818
evakatsynel@gmail.com
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

Wiktoria Myślicka
https://orcid.org/0009-0005-5209-6504
vika.myslitskaya01@gmail.com
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

...

Corresponding author:

Kateryna Bessmylna, kateryna.bessmylna@gmail.com

Abstract

Background. Obesity has reached epidemic proportions and is considered a primary risk factor for gynecologic malignancies. Its evolving influence, aligned with modern molecular classifications, demands a reassessment of clinical strategies.

Aim. This narrative review integrates evidence on the molecular mechanisms linking obesity to gynecologic cancers and evaluates the impact on clinical management and clinical outcomes.

Material and Methods. A literature search of PubMed and Google Scholar (2018–2026) was conducted. Thirty one peer-reviewed articles were selected for qualitative synthesis, focusing on molecular pathophysiology and clinical management.

Results. Adipose tissue promotes carcinogenesis via insulin resistance, chronic inflammation, and estrogen dysregulation. In endometrial cancer, obesity is a primary etiologic factor linked to MMRd (mismatch repair deficiency) and NSMP (no specific molecular profile) molecular subtypes (FIGO 2023). In ovarian cancer, visceral adiposity establishes an omental metastatic niche through lipid-mediated metabolic crosstalk and fatty acid β-oxidation. In cervical cancer, obesity acts as an indirect risk factor by compromising screening participation and diagnostic visualization. Clinical management is challenged by surgical technicalities and chemotherapy dosing dilemmas. Emerging data suggest an "obesity paradox", where inflammatory environments may paradoxically enhance responses to immune checkpoint inhibitors in specific molecular cohorts.

Conclusions. Managing this population requires a shift toward precision metabolic oncology. Future strategies have to prioritize assessing visceral adiposity and integrating metabolic interventions, such as GLP-1 receptor agonists, to improve oncologic outcomes.

Keywords: Obesity, Adiposity, Endometrial Neoplasms, Ovarian Neoplasms, Uterine Cervical Neoplasms, Treatment Outcome

1. Introduction

Obesity has reached epidemic proportions worldwide, emerging as an essential factor of the global cancer burden. Once regarded as a passive reservoir for energy storage, white adipose tissue (WAT) is now recognized as a highly active endocrine and metabolic organ. Through the secretion of bioactive adipokines and pro-inflammatory cytokines, and by modulating systemic metabolism, WAT profoundly alters the cellular and molecular microenvironment of the female reproductive tract.[1]

Among gynecologic malignancies, obesity is most strikingly associated with endometrial cancer (EC), where it serves as a central etiologic factor in the majority of cases. However, its influence significantly impacts to ovarian (OC) and cervical cancers (CC) through distinct biological pathways and unique clinical challenges.[2] The underlying oncogenic mechanisms are multifactorial, characterized by a synergistic relationship between chronic low-grade inflammation, systemic insulin resistance, and dysregulated steroid hormone metabolism.[1,3]

Beyond its role in carcinogenesis, excess adiposity creates formidable hurdles to clinical management. From technical difficulties in imaging and diagnostic visualization to the complexities of surgical staging and chemotherapy dosing, obesity complicates every stage of the oncologic journey.[1] Furthermore, recent advancements, such as the 2023 FIGO staging updates for endometrial cancer, highlight the need to reevaluate how metabolic health intersects with modern molecular classifications.[4]

In this narrative review, we synthesize current evidence on the molecular mechanisms linking obesity to gynecologic cancers and evaluate their impact on clinical outcomes, diagnostic accuracy, and therapy strategies. By bridging the gap between basic pathophysiology and clinical hurdles, this review aims to provide an extensive framework for the management of this high-risk patient population.

2. Methods

2.1. Search Strategy and Data Sources

A comprehensive literature search was performed in PubMed (MEDLINE) and Google Scholar for articles published between January 2018 and February 2026. The search employed combinations of Medical Subject Headings (MeSH) and keywords: “obesity”, “adiposity”, “endometrial neoplasms”, “ovarian neoplasms”, “uterine cervical neoplasms”, “molecular mechanisms”, “insulin resistance”, “adipokines”, “inflammation”, “estrogen”, “clinical outcomes”, “surgical challenges”, “immunotherapy”, “risk”, “survival”, “prognosis”, “screening”, and “diagnosis”.

2.2. Inclusion and Exclusion Criteria

Studies were included if they: were peer-reviewed original research, meta-analyses, narrative or systematic reviews; were published in English; and addressed the molecular or clinical relationship between obesity and the three primary gynecologic cancers. Exclusion criteria included: animal-only studies; case reports; and articles where the full text was unavailable.

2.3. Data Selection and Synthesis

A structured literature search was conducted. A total of 31 sources were selected for qualitative synthesis. Data were organized by oncogenic pathway and disease site to ensure a structured narrative analysis.

3. Biological Mechanisms Linking Obesity and Cancer

The association between obesity and gynecologic malignancies is not simply a consequence of increased body mass but is driven by a complex network of interconnected biological dysfunctions. Excess adipose tissue acts as a highly active endocrine and metabolic organ, initiating systemic changes that create a "permissive" environment for tumor initiation, promotion, and progression through four primary axes: insulin resistance, chronic inflammation, steroid hormone dysregulation, and altered adipokine signaling.

3.1 Insulin resistance

Insulin resistance is a central feature of visceral adiposity and a primary driver of cancer-related metabolic dysregulation. Chronic hyperinsulinemia stimulates carcinogenesis through two synergistic pathways: mitogenic signaling and hormonal modulation. Elevated insulin levels decrease the production of insulin-like growth factor binding proteins (IGFBP-1 and -2), thereby increasing the bioavailability of insulin-like growth factor 1 (IGF-1). Both insulin and IGF-1 bind to their respective receptors (IR and IGF-1R) to activate the PI3K/AKT/mTOR and MAPK/ERK pathways, which synergistically promote cellular proliferation and inhibit apoptosis.[2,5,6] Elevated insulin levels suppress hepatic synthesis of sex hormone-binding globulin (SHBG). This reduction increases the circulating levels of free, biologically active estrogens, creating a potent proliferative stimulus in the endometrium.[3,5,6]

Chronic hyperglycemia provides a direct bioenergetic advantage to malignant cells. To sustain rapid proliferation, cancer cells upregulate glucose transporters such as GLUT-1 and undergo metabolic reprogramming to prioritize glycolysis, even in the presence of oxygen.[7] Furthermore, glucose-driven oxidative stress can induce DNA damage and genomic instability.[5]

3.2 Chronic low-grade inflammation

Obesity-induced expansion of WAT leads to adipocyte hypertrophy, localized hypoxia, and eventual cell death. This triggers macrophage infiltration, which forms “crown-like structures” (CLS) around dying adipocytes. These macrophages, along with dysfunctional adipocytes, secrete pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which contribute to genomic instability, tumor-promoting signaling, and angiogenesis. Additionally, cytokines activate transcription factors, such as NF-κB, which drive survival signals within the tumor microenvironment.[8]

While chronic inflammation generally supports tumor growth, it also modulates the immune landscape. Emerging evidence suggests that this inflammatory state may upregulate immune checkpoint expression (e.g., PD-1/PD-L1), potentially rendering obese patients more responsive to Immune Checkpoint Inhibitors (ICIs).[9]

3.3 Estrogen metabolism

In postmenopausal women, adipose tissue becomes the primary site of estrogen synthesis. This is mediated by the enzyme aromatase, which converts adrenal androgens into estrone, which is then converted into the more potent estradiol. In the absence of progesterone (due to menopause or obesity-related anovulation in premenopausal women), the endometrium is subjected to continuous estrogenic stimulation. This unopposed estrogen leads to pathological hyperplasia and increases the risk of malignant transformation.[3]

As previously noted, hyperinsulinemia reduces SHBG, thereby increasing the percentage of circulating estrogen that remains in its bioactive form.[3,5]

3.4 Adipokines

Adipocytes secrete specialized signaling molecules called adipokines that directly modulate tumor behavior. Leptin levels are increased in obesity and promote tumorigenesis by stimulating proliferation, migration, invasion, angiogenesis, and the epithelial-mesenchymal transition (EMT). Conversely, adiponectin exhibits anti-inflammatory and insulin-sensitizing effects and is typically reduced in obese individuals. The leptin-to-adiponectin (L/A) ratio is now considered a more reliable biomarker for oncogenic risk than either marker alone, representing a shift toward a pro-proliferative state.[10,11]

3.5 The Mechanistic Crosstalk

The potency of obesity as a carcinogen lies in the synergistic crosstalk between these pathways. For instance, chronic inflammation aggravates systemic insulin resistance, which in turn drives estrogen bioavailability. Leptin can further sensitize cells to the effects of estrogen and IGF-1, creating a self-sustaining feedback loop of growth-promoting signals (Table 1). Apprehending these interactions is essential for identifying potential therapy targets and developing more efficient prevention strategies.

Table 1. Summary of key biological mechanisms linking obesity to gynecologic carcinogenesis.

Mechanism	Key Biological Drivers	Primary Impact on Cancer Cells
Insulin Resistance	Insulin, IGF-1, Hyperglycemia	Activation of PI3K/AKT/mTOR and MAPK pathways; inhibition of apoptosis [5,7]
Chronic Inflammation	TNF-α, IL-6, CLS	Genomic instability, angiogenesis, activation of NF-κB and STAT3 pathways [8]
Estrogen Dysregulation	Aromatase, Estradiol, SHBG	Unopposed estrogen exposure and chronic endometrial proliferation [3]

Adipokine Imbalance	↑ Leptin, ↓ Adiponectin	Promotion of EMT, angiogenesis, and cell migration [10,11]
Glucose Metabolism	GLUT-1, Hyperglycemia	Metabolic reprogramming; oxidative DNA damage [5]

4. Obesity and Specific Gynecologic Malignancies

While the metabolic drivers discussed in Section 3 are systemic, their manifestations vary considerably across different gynecologic tissues.

4.1 Endometrial cancer

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries and serves as the prototypical model for obesity-associated carcinogenesis. Historically, EC was classified according to the Bokhman model into type I (endometrioid, estrogen-dependent) and type II (non-endometrioid, estrogen-independent). However, the FIGO 2023 staging system now integrates The Cancer Genome Atlas (TCGA) molecular subtypes: POLEmut (ultramutated), MMRd (mismatch repair deficiency), NSMP (no specific molecular profile), and p53abn (p53 abnormal). Obesity is most heavily correlated with the NSMP and MMRd subtypes, which largely coincide with the classic "estrogen-driven" type I category.[2,4]

Epidemiological data reveal a potent, dose-dependent relationship: every 5-unit increase in BMI is associated with a 50% increase in EC risk. This is driven primarily by the unopposed estrogen effect and systemic insulin resistance, which activate the PI3K/AKT/mTOR pathway, a pathway frequently mutated in endometrioid subtypes.[2,12]

Emerging research on the gut-uterus axis suggests that obesity-driven dysbiosis may increase circulating estrogen via the estrobolome (microbial genes that can influence estrogen levels), additionally worsening the hormonal imbalance.[13]

4.2 Ovarian cancer

Unlike the direct hormonal link in EC, the relationship between obesity and OC is defined by the local adipose microenvironment, particularly within the omentum.

Ovarian cancer exhibits a unique tropism for the omentum, a large fold of visceral adipose tissue, creating the so-called omental niche. In the obese state, adipocytes undergo phenotypic transformation into cancer-associated adipocytes (CAAs), which secrete pro-inflammatory cytokines (IL-6, IL-8) and matrix metalloproteinases (MMP-11), thereby facilitating peritoneal seeding.[14]

One of the most critical aspects of the OC progression is the metabolic shift toward lipid utilization. Ovarian cancer cells induce lipolysis in neighboring adipocytes, triggering the release of free fatty acids (FFAs), which are taken up by upregulated fatty acid-binding proteins (FABP4) and utilized as a primary energy source via β-oxidation, fueling rapid metastatic growth.[14,15]

Adipokines represent a key link between obesity and OC biology. While the L/A ratio remains the primary driver of proliferation and NK-cell suppression, recent research has highlighted the pro-tumorigenic role of "minor" adipokines, such as resistin and chemerin.[10,16]

Similar to EC, recent studies indicate that the microbiome may influence tumor growth in OC both directly and indirectly, including through effects on metabolic pathways and the tumor microenvironment. Specifically, obesity-driven dysbiosis creates a pro-inflammatory milieu that can disrupt metabolic homeostasis and promote adipogenesis. These microbial shifts further facilitate tumorigenesis by enhancing angiogenesis and immunosuppressive signaling within the omental niche. [14,15]

4.3 Cervical cancer

Cervical cancer is primarily caused by persistent high-risk human papillomavirus (HPV) infection, and in contrast to EC and OC, obesity is not considered its direct etiologic factor. However, obesity acts as a critical indirect risk factor by compromising secondary prevention.

Epidemiological data imply that while the risk of invasive cervical cancer is higher in obese women, the detection of precancerous lesions is significantly lower. This indicates that the perceived higher risk of cancer is likely a result of undetected progression from precancer to malignancy due to technical and physical barriers.[17,18]

Women with BMI>40 kg/m^2 are significantly less likely to participate in regular screening. This is caused by a combination of physical discomfort, weight-related stigma in healthcare settings, and the lack of specialized bariatric gynecologic equipment.[19]

In addition to lower screening participation, obesity is a major cause of unsatisfactory cervical smears. Visualization of the transformation zone is frequently obscured by vaginal wall prolapse, leading to a higher rate of false negatives or delayed sampling. These diagnostic limitations frequently lead to stage migration, where patients are diagnosed at more advanced, less treatable stages.[20]

Table 2. Comparative impact of obesity and metabolic dysfunction across gynecologic malignancies.

Mechanism	Endometrial Cancer (EC)	Ovarian Cancer (OC)	Cervical Cancer (CC)
Insulin Resistance	Primary driver; activates PI3K/AKT in MMRd/NSMP subtypes [2,5]	Supportive; fuels systemic growth factor (IGF-1) availability [15]	Indirect; associated with overall metabolic syndrome risk [7]

Chronic Inflammation	Promotes endometrial hyperplasia, angiogenesis, and genomic instability [8]	Local omental focus; supports tumor implantation and progression [14]	Minor contribution
Estrogen Dysregulation	Central etiology; unopposed estrogen promotes endometrial hyperplasia and malignant transformation [2,3]	Limited role; not a primary driver of tumorigenesis [15]	No direct role; disease primarily driven by HPV [17,18]
Adipokine Imbalance	Shift in L/A ratio promotes local tissue proliferation and EMT [11]	Enhances tumor invasion, immune evasion, and metastatic potential [10,16]	Limited impact on carcinogenesis
Glucose/Lipid Metabolism	Increased glycolysis and glucose uptake (GLUT-1 upregulation) [5,7]	Key mechanism; lipid-mediated crosstalk; β-oxidation fuels metastasis [14,15]	Not significant
Microenvironment	Estrobolome and local inflammatory niche [13]	Omental niche; CAAs provide energetic support for lipid-mediated crosstalk [14]	Technical difficulty in cervical visualization due to redundant tissue [20]
Screening & Detection	Symptoms (bleeding) often prompt early detection despite BMI [1]	No effective screening; obesity may mask adnexal masses [1]	Major barrier; reduced participation and higher unsatisfactory smear rates [17,19,20]

5. Clinical management and survival outcomes

The management of gynecologic malignancies in the context of obesity is defined by an increased risk of carcinogenesis coupled with systemic and technical barriers to effective care. These challenges require a multidisciplinary approach that moves past traditional BMI toward a more subtle understanding of metabolic health.

5.1 Diagnostic barriers

The diagnosis of gynecological malignancies in patients with obesity is frequently challenged by physical and technical limitations, which may contribute to delayed detection and a more advanced stage at presentation.

Excess adipose tissue obscures the detection of uterine enlargement or adnexal masses during pelvic exams.[1] Furthermore, imaging resolution is often compromised. Transabdominal ultrasound is limited by tissue depth, while CT and MRI may be hampered by equipment size constraints and artifacts, complicating accurate staging.[1]

In cervical cancer, obesity is a primary driver of unsatisfactory smears due to difficulty in visualizing the cervix and vaginal wall prolapse.[20] This contributes to a failure in detecting precancerous lesions, directly increasing the incidence of invasive disease through delayed intervention.[17,18]

Aside from technical constraints, weight-related stigma and communication barriers represent major obstacles to early detection. Patients may delay reporting critical symptoms, such as abnormal uterine bleeding, due to previous negative healthcare experiences or the anticipation of weight-biased judgment.[20]

5.2 Treatment challenges

Obesity poses considerable challenges in the management of gynecologic cancers, affecting surgical, anesthetic, and pharmacological aspects of treatment, which may affect both perioperative safety and long-term oncologic outcomes.

Obesity increases the technical complexity of surgery, leading to longer operative times, greater estimated blood loss, and higher risks of wound complications and venous thromboembolism.[1,21] While minimally invasive surgery (MIS) is preferred, the steep Trendelenburg positioning required can severely compromise pulmonary ventilation and venous return in the morbidly obese.[1] Interestingly, Gambacorti-Passerini et al., 2019 demonstrated that for the laparoscopic approach, there were no significant differences in intraoperative or postoperative complications, or in long-term survival, between obese and non-obese patients, suggesting that the technique remains oncologically safe in this population.[22] However, recent data suggest that robotic-assisted hysteroscopy further lowers conversion-to-open rates and maintains long-term survival outcomes with fewer perioperative complications compared to traditional laparoscopy, potentially delivering a more reliable platform for the most complex bariatric cases.[23,24]

Determining the optimal chemotherapy dose remains an important clinical dilemma. Concerns regarding toxicity may lead to dose reductions or capping, and may result in suboptimal treatment. Additionally, altered pharmacokinetics in obese patients may affect drug distribution and metabolism.[1] Radiotherapy in obese patients is technically more challenging due to issues with patient positioning, immobilization, and dose distribution.[1]

While obesity complicates conventional therapy, it may provide a unique advantage in immunotherapy. High expression of immune checkpoints in adipose tissue has been shown to enhance the efficacy of PD-1/PD-L1 inhibitors, suggesting that obesity may be a favorable biomarker for immunotherapy in specific molecular subgroups, such as CN-H/TP53abn endometrial cancers.[9]

5.3 Prognosis and survival

The relationship between obesity and survival is characterized by the "obesity paradox", in which a high BMI does not consistently correlate with worse survival.[25]

In endometrial cancer, obese patients often present with low-grade, Type I endometrioid tumors with a favorable prognosis. However, this potential advantage may be offset by high competing mortality from cardiovascular disease and diabetes.[26,27]

The prognostic impact of obesity in OC remains less clear and is often secondary to surgical and systemic factors. Most evidence suggests that prognosis is primarily dictated by stage at diagnosis and residual disease after cytoreductive surgery. Furthermore, obesity may indirectly worsen prognosis through suboptimal chemotherapy dosing.[28] In OC, the paradox is more likely a result of "reverse causation", where the low-BMI group includes patients with advanced cancer cachexia and frailty.[25]

In contrast to the other two malignancies, the impact of obesity on cervical cancer prognosis is more definitive and largely negative. Obese patients exhibit significantly worse overall survival, driven primarily by indirect mechanisms rather than direct tumor biology. These include reduced screening participation, delayed diagnosis (stage migration), and technical challenges associated with radiotherapy and surgery in patients with high visceral adiposity.[29,30] The clinical burden remains significant even after primary management; emerging evidence suggests that obesity is associated with a higher risk of both precancerous lesions and invasive cancer in the post-treatment population, implicating more rigorous surveillance.[31]

Table 3. Clinical management challenges in obese patients with gynecologic malignancies.

Domain	Challenge	Clinical Consequences	
Diagnostic Evaluation	Reduced sensitivity of physical examination and imaging due to adipose tissue depth	Delayed diagnosis; inaccurate surgical staging	1
Cervical Cancer Screening	Lower participation rates; technical difficulty in visualizing the cervix; higher rate of unsatisfactory smears	Missed precancerous lesions; increased incidence of advanced-stage disease at diagnosis	17,18,20

Surgical Management	Increased technical complexity; longer operative times; limited visualization of pelvic structures	Higher risk of intraoperative blood loss and conversion from MIS to open surgery	1,21
Perioperative Risk	Elevated risk of wound complications, infections, and venous thromboembolism (VTE)	Higher postoperative morbidity and prolonged recovery periods	1,21
Minimally Invasive Surgery (MIS)	Cardiopulmonary compromise in steep Trendelenburg position; limited abdominal workspace	Restricted use in morbidly obese patients; robotic surgery may mitigate these limitations	1,23,24
Chemotherapy Dosing	Uncertainty in optimal dosing; tendency toward BSA capping or dose reduction; altered pharmacokinetics	Risk of suboptimal therapeutic intensity and reduced oncologic efficacy	1
Radiotherapy	Technical difficulties in reproducible positioning, immobilization, and dose distribution	Potential reduction in treatment precision and overall effectiveness	1
Immunotherapy Response	Obesity-associated immune modulation (PD-1/PD-L1 expression) may enhance ICI efficacy	Potential therapeutic advantage in specific molecular subgroups ("obesity paradox")	9
Long-Term Outcomes	Presence of high-impact comorbidities (Type 2 diabetes, cardiovascular disease)	Increased non-cancer-related mortality; negative impact on overall survival	26,27
Patient-Provider Interaction	Weight-related stigma and communication barriers	Delayed symptom reporting; reduced patient engagement with healthcare systems	19

6. Future Perspectives

The research landscape is rapidly transitioning from broad epidemiological observations toward precision metabolic medicine. Future efforts ought to prioritize personalized risk stratification and pharmacological interventions that directly target the underlying metabolic, hormonal, and inflammatory drivers of gynecologic malignancies.

Shifting toward precise measures of body composition, such as visceral adiposity index or bioelectrical impedance analysis, will improve both prognostic accuracy and therapeutic decision-making.

The integration of GLP-1 receptor agonists represents a promising opportunity. These agents may offer dual benefits, including significant weight reduction and direct interference with hyperinsulinemic pathways, potentially decreasing the risk of obesity-driven tumor promotion.[13]

The finding that obesity-induced immune dysregulation may prime certain tumors for better responses to ICIs constitutes a paradigm shift.[9] Determining specific biomarkers within this immunological obesity paradox will be essential for selecting candidates for immunotherapy.

Emerging research into the estrobolome, the metabolic crosstalk within the omental niche, warrants deeper investigation. These areas may offer novel targets for adjuvant therapies that disrupt the energetic support systems of metastatic cells.

Finally, confronting the systemic disparities in screening and diagnostic visualization for patients with high BMI is still a public health priority to ensure that metabolic health does not remain a barrier to early cancer detection.

7. Conclusion

Obesity is no longer viewed merely as a passive comorbidity but as a potent, multifactorial driver of gynecologic malignancy. This review highlights that, while the molecular mechanisms driven by insulin resistance, chronic low-grade inflammation, and hormonal dysregulation are systemic, their clinical manifestations are disease-specific.

In endometrial cancer, obesity serves as a primary etiologic driver through the unopposed estrogen and insulin/IGF-1 axes; in ovarian cancer, it facilitates a specialized metastatic niche in the omentum by providing a lipid-rich energetic engine for tumor progression; and in cervical cancer, it acts primarily as a barrier to secondary prevention, compromising screening participation and diagnostic accuracy.

The management of patients with obesity requires an urgent shift from BMI-centric care to precision metabolic oncology. This transition demands an integrated approach that combines an advanced understanding of molecular pathways with tailored clinical strategies. By refining risk stratification and optimizing management for this growing patient population, clinicians can bridge the survival gap and improve outcomes for women living with obesity-related gynecologic cancers.

Disclossure

Author Contributions:

Conceptualization: KB, AC, LZ, AK

Data curation: KB, AC, KW, DV

Formal analysis: KB, AA, KW

Investigation: KB, AK, AC, JŻ

Methodology: KB, KW, AA

Visualization: LZ, AC, AA, DV

Writing – original draft: KB, LZ, VS, WM

Writing – review and editing: JŻ, AK, DV, EK

All authors have read and approved the final version of the manuscript.

Funding Statement: This research received no specific grant from any funding agency in the public, commercial, or non-profit sectors.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Acknowledgments: Not applicable.

Conflict of Interest Statement: The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process:

During the preparation of this work, the authors used AI tools to assist with language and readability, ensuring clarity, consistency, and adherence to scientific writing standards. All scientific content, including literature selection, critical analysis, interpretation of findings, and final conclusions, was developed independently by the authors. The use of AI did not replace human assessment at any stage of the research process. The authors accept full responsibility for the substantive content of the publication.

References:

1. Agnew HJ, Kitson SJ, Crosbie EJ. Gynecological malignancies and obesity. *Best Pract Res Clin Obstet Gynaecol*. Jun 2023;88:102337. doi:10.1016/j.bpobgyn.2023.102337

2. Hooks O, Jhumkhawala V, Sibson K, Shrontz A, Krishnan SS, Ahmad S. Diabetes, Obesity, and Endometrial Cancer: A Review. *Curr Oncol*. Nov 29 2025;32(12)doi:10.3390/curroncol32120672
3. Mili N, Paschou SA, Goulis DG, Dimopoulos MA, Lambrinoudaki I, Psaltopoulou T. Obesity, metabolic syndrome, and cancer: pathophysiological and therapeutic associations. *Endocrine*. Dec 2021;74(3):478-497. doi:10.1007/s12020-021-02884-x
4. Berek JS, Matias-Guiu X, Creutzberg C, et al. FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet*. Aug 2023;162(2):383-394. doi:10.1002/ijgo.14923
5. Byrne FL, Martin AR, Kosasih M, Caruana BT, Farrell R. The Role of Hyperglycemia in Endometrial Cancer Pathogenesis. *Cancers (Basel)*. May 8 2020;12(5)doi:10.3390/cancers12051191
6. Kolano A, Pejas A, Markowiak S, et al. The impact of obesity on endometrial cancer: A comprehensive analysis. *Journal of Education, Health and Sport*. 2024;51:179-197.
7. Lee DY, Lee TS. Associations between metabolic syndrome and gynecologic cancer. *Obstet Gynecol Sci*. May 2020;63(3):215-224. doi:10.5468/ogs.2020.63.3.215
8. Moukarzel LA, Ferrando L, Stylianou A, et al. Impact of obesity and white adipose tissue inflammation on the omental microenvironment in endometrial cancer. *Cancer*. Sep 15 2022;128(18):3297-3309. doi:10.1002/cncr.34356
9. Gómez-Banoy N, Ortiz EJ, Jiang CS, et al. Body mass index and adiposity influence responses to immune checkpoint inhibition in endometrial cancer. *J Clin Invest*. Jun 20 2024;134(17)doi:10.1172/jci180516
10. Kołakowska K, Kiśluk J, Nikliński J. A Novel Insight into the Role of Obesity-Related Adipokines in Ovarian Cancer-State-of-the-Art Review and Future Perspectives. *Int J Mol Sci*. Feb 21 2025;26(5)doi:10.3390/ijms26051857
11. Słabuszewska-Jóźwiak A, Lukaszuk A, Janicka-Kośnik M, Wdowiak A, Jakiel G. Role of Leptin and Adiponectin in Endometrial Cancer. *Int J Mol Sci*. May 10 2022;23(10)doi:10.3390/ijms23105307
12. Lee MA, Tan VY, Pournaras DJ, et al. Adiposity, metabolites and endometrial cancer risk: inference from combinations of Mendelian randomization and observational analyses. *BMC Cancer*. Oct 21 2025;25(1):1619. doi:10.1186/s12885-025-14756-y
13. Burkett WC, Clontz AD, Keku TO, Bae-Jump V. The interplay of obesity, microbiome dynamics, and innovative anti-obesity strategies in the context of endometrial cancer progression and therapeutic approaches. *Biochim Biophys Acta Rev Cancer*. Nov 2023;1878(6):189000. doi:10.1016/j.bbcan.2023.189000
14. Duarte Mendes A, Freitas AR, Vicente R, et al. Adipocyte Microenvironment in Ovarian Cancer: A Critical Contributor? *Int J Mol Sci*. Nov 22 2023;24(23)doi:10.3390/ijms242316589
15. Suratkal J, D'Silva T, AlHilli M. The role of diet, obesity and body composition in epithelial ovarian cancer development and progression: Mechanisms and therapeutic implications. *Gynecol Oncol Rep*. Apr 2025;58:101718. doi:10.1016/j.gore.2025.101718
16. Parafiniuk K, Skiba W, Pawłowska A, Suszczyk D, Maciejczyk A, Wertel I. The Role of the Adipokine Resistin in the Pathogenesis and Progression of Epithelial Ovarian Cancer. *Biomedicines*. Apr 16 2022;10(4)doi:10.3390/biomedicines10040920
17. Clarke MA, Fetterman B, Cheung LC, et al. Epidemiologic Evidence That Excess Body Weight Increases Risk of Cervical Cancer by Decreased Detection of Precancer. *J Clin Oncol*. Apr 20 2018;36(12):1184-1191. doi:10.1200/jco.2017.75.3442
18. Urbute A, Frederiksen K, Thomsen LT, Kesmodel US, Kjaer SK. Overweight and obesity as risk factors for cervical cancer and detection of precancers among screened women: A nationwide, population-based cohort study. *Gynecol Oncol*. Feb 2024;181:20-27. doi:10.1016/j.ygyno.2023.12.002

19. Sand FL, Urbute A, Ring LL, Kjaer AK, Belmonte F, Kjaer SK. The influence of overweight and obesity on participation in cervical cancer screening: A systematic review and meta-analysis. *Prev Med*. Jul 2023;172:107519. doi:10.1016/j.ypmed.2023.107519
20. Urbute A, Kjaer SK, Kesmodel US, Frederiksen K, Thomsen LT. Women with obesity participate less in cervical cancer screening and are more likely to have unsatisfactory smears: Results from a nationwide Danish cohort study. *Prev Med*. Jun 2022;159:107072. doi:10.1016/j.ypmed.2022.107072
21. Harrison R, Iniesta MD, Pitcher B, et al. Enhanced recovery for obese patients undergoing gynecologic cancer surgery. *Int J Gynecol Cancer*. Oct 2020;30(10):1595-1602. doi:10.1136/ijgc-2020-001663
22. Gambacorti-Passerini ZM, López-De la Manzanara Cano C, Pérez Parra C, et al. Obesity in Patients with Endometrial Cancer: May It Affect the Surgical Outcomes of Laparoscopic Approach? *Obes Surg*. Oct 2019;29(10):3285-3290. doi:10.1007/s11695-019-03986-2
23. Cusimano MC, Simpson AN, Dossa F, et al. Laparoscopic and robotic hysterectomy in endometrial cancer patients with obesity: a systematic review and meta-analysis of conversions and complications. *Am J Obstet Gynecol*. Nov 2019;221(5):410-428.e19. doi:10.1016/j.ajog.2019.05.004
24. Lindfors A, Heshar H, Adok C, Sundfeldt K, Dahm-Kähler P. Long-term survival in obese patients after robotic or open surgery for endometrial cancer. *Gynecol Oncol*. Sep 2020;158(3):673-680. doi:10.1016/j.ygyno.2020.05.684
25. Pavone M, Goglia M, Taliento C, et al. Obesity paradox: is a high body mass index positively influencing survival outcomes in gynecological cancers? A systematic review and meta-analysis. *Int J Gynecol Cancer*. Aug 5 2024;34(8):1253-1262. doi:10.1136/ijgc-2023-005252
26. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: A systematic review and meta-analysis. *Obes Rev*. Dec 2021;22(12):e13337. doi:10.1111/obr.13337
27. Arteaga DP, DeKraker C, Ennis M, et al. Body composition and endometrial cancer outcomes. *J Natl Cancer Inst Monogr*. May 4 2023;2023(61):49-55. doi:10.1093/jncimonographs/lgad012
28. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: A systematic review and meta-analysis. *Cancer Rep (Hoboken)*. Nov 2022;5(11):e1618. doi:10.1002/cnr2.1618
29. Gnade CM, Hill EK, Botkin HE, et al. Effect of Obesity on Cervical Cancer Screening and Outcomes. *J Low Genit Tract Dis*. Oct 2020;24(4):358-362. doi:10.1097/lgt.0000000000000570
30. Eide AJ, Halle MK, Lura N, et al. Visceral fat percentage for prediction of outcome in uterine cervical cancer. *Gynecol Oncol*. Sep 2023;176:62-68. doi:10.1016/j.ygyno.2023.06.581
31. Clarke MA, Befano B, Wentzensen N, et al. Associations of obesity with post-treatment risks of cervical precancer and cancer. *Am J Obstet Gynecol*. Jul 2025;233(1):40.e1-40.e16. doi:10.1016/j.ajog.2024.12.002