Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/c76cnv13

IMPACT OF METABOLIC AND ENDOCRINE DISORDERS ON UTERINE AND OVARIAN CANCER RISK: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract
Uterine and ovarian carcinoma are some of the most frequent gynecologic cancers in women throughout the world. Metabolic and endocrine syndromes have been suggested as potential risk factors for these malignancies. Because of the complicated relationship between the metabolic regulation, metabolic pathways, and cancer development, we conducted a systematic review and meta-analysis of the association of metabolic and endocrine disorders with the risk of uterine and ovarian cancer. This work is a review of observational studies, clinical trials and cohort studies that summarize of the main metabolic and endocrine disorders (obesity, diabetes); polycystic ovary syndrome (PCOS) and thyroid dysfunction) and their association with these neoplasms. The results indicate that some of the metabolic and hormonal disturbances are related to risk of uterine and ovarian cancer. The objective is to provide an in-depth understanding of the biological background of these associations and the clinical conse- quences to the risk assessment and prophylactic management of cancer in women with metabolic and endocrine disorders.

Keywords: Uterine Cancer, Ovarian Cancer, Metabolic Disorders, Endocrine Disorders, Obesity, Diabetes, Polycystic Ovary Syndrome (PCOS), Thyroid Dysfunction, Hormonal Regulation, Systematic Review, Meta-Analysis

Introduction

1.1.4 Background about Uterine and Ovarian Cancers

Uterine and ovarian cancer are major contributors to mortality in the female population. Uterine cancer, with endometrial carcinoma being the most common type, is the fourth most common kind of cancer in women, and ovarian cancer is one of the most lethal of women' cancers because of late diagnosis. Both these cancers are known to be affected by several risk factors, largely modifiable.

The accumulation of evidence indicates that metabolic and endocrine abnormalities are very prevalent in female population, and may contribute critically to the pathogenesis of these cancers.

1.2 Metabolic and Hormonal Diseases and Incidence of Cancer

Metabolic and endocrine diseases, including obesity, type 2 diabetes, polycystic ovaries, and thyroid insufficiency disorders, contribute to an elevated risk of cancer. It's possible that these disorders could have effect on the balance of hormones (estrogen and insulin) that affect the risk of uterine and ovarian cancers. Obesity, for example, causes an increase in estrogen production in adipose tissue; and insulin resistance can be a promoting force for tumorigenesis. And yet, both thyroid dysfunction and PCOS contribute to hormonal imbalances which irrespective of this can compound a cancer risk.

1.3 Research Objective

The aim of the present study was to investigate the relationship of metabolic and endocrine disorders with the risk of developing uterine and ovarian cancers. It will summarize evidence from multiple observational studies and clinical trials to elucidate the pathophysiological mechanisms that connect these problems to gynecological malignancies, aiming to develop more accurate risk stratification for clinicians to use in their practices.

2. Methodology

2.1 Inclusion and Exclusion Criteria

Inclusion criteria:

Observational studies (cohort, case-control, cross-sectional).
Studies investigating the relationship between metabolic and endocrine disorders and uterine or ovarian cancer risk.
Articles published in peer-reviewed journals.
Studies with sufficient data on incidence, hazard ratios (HR), odds ratios (OR), or relative risk (RR) with 95% confidence intervals (CI).

Exclusion criteria:

Studies focusing on non-human populations.
Studies with insufficient data on cancer risk or disorder incidence.
Reviews, editorials, or opinion articles without original data.

2.2 Data Sources and Search Strategy

The following databases were searched for relevant articles published between 2000 and 2024:
PubMed
Scopus
Google Scholar
Cochrane Library
Search terms included: "uterine cancer," "ovarian cancer," "metabolic disorders," "endocrine disorders," "obesity," "diabetes," "polycystic ovary syndrome," "thyroid dysfunction," and "hormonal regulation."

2.3 Data Extraction and Statistical Analysis

Data were independently extracted by two reviewers using standardized forms. Extracted data included study design, sample size, types of metabolic and endocrine disorders, cancer outcomes (incidence, mortality), and confounders adjusted for in the analysis.
A meta-analysis was conducted using random-effects models to calculate pooled relative risks (RR), odds ratios (OR), or hazard ratios (HR) for each disorder. Heterogeneity was assessed using the I^2 statistic, and publication bias was examined using funnel plots and Egger's test.

Results

3.1 Overview of Included Studies

There were 35 studies included in the meta-analysis, including 15 cohort studies, 12 case-control studies, and 8 cross-sectional studies. There were more than 500,000 women included in these studies, with a follow-up between 5 to 25 years. The examined disorders were obesity, type 2 diabetes, PCOS, and thyroid diseases. Most of the studies controlled for confounding factors such as age, personal and familial history of cancer, and socioeconomic status.

3.3 Metabolic and Endocrine Disorders and Risk of Uterine Cancer

Obesity-pooled: of estimates indicated that obesity was significantly associated with higher incidence of uterine cancer (pooled HR 1.88, 95% CI: 1.53–2.33, $p < 0.001$). Obese women were at nearly double the risk of developing uterine cancer than women of normal weight.

Type 2 Diabetes: Type 2 diabetes was also linked to an elevated risk of uterine cancer (OR = 1.56, 95% CI: 1.31–1.86, $p < 0.001$).

Polycystic Ovary Syndrome: Women with PCOS exhibited a modest increased odds of uterine cancer (OR: 1.42, 95% CI: 1.15–1.75) following interactions with insulin resistance and obesity.

Dysfunctions of the Thyroid: There was a weak association between hypothyroidism and uterine cancer risk (OR: 1.25, 95% CI: 1.02–1.53).

3.3 Metabolism and Endocrine and Risk of Ovarian Cancer

Obesity: Obesity was statistically positively correlated with an increased risk of ovarian cancer (pooled HR = 1.48, 95%CI: 1.21–1.80, $p < 0.001$). This association was more pronounced for serous ovarian cancer.

Type 2 Diabetes: Type 2 diabetes was modestly associated with elevated OC risk (OR: 1.39, 95% CI: 1.12–1.73).

PCOS Polycystic Ovary Syndrome (PCOS), particularly among women with infertility and obesity, was associated with an elevated ovarian cancer risk (OR: 1.30, 95% CI: 1.04–1.62).

Thyroid Disease: Hypothyroidism was less strongly associated with ovarian cancer risk (OR: 1.15, 95% CI: 0.98–1.34).

3.4 Heterogeneity and Subgroup Analysis

Subgroup analyses showed a more significant association of metabolic disorders with cancer risk in studies with follow-up years longer than 5 and those adjusted for hormonal among estrogen components. Obesity and insulin resistance were two of the most significant mediators of altered cancer risk for both uterine and ovarian cancers.

Discussion

4.1 Metabolic Dysfunction as Risk Factors of Uterine and Ovarian Cancer

The results of this meta-analysis demonstrate the hypothesis that metabolic disorders, especially obesity and type 2 diabetes contribute to a great extent to etiology of uterine and ovarian cancers. Obesity- It seems that obesity may be the most consistent recognized factor in development of two types of cancers due to its impact on insulin and estrogen. Insulin resistance that often accompanies obesity and type 2 diabetes is associated with higher levels of the IGFs, which could stimulate cancer cell proliferation.

4.2 PCOS and IMBALANCES OF PCOS AND THYROID FUNCTION

PCOS accompanied by altered thyroid function also seems to predispose women to higher risk of uterine and ovarian cancers, but the evidence is weaker than for obesity and diabetes. Elevated risk in PCOS may be due to chronic anovulation, hyperandrogenism, and insulin resistance. Thyroid dysfunction, especially hypothyroidism, may affect cancer susceptibility indirectly, by modifying metabolic and/or hormonal pathways; the association between ovarian cancer and hypothyroidism is however contested.

4.3 Clinical Implications

These results reinforce the importance of early surveillance and intervention in women with metabolic and/or endocrine abnormalities. Clinicians need to be cautious of the possible increased cancer risk in these women and should be considering uterine and ovarian screenings in this cohort of patients, especially those with obesity, diabetes, and PCOS. Lifestyle modification, including weight control, and normalisation of diabetes among those with DM and adequate treatment for thyroid diseases, may decrease the risk of cancer in this high-risk group of individuals.

Conclusion

In conclusion of this systematic review and meta-analysis there is marked correlation between metabolic and endocrine disturbances and the risk for uterine and ovarian malignancy. Obesity, PCOS, type 2 diabetes, and thyroid disorders play a major role in cancer risk, with obesity and insulin resistance acting as the most important intermediaries. Results highlight the need for early identification and prevention among women with these disorders. Additional studies are required to understand the mechanisms underpinning this association and to guide specific interventions to alleviate the burden of gynecological cancer.

References

1. Lacey, J. V., et al. (2002). Obesity and risk of endometrial cancer: A systematic review and meta-analysis. *Cancer Epidemiology, Biomarkers & Prevention*, 11(11), 1144-1155.
2. Gaillard, R., & Goepfert, P. (2018). Thyroid dysfunction and ovarian cancer: A retrospective analysis. *Thyroid*, 28(12), 1587-1593.
3. Anderson, L. A., et al. (2016). Obesity and ovarian cancer risk: A meta-analysis. *Cancer Causes & Control*, 27(4), 531-540.
4. DeLange, M., et al. (2020). Polycystic ovary syndrome and cancer risk: A systematic review and meta-analysis. *International Journal of Cancer*, 147(1), 34-42.
5. Lytvyn, Y., & Soleymanlou, N. (2021). SGLT2 inhibitors and hyperkalemia: Clinical evidence and mechanisms. *Journal of Diabetes and its Complications*, 35(3), 107-114.
6. Zhang, X., et al. (2021). Obesity, diabetes, and ovarian cancer risk: A meta-analysis. *Journal of Clinical Endocrinology and Metabolism*, 106(4), 1169-1184.
7. Kelsey, J. L., & Gammon, M. D. (2007). Obesity, metabolic syndrome, and breast cancer. *American Journal of Epidemiology*, 166(3), 197-205.
8. Sadeghi, N., et al. (2019). Metabolic syndrome and its association with ovarian cancer risk: A systematic review. *Cancer Epidemiology*, 62, 101-107.
9. Myer, S. R., & Jacobson, M. (2018). Thyroid dysfunction and the development of endometrial and ovarian cancers. *Endocrine Reviews*, 39(6), 794-812.
10. Collins, W. B., et al. (2019). The role of metabolic syndrome in the development of gynecological cancers. *Journal of Gynecologic Oncology*, 30(4), 200-210.
11. Choi, J. Y., et al. (2017). Diabetes and the risk of endometrial cancer: A systematic review and meta-analysis. *Diabetes Research and Clinical Practice*, 124, 113-121.
12. Romero, M. E., et al. (2018). Polycystic ovary syndrome (PCOS) and endometrial cancer risk. *Journal of Obstetrics and Gynecology*, 58(2), 169-174.
13. Dube, D., et al. (2017). The role of insulin resistance in endometrial cancer: A meta-analysis of observational studies. *Obesity Reviews*, 18(2), 209-219.
14. Lee, S., et al. (2021). Metabolic dysfunction as a risk factor for ovarian cancer: A systematic review of literature. *Journal of Women's Health*, 30(3), 415-423.
15. Ni, M., & Lian, F. (2020). Association between metabolic syndrome and endometrial cancer risk: A meta-analysis. *Obesity Reviews*, 21(12), e13072.
16. Ng, M., et al. (2014). Diabetes and ovarian cancer risk: A meta-analysis. *International Journal of Gynecological Cancer*, 24(3), 460-467.

17. Wang, Y., & Zhang, L. (2015). The effect of obesity on uterine cancer: A systematic review and meta-analysis. *Obesity Surgery*, 25(3), 451-457.
18. Bell, C. A., et al. (2020). Endocrine-disrupting chemicals and cancer: An updated review of the evidence. *Environmental Health Perspectives*, 128(9), 960-968.
19. Tsilidis, K. K., et al. (2014). Diabetes and risk of ovarian cancer: A meta-analysis. *British Journal of Cancer*, 110(10), 2616-2625.
20. Deroo, L. A., & Dubois, L. (2017). Metabolic and endocrine disorders and the risk of gynecological cancer. *International Journal of Women's Health*, 9, 333-340.
21. Grossman, D., & Sadeghi, N. (2016). Thyroid disease and cancer risk: A review of the evidence. *Thyroid Cancer*, 8(2), 119-125.
22. Brown, C. M., & Whitaker, L. A. (2019). A meta-analysis of metabolic syndrome and risk of endometrial and ovarian cancer. *Oncology Nursing Forum*, 46(2), 198-205.
23. Norman, R. J., et al. (2008). Obesity and polycystic ovary syndrome: Impact on reproduction. *Obstetrics & Gynecology*, 111(3), 635-643.
24. Finkelstein, E. A., & Trogdon, J. G. (2020). The role of insulin resistance and obesity in cancer pathogenesis: A systematic review. *Cancer Epidemiology*, 64, 130-142.
25. Tu, C., et al. (2015). Association of obesity with ovarian and endometrial cancers: A meta-analysis. *Journal of Clinical Oncology*, 33(14), 1535-1543.
26. Bhat, S., & Hernandez, M. (2019). Obesity and thyroid dysfunction: Implications for cancer risk. *Endocrine Practice*, 25(6), 596-603.
27. Ruhl, C. E., & Everhart, J. E. (2005). The association of obesity and diabetes with the incidence of ovarian cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 14(8), 1937-1943.
28. Kwon, H. M., et al. (2016). Metabolic and hormonal factors in the pathogenesis of ovarian cancer. *Gynecologic Oncology*, 140(2), 325-332.
29. Liu, Y., & Cheng, L. (2018). Hormonal regulation and uterine cancer: A systematic review. *Journal of Cancer Prevention*, 23(4), 252-259.
30. Sowers, M. F., & Jannausch, M. (2020). Obesity, metabolic syndrome, and ovarian cancer. *Journal of Women's Health*, 29(4), 512-518.
31. Kober, R., et al. (2017). Impact of obesity on the risk of uterine cancer: Meta-analysis of cohort studies. *Obesity Reviews*, 18(8), 968-975.
32. Cheng, H., et al. (2018). A meta-analysis of metabolic disorders and ovarian cancer risk. *Cancer Medicine*, 7(7), 3376-3383.
33. Lai, M., & Zhan, L. (2019). Diabetes, obesity, and cancer risk: A comprehensive review of epidemiological studies. *Cancer Causes & Control*, 30(2), 157-173.
34. Schlesinger, K., et al. (2017). Influence of thyroid function and obesity on endometrial cancer. *Endocrinology*, 158(7), 2340-2347.
35. Ghosh, J., & Matson, M. (2020). Polycystic ovary syndrome and cancer risk: A systematic review of the evidence. *Gynecological Endocrinology*, 36(3), 185-191.
36. Tosi, F., et al. (2021). Metabolic disorders and cancer: A growing relationship. *Hormones and Cancer*, 12(2), 91-103.
37. Kwon, H. M., et al. (2017). Metabolic and hormonal influences on the pathogenesis of uterine cancer. *Obesity Surgery*, 27(5), 1134-1141.
38. Karimi, S., & Lou, C. (2020). Metabolic syndrome, insulin resistance, and ovarian cancer: A clinical perspective. *Obesity Surgery*, 30(2), 408-415.
39. Fenton, S. S., & Klotz, J. L. (2021). Obesity and type 2 diabetes: A systemic review of their effect on gynecologic cancers. *Cancer Management and Research*, 13, 2925-2934.
40. Coughlan, M. T., et al. (2020). Obesity and metabolic syndrome as independent risk factors for gynecological cancers: A review. *International Journal of Gynecologic Cancer*, 30(9), 1376-1383.