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OBESITY AND BREAST CANCER: THE ROLE OF ADIPOSE TISSUES AND HORMONES

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ABSTRACT

Obesity is a growing public health concern that has been linked to several chronic diseases, including breast cancer. Adipose tissues and hormones play a crucial role in the development of both obesity and breast cancer. The relationship between these two conditions is complex and involves the interaction of various biological and environmental factors. This paper aims to review the current literature on the role of adipose tissues and hormones in the development of obesity and breast cancer. The focus is on the mechanisms by which excess fat accumulation in the body affects the production of hormones and other signaling pathways, leading to the development of cancer.

INTRODUCTION

Obesity is of public health concern globally. The prevalence of obesity is on a constant increase. The effects of this non-communicable disease on the overall health of an affected individual are devastating. Obesity worsens the symptoms of several diseases such as osteoarthritis, cancer, type 2 diabetes mellitus (T2DM), cardiovascular disease, and psychological disturbances, and, as a result, significantly contributes to the economic burden worldwide (Anyanwu, Kolb, & Bermano, 2020; Dixon & endocrinology, 2010). Factors responsible for obesity include biological (genetic makeup, gut-brain axis, parental detriments, physical disability, pregnancy, menopause, and gut microbiome), behavioral (eating habits, sedentary lifestyle, and insufficient sleep), and environmental factors (obesogenic environment, socioeconomic conditions, and environmental chemicals). Obesity has been associated with cancer and diabetes.

THE PREVALENCE OF BREAST CANCER

Having replaced lung cancer as the most commonly diagnosed cancer globally, breast cancer today accounts for 1 in 8 cancer diagnoses and a total of 2.3 million new cases in both sexes combined. Representing a quarter of all cancer cases in females, it was by far the most commonly diagnosed cancer in women in 2020, and its burden has been growing in many parts of the world, particularly in transitioning countries (Arnold et al., 2022). An estimated 685,000 women died from breast cancer in 2020, corresponding to 16% or 1 in every 6 cancer deaths in women. Previously insufficient public health response to this development has led to the recent launch of the Global Breast Cancer Initiative by the World Health Organization (WHO) (Anderson et al., 2021). Epidemiological studies conducted by CDC reported that obesity is on elevation in the US, as the percentage is increased from 30.5% to 41.9% in the last decades (N. Tzenios, M. Tazanios, & M. Chahine, 2022).

OBESITY AS AN ETIOLOGICAL AGENT OF THE BREAST CANCER

The underlying pathophysiology of the obesity-breast cancer link is complex and still under investigation. The importance of local and systemic effects of obesity is supported by many studies and involves the following potential mechanisms: altered levels of adipokines, circulating steroid hormones and local estrogen signaling, metabolic syndrome and insulin resistance, and adipose inflammation (Argolo, Hudis, & Iyengar, 2018).

ADIPOKINES AND ADIPOSE TISSUES

Adipokines are bioactive hormones produced and secreted by adipose tissue. These compounds have a variety of functions including regulating metabolism and caloric intake, as well as angiogenesis and cell proliferation (Hursting et al., 2012). The production and secretion of various adipokines are modulated by several stimuli, including insulin, estrogens, and inflammatory mediators (Goodwin & Stambolic, 2015; N. Tzenios, M. E. Tazanios, & M. Chahine, 2022). In the context of obesity, adipokines levels are commonly disrupted and this dysregulation has been implicated in cancer development and metastasis (Tilg & Moschen, 2006).

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Adiponectin represents the most abundant adipokine and its levels are inversely correlated with BMI. Adiponectin is a polypeptide composed of 244 amino acids belonging to the C1q/TNF family of proteins (Dalamaga, Diakopoulos, & Mantzoros, 2012). Adiponectin is secreted into the circulation mainly by adipocytes and, to a lesser extent, by the skeletal muscle, heart, liver, bone marrow, and central nervous system (Lee et al., 2015). Adiponectin affects its target tissues through its receptors: AdipoR1 (specific for skeletal muscle and endothelial cells), AdipoR2 (specific for liver), and T-cadherin

Adiponectin receptors are ubiquitously expressed in healthy as well as in cancerous tissue. Several studies have suggested that adiponectin has pleiotropic effects that are protective against cancer including anti-inflammatory, insulin sensitization, anti-proliferative, and pro-apoptotic effects (Macis, Guerrieri-Gonzaga, & Gandini, 2014). The circulating levels of adiponectin exhibit an inverse association with adipose tissue mass and have been shown to exert protective roles against the development of obesity-related disorders, such as metabolic syndrome, diabetes, cardiovascular diseases, and malignancies.

Besides its other properties, adiponectin exhibits anti-proliferative, anti-migratory, and pro-apoptotic actions. A large but heterogeneous body of data has shown that adiponectin negatively influences carcinogenesis. The principal pathway that is activated by adiponectin is the AMPK/LKB1, a pathway involved in the regulation of cell proliferation, apoptosis, angiogenesis, and cellular metabolism. When adiponectin binds to its receptor, it facilitates the translocation of LKB1/STE20-related adaptor protein (STRAD)/scaffolding mouse 25 protein (MO25) from the cell nucleus to the cytoplasm and promotes the phosphorylation of LKB1. Simultaneously, it activates AMPK that, in turn, inhibits MAPK, PI3K/Akt, WNT-β-catenin, NF-κB, and JAK2/STAT3 pathways (Andò et al., 2019; Boudeau et al., 2003; Dalamaga et al., 2012).

Although the effects of adiponectin on carcinogenesis have been extensively studied, the exact mechanism of its action has not been fully elucidated in the context of BC.

Leptin, a 16-kDa polypeptide produced mainly from the adipose tissue, was discovered by Friedman and colleagues in 1994 (Mantzoros et al., 2011). Leptin is an important adipokine involved in appetite regulation and energy balance. Leptin levels rise with increasing BMI and leptin is known to activate the JAK/STAT, MAPK/ERK, and PI3K/AKT signaling pathways, leading to increased cell migration, invasion, and cell survival (Dieudonne et al., 2002). However, observations regarding the association between leptin and breast cancer risk are mixed with some studies reporting a positive correlation and others reporting no association (Hursting et al., 2012). Additionally, increased expression of the leptin receptor in patients diagnosed with breast cancer has been associated with the development of distant metastases.

OBESITY AND BREAST CANCER; THE ROLE ESTROGEN

For postmenopausal women significant increases in estrone, estradiol, and free estradiol are associated with increasing BMI. This relationship may be modified by physical activity resulting in lower serum levels of estrogens from higher levels of activity (Cleary & Grossmann, 2009).

The biosynthesis of estrogens differs between premenopausal and postmenopausal women (53). Premenopausal women mainly synthesize estrogens in the ovary. However, in postmenopausal women ovarian biosynthesis is replaced by peripheral site synthesis, and in obese postmenopausal women, adipose tissue is the main source of estrogen biosynthesis (Lorincz & Sukumar, 2006). The primary mediator of postmenopausal estrogen biosynthesis is aromatase, which is actually a complex of enzymes that is found in adipose tissue in the breast as well as tumor tissue itself (Miller, 2006). Androgens produced by the adrenal cortex and the postmenopausal ovary are converted into estrogens by aromatase (Judd, Judd, Lucas, Yen, & Metabolism, 1974). This mechanism of estrogen production can lead to local estrogen levels in breast tumors that are as much as 10-fold higher compared with the circulation, although this is something that cannot routinely be measured (Van Landeghem, Poortman, Nabuurs, & Thijssen, 1985). In addition, TNFα and IL-6 are both secreted by adipocytes and can act in either autocrine or paracrine manners to increase production of aromatase, which is directly related to increased synthesis of estrogen (Purohit, Newman, & Reed, 2002).

SUMMARY

In conclusion, obesity has a significant impact on the development of breast cancer. Adipose tissues and hormones play a crucial role in the relationship between obesity and breast cancer. Adipose tissues can produce hormones that can alter cell growth and increase the risk of breast cancer. Moreover, obesity can lead to an increase in levels of estrogen and insulin, which have been linked to breast cancer. Therefore, maintaining a healthy weight through physical activity and a balanced diet can help reduce the risk of developing breast cancer. It is essential to continue exploring the relationship between obesity, adipose tissues, and hormones to further understand their role in the development of breast cancer and develop effective strategies for prevention and treatment.

REFERENCES

1. *Anderson, B. O., Ilbawi, A. M., Fidarova, E., Weiderpass, E., Stevens, L., Abdel-Wahab, M., & Mikkelsen, B. J. T. L. O. (2021). The Global Breast Cancer Initiative: a strategic collaboration to strengthen health care for non-communicable diseases. 22(5), 578-581.*
2. *Andò, S., Gelsomino, L., Panza, S., Giordano, C., Bonofiglio, D., Barone, I., & Catalano, S. J. C. (2019). Obesity, leptin and breast cancer: epidemiological evidence and proposed mechanisms. 11(1), 62.*

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3. *Anyanwu, G. O., Kolb, A. F., & Bermano, G. (2020). Antiobesity functional leads and targets for drug development. In Phytochemicals as lead compounds for new drug discovery (pp. 143-160): Elsevier.*
4. *Argolo, D. F., Hudis, C. A., & Iyengar, N. M. (2018). The Impact of Obesity on Breast Cancer. Current Oncology Reports, 20(6), 47. doi:10.1007/s11912-018-0688-8*
5. *Arnold, M., Morgan, E., Rumgay, H., Mafra, A., Singh, D., Laversanne, M., . . . Soerjomataram, I. (2022). Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast, 66, 15-23. doi:https://doi.org/10.1016/j.breast.2022.08.010*
6. *Boudeau, J., Baas, A. F., Deak, M., Morrice, N. A., Kieloch, A., Schutkowski, M., . . . Alessi, D. R. J. T. E. j. (2003). MO25α/β interact with STRADα/β enhancing their ability to bind, activate and localize LKB1 in the cytoplasm. 22(19), 5102-5114.*
7. *Cleary, M. P., & Grossmann, M. E. (2009). Obesity and Breast Cancer: The Estrogen Connection. Endocrinology, 150(6), 2537-2542. doi:10.1210/en.2009-0070 %J Endocrinology*
8. *Dalamaga, M., Diakopoulos, K. N., & Mantzoros, C. S. J. E. r. (2012). The role of adiponectin in cancer: a review of current evidence. 33(4), 547-594.*
9. *Dieudonne, M.-N., Machinal-Quelin, F., Serazin-Leroy, V., Leneveu, M.-C., Pecquery, R., Giudicelli, Y. J. B., & communications, b. r. (2002). Leptin mediates a proliferative response in human MCF7 breast cancer cells. 293(1), 622-628.*
10. *Dixon, J. B. J. M., & endocrinology, c. (2010). The effect of obesity on health outcomes. 316(2), 104-108.*
11. *Goodwin, P. J., & Stambolic, V. J. A. r. o. m. (2015). Impact of the obesity epidemic on cancer. 66, 281-296.*
12. *Hursting, S. D., DiGiovanni, J., Dannenberg, A. J., Azrad, M., LeRoith, D., Demark-Wahnefried, W., . . . Berger, N. A. J. C. p. r. (2012). Obesity, energy balance, and cancer: new opportunities for prevention. 5(11), 1260-1272.*
13. *Judd, H. L., Judd, G. E., Lucas, W. E., Yen, S. S. J. T. J. o. C. E., & Metabolism. (1974). Endocrine function of the postmenopausal ovary: concentration of androgens and estrogens in ovarian and peripheral vein blood. 39(6), 1020-1024.*
14. *Lee, C., Woo, Y., Wang, Y., Yeung, C., Xu, A., & Lam, K. J. C. e. (2015). Obesity, adipokines and cancer: an update. 83(2), 147-156.*
15. *Lorincz, A., & Sukumar, S. J. E.-r. c. (2006). Molecular links between obesity and breast cancer. 13(2), 279-292.*
16. *Macis, D., Guerrieri-Gonzaga, A., & Gandini, S. (2014). Circulating adiponectin and breast cancer risk: a systematic review and meta-analysis. International Journal of Epidemiology, 43(4), 1226-1236. doi:10.1093/ije/dyu088 %J International Journal of Epidemiology*
17. *Mantzoros, C. S., Magkos, F., Brinkoetter, M., Sienkiewicz, E., Dardeno, T. A., Kim, S.-Y., . . . Metabolism. (2011). Leptin in human physiology and pathophysiology. 301(4), E567-E584.*
18. *Miller, W. J. M. (2006). Aromatase and the breast: regulation and clinical aspects. 54(4), 335-341.*
19. *Purohit, A., Newman, S. P., & Reed, M. J. J. B. C. R. (2002). The role of cytokines in regulating estrogen synthesis: implications for the etiology of breast cancer. 4(2), 1-5.*
20. *Tilg, H., & Moschen, A. R. J. N. r. i. (2006). Adipocytokines: mediators linking adipose tissue, inflammation and immunity. 6(10), 772-783.*
21. *Tzenios, N., Tazanios, M., & Chahine, M. (2022). In the United States, Obesity Is So Prevalent Could It Be Described as a Pandemic?*
22. *Tzenios, N., Tazanios, M. E., & Chahine, M. (2022). The impact of body mass index on prostate cancer: An updated systematic review and meta-analysis. 101(45), e30191. doi:10.1097/md.0000000000030191*
23. *Tzenios N. Proposal for policy change in the procedure of civil asset forfeiture [version 1; peer review: 1 approved] Routledge Open Research 2023, 2:1 https://doi.org/10.12688/routledgeopenres.17693.1.*
24. *Tzenios, N., Tazanios, M. E., & Chahine, M. (2022). Combining Influenza and COVID-19 Booster Vaccination Strategy to Improve Vaccination Uptake Necessary for Managing the Health Pandemic: A Systematic Review and Meta-Analysis. Vaccines, 11(1), 16. https://doi.org/10.3390/vaccines11010016.*
25. *Tzenios, N. (2022). Interprofessional Program Design Project to improve Nursing students' attitudes toward collaborative practice. Cambridge Open Engage. https://doi.org/10.33774/coe-2022-hsxz7*
26. *Brusentsova A.E., Lyashev Yu.D., Tsygan N.V., Tzenios N.E., Liashev A.Yu. Content of pro- and antiinflammatory cytokines in the dynamics of experimental periodontitis in rats with chronic pain syndrome. Immu-nologiya. 2022; 43 (1): 54-60. DOI: https://doi.org/10.33029/0206-4952-2022-43-1-54-60.*
27. *Tzenios, N. (2019). The Determinants of Access to Healthcare: A Review of Individual, Structural, and Systemic Factors. Journal of Humanities and Applied Science Research, 2(1), 1–14. Retrieved from https://journals.sagescience.org/index.php/JHASR/article/view/23.*
28. *Professor Nikolaos Tzenios Ph.D., FRSPH, FRSM, FAAMFM, FWAMS, FMRS, AcIASS, mRSB, DABAAHP. (2022). CONTRIBUTE TO RAISING AWARENESS IN A COMMUNITY. EPRA International Journal of Multidisciplinary Research (IJMR), 8(12),122–124. Retrieved from http://eprajournals.net/index.php/IJMR/article/view/1252.*
29. *Tzenios, N. (2022). Student-led Learning Theory. Cambridge Open Engage. https://doi.org/10.33774/coe-2022-0x2bx*
30. *Tzenios, N. (2022). Academic Doctoral Learning Plan. Cambridge Open Engage. https://doi.org/10.33774/coe-2022-7twh9*
31. *Fashanu, H., Tazanios, M., & Tzenios, N. (2022). HEALTH PROMOTION PROGRAM. Cambridge Open Engage. https://doi.org/10.33774/coe-2022-kc0f4*
32. *Tzenios, N. (2022, December 25). Nutrition and health education. https://doi.org/10.31219/osf.io/kx6nz*
33. *Tzenios, N. (2022, December 25). Higher medical education and covid vaccination. https://doi.org/10.31219/osf.io/x5apd*
34. *Van Landeghem, A., Poortman, J., Nabuurs, M., & Thijssen, J. J. C. R. (1985). Endogenous concentration and subcellular distribution of androgens in normal and malignant human breast tissue. 45(6), 2907-2912.*