OBESITY AS A RISK FACTOR FOR DIFFERENT TYPES OF CANCER

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ABSTRACT
Over the last few decades, the incidence of obesity is increasing which is now recognized as public health issue worldwide. Obesity has been associated with an elevated risk of several types of metabolic syndrome and malignancies. This article reviews the latest evidence on the association between higher Body Mass Index (BMI) and cancer, discovering the essential biological mechanism and pathways such as the interplay of adipokines, cytokines, and growth factors. Furthermore, it provides intuition into the effects of obesity on proliferation and metastasis. In last, it highlights the need for a comprehensive approach to tackle the obesity pandemic including changes in lifestyle and regular cancer to enhance the quality of life.

INTRODUCTION

Obesity leads the human body to deviate from normal metabolic conditions to abnormal one, which in term play important role in the pathophysiology of diverse metabolic syndrome (Bitzur et al., 2016). The stored body fat is not primarily for energy generation but is also involved in the secretion of different types of hormones which modulates harmful metabolic effects ranging from insulin resistivity to chronic metabolic syndromes. A few decades ago, it was believed that obesity is just related to hyperinsulinemia, hyperglycemia, hypertension, and cardiovascular diseases. But recent studies revealed that different molecular mechanisms associated with adipose tissues in obese can lead to different types of cancers (Nimptsch, Pischon, & investigation, 2015).

THE ROLE OF OBESITY IN DIFFERENT TYPES OF CANCER

The growing body of scientific information is evident on the fact that obesity plays a crucial role in the pathophysiology of different cancer like liver cancer (Saitta, Pollicino, & Raimondo, 2019), prostate cancer (N. Tzenios, M. E. Tazanios, & M. Chahine, 2022a; N. Tzenios, M. E. Tazanios, & M. J. M. Chahine, 2022b), breast cancer (Kang, LeRoith, & Gallagher, 2018), and colorectal cancer (Dai, Xu, & Niu, 2007).

THE ROLE OF OBESITY IN LIVER CANCER

Non-alcoholic fatty liver disease (NFLD) is considered a major threat to liver health in the 21st century which is caused by the increased prevalence of obesity. Non-alcoholic fatty liver disease (NFLD) is defined as the excessive accumulation of triglycerides ($\geq$ 5% TGs) into the liver tissues without hyper-alcoholism and other liver morbidities like chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections. Sometimes, the disease may acquire an advanced stage called Non-alcoholic steatohepatitis (NASH) (Chalasani et al., 2018). NAFLD is regarded as the hepatic manifestation of the metabolic syndrome and is associated with several metabolic comorbidities in addition to obesity, including Type 2 diabetes mellitus (T2DM), hyperlipidemia, and arterial hypertension (Cholongitas et al., 2021). In regard of the epidemiology of NAFLD, one fourth of the world population is affected by NAFLD which may exceeded in coming 10 years upto 56%. NAFLD is also considered a major cause of hepatocellular carcinoma (HCC) (de Hoon, Eichenberger, & Vitkup, 2010).

THE ROLE OF OBESITY IN PROSTATE CANCER

As previously said that obesity is a serious threat to public health affecting more than 30% of individuals in the United States. There are certain extrinsic (environmental) and intrinsic (psychology, neuroendocrine and genetic) factors that are that play their role in the development of obesity (Tzenios, Tazanios, et al., 2022a).

In worldwide, prostate cancer is the second most common type of cancer found and also second prominent death causing cancer in men (Jemal et al., 2011). The link between higher BMI and pathophysiology of prostate cancer is very ambiguous but a lot of studies have found substantial link between the obesity and the prognosis of prostate cancer (Guerrios-Rivera et al., 2017). A scientist reported that obesity at the early stage of life is inversely related to the prognosis of the prostate cancer (Möller et al., 2016). Another study revealed that higher BMI was linked with higher mortality related to the prostate cancer (Taghizadeh et al., 2015). The analysis of data from Prostate Cancer Prevention Trial (PCPT) revealed that obesity raises the chance of high-grade prostate cancer (Gong et al., 2006). As a result, obesity-mediated cancer progression is a major issue. Obesity is related to lower disease-free survival and overall survival across all breast cancer subtypes (Lohmann et al., 2021).

THE ROLE OF OBESITY IN BREAST CANCER

The most frequent type of cancer reported in women is breast cancer. According to the Global cancer statistics 2020, the prevalence of breast cancer has surpassed the lung cancer worldwide (Sung et al., 2021). The prominent factor involved in the pathophysiology is higher BMI which lead to postmenopausal breast cancer. This type of cancer is easily preventable by adopting healthy and active life style (Clinton, Giovannucci, & Hursting, 2020).

The primary source of estrogen in premenopausal women is ovaries. While in menopause, adipose tissue becomes the major site of estrogen production. As a result, obese women have higher postmenopausal estrogen levels and, as a result, are more vulnerable to estrogen's protumorigenic effects (Bhardwaj et al., 2019). However, the scientific evidence on the correlation between obesity and breast cancer is convoluted by subtype and menopausal state. Obesity in postmenopausal women enhances the overall relative risk of acquiring breast cancer to 1.33, owing mostly to higher frequencies of estrogen receptors (ER) + breast cancers. While obesity, is linked to the emergence and progression of postmenopausal tripe negative breast cancer (TNBC). The genetic biomarkers of higher BMI such as several single nucleotide polymorphisms associated with fasting glucose and insulin, also correlate with breast cancer risk regardless of family background, age, or menopausal status, highlighting the significance of the connection among obesity, breast cancer risk, and genetics (Devericks, Carson, McCullough, Coleman, & Hursting, 2022). Furthermore, the obese people have an altered metabolism along chronic inflammatory state as shown by the increase of inflammatory cells and makers (Shoelson, Herrero, & Naaz, 2007).

There is a direct impact of higher BMI of obese people on the progression of breast cancer. In postmenopausal individuals, a higher peripheral estrogen production in adipose tissues was associated with a higher BMI. Patients with a high BMI showed a limited concentration of sex hormone-binding globulin, which may be the cause of their poor BC prognosis. The significant rise in estrogen production and aromatase activity was also associated with uncontrollable BC cell growth (Shoelson et al., 2007). However it is still ambiguous that most of the breast cancer patient with overweight psyche has an elevated concentration of insulin, insulin growth factor and sex hormones which could cause a significant mitogenic activity (Stephenson, Rose, & cancer, 2003).

THE ROLE OF OBESITY IN COLORECTAL CANCER

Colorectal cancer (CRC) is the third most frequent malignancy and the third major cause of cancer mortality in both men and women in the United States. Recent epidemiological research indicates that CRC has been steadily increasing, implying a continuing need to identify the factors that may be contributing to its development. Obesity is one risk factor that is persisting and increasing day by day in modern world. Obesity is a complex condition with several metabolic and physiological alterations that promote carcinogenesis. The gut microbiome is another component that is changed in obesity and has been linked to CRC (Goldbaum, 2022).

Higher BMI is the fifth leading cause of death in adults, accounting for at least 2.8 million deaths per year. Furthermore, in Europe, being overweight and obese have been linked to 11% of colorectal cancer (CRC) incidences. Furthermore, some studies predict that higher BMI is linked with more than 30-70% increased colorectal cancer in men unlike in women (Bardou, Barkun, & Martel, 2013). Although visceral and subcutaneous compartments are the sites where excessive fat is stored, it's fascinating to see that this recent study found a higher incidence of abdominal obesity (27.8% of men and 45.9% of women) (Abajo et al., 2012). The metabolic syndrome (MS) only affects roughly two-thirds of people who are obese. On the other hand, some obese subjects retain normal

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metabolisms.   MS is crucial in associating obesity to the majority of its side effects, including diabetes, cardiovascular disease, or an elevated risk of cancer in various locations, although it may vary across different ethnicities (Wildman et al., 2008).

In summary, a few number of available studies propose weight loss may be lowers the risk of developing cancer (Tzenios, Tazanios, Poh, & Chahine, 2022) specially colorectal cancer. Weight loss achieved by healthy diet with or without bariatric surgery obstructs with gut microbiota and host metabolic and physiological functions which lead to decrease incidence of metabolic syndrome and maintain a proper concentration of growth factors, inflammatory cytokines and adipokines.

REFERENCES
1. Abajo, A., Bitarte, N., Zarate, R., Boni, V., Lopez, I., Gonzalez-Huarriz, M., . . . Garcia-Foncillas, J. (2012). Identification of colorectal cancer metastasis markers by an angiogenesis-related cytokine-antibody array. World J Gastroenterol, 18(7), 637-645. doi:10.3748/wjg.v18.i7.637
2. Bardou, M., Barkun, A. N., & Martel, M. (2013). Obesity and colorectal cancer. 62(6), 933-947. doi:10.1136/gutjnl-2013-304701 %J Gut
3. Bhardwaj, P., Au, C. C., Benito-Martin, A., Ladumor, H., Oshchepkova, S., Moges, R., . . . biology, m. (2019). Estrogens and breast cancer: Mechanisms involved in obesity-related development, growth and progression. 189, 161-170.
4. Bitzur, R., Brenner, R., Maor, E., Antebi, M., Ziv-Baran, T., Segev, S., . . . Kivity, S. (2016). Metabolic syndrome, obesity, and the risk of cancer development. European Journal of Internal Medicine, 34, 89-93. doi:https://doi.org/10.1016/j.ejim.2016.08.019
5. Chalasani, N., Younossi, Z., Lavine, J. E., Charlton, M., Cusi, K., Rinella, M., . . . Sanyal, A. J. J. H. (2018). The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. 67(1), 328-357.
6. Cholongitas, E., Pavlopoulou, I., Papatheodoridi, M., Markakis, G. E., Bouras, E., Haidich, A.-B., & Papatheodoridis, G. J. A. o. g. (2021). Epidemiology of nonalcoholic fatty liver disease in Europe: a systematic review and meta-analysis. 34(3), 404.
7. Clinton, S. K., Giovannucci, E. L., & Hursting, S. D. J. T. j. o. n. (2020). The world cancer research fund/American institute for cancer research third expert report on diet, nutrition, physical activity, and cancer: impact and future directions. 150(4), 663-671.
8. Dai, Z., Xu, Y.-C., & Niu, L. J. W. j. o. g. W. (2007). Obesity and colorectal cancer risk: a meta-analysis of cohort studies. 13(31), 4199.
9. de Hoon, M. J. L., Eichenberger, P., & Vitkup, D. (2010). Hierarchical Evolution of the Bacterial Sporulation Network. Current Biology, 20(17), R735-R745. doi:https://doi.org/10.1016/j.cub.2010.06.031
10. Devericks, E. N., Carson, M. S., McCullough, L. E., Coleman, M. F., & Hursting, S. D. (2022). The obesity-breast cancer link: a multidisciplinary perspective. Cancer and Metastasis Reviews, 41(3), 607-625. doi:10.1007/s10555-022-10043-5
11. Goldbaum, A. A. (2022). Role of the gut microbiota, diet, and obesity in colorectal cancer risk. Purdue University Graduate School, Retrieved   from https://hammer.purdue.edu/articles/thesis/Role_of_the_gut_microbiota_diet_and_obesity_in_colorectal_cancer_risk/19678431
12. Gong, Z., Neuhouser, M. L., Goodman, P. J., Albanes, D., Chi, C., Hsing, A. W., . . . Prevention. (2006). Obesity, diabetes, and risk of prostate cancer: results from the prostate cancer prevention trial. 15(10), 1977-1983.
13. Guerrios-Rivera, L., Howard, L., Frank, J., De Hoedt, A., Beverly, D., Grant, D. J., . . . Freedland, S. J. J. U. (2017). Is body mass index the best adiposity measure for prostate cancer risk? Results from a veterans affairs biopsy cohort. 105, 129-135.
14. Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., & Forman, D. J. C. a. c. j. f. c. (2011). Global cancer statistics. 61(2), 69-90.
15. Kang, C., LeRoith, D., & Gallagher, E. J. J. E. (2018). Diabetes, obesity, and breast cancer. 159(11), 3801-3812.
16. Lohmann, A. E., Soldera, S. V., Pimentel, I., Ribnikar, D., Ennis, M., Amir, E., & Goodwin, P. J. J. J. J. o. t. N. C. I. (2021). Association of obesity with breast cancer outcome in relation to cancer subtypes: a meta-analysis. 113(11), 1465-1475.
17. Möller, E., Wilson, K. M., Batista, J. L., Mucci, L. A., Bälter, K., & Giovannucci, E. J. I. j. o. c. (2016). Body size across the life course and prostate cancer in the Health Professionals Follow-up Study. 138(4), 853-865.
18. Nimptsch, K., Pischon, T. J. H. m. b., & investigation, c. (2015). Body fatness, related biomarkers and cancer risk: an epidemiological perspective. 22(2), 39-51.
19. Saitta, C., Pollicino, T., & Raimondo, G. (2019). Obesity and liver cancer. Annals of Hepatology, 18(6), 810-815. doi:https://doi.org/10.1016/j.aohep.2019.07.004
20. Shoelson, S. E., Herrero, L., & Naaz, A. J. G. (2007). Obesity, inflammation, and insulin resistance. 132(6), 2169-2180.
21. Stephenson, G. D., Rose, D. P. J. N., & cancer. (2003). Breast cancer and obesity: an update. 45(1), 1-16.
22. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. J. C. a. c. j. f. c. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. 71(3), 209-249.
23. Taghizadeh, N., Boezen, H. M., Schouten, J. P., Schröder, C. P., Vries, E. E. d., & Vonk, J. M. J. P. o. (2015). BMI and lifetime changes in BMI and cancer mortality risk. 10(4), e0125261.
24. Tzenios, N., Tazanios, M., Poh, O. B. J., & Chahine, M. (2022). Does Losing Weight Lower the Risk of Cancer: A Systematic Review and Meta-analysis.
25. Tzenios, N., Tazanios, M. E., & Chahine, M. (2022a). The impact of body mass index on prostate cancer: An updated systematic review and meta-analysis. 101(45), e30191. doi:10.1097/md.0000000000030191

26. *Tzenios, N., Tazanios, M. E., & Chahine, M. J. M. (2022b). The impact of body mass index on prostate cancer: An updated systematic review and meta-analysis. 101(45), e30191.*
27. *Tzenios, N., Tazanios, M., & Chahine, M. (2022). In the United States, Obesity Is So Prevalent Could It Be Described as a Pandemic?*
28. *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*
29. *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.*
30. *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.*
31. *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*
32. *Wildman, R. P., Muntner, P., Reynolds, K., McGinn, A. P., Rajpathak, S., Wylie-Rosett, J., & Sowers, M. R. (2008). The Obese Without Cardiometabolic Risk Factor Clustering and the Normal Weight With Cardiometabolic Risk Factor Clustering: Prevalence and Correlates of 2 Phenotypes Among the US Population (NHANES 1999-2004). Archives of Internal Medicine, 168(15), 1617-1624. doi:10.1001/archinte.168.15.1617 %J Archives of Internal Medicine*