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Obesity, Cancer and Cardiovascular Diseases: Can They Have to-and-Fro Communications with Sleep?

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Abstract: Obesity, characterized by the excessive accumulation of body fat, contributes to a multitude of physiological dysfunctions. This paper explores the complex relationship between obesity and various risk factors and complications, shedding light on critical health implications. Obesity triggers alterations in insulin, leptin, adiponectin, cytokines, and insulin-like growth factors, fostering conditions conducive to cancer initiation. Aberrations in nutrient-dependent intracellular signaling pathways, driven by the excess nutrition characteristic of obesity, contribute to the neoplastic transformation of cells. The Body Mass Index (BMI) correlates directly with adiposity, underlining its significance in cancer risk. Furthermore, insulin and insulin-like growth factors, notably IGF-2, play pivotal roles in this relationship. The expression of IR-A receptors is elevated in cancer. Obesity and cardiovascular diseases share a strong association. Obesity elevates the risk of fatal events like myocardial infarction. High cholesterol levels contribute to atherosclerosis in the aorta and coronary arteries. The severity of coronary artery disease is influenced by plaque formation characterized by calcium deposits. Obesity is also linked to hypertension and increased ventricular mass, exacerbating cardiovascular risks. Hypercholesterolemia and hypertension correlate with a high Body Mass Index (BMI). Obesity is intricately connected to insulin resistance, particularly evident in childhood obesity. It entails a gradual decline in insulin sensitivity, leading to elevated insulin levels in the bloodstream. Insulin resistance is a central factor in the development of Type 2 Diabetes Mellitus. Obesity also results in elevated triglyceride levels and reduced high-density lipoproteins, contributing to atherogenic dyslipidemia and a heightened risk of atherosclerosis. Additionally, obesity is associated with various other disorders, including epilepsy, depression, and neuropsychological problems. Beyond its physiological impact, obesity is associated with significant psychosocial challenges. Studies indicate that individuals with obesity face a higher risk of depressive symptoms, often related to overeating and unhealthy dietary patterns. The social withdrawal tendencies of obese individuals exacerbate these symptoms, with higher rates of depression observed in this group. OSA, a sleep disorder characterized by intermittent breathing cessation during sleep, is strongly correlated with obesity. Approximately 58% of obese individuals experience OSA, with higher Body Mass Index (BMI) associated with an increased risk. Weight reduction has been found to mitigate the severity of OSA and related arrhythmias. Continuous positive airway pressure (CPAP) therapy demonstrates effectiveness in reducing visceral fat accumulation and leptin levels. This comprehensive review underscores the intricate web of health implications associated with obesity, emphasizing the critical need for preventive measures and intervention strategies to address the multifaceted challenges posed by this global health concern.

Keywords: obesity; cancer, cardiovascular disease, insulin resistance. psychosocial impact; sleep apnea

Introduction

Obesity is a disease which involves accumulation of excess body fats leading to several physiological dysfunction^{1,2}. In childhood obesity there is replication of adipocytes leading to elevated number of the fat cells in the body, whereas obesity seen in adults is related to expansion in the size of adipocytes³⁻⁵. Interventions taken to reduced weight will only reduce the size of the fat

cells and not the number of fat cells. Restrictions in diet may lead to reduction in lipogenesis and release of free fatty acids⁶⁻⁹.

Some of the risk factors and complications related with obesity:

1. **Cancer:** In obese people alteration in the level of insulin, leptin, adiponectin (hormone secreted by adipocytes), cytokines and insulin like growth factors is seen¹⁰. All these alterations promote the initiation of cancer inside our body. Cancer is a disease in which normal cells due to oncogenic mutations will undergo neoplastic transformation. Inside our cells the signalling taking place that controls the growth of a cell majorly depends upon the nutrients taken by us¹¹⁻¹³. In obesity there is excess nutrition inside our body that drastically affects the intracellular signalling thus promoting the neoplastic transformation of cells. The BMI (Body mass index) is directly related with the adiposity, the higher the adiposity the higher is the BMI. Adipose tissue is an important part of signalling networks; therefore, deposition of adipose tissue adversely changes the signalling pattern inside a cell. Endocrine system helps in the communication between the cells and nutrition intake. Some more factors are related with obesity and cancer as follows:
 - a. **Insulin:** It is one of the most important hormones. Insulin binds with insulin receptors (IR) which is present on the cell surface and upon binding signalling cascades will be initiated that will further affect several cellular responses, one of the response is that it will help to trade glucose transporters to the cell membrane so that uptake of glucose can be increased. Insulin is secreted by beta cells of pancreas. The insulin will then go and bind to the IR present on the cell surface, once this happens tyrosine kinase domain gets activated that will further go and phosphorylate IR substrate proteins 1 and 2. Upon phosphorylation of these proteins several signalling pathways gets activated. In cancer it has been seen that there is high expression of IR-A receptors.
 - b. **Insulin like growth factors (IGF):** liver produces IGF-1 in response to growth hormones. High levels of IGF-1 are directly proportional with the cancer. IGF-1 Binds with insulin like growth factor binding proteins (IGFBP) and inhibit the binding of IGF-1 to its receptor. IGF-2 acts through IR-A and is highly related with BMI. Generally, higher concentration of IGF-2 has been seen in people with obesity. In wilm's tumour there was high expression of IGF-2. In mesenchymal tumours IGF-2 imprinting genes are not found.
 - c. **Steroid Hormones:** Oestrogen signalling is chronically involved in tumorigenesis by stimulating proliferation of cells and inducing angiogenesis. In this inhibition of apoptosis also takes place. Moreover, obesity is also associated with reduced levels of sex hormone-binding globulin, which elevates the free oestradiol that is associated with a higher cancer risk. Relation of other steroid hormones with cancer and obesity is still not clear¹⁴
2. **Cardiovascular disease (CVD):** Obesity and cardiovascular diseases are strongly linked with each other. Some studies have shown that in obese people risk of myocardial infarction increases which can be fatal. Atherosclerosis in Aorta and coronary artery is because of high cholesterol level in an individual. The level of calcium deposits which is plaque formation determines the severity of coronary artery disease. Obesity and high blood pressure are also linked with each other, an increase in the ventricular mass is seen in people who are obese and have hypertension. Hypercholesterolemia and hypertension are both linked with high body mass index¹⁵
3. **Metabolic Alterations:** In obesity there is involvement of insulin resistance, some studies have shown that in childhood obesity there is a gradual decrease in the insulin sensitivity and an elevated level of insulin the blood circulation can be seen. Insulin resistance is one of the major factors responsible for Type 2 Diabetes mellitus. There is an increase seen in insulin resistance with age, but if there is high insulin resistance which is generally in the case of obesity then it leads to glucose intolerance which further leads to type 2 diabetes. In obesity there is an elevated levels of triglycerides (TG) and reduction in high density lipoproteins, this can lead to Atherogenic dyslipidemia. This condition eventually increases the changes of atherosclerosis in obese people¹⁵. Many other disorders like epilepsy¹⁶⁻¹⁸, depression and other neuropsychological problems can also occur.¹⁹

4. **Psychosocial problems:** Obesity along with physiological conditions also have certain psychological problems, like studies have shown people with obesity have high risk of showing depressive symptoms. Also, depression can be related to overeating or unhealthy dietary patterns. People who are obese tend to be reluctant in getting socially involved with people and these worsens the symptoms. People who are obese shows more symptoms of depression than people who are already suffering from depression.
5. **Obstructive Sleep apnoea:** It is a sleep disorder in which during sleeping the breathing stops suddenly and after few seconds the breathing will again start. This disorder is highly associated with obesity, 58% of people who are obese shows that they also suffer from sleep apnoea. The higher the BMI (body mass index) the higher is the chance of suffering from this sleep disorder. People who suffer with this disorder shows. Reducing weight can decrease the severity of the sleep apnoea and sleep apnoea-related arrhythmias^{20,21}. Continuous positive airway pressure (CPAP) therapy has shown to decrease the visceral fat accumulation in the body and reduced leptin levels²¹.

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