



Effectiveness Of Intermittent Fasting in Preventing Immune Diseases and Cancer

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Abstract

Background: Nutrition interventions are recommended for most cancer patients. Chronic caloric restriction has powerful anticarcinogenic actions, also, fasting has demonstrated reductions in chemotherapy related side effects and improved treatment tolerability and effectiveness, evidence suggests that fasting or prolonged fasting is safe and may have a protective effect on healthy cells from chemotherapy toxicity, also decreasing tumor growth. Fasting and exercise is recommended because lead to improve cancer related outcomes, the studies showed that intermittent fasting between 24 and 72 hours can be safe and feasible as determined by treatment side effects, it has become in growing interest in both the scientific and lay community as an alternative to caloric restriction. Materials: According to a survey by the international food information council foundation, intermittent fasting has become the most popular diet in the last year, and patients with cancer are seeking about its beneficial effects for cancer prevention and treatment. However, we needs additional trials are needed to elucidate the risks and benefits of fasting for patients with cancer. Results: the findings suggest that the combined fasting and exercise is improve the health and helps on the preventing from tumor. Intermittent fasting may be usefule in adults with cancer through means of weight managment. The health benefits of caloric restriction result from a passive reduction in the production of damaging oxygen free radicals. In this review, we provide evidences of fasting as intervention in the cancer and discuss the potential benefits and mechanisms of fasting for cancer patients. Conclusion: Diet and fasting play an important role of in targeted therapies for any cancer type, where tumor cells adapttheir metabolism to produce energy for growth and survival; fasting decreases circulating glucose,which is the preferential energy source of cancer, thus fasting could make therapies more effective by sensitizing cancer cells to protecting healthy cells from treatment toxicity, through decreasing circulating insulin-like growth factor-1, which limiting tumor development pathways.

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Introduction

Despite significant advances in the oncology, cancer is the second leading cause of mortality and morbidity in the United States [1], it is accounting 608,570 deaths in 2021 [2], with aaging, it may expected to increase the risk of cancer, which estimated 40.14% for males and 38.70% for [3]. cancer patients suffers from undesirable alterations including, body composition and reductions in quality of life, thus, lead to development of comorbidities, and mortality [4], the side effects risks are related to patient characteristics such as obesity, functional status, nutritional intake,

presence of comorbidities, and genetic predispositions [5-6]. particular, the estimations indicated that 42% of all cancers and 45% of cancer deaths due to lifestyle risk factors, including tobacco, physical inactivity, excessive adiposity, and dietary factors such as processed food consumption, red meat, processed meat, low intake of plant foods rich in dietary fiber, antioxidant, vitamins and phytochemicals [7]. Overweight and obesity are associated with an increased risk for different cancers, therefor, cancer outcomes could be prevented and improved by healthful lifestyle [8].

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For example, Calorie restriction without malnutrition is the most robust intervention for cancer prevention in rodents and monkeys, and, in humans, decreased production of growth factors, inflammatory cytokines, and anabolic hormones, decreased oxidative stress and free radical induced DNA damage can be promote by anticarcinogenic adaptations [9]. On other hand, Calorie restriction and exercise improves and protects from cancer, treatment the changes in body composition, functional status, inflammatory environments and prevent obesity comorbidities including, cardiovascular disease, type 2 diabetes, and metabolic syndrome [10]. Intermittent fasting is becoming a popular alternative to daily Calorie restriction, with intermittent fasting being the most frequently cited diet pattern in 2020 among Americans aged 18 to 80 years according to the international food information council survey [11]. Calorie restriction has various forms, including fasting for 24 hours on alternate days, fasting 2 days per week on nonconsecutive days, or time-restricted feeding, Fasting is the avoidance of food, and in some cases drink, for a specific amount of time, it is practiced for a variety of reasons including religious purposes, like Ramadan fast, and health purposes, such as alleviate toxicities and cancer symptoms, it impact body and cardiometabolic outcomes [12], fasting is considered as safe intervention while receiving treatment for cancer [13], also, fasting of 12 to 72 h with feeding during fed hours may be feasible for cancer patients and improvement the risk factors associated with cancer related outcome [14]. several studies have reported that exercise play a role in improving treatment tolerance and efficacy such as relative dose intensity and treatment delivery and tumor size [15-16]. In this review, we examine the data of different forms fasting, with focusing on the biologic adaptations

that may reduce cancer incidence and improve cancer outcomes. also, We highlight new scientific trends on the role of intermittent fasting as a potential new adjunctive therapy for patients undergoing chemotherapy. The daily fasting period of up to 20 hours, result in ketogenesis occurs, thus, metabolic switching from liver-derived glucose to adipose cell-derived ketones occurs daily or several days each week. Some studies in animals and humans have shown that the health benefits of intermittent fasting are not only reduced free-radical production or weight loss, but, intermittent fasting elicits adaptive cellular responses between and within organs in a manner that improves glucose regulation, increases stress resistance, and suppresses inflammation. During fasting, cells activate pathways that enhance intrinsic defenses against oxidative and metabolic stress and that remove and repair damaged molecules [17-18]. On other hand, studies show the efficacy of intermittent fasting in modifying diseases in animals, including obesity, diabetes, cardiovascular disease, cancers, neurodegenerative brain diseases [19], it affects general health indicators, slows aging and disease processes [20]. Also, the combination and synergism fasting and exercise in the non cancer population is improve health related outcomes [21]. This research present some reviews studies in animals and humans that have shown how intermittent fasting affects general health indicators and slows aging and disease processes. First, it was describe the most commonly studied intermittent fasting regimens, then, present and discuss findings the intermittent fasting regimens in healthy persons and in patients with metabolic disorders (obesity, insulin resistance, hypertension and cancer). Finally, presenting practical information on how intermittent-fasting regimens can be prescribed and implemented.

Table 1: Different Definition of intermittent fasting types according to [21]

Type	Definition
Intermittent energy restriction	It is known as restricting energy intake to 60–75% below energy requirements for short periods, followed by periods normal energy intake. For example, 5:2 diet, consisting of pproximately 5 days of eucaloric feeding and approximately 2 days of a very-low-calorie diet per week.
Long term fasting	It means temporarily fasting for a period more than 72 hours.
Short term fasting	It is known as Temporarily fasting for a period between 12



	and 72 hours, an example alternate day fasting.
Time restricted feeding	It means reducing food intake to a set number of hours each day , for example, eating in less than 10 hours daily period and fast between (12-16 hours).
Ramadan fast	It means Religious fasting, which require abstinence from foods and beverages for a short period of time.
Fasting mimicking diet	It known as very low-calorie and low protein diet.

Intermittent fasting healthy benefits

Body composition during fasting

Fasting induce synergistic effects on improved metabolic outcomes such as body composition, cholesterol, and insulin sensitivity. Fasting and exercise have achieve health and therapeutic benefits in oncology [22]. Body composition changes during fasting, which associate with the length of time fasting. In a pilot crossover study among cancer patients undergoing chemotherapy, comparing short term fasting to normocaloric diet, it was observed a significant loss in mean fat mass , which led to a significant weight loss, also, fasting may achieve the baseline weight, so fasting is the better option for cancer patients [23]. An increase in fat mass and decline in lean mass loss occurs in cancer patients as a result of extended bedrest, stress-related eating, decreased physical activity [24], thus, the quantity and distribution of fat mass and lean mass are influential in the effectiveness of treatment, development of cancer and treatment related side effects [25]. Also changes in fat mass and lean mass can play critical roles in the development of cardiometabolic outcomes, which contribute to the development of comorbidities and reducing the health of a cancer patient, so lifestyle intervention strategies, such as fasting and its different types is critical to a cancer patient's care to improve body composition and prevent cancer [4].

Fasting insulin like growth factor

During the fasting, the body utilizing glycogen stores for energy to maintain glucose homeostasis. Insulin like growth factor is a mediator of growth hormone and has significant metabolic effects. Obesity has been attributed to 15–20% of cancer related deaths where obese individuals often present with higher levels of Insulin like growth which associating obesity, increased cancer risk and disease progression [26]. Some studies utilizing short term fasting have demonstrated a reduction in Insulin like growth factor with a reduction in insulin [23]. In study about women with breast cancer, data analysis that each 2 hours

increase in overnight fasting was associated with a significant reduction in hemoglobin [27]. Some literature suggests that the short term fasting, which is a type of intermittent fasting may play a role in improvement cancer outcomes, such as treatment toxicity and efficacy, through normalization of metabolic markers [13]. obesity and high levels of insulin and Insulin like growth factor, in addition to diabetes mellitus are associated with cancer [28].

Diet, intermittent fasting and cancer prognosis

weight loss is considered without a significant change in diet composition, has a role in reducing cancer risk. For example, a low fat dietary pattern resulted in weight loss in Study of early stage breast cancer survivors [29]. Chronic daily without malnutrition has a powerful effect in preventing spontaneous and chemically induced tumors in animals and reduce the development of mammary tumors in rodents [30]. On other hand, [31] studied the role of intermittent fasting in the prevention and treatment of cancer, Studies suggest that prolonged fasting in some patients with cancer is safe and capable of decreasing chemotherapy related toxicity and tumor growth.

Cancer related outcomes during fasting

Lifestyles, including physical activity and the consumption of a healthy diet are factors that decrease the risk of cancer development. Cancer cells rely on aerobic glycolysis deriving their energy from glucose converted to lactate for energy followed by lactate fermentation, even when oxygen is available. During fasting, a shift in energy metabolism from glycolytic metabolism to oxidative phosphorylation, may be a means by which cancer growth rate is altered [32]. There are studies on long term calorie restriction in humans have demonstrated a reduction in metabolic and hormonal factors associated with cancer risk [33]. Short term fasting from 12 to 72 hours may be feasible for cancer patients. on other hand, in mice, shorter periods of fasting have been shown to slow cancer growth as effectively, with the effects of the



short term fasting improving response between healthy somatic cells and cancer cells, thus, short term fasting increase sensitivity of tumor cells to chemotherapy [34-35]. During fasting, shuts down pathways promoting growth to provide energy to repair pathways that contribute to resistance to chemotherapy, which is known stress resistance [36-37], also, fasting reducing leukocyte damage. In a pilot study of short term fasting in negative breast cancer patients, compared to unfasted women, experienced reduced hematological toxicities 7 days post chemotherapy administration for erythrocyte and thrombocyte counts. Patients undertaking short term fasting have a response to chemotherapy, compared to non fasted patients [23]. According to [38] demonstrated that lifestyle, including fasting is considered the best support cancer patients and health outcomes, thus, the mplementation of fasting depended on the patient has to limit their food intake for a certain period of time, as opposed to changing the type of food they consume, may be more appealing and easier to adhere. Finally, fasting demonstrates as a potential modality to bolster antitumor immunity, prolonged overnight fasting reduce inInsulin like growth factor levels and protein kinase A activity. Further, fasting lessened immunosuppression and chemotherapy induced mortality, and alternate day fasting for two weeks led to inhibited inhibiting tumor growth through decreased levels of adenosine, and increased autophagy of tumor cells [39-40].

Mechanisms of intermittent fasting in cancer

Cancer occurs through a combination of mutations and damage to deoxyribonucleic acid that lead to atypical rapid reproduction of cells [41]. Those mutations make cancer cells less able to adapt such as those created during fasting. Conversely, healthy cells make maintenance phase in response to fasting, the benefits of fasting related to cancer are known as differential stress resistance , which protects healthy cells from chemotherapy toxicity [42], which sensitizes cancer cells to the chemotherapy, This occurs because fasting reduces the levels of hormones in the body including glucose, insulin, and insulin-like growth factor-1 , which reduce cell division and growth, thereby protecting them from chemotherapy [43]. In addition to, fasting promote the regeneration of stem cells in the nervous system, muscle and liver damaged by chemotherapy, as well as regenerate white blood cells [44]. Furthermore, fasting reduces

of heme oxygenase-1 , heme oxygenase-1 is a protein protects cancer cells from cell death, thereby sensitizing the cancer cells to chemotherapy and inducing apoptosis, also, fasting inhibits the development of new blood vessels in tumors that prevents tumor growth [41]. In general, intermittently fasting during chemotherapy is safe and does not contribute to adverse side effects or malnutrition in women with breast cancer and without significantly impacting quality of life.

Search Strategy

PubMed databases were used to search the literature about the “Fasting, cancer and (chemotherapy, treatment, toxicity). Articles were include studies of human adults 18 years or older with suffering from breast cancer and undergoing chemotherapy. studies were excluded if fasting was limited to fasting blood work and if they did not involve an intermittent fasting protocol, studies that includedpatients with other cancers, in addition to patients with breast cancers. According to [36]. was including four patients with ovarian cancer in addition to twenty nine patients with breast cancer and one patient with advanced breast cancer as they studied the effects of intermittent fasting on quality of life. Also, men patients suffering from several other cancers such as urothelial, non small cell lung cancer, ovarian, and uterine, in addition to breast cancer. In addition to provided valuable insight into fasting in relation to 2 different standard of care chemotherapy regimens for patients with breast cancer.

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Literature review

According to [36] investigated the effectiveness of fasting for twenty four hours on women with breast cancer to fast and they treat by chemotherapy , these women were permitted to drink water and sugarless coffee and tea during the fasting time period, fasting did not contribute to chemotherapy toxicities, addressed fasting protocol and quality of life on chronic illness therapy for participants with several others of cancer such as breast cancer, advanced breast cancer and ovarian cancer and they treat by chemotherapy, the participants were fast for 36 hours before chemotherapy and for 24 hours after chemotherapy. Those participants who started with fasting reported better quality of life and less fatigue than those following the Mediterranean diet. All reported side effects of



fasting was low grade and included headache, hunger, nausea after intake of broth or juice. Also, depend on increasing the length of the fast for 24 hours before platinum-based chemotherapy cycle, the length of the fast was gradually increased in each cycle, with the maximum length of fasting being 72 hours. No evidence of malnutrition was found in this study. Fasting-related symptoms included headache, dizziness, hypoglycemia, grade I weight loss, hyponatremia, and hypotension. These studies concluded that intermittent fasting is safe during the chemotherapy regimens, including lack of toxicity, weight loss, and malnutrition. In addition to fasting reduces the levels of glucose and insulin circulating in the body. Also, fasting was safe in that insulin levels were not significantly increased, intermittent fasting by a minimal amount of calories may promote feasibility in that 200 to 350 calories was generally feasible for the participants who were able to adhere to the fasting protocol but not for all. On other hands, [45] studied the safety and feasibility of intermittent fasting during chemotherapy for breast cancer. Intermittent fasting has been shown to protect healthy cells from chemotherapy toxicity while sensitizing cancer cells, intermittent fasting between 24 and 72 hours can be safe and feasible by treatment side effects, blood work, adherence to a fasting protocol, and quality of life.

Discussion

Previous studies [36] indicated that intermittently fasting was safe, it is not contributing in the side effects of chemotherapy, but it improve of the effectiveness of chemotherapy and prevent the healthy cells toxic during chemotherapy, the number of participants with nausea and vomiting decreased as the length of the fast increased, with improvement in quality of life and fatigue in participants who started chemotherapy. In addition, the safety through non increasing insulin and glucose levels during the analyzing biochemical laboratory. Most, of the participants in this studies, but not all were able to the fasting protocol, demonstrating inconsistent feasibility of fasting during chemotherapy. participants met eligibility criteria, they were not malnourished before starting the fasting regimen and excludation participants with a body mass index of less than 19 kg/m², with boody mass index of less than 20.5 kg/m² or with greater than 10% weight loss in the previous year, therefore, the results of these studies cannot be generalized to anyone with a low boody

mass index, although many clinicians characterize malnutrition based on weight, making weight loss and low boody mass index important safety criteria to consider. In the final, the minimal caloric intake is considered as part of fasting protocol. Fasting demonstrated a significant benefit on quality of life, it protects healthy cells and decrease the damage from chemotherapy. In addition, it limits the amount of glucose and insulin (among other hormones and metabolites) circulating in the body.

Conclusion

Preclinical studies and clinical trials have shown that intermittent fasting has benefits for many health conditions, including, obesity, diabetes mellitus, cardiovascular disease, cancers, and neurologic disorders, improvement health throughout the life span. Furthermore, cannot generalize to other age groups. Studies provided some benefits, the safety and feasibility to fasting of breast cancer diagnosis and treatment during chemotherapy. Overall the studies did show that intermittently fasting is safe and generally feasible for the majority of participants who were able to adhere to the fasting protocol. Future research should include protocols that study the length of fasting and that standardize whether caloric intake is beneficial while intermittently fasting or decreasing the length of fasting with consuming no calories is more or less beneficial than a longer fast that allows some caloric intake on the fasting day. The nutritional status of the participants must be taken into account, while overweight and obesity are risk factors for postmenopausal patients with breast cancer; fasting is a restrictive way of eating, thus, it is exclude participants who are malnourished at the start of chemotherapy, through poor outcomes associated with malnutrition in oncology. Fasting could also have important implications on cancer prevention, not only during chemotherapy, but the safety and feasibility of long-term fasting in cancer prevention among those at high risk. Finally, diet and fasting play an important role of in targeted therapies for any cancer type. Normal cells produce energy through oxidative phosphorylation in the mitochondria. with the effect of aerobic glycolysis, tumor cells adapt their metabolism to produce energy by converting glucose to lactate to sustain the high energy demands necessary for growth and survival; fasting decreases circulating glucose, which is the preferential energy source of cancer, thus fasting could make therapies more

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effective by sensitizing cancer cells to targeted therapies and protecting healthy cells from chemotherapy toxicity. Fasting could have important implications on targeted therapies by decreasing circulating insulin-like growth factor-1 and potentially limiting tumor development pathways.

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