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Review Article

Effect of Intermittent Fasting on Cancer

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Abstract:

Diet is a modifiable factor that may affect cancer risk, treatment and recurrence, currently there is a high level of interest in fasting and cancer in the scientific community but no clear information about the purported health benefits, fasting and fasting mimicking diets leads to wide alterations in growth factors and in metabolite levels giving rise to an unfavorable environment for cell proliferation, there are multiple examples of fasting diets that might regenerate antitumor immunity and may even prevent some types of tumors which are most likely to be sensitive to these dietary interventions, thus, the biologically-relevant interplay between fasting or nutrient deprivation and current cancer treatments encourages the design of future trials to maximize efficacy and achieve the lowest toxicity of current cancer treatments.

Key words: fasting; cancer; treatment; recurrence

Introduction

Humans evolved in environments where food was scarce, enabling them to function at high energy levels [1]. However, modern sedentary lifestyles and overconsumption of high-calorie foods have compromised health, leading to issues like insulin resistance, obesity, cardiovascular diseases, depression, and even cancer [1,2]. Fasting, a practice dating back to Hippocrates [2,3], is a safe and well-tolerated method that reduces oxidative stress, enhances stress resistance, delays aging, and potentially combats cancer [4,5]. Intermittent fasting (IF) is a specific eating pattern involving alternating periods of fasting (16-48 hours) and eating (8-12 hours) [6,7]. Lifestyle factors, including diet, contribute to approximately 42% of cancers and 45% of cancer-related deaths [8]. Despite significant advancements in oncology, cancer remains a major global health concern, affecting 19.97 million people and causing 10 million deaths in 2022 [9]. Survival rates and prognoses for cancer patients remain unsatisfactory. Recently, the fasting concept has become popular among scientists and the general population. In particular, fasting reputedly slows down ageing, improves overall health [4-7]. Proposed mechanisms for this effect include an induction of autophagocytosis of cancer cells and/or the idea that fasting may also protect healthy cells in cancer patients against the stress induced by chemotherapy [8-9]. In this review, we aim to describe the various types of fasting, their relationships with cancer treatments, and their effects on cancer, treatment responses, and survival in cancer patients.

Types of fast:

Based on traditional, cultural or religious backgrounds, there are many types of periodic fasting, many types of fasting experience no or small caloric intake (eg 500 kcal daily) with an unlimited amount of caloric-free beverages (coffee without sugar or milk, water, diet soft drinks.) (Table1) [8,10].

Types of fast	Description
Complete alternate day fasting	Involves alternating fasting days and feeding days
Modified fasting regimens	Severe energy restriction for 2 non-consecutive days per week and ad libitum eating for the other 5 days.
Time restricted feeding	Allows ad libitum energy intake within specific time frames, inducing regular, extended fasting intervals.
Religious fasting	Variety of fasting regimens undertaken for religious or spiritual purposes.
Ramadan fasting	A fast from sunrise to sunset during the holy month of Ramadan, with one large meal after sunset and

	one lighter mean before dawn. Thus, for about 12 hours of length.
Other religious fasts	Some Christians routinely abstain from food and drink for extended periods of time, some seventh –day Adventists consume their last of two daily meals in the afternoon, resulting in an extended nighttime fasting interval.

Table 1: Type of fasting

Because Calorie Restriction (CR) can have both very positive and negative effects and is unlikely to be adopted by a significant portion of the populations since it unavoidably causes severe weight loss, intermittent and periodic fasting are emerging as novel interventions which could maintain many of the beneficial effects of CR while reducing the burden and many of the side effects [10]. Fasting, the complete elimination of nutrients from the diet, is the most extreme of the dietary restrictions [11,12]. Fasting regimens can be implemented in various formats (table2). Intermittent fasting (IF) involves short-term, frequent fasting periods, such as alternate-day fasting (ADF) or time-restricted eating (TRE) [11-14]. In contrast, prolonged and periodic fasting (PF) entails less frequent but longer periods of fasting, often lasting 2-5 days or involving fasting-mimicking diets (FMD) for 4-7 days [15-18].

	Type of Fasting	**Schedule**	**Description**
Intermittent Fasting (IF)	ADF	24 h fast/ 24 h eating period	Water only fasting every other day
	5:2	2 days fast or very low-calorie consumption (500–700 kcal)/ 5 days eating period	Alternation of 2 days of very low-calorie consumption with a 5 days ad libitum re-feeding period
	TRF	12- to 18 h fast/ 6- to 12 h eating period	Food intake restricted to 6–12 h per day
Periodic Fasting (PF)	Prolonged fasting	2–5 days of water fast/ 7 days eating period (or longer)	Water only fasting period followed by an ad libitum re-feeding period
	Prolonged FMD	4- to 7 days FMD/ 10- to 25days eating period	30–50% of the normal caloric intake using a fasting mimicking diet for 4–7 days followed by an ad libitum re-feeding period

Table 2: Dietary approaches to promote health span [15]

While IF typically involves alternating fasting and feeding phases, PF can be implemented sporadically throughout the year [11]. Both IF and PF induce metabolic adaptations, including decreased blood glucose levels, reduced glycogen stores, lower leptin levels, and increased fatty acid mobilization with ketone body production [11,18]. Additionally, fasting periods, particularly those involving FMD, can positively impact cognitive function, leading to heightened awareness, attention, mental acuity, vigilance, and reduced depressive symptoms [19].

Circadian Biology Cycle

The master biological clock is in the suprachiasmatic nucleus of the hypothalamus and is entrained to light and dark stimuli, it plays a major role in integrating metabolism and energetics, similar clock oscillators have been found in peripheral tissues (liver, fat and skeletal muscle..) desynchronization of this biological brain and peripheral clock may increase the risk of cancer, a large literature indicates that shift work is associated with increased risks of obesity, diabetes, cardiovascular disease and cancer, similarly consuming the majority of the day's energy earlier in the day causes a lower weight and improves health [10].

Gastrointestinal microbiota

The diversity of the Gut microbiota is regulated by fasting, it increases production of short chain fatty acids, which can regulate insulin response and decreases inflammation [3].

Intermittent fasting should be contraindicated if there is a history of an eating disorder (anorexia, bulimia, malnutrition.) or pregnancy [3, 20-22].

Intermittent fasting and cancer

Fasting leads to wide alterations in systemic levels of hormones, growth factors (insulin, glucagon, GH, IGF-1) which reduces the ability of tumor cells to adapt and survive, it can modulate cancer initiation, progression, and recurrence [3, 23-25].

In fasting, low serum levels of glucose impose extra stress on tumor cells, while healthy one's function normally, these different responses cause more DNA damage and apoptosis in tumor cells and protects healthy cells from treatment damages, it is called **differential stress sensitization –DSS [26-27].**

IF promotes also stem cell-based regeneration, interestingly, in fasting, cytotoxic agents elicited differential response in normal and tumor cells, a phenomenon known as differential stress **resistance –DSR-** In healthy cells (Figure1), fasting shuts down pathways promoting growth to re-invest in repair pathways, thus tumor cells lose ability to adapt to extreme environments including caloric deprivation [1, 28,29].

This metabolic stress causes insulin levels to drop and glucagon levels to rise, increasing the breakdown of glycogen into glucose and triglycerides into free fatty acids, lipolysis is maintained by glucocorticoids and adrenalin as a result, fasting benefits the brain, muscle, liver, and adipose tissue, IF boosts fatty acid oxidation and induces a transition from aerobic glycolysis to mitochondrial oxidative phosphorylation in tumor cells [30]. The brain progressively adjusts using the ketone bodies in addition to glucose to satisfy its energy requirements, while other tissues use fatty acids to function. "Warburg effect" in fasting, the normal cells can replace glucose deprivation by ketone bodies and fatty acids, in contrast tumor cells depend on glucose, so it stimulates the aerobic glycolysis and produces lactic acid it's "Warburg effect, sometimes an "anti-Warburg" effect result in oxidative stress and induced apoptosis of tumor cells [20,31,32].

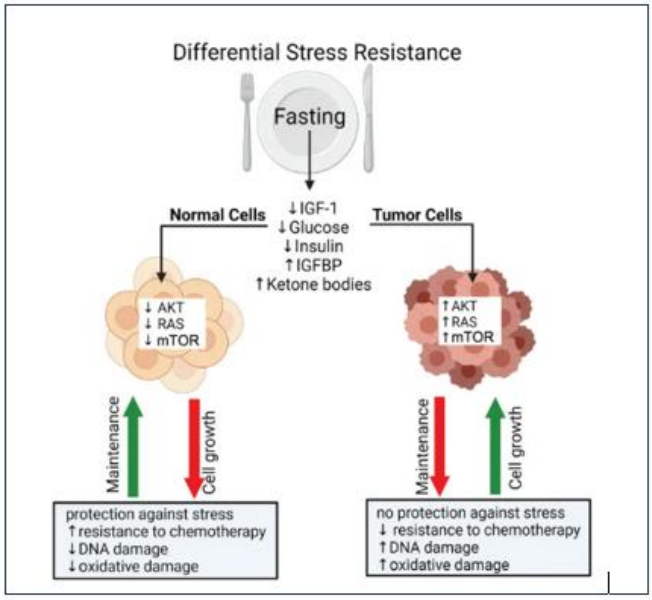

Figure 1: Differential stress resistance mechanisms [30]

The possible mechanisms associated with the differential stress resistance theory. AKT: protein kinase B; IGF-1: insulin-like growth factor 1; IGFBP: insulin-like growth factor binding protein; mTOR: mechanistic target of rapamycin; RAS: rat sarcoma virus.

The related progression on IF combined with tumor therapy was listed in the Table 3.

Fasting has also several effects [3,15,21,31-34]:

- FGF-21 increases and IGFBP1 binds IGF-1 thus causes IGF-1 deficiency, it can protect against cancer progression
- Vitamin B9 promotes DNA replication in cancer cells
- Vitamin B12 and folic acid could also promote tumor progression
- Vitamin D increases calcium absorption
- Autophagy eliminates intracellular signals and thus suggests cancer prevention role
- Decreases the production of free radicals
- Increases resistance to stress
- Improves anti-stress ability
- Reduces the level of reactive oxygen species (ROS and the expression of hypoxia inducible factor-1α
- Current evidence suggests that intermittent

However, in practice, many physicians may consider fasting harmful for some kind of cancer patients weakened by a prior chemotherapy (aging with decreased appetite, nausea, taste changes.) [4].

Figure2: The action of IF in tumor cell growth [7]

The molecular mechanism by which intermittent fasting (IF) affects tumor cell growth.

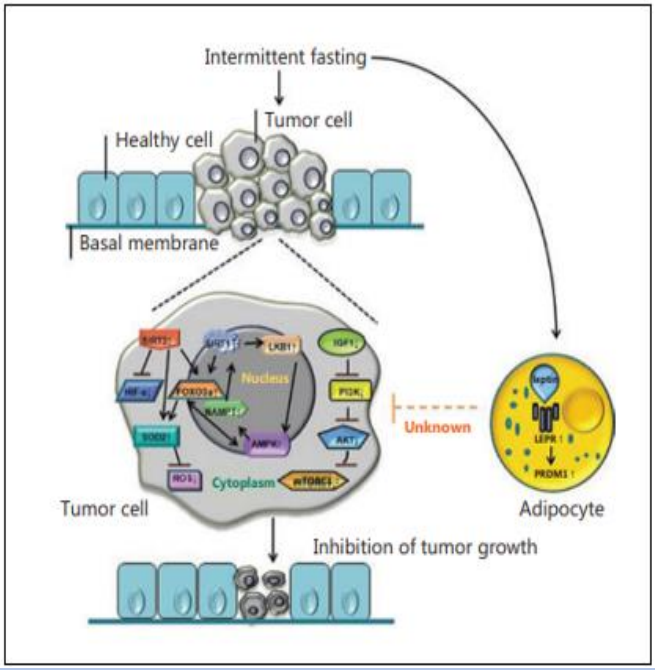

Figure 2: The action of IF in tumor cell growth [7]

The molecular mechanism by which intermittent fasting (IF) affects tumor cell growth. Mechanistically, IF inhib is the IGF-1/AKT and mTORC1 pathways in tumor cells, while the AMPK, SIRT1, and SIRT3 pathways are activated. In addition, AMPK and SIRTs depend on each other in IF-associated metabolic adaptation. However, AMPK can induce activation of SIRT1 through NAMPT, while SIRT1 can activate AMPK through LKB1 regulation. FOXO3a (a downstream molecule of SIRT1 and SIRT3) and AMPK can each enhance the other's transcriptional activities. Furthermore, SIRT3 inhibits tumor growth by activating FOXO3a and the expression of superoxide dismutase (SOD), thereby reducing the level of reactive oxygen species and negatively regulating the expression of HIF-1α. SIRT3 activates SOD2 via up regulation of FOXO3a. Furthermore, IF can selectively inhibit tumor growth by upregulating LEPR and its downstream signaling path way protein, PRDM1.

Year	Disease(s)	Dietary regimen	Outcome
2020[35]	Colorectal cancer and other KRAS-mutant tumors	Standard feeding or on the last day of the first IF cycle, vitamin C (4 g/kg in saline) began via intraperitoneal injection twice a day, with at least 6–8 between the 2 daily administrations	The combination of IF and vitamin C represented a promising low toxicity intervention
2019[36]	Orthotopic pancreatic tumors	Fed or fasted for 24 h and then exposed to total abdominal radiation at a dose of 11.5 Gy	IF improved the survival of mice with orthotopic pancreatic tumors subjected to lethal abdominal radiation
2017[37]	Colon cancer	24 h fasting on alternate days for 2 weeks	IF inhibited colon cancer growth and decreased the production of extracellular adenosine by cancer cells by suppressing CD73 expression
2016[38]	Fibrosarcoma	48 h fasting (water only) once vs. ad libitum feeding; animals were injected with mitoxantrone or oxaliplatin at the end of fasting	IF improved the efficacy of chemotherapy in an immune system-dependent and autophagy-dependent fashion
2016[39]	Breast cancer; melanoma	48–60 h fasting (water only) or a 96 h FMD once a week for 2–4 weeks vs. ad libitum feeding; animals were injected with chemotherapy at the end of each fasting and/or FMD cycle	IF slowed tumor progression when combined with doxorubicin or cyclophosphamide, expanded lymphoid progenitors and boosted anticancer immunity
2015[40]	Colon cancer	48 h fasting (water only) once a week for 2 weeks, 24 h prior to and 24 h after oxaliplatin injection vs. ad libitum feeding	IF improved the anticancer effects of oxaliplatin, exerted anti-Warburg effects and promoted oxidative stress and apoptosis in cancer cells
2015[41]	Lung cancer; colorectal cancer	48 h fasting (water only) once a week for 3 weeks with daily treatment with crizotinib or regorafenib vs. ad libitum feeding	IF improved the clinical activities of crizotinib and regorafenib
2012[42]	Mesothelioma; lung cancer	48 h fasting (water only) given once a week for 3 weeks, 32 h prior to and 16 h after cisplatin injection vs. ad libitum feeding	IF sensitized human mesothelioma and lung cancer xenografts to cisplatin

Table 3: Overview of intermittent fasting (IF) combined with tumor therapy

Intermittent fasting in clinical trials

Most clinical trials of fasting in cancer patients performed to date are retrospective trials, observational studies evaluated in supportive care outcomes or phase I, II clinical trials, currently several well-powered studies are underway to address outstanding questions however, more extensive data are needed before intermittent fasting can be a routine clinical use [3], the DIRECT study evaluated the fasting mimicking diet (FMD) + neoadjuvant chemotherapy in women with HER 2 negative breast cancer, patients in the FMD group had a better pathological response and a decreased chemotherapy induced DNA damage to normal cells [30,43].

Another study on patients with breast cancer identified a potential beneficial of IF on chemotherapy induced toxicity [44].

Fasting and Cancer Prevention

Data on the effect of IF suggest has a beneficial effect in preventing 60% of cancers in animal studies, a Swedish study found a 29% reduction in cancer incidence and 23% lower cancer mortality in a population who underwent a bariatric surgery, the look AHEAD trial of 4859 overweight patients who were randomized to an intensive group of CR (1200-1800 kcal daily) and an observational group, after 11 years patients in the intensive lifestyle group had a 16% lower incidence of obesity-related cancers (including esophagus, colon, rectum, kidney, pancreas, stomach, liver, gallbladder, thyroid, uterine, ovarian…) which the authors proposed was secondary to weight loss, though, there are no known, reproductible diets, to cure or prevent cancer recurrence, future well designed

randomized clinical trials should examine the effect of IF over longer periods, different cancers and populations [8,29,45,46].

Fasting during specific treatments of cancer

IF has the potential to lower the ratio of fat to lean body mass, which may benefit patients at risk of weight–related side effects of some cancer treatments, many studies report improvements in quality of life, fatigue and GI toxicities [34], the fasting glucose, insulin and HbA1c of adults with obesity decreases significantly after short alternate- date regimens in some studies [10,47]. Glutamine is another metabolic substrate that has a high conversion rate in tumor cells, the catabolism of glutamine can protect tumor cells from chemical toxicity, fasting can increase chemosensitivity of cancer cells by affecting glutaminase and glutamine transporter levels [32].

Chemotherapy and radiotherapy

Fasting increases autophagy which is a catabolic process providing primary materials such as amino acids, fatty acids, nucleosides/nucleotides, sugars often induced by chemotherapeutic agents [48], many trial evaluates the combination of fasting with chemotherapy represents a potentially promising strategy to increase efficacy, reduce resistance and prevent side effects [25].

Normal cells are protected from chemotherapeutic agents by changes in circulating hormones and metabolites, during nutrient deprivation, they

re-invest energy in maintenance and repair that contribute to resistance to chemotherapy while tumor cells are unable to slow-down growth due to mutations in tumor suppressor genes and mitogenic pathways, this different reaction makes tumor cells more susceptible to chemotherapy and other treatments since they violate the anti- proliferation signals required by fasting environment [31].Two days of fasting before chemotherapy treatment is safe and protect against the side effects of chemotherapy, this type of fasting is shown to delay the progression of several tumors especially in mice [27,49,].In addition, IF has been shown to increase tumor sensitivity to radiation therapy (RT) and prolong the survival of fasting experimental animals [Icard]. Specifically, mice with pancreatic tumors subjected to lethal abdominal radiation exhibited improved survival rates when subjected to IF compared to those with ad libitum food access. Additionally, IF did not impair RT-induced tumor cell killing and even enhanced γ-H2AX staining post-RT, suggesting a potential radio sensitizing effect [50]. Encouragingly, preclinical and preliminary clinical data support the notion that IF could serve as a complementary therapy to improve RT outcomes, both in terms of tumor control and reduced normal tissue toxicity [51,52]. While these basic studies have yielded promising results, further preclinical research is necessary to establish clinical relevance, as human data, including clinical outcome studies, safety data, and randomized controlled trials, remain limited [53]. Future investigations should prioritize safety and explore the potential of IF to enhance the efficacy of lower doses of chemotherapy and radiation therapy.

Hormones and fasting

Many studies demonstrate the link between nutrients and particularly protein intake, growth hormones, DNA damage and cancer, two major hormonal pathways appear to affect cancer incidence the IGF-1 and the insulin signaling [15].

Many dietary patterns, including the Western diet, are associated with reduced lifespan and health span and appear to affect cancer incidence by two major hormonal axes/pathways: the growth hormone-IGF1; the insulin signaling [54-56]. Breast cancer, particularly hormone receptor-positive (HR+) breast cancer, represents a significant health challenge. While endocrine therapies like Tamoxifen and Fulvestrant are effective, primary and acquired resistance often limits their long-term efficacy [57, 58].

A periodic fasting or a fasting-mimicking diet can enhance the effectiveness of endocrine therapies in mouse models of HR+ breast cancer. By lowering circulating levels of IGF-1, insulin, and leptin, and inhibiting the AKT-mTOR signaling pathway, these dietary interventions can potentiate the effects of tamoxifen and Fulvestrant. Moreover, combining a fasting-mimicking diet with a cyclin-dependent kinase 4/6 inhibitor like Palbociclib can lead to sustained tumor regression and overcome acquired drug resistance. (57,59) Importantly, fasting and fasting-mimicking diets can also mitigate the side effects of endocrine therapy, such as endometrial hyperplasia caused by tamoxifen. In human clinical trials, fasting-mimicking diets have been shown to induce similar metabolic changes as observed in mice, including reductions in insulin, leptin, and IGF-1 levels. (59,60) These findings suggest that fasting-mimicking diets hold promise as a potential adjuvant therapy for HR+ breast cancer. Further clinical studies are warranted to explore the optimal timing and duration of these dietary interventions and their impact on patient outcomes.

In a study by Lende et al., post-surgical breast cancer patients who fasted prior to surgery demonstrated significantly improved relapse-free and breast cancer-specific survival compared to those who received a carbohydrate-based nutritional supplement. This positive effect was particularly pronounced in patients with estrogen receptor-positive (ER+) breast cancer. Fasting appeared to favorably influence the hormonal environment, potentially enhancing the efficacy of subsequent treatments. While no significant difference was observed in estrogen receptor-negative patients, the study highlights the potential benefits of fasting for a specific subset of breast cancer patients [61].

Fasting and targeted therapy

Intermittent fasting (IF) has been shown to modulate various cellular pathways implicated in cancer progression. By decreasing insulin-like growth factor-1 (IGF-1) levels, IF can activate AMP-activated protein kinase (AMPK) and inhibit the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT) pathway [3,26,31,32]. Additionally, IF can enhance the efficacy of cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, particularly Palbociclib, by reducing pharmacokinetic variability [26]. Furthermore, IF-induced inhibition of mechanistic target of rapamycin (mTOR) and activation of AMPK can stimulate autophagy, a cellular process that removes damaged organelles and misfolded proteins (Kalam, Psara). By reducing IGF-1 levels, IF can also inhibit the RAS/mitogen-activated protein kinase (MAPK) signaling pathway, leading to decreased activity of transcription factors involved in cell proliferation and growth [26, 32]. Overall, these findings suggest that IF can improve the efficacy of targeted therapies, such as tyrosine kinase inhibitors (TKIs), by inhibiting key signaling pathways involved in cancer cell growth and survival [31,32].

Immunotherapy and fasting

When butyrate metabolism is disrupted in colon cancer, it accumulates, inhibits cell development and causes cell death suggesting that microbiota may play a role in immunotherapy as well [10]. There is a growing appreciation for how the metabolic pathways activated in fasting interact with immune responses to control tumor growth [3] Anti-PD1 treatment is effective in melanoma with high levels of A. muciniphila low levels of circulating IGF-1 sensitize tumor cells to anti PD L1 [26,31]. fasting was also associated with fewer instances of immunotoxicity and adverse events. No study has reported the effects of ketogenic diet on immunotherapy outcomes; thus, it is not clear whether the glucose limitation will affect anti-tumor immunity [62].

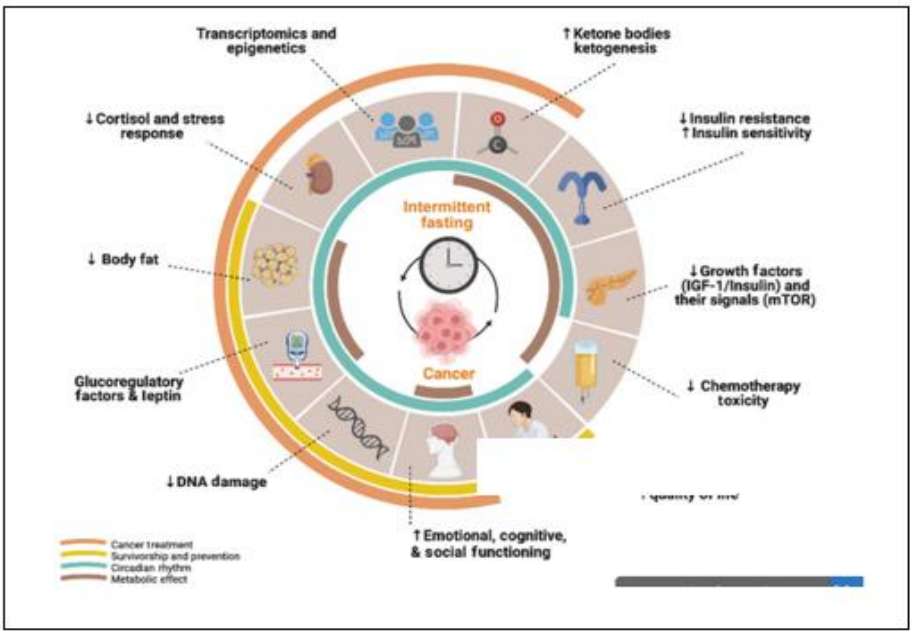

Figure 3: the impact of intermittent fasting in cancer prevention and treatment [3]

Conclusion

While intermittent fasting holds significant potential as a tool to combat cancer, its current role in clinical practice remains limited. While preliminary evidence suggests potential benefits in specific contexts, such as reducing side effects of certain treatments, more robust and conclusive data is needed. It's crucial to acknowledge the potential risks, particularly for patients at risk of malnutrition or eating disorders. Unintentional weight loss can severely impact clinical outcomes, making fasting inadvisable in such cases. As such, a personalized approach is essential. Patients with cancer should consult with a registered dietitian specializing in oncology to determine the most appropriate dietary strategy for their individual needs. Future research will undoubtedly shed lighter on the optimal implementation of fasting regimens in cancer care. Ongoing clinical trials are exploring the impact of intermittent fasting on cancer incidence, treatment response, and overall survival. By carefully considering the potential benefits and risks, we can harness the power of fasting to improve cancer outcomes.

References

1. Mattson M.P. and al: (2017). impact of intermittent fasting on health and disease processes. Ageing research reviews, (39), 46-58.
2. Wang Y., Wu R.: (2019). Fasting - Effects on the Human Body and Psyche]. Praxis (Bern 1994). Jul;108(9):593-597
3. Kalam F. and al: (2023). intermittent fasting interventions to leverage metabolic and circadian mechanisms for cancer treatment and supportive care outcomes. Journal of the National Cancer Institute Monographs, (51), 84-103.
4. Safdie F.M. and al: (2009). fasting and cancer in humans: a case series report, AGING, December, 1(12).
5. Cathcart P. and al: (2017). fasting starving cancer, cancer and society, quackery. The Lancet Oncology.18(4),431.
6. Schmidt M.W. and al: (2023). effects of intermittent fasting on quality of life, tolerance of chemotherapy in patients with gynecological cancers: study protocol of a randomized-controlled multi-center trial, front oncol., SEC gyneacological Oncology.;13.
7. Zhao X, Yang J, Huang R, Guo M, Zhou Y, Xu L. (2021). The role and its mechanism of intermittent fasting in tumors: friend or foe? Cancer Biol Med.; 18: 63-73.
8. Clifton K.K. and al: (2021). intermittent fasting in the prevention and treatment of cancers, CA CANCERJ CLIN;71:527-546.
9. Globocan 2022
10. Patterson R., Sears D.: (2017). metabolic effects of intermittent fasting, annual review of nutrition, volume 31, p 371-393.
11. Longo, V.D.; Mattson, M.P. (2014). Fasting: Molecular mechanisms and clinical applications. Cell Metab., 19, 181–192
12. Trepanowski, J.F.; Canale, R.E.; Marshall, K.E.; Kabir, M.M.; Bloomer, R.J. (2011). Impact of caloric and dietary restriction regimens on markers of health and longevity in humans and animals: A summary of available findings. Nutr. J., 10, 107.
13. Regmi, P.; Chaudhary, R.; Page, A.J.; Hutchison, A.T.; Vincent, A.D.; Liu, B.; Heilbronn, L. (2021). Early or delayed time-restricted feeding prevents metabolic impact of obesity in mice. J. Endocrinol., 248, 75–86.
14. Chaix, A.; Lin, T.; Le, H.D.; Chang, M.W.; Panda, S. (2019). Time-Restricted Feeding Prevents Obesity and Metabolic Syndrome in Mice Lacking a Circadian Clock. Cell Metab., 29, 303–319.e304.
15. Salvadori, G.; Mirisola, M.G.; Longo, V.D. (2021). Intermittent and Periodic Fasting, Hormones, and Cancer Prevention. Cancers, 13, 4587.
16. Raffaghello, L.; Lee, C.; Safdie, F.M.; Wei, M.; Madia, F.; Bianchi, G.; Longo, V.D. (2008). Starvation-dependent differential stress resistance protects normal but not cancer cells against high-dose chemotherapy. Proc. Natl. Acad. Sci. USA, 105, 8215–8220.
17. Brandhorst, S.; Choi, I.Y.; Wei, M.; Cheng, C.W.; Sedrakyan, S.; Navarrete, G.; Dubeau, L.; Yap, L.P.; Park, R.; Vinciguerra, M.; et al. (2015). A Periodic Diet that Mimics Fasting Promotes Multi-System Regeneration, Enhanced Cognitive Performance, and Healthspan. Cell Metab., 22, 86–99.
18. Longo, V.D.; Panda, S. (2016). Fasting, Circadian Rhythms, and Time-Restricted Feeding in Healthy Lifespan. Cell Metab., 23, 1048–1059.
19. Maniaci, G.; La Cascia, C.; Giammanco, A.; Ferraro, L.; Chianetta, R.; Di Peri, R.; Sardella, Z.; Citarrella, R.;

Mannella, Y.; Larcan, S.; et al. (2020). Efficacy of a fasting-mimicking diet in functional therapy for depression: A randomised controlled pilot trial. J.Clin. Psychol. 76, 1807–1817.
20. Kuçuk A.N. and al: (2023). the role of intermittent fasting and the ketogenic diet in cancer disease: can they replace the mediterranean diet? European journal of cancer prevention 32(6): p 533-543, November.
21. Ferro Y. and al: (2023). therapeutic fasting in reducing chemotherapy side effects in cancer patients: a systematic review and meta-analysis, nutrients, 15(12), 2666.
22. Liu and al: (2023). intestinal microbiota: a bridge between intermittent fasting and tumors, biomedicine & pharmacotherapy, vol 167, November, 115484.
23. Pio R. and al: (2024). fasting and fasting mimicking conditions in the cancer immunotherapy era, J Phisiol Biochem.
24. Nencioni A. and al: (2018). fasting and cancer: molecular mechanisms and clinical application, nature reviews cancer, 18, 707-719.
25. Crespo A. and al (2022). intermittent fasting and cancer, journal of restorative medicine, 12(1).
26. Kikomeko J. and al: (2023). short-term fasting and fasting mimicking diets combined with chemotherapy: a narrative review, therapeutic advances in medical oncology, vol 15, 1-14.
27. Sun L. and al: (2017). effect of fasting therapy in chemotherapy-protection and tumor –suppression: a systematic review, translational cancer research, vol 6, n°2(April 28).
28. Antunes F. and al: (2018). autophagy and intermittent fasting: the connection for cancer therapy? CLINICS;73(suppl 1): e814s.
29. Blazevits O. and al: (2023). fasting and fasting mimicking diets in cancer prevention and therapy, trends in cancer vol 9, issue 3, march, 212-222.
30. Gabel K. and al: (2022). current evidence and directions for intermittent fasting during cancer chemotherapy, Adv Nutr; 13667-1680.
31. Tiwary S. and al: (2022). effect of fasting on cancer: a narrative review of scientific evidence, Cancer Science.:113:3201-3302.
32. Zhang J. and al: (2020). fasting to enhance cancer treatment in models the next steps, journal of biomedical science;27 (58).
33. Alidadi M. and al: (2021). the effect of caloric restriction and fasting on cancer, seminars in cancer biology; 73: 30-44.
34. Sucholeiki R. Li and al: (2024). intermittent fasting and its impact on toxicities, symptoms and quality of life in patients on active cancer treatment, cancer treatment reviews, vol 126, may.
35. Di Tano M, Raucci F, Vernieri C, Caffa I, Buono R, Fanti M, et al. (2020). Synergistic effect of fasting-mimicking diet and vitamin C against KRAS mutated cancers. Nat Commun.; 11: 23-32.
36. De la Cruz Bonilla M, Stemler KM, Jeter-Jones S, Fujimoto TN, Molkentine J, Asencio Torres GM, et al. (2019). Fasting reduces intestinal radiotoxicity, enabling dose-escalated radiation therapy for pancreatic cancer. Int J Radiat Oncol Biol Phys.; 105: 537-547.
37. Sun P, Wang H, He Z, Wu Q, Chen W, Sun Z, et al. (2017). Fasting inhibits colorectal cancer growth by reducing M2 polarization of tumor-associated macrophages. Oncotarget.; 8(74):649-650.
38. Di Biase S, Lee C, Brandhorst S, Manes B, Buono R, Cheng CW, et al. (2016). Fasting-mimicking diet reduces HO-1 to promote T cell mediated tumor cytotoxicity. Cancer Cell.; 30: 136-146.
39. Pietrocola F, Pol J, Vacchelli E, Enot DP, Baracco EE, Levesque S, et al. (2016). Caloric restriction mimetics enhance anticancer immunosurveillance. Cancer Cell.; 30: 147-160.
40. Caffa I, D'Agostino V, Damonte P, Soncini D, Cea M, Monacelli F, et al. (2015). Fasting potentiates the anticancer activity of tyrosine kinase inhibitors by strengthening MAPK signaling inhibition. Oncotarget.; 6(11):820-832.
41. Bianchi G, Martella R, Ravera S, Marini C, Capitanio S, Orengo A, et al. (2015). Fasting induces anti-Warburg effect that increases respiration but reduces ATP-synthesis to promote apoptosis in colon cancer models. Oncotarget.; 6(11):806-819.
42. Shi Y, Felley-Bosco E, Marti TM, Orlowski K, Pruschy M, Stahel RA. (2012). Starvation-induced activation of ATM/Chk2/p53 signaling sensitizes cancer cells to cisplatin. BMC Cancer.; 12: 571.
43. De gruil N. and al: (2022). short-term fasting synergizes with solid cancer therapy by boosting antitumor immunity, cancers °, 14(6), 1390.
44. Anemoulis M. and al: (2023). intermittent fasting in breast cancer, a systematic review and critical update of available studies Nutrients, 15(3), 532.
45. Stringer E. and al: (2022). intermittent fasting in cancer: a role in survivorship? curr nutr rep, 11:500-507.
46. Giannakou K. and al: (2020). the effect of intermittent fasting on cancer prevention: a systematic review, European journal of public health, volume 30 (5):166-216.
47. De Azevedo FR, Ikeoka D, Caramelli B. (2013). Effects of intermittent fasting on metabolism in men. Rev Assoc Med Bras. ;59(2):167-173
48. Ibrahim EM, Al-Foheidi MH, Al-Mansour MM. (2021). Energy and caloric restriction, and fasting and cancer: a narrative review. Support Care Cancer. May;29(5):2299-2304.
49. Lee C. and al: fasting cycles retard crowth of tumors and sensitize a range of cancer cell types to chemotherapy, science translational medicine, 4(124):124-127.
50. Icard P, Ollivier L, Forgez P, Otz J, Alifano M, Fournel L, et al. (2020). Perspective: do fasting, caloric restriction, and diets increase sensitivity to radiotherapy? A literature reviews. Adv Nutr.11: 1089-1101.
51. Klement RJ. (2019). The influence of ketogenic therapy on the 5 Rs of radiobiology. Int J Radiat Biol.; 95: 394-407.
52. Klement RJ. (2018). Fasting, fats, and physics: combining ketogenic and radiation therapy against cancer. Complement Med Res.25: 102-113.
53. Horne BD, Muhlestein JB, Anderson JL. (2015). Health effects of intermittent fasting: hormesis or harm? A systematic review. Am J Clin Nutr.102: 464-470.
54. Sugimura, T. (2000). Nutrition and dietary carcinogens. Carcinogenesis, 21, 387–395.
55. Kushi, L.H.; Byers, T. and al.; American Cancer Society, N.; et al. (2006). American Cancer Society Guidelines on Nutrition and Physical Activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J. Clin. 56, 254–281.
56. Guevara-Aguirre, J.; Rosenbloom, and al. (2015). GH Receptor Deficiency in Ecuadorian Adults Is Associated with Obesity and Enhanced Insulin Sensitivity. J. Clin. Endocrinol. Metab., 100, 2589–2596.
57. AlFakeeh A, Brezden-Masley C. (2018). Overcoming endocrine resistance in hormone receptor-positive breast cancer. Curr. Oncol 25, S18–S27.

58. Garofalo C, Sisci D & Surmacz E. (2004). Leptin interferes with the effects of the antiestrogen ICI 182,780 in MCF-7 breast cancer cells. Clin. Cancer Res 10, 6466–6475.
59. Shajahan-Haq AN et al. (2017). EGR1 regulates cellular metabolism and survival in endocrine resistant breast cancer. Oncotarget 8, 96865–96884.
60. Hu R, Hilakivi-Clarke L & Clarke R. (2015). Molecular mechanisms of tamoxifen-associated endometrial cancer (Review). Oncol. Lett 9, 1495–1501.
61. Lende, T. H., et al. (2019). Influence of pre-operative oral carbo hydrate loading vs. standard fasting on tumor proliferation and clinical outcome in breast cancer patients─ a randomized trial. BMC Cancer, 19(1), 1–22.
62. Turbitt WJ, Orlandella RM, Gibson JT, Peterson CM, Norian LA. (2020). Therapeutic time-restricted feeding reduces renal tumor bioluminescence in mice but fails to improve anti-CTLA-4 efficacy. Anticancer Res.;40: 5445-5456.

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