

The Emerging Role of Fasting in Cancer Treatment


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Article Info	Abstract
<p>Article type: Research Article</p> <p>Article history: Received 25 November 2024 Received in revised from 18 December 2024 Accepted 25 December 2024 Published online 28 January 2025</p> <p>Keywords: Fasting-Mimicking Diets, Intermittent Fasting, Cancer, Systemic therapy, Radiotherapy</p>	<p>Fasting-based dietary interventions have emerged as promising therapeutic strategies. They show efficacy in weight control, metabolic regulation, and gastrointestinal health. Growing preclinical and clinical evidence indicates that these regimens may influence cancer outcomes by altering tumor metabolism, enhancing treatment efficacy, and reducing therapy-related toxicity. This review critically evaluates current research on fasting mechanisms and their applications in cancer prevention and treatment. Most existing protocols differ from the specific structure of Islamic fasting, highlighting the need for rigorous assessment of its unique physiological features. Fasting affects several oncogenic pathways through metabolic reprogramming, immune modulation, and cellular stress responses. Preliminary studies suggest synergistic effects when fasting is combined with chemotherapy, radiotherapy, or targeted therapy. However, evidence remains inconsistent across cancer types. Major challenges include the lack of standardized protocols, limited criteria for patient selection, and insufficient data on long-term safety. Significant knowledge gaps persist and require well-designed randomized controlled trials. We propose a translational research framework to systematically study fasting in oncology. This approach emphasizes protocol standardization, biomarker-based mechanisms, and personalized designs guided by tumor biology and patient characteristics. Overall, fasting shows strong potential as an adjuvant cancer therapy, while key areas for future investigation must be addressed to develop evidence-based clinical guidelines.</p>
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Introduction

Fasting represents one of the most significant religious observances and a divine obligation for Muslims during the holy month of Ramadan, as ordained in verses 183 and 184 of Surah Al-Baqarah. This practice is fundamentally rooted in spiritual purification and the pursuit of divine proximity. Within the Islamic tradition, fasting entails complete abstinence from food and drink during the daylight hours specified by the Islamic calendar (from dawn to sunset). The Quran explicitly commands fasting in verse 183 of Surah Al-Baqarah. In contrast, verse 184 provides exemptions for the ill and those incapable of observing this obligation. Still, it emphasizes its virtues through the phrase "fasting is better for you, if only you knew."

Extensive scientific research has investigated the physiological effects of fasting on cellular aging, longevity, and various pathological conditions, including neurological disorders, autoimmune diseases, cardiovascular conditions, and metabolic syndromes¹. Notably, the groundbreaking work of Yoshinori Ohsumi, the Japanese cell biologist awarded the 2016 Nobel Prize in Physiology or Medicine, demonstrated that fasting activates autophagy a crucial cellular recycling and regeneration process while simultaneously decelerating aging². However, the specific implications of fasting on individuals with illnesses, especially cancer patients, remain incompletely understood, with current research failing to provide conclusive evidence regarding its potential benefits or risks in this group.

Cancer, recognized as one of the most formidable diseases of the modern era, typically necessitates comprehensive nutritional support for affected individuals. This presents a complex clinical dilemma for Muslim patients during Ramadan, when the decision to fast or abstain becomes particularly challenging. Current medical practice generally recommends avoiding fasting during active cancer treatment and for up to two years following therapy. However, the global scientific community continues to debate the potential therapeutic effects of fasting in oncology, with some studies highlighting detrimental impacts on cancer cell proliferation. In contrast, others report possible benefits and safety.

This critical dichotomy raises essential questions: Which findings merit greater scientific credibility? Under what specific conditions might fasting serve as either a preventative measure or a therapeutic intervention for cancer? The present review systematically explores existing research to elucidate the potential role of fasting in preventing and treating malignancies, with a focus on developing evidence-based guidelines for clinical practice.

¹ Valter D. Longo et al., "Intermittent and Periodic Fasting, Longevity and Disease," *Nature Aging* 1, no. 1 (2021): 47–59.

² The Nobel Assembly at Karolinska Institutet, "The 2016 Nobel Prize in Physiology or Medicine Awarded to Yoshinori Ohsumi for His Discoveries of Mechanisms for Autophagy," *The Nobel Prize*, 2016.

1. Research Background

Fasting regimens, whether practiced for several days per week or during specific hours per day, have gained widespread popularity as a therapeutic approach for weight management, gut rest, and various other health benefits¹. Multiple fasting patterns have emerged globally, including fasting-mimicking dietary (FMD), short-term fasting (STF), periodic fasting and calorie restriction (PFCR), and intermittent fasting (IF), which are classified based on their duration, period length, and nutritional modifications. While some studies suggest that fasting may stimulate the proliferation and metastasis², and that tumor eradication through nutrient deprivation is challenging because all cells—both cancerous and normal—depend on glucose for energy³, other groundbreaking studies report remarkable findings regarding its safety and potential benefits for cancer patients. Still, these positive results have been interpreted with considerable caution in the scientific community⁴.

Emerging evidence suggests that fasting regimens may be a viable strategy for preventing and treating certain types of solid tumors in specific cases⁵. When combined with conventional cancer therapies, dietary restriction appears to create metabolic conditions that limit cancer cell adaptation, survival, and growth, potentially playing a pivotal role in cancer remission⁶. This synergistic approach has shown particular promise when integrated with chemotherapy, immunotherapy, and hormone therapy⁷, while also demonstrating the capacity to mitigate the side effects of radiation therapy⁸. The observed therapeutic benefits may be mediated through multiple mechanisms, including reduced blood glucose production, stimulation of stem cells for immune system regeneration, and nutritional homeostasis⁹. Furthermore, fasting has significant

¹ N. Kanarek, B. Petrova, and D. M. Sabatini, “Dietary Modifications for Enhanced Cancer Therapy,” *Nature* 579, no. 7800 (2020): 507–517.

² R. Caccialanza et al., “Fasting in Oncology: A Word of Caution,” *Nature Reviews Cancer* 19, no. 3 (2019): 177.

³ D. R. Grimes and E. O’Riordan, “Starving Cancer and Other Dangerous Dietary Misconceptions,” *The Lancet Oncology* 24, no. 11 (2023): 1177–1178.

⁴ O. Blaževičs, M. Di Tano, and V. D. Longo, “Fasting and Fasting-Mimicking Diets in Cancer Prevention and Therapy,” *Trends in Cancer* 9, no. 3 (2023): 212–222.

⁵ S. de Groot et al., “Effects of Short-Term Fasting on Cancer Treatment,” *Journal of Experimental & Clinical Cancer Research* 38, no. 1 (2019): 209.

⁶ S. de Groot et al., “Fasting-Mimicking Diet as an Adjunct to Neoadjuvant Chemotherapy for Breast Cancer in the Multicentre Randomized Phase 2 DIRECT Trial,” *Nature Communications* 11, no. 1 (2020): 3083.

⁷ J. Zhang, Y. Deng, and B. L. Khoo, “Fasting to Enhance Cancer Treatment in Models: The Next Steps,” *Journal of Biomedical Science* 27, no. 1 (2020): 58.

⁸ M. Barradas et al., “Fatty Acids Homeostasis during Fasting Predicts Protection from Chemotherapy Toxicity,” *Nature Communications* 13, no. 1 (2022): 5677.

⁹ A. Nencioni et al., “Fasting and Cancer: Molecular Mechanisms and Clinical Application,” *Nature Reviews Cancer* 18, no. 11 (2018): 707–719.

effects on lipid metabolism, gut microbiota activity, and caloric intake¹ while also enhancing cholesterol efflux from malignant cells².

Notably, the combination of fasting and chemotherapy has been shown to decelerate progression in breast and skin cancers³ while increasing the production of lymphoid progenitor cells (CLPs) and tumor-infiltrating lymphocytes that contribute to tumor elimination. Caloric restriction in fasting-based regimens not only reduces treatment toxicity in healthy cells⁴ but also inflicts substantial damage to cancerous cell⁵. Current evidence suggests that while dietary manipulation of various metabolites demonstrates clear preclinical advantages, some show clinical promise; however, no established guidelines or recommended dietary modifications currently exist for cancer patients⁶. The development of tailored nutritional recommendations is particularly crucial given the metabolic heterogeneity among different cancer types, including variations in energy sources and specific nutrient dependencies.

2. Research Methodology

2-1. Religious and Quranic Research Methodology

This investigation employed a comprehensive analysis of verses 183 and 184 of Surah Al-Baqarah, referencing authoritative Quranic translations and exegeses. Through systematic examination of these scriptural sources, fasting was identified as the primary keyword for subsequent scientific inquiry. The extracted studies were rigorously compared with Islamic jurisprudential rulings on the subject to ensure theological alignment.

2-2. Scientific Research Methodology

The review incorporated evidence from reputable scientific databases, primarily PubMed (MEDLINE), Scopus, and Embase, as well as Nature family journals, focusing on publications from 2014 to 2024. Search strategies utilized controlled vocabulary including "Fasting", "FMD", "STF", "PFRC", "DR", "IF", and "Cancer", among others. Priority was given to highly cited articles that demonstrate significant scholarly impact, as measured by citation frequency and their influence on subsequent research. The selection process emphasized studies that have made substantial contributions to the evolving understanding of fasting's role in oncology.

¹ K. K. Clifton et al., "Intermittent Fasting in the Prevention and Treatment of Cancer," *CA: A Cancer Journal for Clinicians* 71, no. 6 (2021): 527–546.

² A. Khalifa et al., "Cyclic Fasting Bolsters Cholesterol Biosynthesis Inhibitors' Anticancer Activity," *Nature Communications* 14, no. 1 (2023): 6951.

³ I. Caffa et al., "Fasting-Mimicking Diet and Hormone Therapy Induce Breast Cancer Regression," *Nature* 583, no. 7817 (2020): 620–624.

⁴ Zhang, J., Y. Deng, and B. L. Khoo. "Fasting to Enhance Cancer Treatment in Models: The Next Steps." *Journal of Biomedical Science* 27, no. 1 (2020): 58.

⁵ Weng, M.-L., et al. "Fasting Inhibits Aerobic Glycolysis and Proliferation in Colorectal Cancer via the Fdft1-Mediated AKT/mTOR/HIF-1 α Pathway Suppression." *Nature Communications* 11, no. 1 (2020): 1869.

⁶ Pomatto-Watson, L. C. D., et al. "Daily Caloric Restriction Limits Tumor Growth More Effectively Than Caloric Cycling Regardless of Dietary Composition." *Nature Communications* 12, no. 1 (2021): 6201.

2-3. Defining Fasting: Islamic and Scientific Perspectives

In Islam, fasting (*Sawm*) during Ramadan entails complete abstinence from food, drink, and other physical needs (e.g., smoking, sexual activity) from dawn (*Fajr*) until sunset (*Maghrib*), with additional spiritual and behavioral intentions (*niyyah*). This practice extends beyond caloric restriction, incorporating discipline, self-purification, and heightened devotion.

In contrast, scientific literature often examines fasting through structured dietary interventions, including Fasting-Mimicking Diets (FMD)—cyclic, very-low-calorie (300–600 kcal/day) regimens with low protein. Caloric Restriction (CR) is a sustained 15–30% reduction in daily caloric intake without malnutrition. Other dietary interventions include Very Low-Carbohydrate Diets (VLCD), which restrict carbohydrates to induce selective metabolic shifts; Low-Fat Diets (LFD) (<30% fat intake); and Amino Acid Restriction.

3. Results and Discussion

3-1. Metabolic Vulnerabilities of Cancer

Cancer cells exhibit distinct alterations in nutrient metabolism pathways to meet their heightened energy and biosynthetic demands¹. These adaptations include enhanced nutrient uptake and activation of intracellular anabolic pathways, with three primary nutritional sources: glucose, amino acids, and lipids.

The Warburg effect characterizes the preferential use of glycolysis over oxidative phosphorylation in cancer cells, even under normoxic conditions². While less efficient, this metabolic reprogramming provides rapid ATP generation and biosynthetic intermediates. Lactate, once considered a byproduct of glycolysis, now emerges as a significant energy source for many tumors, sometimes surpassing glucose in utilization by the TCA cycle³. Fructose metabolism similarly supports tumorigenesis through the activation of the glycolytic pathway and metabolic reprogramming⁴.

Amino acid metabolism reveals critical dependencies, particularly on glutamine, a versatile substrate converted to α -ketoglutarate to fuel the TCA cycle and support fatty acid synthesis⁵. Branched-chain amino acids (leucine, isoleucine, valine) serve dual roles in protein synthesis and energy production⁶.

¹ D. Hanahan and R. A. Weinberg, “Hallmarks of Cancer: The Next Generation,” *Cell* 144, no. 5 (2011): 646–674.

² N. S. Chandel, “Glycolysis,” *Cold Spring Harbor Perspectives in Biology* 13, no. 5 (2021): a040535.

³ S. Hui et al., “Glucose Feeds the TCA Cycle via Circulating Lactate,” *Nature* 551, no. 7678 (2017): 115–118.

⁴ *Ibid.*

⁵ M. D. Neinast et al., “Quantitative Analysis of the Whole-Body Metabolic Fate of Branched-Chain Amino Acids,” *Cell Metabolism* 29, no. 2 (2019): 417–429.e4.

⁶ M. D. Neinast et al., “Quantitative Analysis of the Whole-Body Metabolic Fate of Branched-Chain Amino Acids,” *Cell Metabolism* 29, no. 2 (2019): 417–429.e4.

Lipid metabolism in cancer involves complex adaptations. Fatty acids undergo β -oxidation for ATP production, contribute to membrane biosynthesis, or convert to ketones in the liver - an alternative energy source for some malignancies¹. Hypoxic conditions further exacerbate metabolic flexibility, with cancer cells increasing glycolysis while reducing NADH production to maintain energy homeostasis².

These metabolic vulnerabilities present promising therapeutic targets, including:

- Glucose/glutamine restriction
- Specific amino acid depletion
- Pentose phosphate pathway inhibition

Precision targeting requires a comprehensive understanding of tumor-specific metabolic dependencies.

3-2. Tissue-Specific Metabolic Profiles

Neoplastic transformations induce unique metabolic adaptations across different tissues³:

Central Nervous System:

- Gliomas preferentially utilize glycolysis while maintaining capacity for glutamine/ketone metabolism⁴
- IDH1/IDH2 mutations increase nutrient sensitivity, revealing therapeutic opportunities

Mammary Tissue:

- ER+ tumors employ oxidative pathways (lactate/citrate consumption)⁵
- Triple-negative subtypes demonstrate glycolytic dominance and external fatty acid dependence

Hepatic Carcinomas:

- HCC upregulates glycolysis/lipogenesis with fructose/fatty acid dependency⁶
- Portal venous position creates a unique metabolic microenvironment

Colorectal Malignancies:

- WNT/PI3K/KRAS mutations drive glycolytic/flux⁷
- Dietary fructose may unexpectedly fuel tumor progression

Prostatic Neoplasms:

¹ R. J. DeBerardinis and C. B. Thompson, "Cellular Metabolism and Disease: What Do Metabolic Outliers Teach Us?" *Cell* 148, no. 6 (2012): 1132–1144.

² N. S. Chandel, "Glycolysis," *Cold Spring Harbor Perspectives in Biology* 13, no. 5 (2021): a040535.

³ E. Reznik et al., "A Landscape of Metabolic Variation across Tumor Types," *Cell Systems* 6, no. 3 (2018): 301–313.e3.

⁴ S. Venneti and C. B. Thompson, "Metabolic Reprogramming in Brain Tumors," *Annual Review of Pathology: Mechanisms of Disease* 12, no. 1 (2017): 515–545.

⁵ M. D. Goncalves, B. D. Hopkins, and L. C. Cantley, "Phosphatidylinositol 3-Kinase, Growth Disorders, and Cancer," *New England Journal of Medicine* 379, no. 21 (2018): 2052–2062.

⁶ H. Nakagawa et al., "Lipid Metabolic Reprogramming in Hepatocellular Carcinoma," *Cancers* 10, no. 11 (2018): 447.

⁷ S. R. Taylor et al., "Dietary Fructose Improves Intestinal Cell Survival and Nutrient Absorption," *Nature* 597, no. 7875 (2021): 263–267.

- Metabolic reactivation of oxidative pathways¹
- Citrate/lactate/fatty acid utilization with fructose mediation

Pulmonary Tumors:

- NSCLC activates parallel glycolytic/lipolytic pathways²
- KRAS mutations enhance BCAA dependence

Pancreatic Adenocarcinomas:

- Glutamine/fatty acid addiction with hypoxic adaptation³
- Unsaturated fatty acid scavenging capability

Endometrial Cancers:

- PI3K-mediated glucose dependence⁴
- Hormonally influenced metabolic programming

These tissue-specific profiles enable the development of precision nutritional interventions tailored to tumor metabolic signatures.

3-3. Classification of Dietary Interventions

To date, various types of dietary interventions have been used in cancer treatment⁵. Some approaches mainly target nutritional content, such as calorie-restriction, low-carbohydrate, and low-fat diets, while others focus on the timing of food intake, including fasting-mimicking diets and intermittent fasting regimens, which involve complete or partial periods of energy restriction regardless of meal composition. Notably, Taylor et al.⁶ published a comprehensive review of these dietary strategies in *Nature*, thoroughly examining their metabolic effects, implementation, and clinical relevance. In this section, we highlight and discuss several key aspects from that review that are most relevant and closely aligned with our focus on Islamic fasting. This provides a framework for a brief overview of the reported effectiveness and the potentially beneficial metabolic responses that may occur in cancer patients.

¹ Y. Liu, "Fatty Acid Oxidation Is a Dominant Bioenergetic Pathway in Prostate Cancer," *Prostate Cancer and Prostatic Diseases* 9, no. 3 (2006): 230–234.

² S. M. Davidson et al., "Direct Evidence for Cancer-Cell-Autonomous Extracellular Protein Catabolism in Pancreatic Tumors," *Nature Medicine* 23, no. 2 (2017): 235–241.

³ A. M. Zhang et al., "Endogenous Hyperinsulinemia Contributes to Pancreatic Cancer Development," *Cell Metabolism* 30, no. 3 (2019): 403–404.

⁴ A. Frolova et al., "Facilitative Glucose Transporter Type 1 Is Differentially Regulated by Progesterone and Estrogen in Murine and Human Endometrial Stromal Cells," *Endocrinology* 150, no. 3 (2009): 1512–1520.

⁵ B. A. Helmink et al., "The Microbiome, Cancer, and Cancer Therapy," *Nature Medicine* 25, no. 3 (2019): 377–388.

⁶ R. Taylor, J. N. Falcone, L. C. Cantley, and M. D. Goncalves, "Developing Dietary Interventions as Therapy for Cancer," *Nature Reviews Cancer* 22, no. 8 (2022): 452–466.

Calorie Restriction (CR)

In this type of dietary intervention, the total daily energy intake is reduced (in most clinical settings by approximately 15-30% of the daily energy consumption), while a balanced ratio of major nutrients is maintained¹. In Eastern medicine, particularly in traditional Iranian systems, fasting holds a special and longstanding status, consistently regarded as an essential means of maintaining health and treating certain diseases. In some cases, even extreme approaches to fasting have been observed; for example, some practitioners and specialists in traditional medicine recommend highly stringent dietary restrictions for their patients, including so-called “water fasting” protocols, wherein the patient is permitted to consume only water, abstaining from all solid foods. This represents a near 100% reduction in daily caloric intake. Documentation for these extreme approaches is based on the authors’ verbal communications with experts and experienced individuals in the field of traditional medicine.

Such extreme recommendations are sometimes even employed in the treatment of cancer or benign disorders, reflecting the deep roots and influence of these beliefs within Iranian health culture. Despite the passage of many years, there still exist individuals who employ these extreme methods. However, the prevailing approach in contemporary scientific and academic circles is increasingly shifting towards the documentation and validation of therapeutic strategies. Below, relevant cases and evidence formally recorded in credible academic sources will be introduced.

In preclinical animal studies, researchers have observed beneficial effects of calorie restriction, including decreased tumor incidence, slowed cancer progression, and reduced metastasis². To date, only a limited number of human studies have described the effects of calorie restriction as a therapeutic intervention for cancer³. In 2007, a phase III trial was initiated to evaluate the impact of calorie restriction in breast cancer patients. The available data have demonstrated favorable results, with improved disease-free survival reported⁴. Soon, results from a randomized phase III trial for breast cancer, evaluating calorie restriction as an adjunct therapy in early-stage breast cancer⁵, will be published—a development that is expected to substantially advance researchers’ understanding of this dietary intervention in cancer therapy.

¹ S. K. Das et al., “Low or Moderate Dietary Energy Restriction for Long-Term Weight Loss: What Works Best?” *Obesity* 17, no. 11 (2009): 2019–2024.

² M. Lv et al., “Roles of Caloric Restriction, Ketogenic Diet and Intermittent Fasting During Initiation, Progression and Metastasis of Cancer in Animal Models: A

³ H. Shaikh et al., “Body Weight Management in Overweight and Obese Breast Cancer Survivors,” *Cochrane Database of Systematic Reviews* 2020, no. 12 (2020).

⁴ P. J. Goodwin et al., “The LISA Randomized Trial of a Weight Loss Intervention in Postmenopausal Breast Cancer,” *NPJ Breast Cancer* 6, no. 1 (2020): 6.

⁵ J. A. Ligibel et al., “Randomized Phase III Trial Evaluating the Role of Weight Loss in Adjuvant Treatment of Overweight and Obese Women with Early Breast Cancer (Alliance A011401): Study Design,” *NPJ Breast Cancer* 3, no. 1 (2017): 37.

Fasting-Mimicking Diets (FMD)

In the context of calorie-restriction interventions, the duration of fasting intervals between meals is often overlooked. Mice subjected to calorie restriction typically consume their total daily caloric intake in a single meal, resulting in intermittent phases of high caloric consumption followed by fasting-like intervals. This phenomenon has led researchers to investigate whether the benefits observed in mouse models are attributed to calorie restriction itself or to the fasting periods that accompany it.

In carefully controlled studies on mice, fasting—defined as receiving daily calories in a single meal—was compared to calorie restriction. Results showed that, independent of total caloric intake, diet composition, or body weight, fasting led to similar improvements in health and survival rates¹. Additionally, in animal cancer models, cyclic fasting-mimicking diets (FMD) have been shown to improve therapeutic outcomes when used in conjunction with conventional cancer treatments.²

In studies involving cancer patients undergoing chemotherapy, fasting has been shown to decrease tumor-associated hormones, lessen side effects, and enhance overall quality of life³. Additionally, fasting can modify peripheral immune cell populations, potentially contributing to anti-tumor effects⁴. Despite these benefits, sustaining prolonged fasting periods poses challenges⁵. To address this, various intermittent fasting protocols have been developed to emulate the advantages of fasting while improving long-term compliance⁶.

Preclinical and clinical studies have demonstrated that FMD can inhibit cancer-related processes by reducing tumor-promoting hormones, including insulin, IGF-1, and leptin. These metabolic changes are accompanied by a reduction in peripheral immunosuppressive cells and enhancement of antitumor immune responses within the tumor microenvironment. Numerous

¹ S. J. Mitchell et al., “Daily Fasting Improves Health and Survival in Male Mice Independent of Diet Composition and Calories,” *Cell Metabolism* 29, no. 1 (2019): 221–228.e3.

² F. Valdemarin et al., “Safety and Feasibility of Fasting-Mimicking Diet and Effects on Nutritional Status and Circulating Metabolic and Inflammatory Factors in Cancer Patients Undergoing Active Treatment,” *Cancers* 13, no. 16 (2021): 4013.

³ F. M. Safdie et al., “Fasting and Cancer Treatment in Humans: A Case Series Report,” *Aging (Albany NY)* 1, no. 12 (2009): 988.

⁴ S. Jordan et al., “Dietary Intake Regulates the Circulating Inflammatory Monocyte Pool,” *Cell* 178, no. 5 (2019): 1102–1114.e17.

⁵ J. F. Trepanowski et al., “Effect of Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection Among Metabolically Healthy Obese Adults: A Randomized Clinical Trial,” *JAMA Internal Medicine* 177, no. 7 (2017): 930–938

⁶ aNencioni et al., “Fasting and Cancer: Molecular Mechanisms and Clinical Application,” *Nature Reviews Cancer* 18, no. 11 (2018): 707–719

studies have been conducted in recent years to investigate FMD regimens¹, and there is considerable anticipation for further clinical trials in this area².

Other Fasting-Based Approaches

In addition to FMD, other fasting-based approaches, such as time-restricted feeding (TRF), have attracted attention as effective nutritional strategies with potential anticancer properties. TRF primarily focuses on extending the daily fasting period to at least 14 hours without necessarily reducing calorie intake. Unlike FMD, which emphasizes severe caloric and nutrient composition restrictions over specified periods, TRF limits the eating window to certain hours of the day. This type of dietary regimen most closely resembles Islamic fasting protocols.

Studies have shown that the timing of food intake during the day can affect the efficacy of this nutritional approach; for example, early time-restricted feeding (eTRF)—with food intake concentrated in the early hours of the day—has been shown to be more beneficial compared to feeding periods in the afternoon or evening, with nearly all patients able to comply without any reported adverse effects. Animal models have demonstrated that this method can effectively reduce the growth of obesity-related tumors and metastasis without the need for calorie restriction or weight loss. The anticancer effects of TRF have been mainly attributed to³ reductions in hyperinsulinemia, which plays a central role in tumor progression.⁴ To date, no clinical trials have been initiated to evaluate TRF in cancer patients. Still, data from animal models suggest that this approach may be effective in managing cancer. These two innovative approaches, through metabolic impacts such as reductions in insulin, IGF-1, and leptin levels, demonstrate significant potential to improve cancer treatment outcomes, especially when combined with conventional therapies⁵.

Very Low-Carbohydrate Diets (VLCD)

Some of the systemic metabolic benefits of calorie restriction and fasting can be recapitulated through nutritional interventions with altered macronutrient ratios. For instance, very low-carbohydrate diets (VLCD) or low-fat diets (LFD) have been shown to reduce food intake and modulate tumor-promoting hormones compared to standard diets. These nutritional regimens have been studied for decades among cancer patients, demonstrating safety, feasibility, and in some cases, promising anticancer effects.

¹ S. Vingeliene et al., “An Update of the WCRF/AICR Systematic Literature Review and Meta-Analysis on Dietary and Anthropometric Factors and Esophageal Cancer Risk,” *Annals of Oncology* 28, no. 10 (2017): 2409–2419.

² S. de Groot et al., “The Effects of Short-Term Fasting on Tolerance to (Neo)Adjuvant Chemotherapy in HER2-Negative Breast Cancer Patients: A Randomized Pilot Study,” *BMC Cancer* 15 (2015): 1–9.

³ M. Das et al., “Time-Restricted Feeding Normalizes Hyperinsulinemia to Inhibit Breast Cancer in Obese Postmenopausal Mouse Models,” *Nature Communications* 12 (2021): 565.

⁴ M. Das et al., “Time-Restricted Feeding Normalizes Hyperinsulinemia to Inhibit Breast Cancer in Obese Postmenopausal Mouse Models,” *Nature Communications* 12 (2021): 565.

⁵ G. Salvadori et al., “Fasting-Mimicking Diet Blocks Triple-Negative Breast Cancer and Cancer Stem Cell Escape,” *Cell Metabolism* 33, no. 11 (2021): 2247–2259.e6.

For example, Cohen and colleagues conducted a 12-week randomized controlled trial in women with ovarian or endometrial cancer to investigate the effects of VLCD intervention on metabolic parameters¹. Only mild adverse effects were observed, and participants experienced a reduction in fat mass while maintaining lean mass, with no change in blood lipid profiles².

Encouraging data have also been reported for the implementation of VLCD in patients with breast cancer. In a randomized controlled trial involving 80 breast cancer patients undergoing chemotherapy, a 12-week VLCD intervention reduced tumor diameter compared to the control group receiving a standard diet. However, these results should be interpreted cautiously, as standard criteria for measuring tumor size should be applied, and there are also reports suggesting that dietary fat intake may be associated with increased risk of breast cancer and its recurrence in specific subgroups.

Low-Fat Diets (LFD)

These diets limit fat intake to less than 30% of total daily calories and emphasize consumption of vegetables, fruits, and whole grains. Apart from their exhaustive examination in non-cancer populations³, LFDs—unlike other dietary interventions discussed in this article—have been extensively tested in large cancer cohorts, and have been deemed safe. A randomized controlled study in postmenopausal women—specifically designed to evaluate the long-term benefits and risks of LFD for breast cancer, colorectal cancer, and cardiovascular disease—was conducted. Although no long-term decreases in cancer incidence or overall mortality were observed⁴, the LFD intervention lowered the incidence of deaths after breast cancer diagnosis.⁵

Other Dietary Interventions: Amino Acid Restriction Approaches

Novel strategies have also emerged to assess the antitumor effects of targeted amino acid restrictions. Preclinical studies have demonstrated that deprivation of amino acids, such as serine, glycine, cysteine, and methionine, can inhibit tumor growth. The translational potential of these findings should be evaluated in clinical studies.

A comparison of these scientific protocols and Islamic fasting

While most dietary interventions (including CR and FMD) permit water consumption, Islamic fasting strictly prohibits both food and liquid intake during daylight hours. This

¹ C. W. Cohen et al., “A Ketogenic Diet Reduces Central Obesity and Serum Insulin in Women with Ovarian or Endometrial Cancer,” *The Journal of Nutrition* 148, no. 8 (2018): 1253–1260.

² C. W. Cohen et al., “A Ketogenic Diet Is Acceptable in Women with Ovarian and Endometrial Cancer and Has No Adverse Effects on Blood Lipids: A Randomized, Controlled Trial,” *Nutrition and Cancer* 72, no. 4 (2020): 584–594

³ A. B. Evert et al., “Nutrition Therapy Recommendations for the Management of Adults with Diabetes,” *Diabetes Care* 37 (Supplement_1) (2014): S120–S143.

⁴ C. A. Thomson et al., “Cancer Incidence and Mortality During the Intervention and Postintervention Periods of the Women's Health Initiative Dietary Modification Trial,” *Cancer Epidemiology, Biomarkers & Prevention* 23, no. 12 (2014): 2924–2935.

⁵ R. T. Chlebowski et al., “Low-Fat Dietary Pattern and Breast Cancer Mortality in the Women's Health Initiative Randomized Controlled Trial,” *Journal of Clinical Oncology* 35, no. 25 (2017): 2919–2926.

fundamental difference in hydration protocols may significantly impact metabolic and cellular responses. Furthermore, dietary approaches such as VLCD, LFD, and amino acid restriction demonstrate even more fundamental differences from Islamic fasting in terms of nutrient and fluid intake. Unlike CR and FMD, which primarily restrict calories while maintaining hydration, these interventions involve specific macronutrient modifications (carbohydrate or fat restriction) or selective amino acid elimination while typically permitting normal fluid consumption. This creates a more pronounced contrast with the Islamic fasting paradigm of complete abstinence, potentially leading to divergent metabolic consequences. The nutritional permissibility in these protocols versus the comprehensive prohibition in religious fasting may yield substantially different biological effects that warrant careful consideration in comparative studies.

3-4. Dietary Adjuncts to Radiotherapy

One promising application of dietary interventions in oncology is enhancing the efficacy of radiotherapy. Since radiotherapy is typically delivered within a defined treatment window, dietary modifications can be precisely timed to this period, potentially enabling more aggressive intervention strategies. A key mechanism by which dietary approaches may improve radiotherapy outcomes involves impairing the capacity of tumor cells to repair DNA damage. For instance, in murine models, methionine-restricted diets radiosensitize tumor cells by altering one-carbon metabolism¹. A similar dietary approach has been implemented in a controlled human clinical study, though its effects on tumor outcomes remain under evaluation².

Dietary regimens that reduce circulating glucose levels have also been investigated as adjuncts to radiotherapy. Preclinical studies in murine models of lung and brain cancers demonstrate that low-glucose culture conditions or carbohydrate-restricted diets specifically enhance tumor cell radiosensitivity³. Recently, the ERGO2 trial—a small, randomized study in patients with recurrent malignant glioma—examined a very low-carbohydrate diet (VLCD) combined with intermittent fasting as an adjunct to radiotherapy. While this study found no statistically significant difference in progression-free or overall survival between dietary groups, post-hoc analysis revealed that patients achieving lower circulating glucose levels by day 6 demonstrated significantly improved survival outcomes⁴.

These findings collectively suggest that:

1. Metabolic modulation through dietary restriction may potentiate radiotherapy effects
2. The timing of dietary interventions relative to radiation treatment is crucial
3. Biomarkers like circulating glucose levels may help identify responsive patient subsets

¹ X. Gao et al., “Dietary Methionine Influences Therapy in Mouse Cancer Models and Alters Human Metabolism,” *Nature* 572, no. 7769 (2019): 397–401.

² Ibid.

³ B. G. Allen et al., “Ketogenic Diets Enhance Oxidative Stress and Radio-Chemo-Therapy Responses in Lung Cancer Xenografts,” *Clinical Cancer Research* 19, no. 14 (2013): 3905–3913.

⁴ M. Voss et al., “ERGO2: A Prospective, Randomized Trial of Calorie-Restricted Ketogenic Diet and Fasting in Addition to Reirradiation for Malignant Glioma,” *International Journal of Radiation Oncology* 108, no. 4 (2020): 987–99

Further clinical investigation is warranted to establish optimal dietary protocols and validate predictive biomarkers for this emerging therapeutic strategy. Current evidence highlights the need for larger, biomarker-stratified trials to determine which tumor types and patient populations might benefit most from dietary-radiotherapy combinations.

3-5. Toward Evidence-Based Implementation of Islamic Fasting in Clinical Settings

Defining a clinical trial for the implementation of Islamic fasting regimens in the clinic is still premature, as rigorous preclinical evaluation—including in vitro, animal, and sequential phase I, II, and III studies—must precede clinical translation. Transitioning toward an Islamic fasting paradigm requires substantial preliminary work, beginning with the evaluation of established fasting-mimicking diets and then systematically approaching protocols that resemble Islamic fasting, step by step. For instance, it is necessary first to determine whether altering a single dietary component or the entire diet is warranted, and to evaluate site-specific effects. For example, fat restriction is recommended for specific organs, such as the pancreas and gallbladder, but dietary modifications may need to be tailored for each anatomical site. Advancing science demands a meticulous, incremental research approach that builds upon existing evidence, initially replicating validated protocols and then gradually introducing minor modifications, such as restricting food intake to daylight hours. This approach, unlike current fasting-mimicking diet trials, aligns more closely with the principles of time-restricted feeding. To ensure clinical relevance, protocols previously tested and published by other researchers should be carefully reviewed, with shifts toward Islamic fasting implemented cautiously and only after establishing safety and efficacy in prior models. We hypothesize that metabolic changes regulated by exposure to sunlight, which profoundly influences circadian rhythms, sleep, metabolism, mood, and numerous other physiological processes, may lead to distinct outcomes; however, the optimal strategies for incorporating this element remain to be defined. Notably, limiting fasting protocols to daylight hours could offer significant benefits while reducing the risks and discomfort associated with prolonged fasting intervals.

Nevertheless, such approaches necessitate thorough investigation, with close clinical follow-up for each patient, careful consideration of eligibility and exclusion criteria, and stepwise, cautious adjustment of factors such as fluid restriction. All such interventions should undergo comprehensive preclinical evaluation, as, to our knowledge, such integrative mechanisms have not yet been systematically explored. Overall, we encourage oncologists and biologists interested in this domain to consider these research questions while adhering rigorously to the conventional scientific pathway.

4. Conclusion and Future Research Directions

This comprehensive review highlights the growing potential of dietary interventions particularly fasting regimens as adjunctive strategies in cancer therapy. Emerging evidence indicates that metabolic targeting via nutritional modulation can affect tumor progression, therapeutic

efficacy, and patient outcomes; however, most data remain preclinical and have seen limited translation into routine clinical practice.

Historically, oncology has treated nutrition primarily as supportive care. Recent advances, however, point to a paradigm shift: the metabolic vulnerabilities of cancer cells once regarded as peripheral are now being considered actionable therapeutic targets. The central question is whether selective metabolic restriction can amplify these vulnerabilities while sparing normal tissues.

This question generates several subordinate inquiries: Which nutrients serve as the principal fuel sources for specific cancers? Does restricting those substrates improve therapeutic response? Researchers have investigated both targeted nutrient limitations (for example, fats or carbohydrates) and broader caloric-restriction strategies. Preclinical models particularly murine studies are encouraging, yet the timing and scheduling of nutrient delivery constitute major confounders, which is why intermittent fasting has attracted substantial interest.

To date, low-fat diets and caloric restriction have progressed furthest toward clinical implementation; fasting-mimicking diets remain at an earlier stage of development. Several randomized controlled trials are currently underway, but comparative effectiveness across approaches has not been established.

Notably, Islamic fasting traditions grounded in Qur'anic principles provide a culturally informed framework that merits rigorous scientific evaluation. We therefore advocate conducting well-designed randomized controlled trials that assess fasting as an adjunct to standard cancer therapies. Such trials should incorporate tumor-specific metabolic profiling to identify optimal fasting regimens for distinct malignancies and should include comprehensive safety, tolerability, and quality-of-life endpoints.

Looking forward, several research priorities require concentrated effort. First, defining tumor-specific metabolic dependencies is essential for the development of precision-nutrition strategies tailored to cancer type. Second, fasting protocols must be optimized particularly with respect to duration and frequency to maximize therapeutic benefit while minimizing patient burden. Third, robust predictive biomarkers are needed for patient stratification and treatment personalization. Fourth, the immunomodulatory consequences of fasting demand deeper investigation, especially in combination with contemporary immunotherapies. Finally, integrating fasting regimens with next-generation targeted agents may reveal synergistic mechanisms and help overcome existing therapeutic limitations.

In summary, the intersection of nutritional science and oncology calls for interdisciplinary collaboration to establish evidence-based clinical guidelines. Early results especially for caloric restriction and low-fat diets are promising, but fasting-mimicking regimens require further validation. This evolving field not only offers therapeutic innovation but also invites a fundamental reappraisal of cancer metabolism within modern oncology.

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