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Recent Advancements in Nutrition and Dietary Intervention in the Management of Cancer

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Abstract

Globally, the main cause of death is cancer. Most of the doctors treat it using methods such as surgery, chemotherapy, and radiation. These treatments help improve health, but they also destroy our healthy body tissues along with cancerous cells during therapies, such as toxicity, a weakened immune system, and resistance to treatments. Due to several issues, most cancer patients end up malnutrition, also called cancer cachexia, a condition in which patients lose weight and muscle, and it affects 60% of those having advanced cancer which causes difficulty and leads to worsen outcomes. Recent research advancements have been focused on personalized nutrition, were doctors design custom plans using genomics. Certain diet plans are also being tested to make current cancer treatments work effectively. An example of cutting down calories and fasting for a short duration makes cancer cells more sensitive to treatment. Furthermore, the ketogenic diet uses methods that prevent cancer cells from getting energy and kill cancer cells more easily. Arginine and Probiotics can help fix problems with cancer, according to early results by using Patient Generated Subjective Global Assessment (PGSGA), diet changes can affect patients, and it would be difficult to follow these plans. Consistent measures with Randomized Controlled Trials (RCTs) should be the priority. Oncologists and Supportive care, need to work together closely on the patient get care.

Keywords: Cancer; Nutrition; Dietary Intervention; Management; Ketogenic Diet

Abbreviations: PGSGA: Patient Generated Subjective Global Assessment; RCTs: Randomized Controlled Trials; IARC: International Agency for Research on Cancer; MNA®: Mini Nutritional Assessment; PNI: Prognostic Nutritional Index; KD: Ketogenic Diet; CR: Calorie Restriction; DSS: Differential Stress Sensitization; DSR: Differential Stress Resistance; Gln: Glutamine; QoL: Quality of Life; CRF: Cancer-Related Fatigue; ROS: Reactive Oxygen Species; LOS: Length of Stay; TPN: Total Parenteral Nutrition

Introduction

Cancer is described as the multifactorial uncontrolled development and growth of body cells. There are more than 100 varieties of cancer, which are divided by the type of tissue or organ affected by the human body including genomic and environmental interactions [1,2]. The characteristic features of the cancer include unrestrained proliferation, lack of responsiveness to growth factors, sustained angiogenesis, anti-apoptotic properties, and invasion of other tissues [3]. Global cancer burden estimates (GLOBOCAN) are provided by agencies such as International Agency for Research on Cancer (IARC) [3-6] The types of cancers are treated either with standard remedies, i.e., surgery, radiation therapy, and chemotherapy, or using nonconventional or complementary or traditional treatment, i.e., hormone therapy, immunotherapy, nano-therapy, etc. [7] The choice of effective cancer treatment method is based on the nature of detected malignancies, their growth stage, age, the frequency, dosage of drugs, and the health of the patients. [3,8-12] Chemotherapy damages rapidly dividing cells but harms normal tissues, manifested by side effects such as myelosuppression, nausea, and loss of hair. Moreover, it is hindered by drug resistance [8,13]. Radiotherapy uses ionizing radiation to produce local tumor

damage but can damage nearby healthy tissues, leading to fibrosis, dysfunction of an organ, or secondary malignancies [9,14-16]. On the whole, these traditional treatments cause collateral damage to normal somatic tissues often inducing malnutrition, cachexia and metabolic imbalances which negatively affect immune competence and worsen prognosis [17,18].

The dietary impact on cancer metabolism is one of the modern academic research topics. Though the word prevention might be slightly exaggerated. Healthy habits are linked to reducing cancer risk and nutritional modulation has shown promise in decimation of cancer growth in preclinical models [19,20-23]. Proper nutritional care helps maintain strength, boost immune system and improve tolerance to therapy, and enhance quality of life [17]. Evidence suggests that diets rich in fruits, vegetables, wholegrains, and omega-3 fats can enhance treatment outcomes by regulating inflammation and oxidative stress [24-26].

By Incorporating evidence-based, customized nutrition plans, which can regulate fundamental intracellular pathways involved in tumor development; clinicians can mitigate undesirable treatment outcomes, enhanced efficacy, and promote long-term survivorship [26]. This mini review is focused to elaborate nutrition in cancer management, recent advancements and its integration of nutrition with conventional cancer therapies.

Overview of Nutrition in Cancer Management

Cancer patients have a high rate of malnutrition that is closely associated with poor clinical outcomes. Mini Nutritional Assessment (MNA®) is commonly used to individuals with cancer who may suffer from older age, but it is questionable whether it has any predictive validity in terms of patient prognosis. One of the common occurrences in cancer patients is malnutrition, a phenomenon that has the capability to affect the course of the disease as well as the survival [27]. Recent evidence shows that Prognostic Nutritional Index (PNI) is a statistically significant prognostic determinant of survival as shown in univariate and multivariate analyses. Further, pre-operative serum albumin was observed to have poorer outcomes, which work as autonomous prognostic markers in various studies [28,29].

Cancer cachexia is a multidimensional wasting syndrome involving progressive weight loss that significantly contributes to cancer morbidity and mortality, and although reduced dietary intake is common and strongly correlated with the degree of weight loss, many patients fail to achieve the recommended dietary intake even after nutritional counseling [30-32]. This condition is metabolically distinct from simple starvation, as tumors actively affect neural mechanisms regulating appetite and energy expenditure while promoting catabolism and wasting of peripheral tissues, including cardiac and skeletal muscle, adipose tissue, and bone. Defining effective and multimodal interventions for cachexia remains challenging due to a lack of consensus on definitions, low strength of evidence from clinical trials, and a scarcity of robust, rigorous, and mechanistic studies [30]. Malnutrition is also a prevalent and challenging health concern in older adults, linked to increased mortality, morbidity, physical decline, and reduced quality of life [33]. In oncology, the prevalence of malnutrition (or risk of it) increases with the stage of the disease, affecting about 60% of advanced cancer patients, and critically, malnutrition defined by involuntary weight loss (>5% in 3–6 months) is a potent predictor of poor outcome, with weight loss before or during chemotherapy linked to worse overall survival, though conversely, weight gain in patients with non-small cell lung cancer has been reported to be associated with a significant improvement of overall survival [34-37].

The resolution of clinical decisions in practice still involves diagnosing and treating a given condition through the assessment of the signs and symptoms, the pathophysiology of the organ systems, the underlying cause(s), and the corresponding therapy [38].

The Food and Nutrition Board of the Institute of Medicine has established the Recommended Dietary Allowance of certain nutrients 22 and Dietary Reference Intakes from the applications of evidence-based reviews conducted by expert panels [39-41].

Recommendations from IARC and WCRF/AICR/NCI are consistent and streamlined, advising individuals to maintain their weight on the lower end of the healthy range (between 18.5 and 25 kg/m^2), to avoid gaining more than 5 kg during adulthood, and to lose 5-10% of body weight if already overweight or obese, along with moderate activities like brisk walking or cycling for 30 minutes on most days of the week, for a reduction in chronic disease (coronary heart disease and diabetes) and for overall health. For those who do drink alcohol, consumption should be restricted to <5% of total energy for men and <2.5% of total energy for women, or fewer than 2 drinks per day for men and one for women [42-44]. According to recommendation of IARC, consuming at least 400 g/d of a variety of fruits and vegetables, including fiber, and NCI suggests 5–9 servings/d [43].

Recent Advancements in Dietary Interventions

Indeed, the future direction of cancer care is more personalized and precision nutrition that is no longer based on a standard diet due to the high degree of cancer classification, patient-specific environment and lifestyle [26]. The essence of the proposed project is the creation of individualized nutrition plans that enhance patient outcomes. The rationale behind this method is that dietary manipulation affects the amount of metabolites accessible to the tumor cell in its microenvironment and, thus, the way in which cancer cells use nutrients to grow, develop, and survive [45]. Other tools like genetics and genomics that are necessary in comprehending the genetic predisposition (for example, particular sub-types of breast cancer in women of African descent) and deriving the genomic insights are crucial to the prognosis (as in ovarian cancer, progression-free survival) are

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also incorporated into precision care. Moreover, metabolomics is also used as a state-of-the-art analytical technique to monitor the metabolic alteration and identify mechanistic connections among the host, the disease, and the gut microbiome. The role of the gut microbiota in cancer susceptibility is that nutritional factors can regulate the gut flora to promote the development of tumor-suppressing or carcinogenic bacteria [46,47].

Nutrigenetics involves the study of the impact of nutrition on the gene level, with its focus being on the effect and the way in which specific genetic variants are affected by nutrient interactions. It incorporates environmental exposure, nutrition, with the human genome, with the focus on the gene [48,49].

Nutrigenomics examines how nutrients alter genomic and transcriptomic profiles and then examines the resultant effects on proteomics and metabolomics. In this method, the nutrients are studied holistically regarding the way they alter gene expression and transcript patterns and, thus, affect proteomic and metabolomic mechanisms [50].

The overall objective of the integration of nutrigenetics and nutrigenomics is to use personalized medicine and customized cancer therapy, such as considering of genomic profile and nutrient intake of a patient or adjuvant nutrition support of cancer treatment, apoptosis regulation or angiogenesis prevention [51-53]. Refer below to the Table 1 that provides information about the key components in nutrients and its approximate Energy Distribution in cancer therapy.

Ratio: 3:1 or 4:1 (Fat: Carbohydrates + Protein) [54]

Ketogenic diet (KD) has become one of the leading methods that seek to attack the metabolic processes of the cancer cells [55]. In comparison to traditional dietary interventions, KD is theorized as a metabolic therapy that aims to provide an inhospitable environment to the malignant cell [56]. The main aim of the KD is to force the organism to change its metabolic state of utilizing glucose to produce ATP to the oxidation of lipid substances to produce ketone body and put the organism in a ketonic state [57]. The basis of the application of KD is the exploitation of the underlying metabolic differences between normal and cancerous cells which is often known as the Warburg effect [58,59].

It has been demonstrated that dietary intake affects many pathways involved in carcinogenesis and tumor progression. Dietary guidelines have recommended the use of a plant-based diet as a way of preventing cancer [56,60-62] (Figure 1).

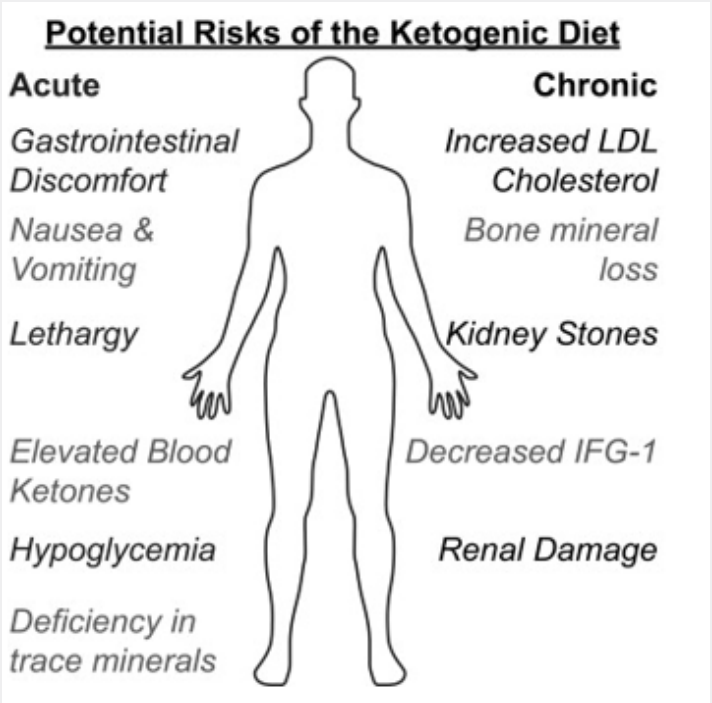

Figure 1: Possible acute and chronic side effects associated with the ketogenic diet [54].

Integration of Nutrition with Conventional Cancer Therapies

Dietary strategies are employed to enhance the effectiveness of conventional cancer therapies by exploiting metabolic differences between cancer and normal cells or providing protective effects [63]. Calorie Restriction (CR) and short-term fasting are researched interventions because they induce differential stress sensitization (DSS) in cancer cells, increasing their susceptibility

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to chemotherapy and radiation, while simultaneously promoting differential stress resistance (DSR) in normal cells, shielding them from toxic damage [64,65]. Other than the regulation of dietary intake, additional intake of particular nutrients could be beneficial. As an example, glutamine (Gln) might alleviate the undesirable radiational effects and promote the effectiveness of chemotherapy because of diminishing the harmful side effects. In addition, omega fatty acids (ω-3) could be used to enhance the efficacy of chemotherapy in preventing the growth of cancerous cells at the same time they are used alongside chemotherapy. The Ketogenic Diet (KD) is thought to be a way to change how your body works to fight cancer by making things challenging for cancer cells. [23,66] The manipulation of the gut microbiota is extremely important as evidenced. Nucleotide synthesis by intestinal bacteria can also change the reaction of rectal cancer patients to pre-operative chemo-radiotherapy, which means that the adjustment of the microbiota may enhance treatment outcomes [67].

Efficient and carefully designed nutritional support is invaluable to neutralizing the negative impact of treatment plans, promoting immune efficiency, and enhancing the Quality of Life (QoL). Optimal nutrition care provision requires that there is an energy intake of between 25-30 kcal per kilogram of body weight per day with a protein intake of above 1g/kg/day and ideally above 1.5g/kg/day, to protect lean body mass, tissue repair, and prevent the development of sarcopenia [68,69] Much has been done in the control of common toxicities that affect the eating habits. Nausea and vomiting (N/V) are now better controlled using advanced anti-emetic regimens, including 5-HT3 antagonists for immediate N/V, neurokinin receptor antagonists for delayed nausea, and the inclusion of corticosteroids and olanzapine. To address mucositis damage to the mucosal lining's strategies, include oral cryotherapy (ice chips), keratinocyte growth factor (palifermin), and glutamine, which protects the intestines and can reduce chemotherapy-induced complications like GI-mucositis and diarrhea [70,71]. Although systematic reviews suggest that nutrition therapy alone has no definitive overall effect on QoL or Cancer-Related Fatigue (CRF), there is preliminary evidence that plant-based dietary patterns (anti-inflammatory diets high in fruits, vegetables, fish, nuts, and seeds) may offer improvements in CRF. Importantly, interventions that successfully utilized nutritional assessment tools like the Patient-Generated Subjective Global Assessment (PGSGA) to improve nutritional status often correlated with subsequent improvements in patient quality of life [72-74] (Figure 2).

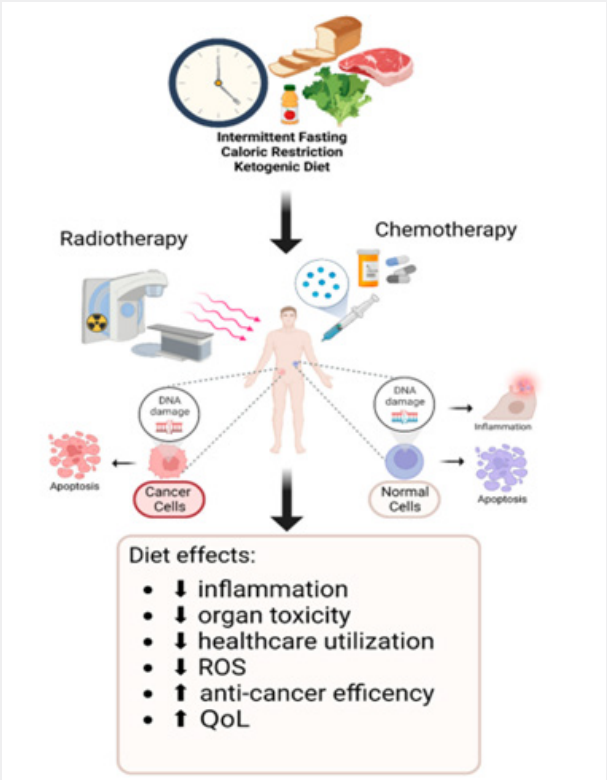

Figure 2: Potential positive effects of dietary interventions on patients receiving cancer treatment. Quality of life (QoL) is a parameter that is used to determine the well-being of an individual both physically and psychologically. Reactive oxygen species (ROS) are unstable molecules which induce DNA damage, thereby leading to cell death [74].

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Table 1: Key nutrients in cancer therapy outcome chart.

Component	Approximate Energy Distribution
Fat	90% of total calories
Protein	8% of total calories
Carbohydrates	2% of total calories

Immuno-nutrition consists of modulating the immunological responses and fostering the rehabilitation of tissues by the oral, enteral, or parenteral administration of immune system-boosting nutrients [75]. These nutrients include arginine, glutamine, omega-3 fatty acids, and nucleotides [76]. Recommended timeframes include the postoperative period and postoperative care of patients after upper gastrointestinal cancer surgery. Immune system boosts during the postoperative period have been documented to improve safety and efficacy by lowering complication rates, especially infectious ones, and shortening hospital length of stay (LOS) [75]. Specifically, postoperative, Gln-enriched total parenteral nutrition (TPN) improves nutritional status, nitrogen balance, and diminishing inflammatory status (IL-6 and CRP) [77]. Dysbiosis induced by cancer therapy, exacerbating gastrointestinal (GI) mucositis and malnutrition, necessitates explicit attention to modulation of Gut Microbiota (GM). Probiotics and symbiotic have clinical benefits and in one study, the authors describe reduced infectious complications postoperatively in patients with colorectal cancer [78]. Another study in patients undergoing neoadjuvant chemotherapy for esophageal cancer documented a reduction of chemotherapy-associated diarrhea, thus lowering the need for prophylactic antibiotics. Specific nutrients, such as omega-3 fatty acids and arginine, are known to beneficially alter certain in-body processes [79].

Challenges and Limitations

Results don't seem to be materializing as our integration of good nutrition into therapeutic plans still encounters severe hurdles. Some hurdles like differentiating level of implications and effects inflicted on and by different types of cancer. Other hurdles, like a lack of uniform guidelines in clinical and cross-sectional literature, and therefore a lack of conclusive analyses on the therapeutic impacts of nutrition on cancer, are to be used in studies on Cancer-Related Fatigue (CRF) and Quality of Life (QoL) [80]. Cancer patients shut down on compliance and on limits set by practical considerations. Many conventional strategies for Cancer care cause distressing toxicities [81]. It is the toxicities like nausea and mucositis that literally make eating on un-impacted days of the cancer care cycle a considerable emotional and physical challenge as well as a cause of shame for the patient. It is these unconsumed calories that fuel the patient's decline and worsen prognostic outcomes [82].

Conclusion and Future Perspectives

In conclusion, while the overall pooled data continues to show no conclusive value of nutrition therapy on CRF or QoL, certain focused approaches show potential promise, especially where Patient-Generated Subjective Global Assessment (PGSGA) tools have been designed to drive personalized assistance and where plant-centric or anti-inflammatory eating patterns have been utilized. Personalized nutrition and precision nutrition research with tools like metabolic profiling and genomics must be the focus of upcoming studies. To secure credible data, the field requires more large-scale Randomized Controlled Trials (RCTs) that incorporate reliable and standardized instruments to measure CRF and QoL, determine the most strategic implementation of an intervention (pre-, during- or post-treatment), and address hypermetabolic energy needs, dietitians, and palliative care teams in anticipatory, predictable supportive care. For clinical outcomes, interdisciplinary interaction should be highlighted to deal with the toxicities through proactive therapeutic relationships involving oncologists, dietitians, and palliative care teams to facilitate predictable and anticipatory supportive care.

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