VER
Vascular & Endovascular Review

Nutritional Significance and Its Impact on Cancer Patient Outcomes

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ABSTRACT

Nutrition plays a critical role in influencing treatment response, recovery, and overall clinical outcomes in cancer patients. Malnutrition is highly prevalent among individuals undergoing cancer therapy due to factors such as reduced appetite, metabolic alterations, treatment-related side effects, and disease progression, leading to compromised immune function, delayed healing, and decreased quality of life. This review explores the nutritional significance in cancer care and its direct impact on patient outcomes, including therapeutic tolerance, survival rates, and functional status. Adequate nutritional support has been shown to improve treatment efficacy, reduce complications, minimize hospital stays, and enhance physical strength and psychological well-being. Emphasis is placed on individualized nutritional assessment, early intervention, and the integration of dietetic therapy as a component of comprehensive oncology management. The study highlights the importance of balanced macro- and micronutrient intake, oral nutritional supplements, and enteral or parenteral nutrition when necessary. Optimizing nutritional strategies is pivotal in improving prognosis and promoting holistic recovery in cancer patients.

KEYWORDS: Cancer nutrition, Malnutrition, Clinical outcomes, Dietary intervention, Oncology care

How to Cite: Syrsulu Myrzagulova, Tolepbergenova M, Zhexenova Azhar N, Muratbekova Raikhan Abdurazakovna, Muratova Ainur Nurzhigitovna, Sajad Ahmad Bhat., (2025) Experimental Models for Evaluating Learning and Memory: A Neuropharmacological Perspective, Vascular and Endovascular Review, Vol.8, No.13s, 13-18.

INTRODUCTION

Nutritional problems are often encountered during the treatment of cancer. A prospective observational study reported that 51.1% of all cancer patients presented nutritional impairment, and 64% of patients showed reduction in weight 6 months after diagnosis [1]. Weight loss, especially cachexia, are widely recognized as not only reduced physical function and quality of life, but also poor prognostic factors in cancer patients. Classically, BMI is often used for measuring nutritional status of a patient, and recent studies have focused more on sarcopenia [2]. However, nutritional problems are complex and vary depending on the location and stage of cancer [1,3]. Therefore, nutritional support for cancer patients should be based on the assessment of each patient's condition and appropriate planning of the outcome. In this review, we will look at what should be considered to prevent malnutrition by providing adequate nutrition to cancer patients.

Cachexia, usually found in cancer patients, is not only caused by malnutrition owing to anorexia. It is a more complicated condition combining lower intake, metabolic malfunction, and higher energy need. This process comprises a range of inflammatory cytokines in cancer cells, abnormalities in protein and lipid metabolism, and an imbalance in the creation and degradation processes of muscle proteins.

Dysfunction in the control of human inflammatory process is documented in numerous disorders, including cancer. Researches have revealed that elevated inflammatory cytokines, such as TNF-α and interleukin-6 (IL-6), play significant roles in the nutritional metabolism of cancer patients [4]. TNF-α is a cytokine associated to cachexia, and it was initially dubbed cachectin [5]. It has long been recognized that TNF-α infusion induces loss of skeletal muscle mass in mice, while TNF-α blocking immunoglobulin decreased muscle loss in tumor-bearing rats [6,7]. Although it is controversial if TNF-α levels in blood are higher in cancer patients, it is believed that TNF-α activates nuclear factor kappalight-chain-enhancer of activated B cells (NF-κB) and promotes the degradation of proteins through a pathway independent of the ubiquitin-proteasome pathway [8]. Furthermore, TNF-α stimulates other cytokines and may elicit symptoms linked with cachexia, such as anorexia [9]. A research utilizing an antiTNF-α drug, etanercept, in cancer patients revealed that etanercept improved chemotherapy adherence and tiredness during cancer treatment [10]. IL-6 is also considered to have a very essential role in cancer-related cachexia. In a research utilizing ApcMin/+ mice, increase of IL-6 did not produce cachexia in the tumor-free animals. However, elevation of IL-6 was associated with decreased skeletal muscle and fat mass, and increased tumor burden in ApcMin/+ mice [11]. In cancer patients, IL-6 increases the acute phase reactants such as CRP through signal transducer and activator of transcription 3 (STAT3), and it is associated with muscle wasting [12]. However, in a trial of lung cancer patients, treatment of humanized anti-IL-6 antibody was beneficial in reducing symptoms such as anorexia, but it did not stimulate weight gain [13]. Therefore, it is found that cancer-associated cachexia is not only connected to one cytokine, but is controlled by the interactions of multiple signaling molecules.

In catabolic illnesses, different hormones and cytokines control protein synthesis and breakdown via the ubiquitin-proteasome pathway, autophagy, and transforming growth factor beta family ligands. Up-regulation of the ubiquitin-proteasome system by catabolic stress in numerous animal tumor models has been related with muscle atrophy. Myofibrillar components of muscle protein are predominantly degraded in the ubiquitin-proteasome pathway, and this leads to diminished muscular strength [14]. Moreover, the stress hormones and inflammatory cytokines induce autophagy and mitochondrial malfunction, which contribute to muscular atrophy. These processes are controlled by atrogenes and transcription factors, such as NFκB and forkhead box protein O (FOXO). 14 Especially in cancer patients, chemotherapy itself and malabsorption by consequences of treatment, such as mucositis, may directly trigger muscle atrophy [15]

It is widely recognized that impairment of glucose metabolism occurs in cancer patients. Cancer cells display significant glycolysis, and glucose is generated via gluconeogenesis in the liver utilizing lactate produced by the cancer cells [16]. During cancer-associated cachexia, elevated level of insulin-like growth factor-1 is detected, leading in insulin resistance [17]. Thus, most of the glucose produced is consumed by the cancer cells; thus, cancer patients have a very high energy need. However, in real clinical investigations, insulin resistance is not invariably related with weight reduction [18].

Lipid metabolism is also disturbed in cancer patients. The loss of adipose tissue by metabolic impairment further worsens cancer-associated cachexia. The buildup of triglycerides in the cytoplasm of adipocytes is the most effective way of energy storage. Free fatty acid and glycerol from triglyceride rise in individuals with cancer-associated cachexia [19]. Higher lipolysis and fat oxidation rates were seen in cancer patients decreasing weight as compared to those of healthy control [20]. This lipolysis was increased by hormones, pro-inflammatory cytokines, and lipid-mobilizing factor [21]. One noteworthy result of lipid metabolism in cancer patients is fat browning. White adipose tissue cells transform to brown adipose tissue-like cells (beige cells) during cancer-associated cachexia, similar to the process in cold conditions [22]. The numerous mitochondrial components of beige cells create heat (thermogenesis) from ATP production via enhanced uncoupling protein-1 [17]. Fat browning in cancer-associated cachexia signifies imbalance of homeostasis and leads to catabolic wasting unlike normal physiologic settings.

IMPACT OF MALNUTRITION ON TREATMENT OUTCOMES IN CANCER PATIENTS

Although the stage and type of cancer and the response to treatment are the most significant prognostic markers, several studies have revealed that patients who sustained weight gain showed better prognosis than those who did not. Malnutrition is related with longer hospital stay and greater incidence of admission, delayed wound healing, weakening of the immune system, and cancer-associated mortality [23-25]. An essential link beyond simple cause and effect has been established between malnutrition and exacerbation of the condition. In a multicenter research assessing the incidence of malnutrition in patients after cancer therapy, old age, hospital stay, and metastasis indicated a connection with malnutrition. Moreover, malnutrition was connected with increased infection incidence and longer hospital stay [26]; consequently, simply emphasis on raising the weight of cancer patients does not improve the patient's clinical prognosis favorably.

Sarcopenia in patients with cachexia has lately been highlighted for contributing to poor prognosis in cancer patients. In a research that studied prognosis of patients with cholangiocarcinoma following major surgery, preoperative sarcopenia was related with longer hospital stay, greater incidence of liver failure, and higher postoperative infection rate [27]. Sarcopenia exhibited favorable connection with higher toxicity from chemotherapy and quicker tumor growth in patients with metastatic breast cancer [28], and was connected to shorter survival rate. In a retrospective research examining 229 stage III colon cancer patients, one standard deviation decrease of the psoas muscle mass index was connected to an increased hazard of overall death in multivariate analysis [29]. Likewise, in a prospective analysis of patients with foregut cancer treated with neoadjuvant chemotherapy, decrease in skeletal muscle mass was a predictor of lower survival rate [30]. Several additional investigations of various cancer types revealed that sarcopenia negatively influenced the prognosis linked with cancer therapy and was related with comorbidities.

for 15 s. During the second test, animals were removed from shock free zone if they did not step down for a period of 60 s. Retention was tested after 24 h in a similar manner, except that the electric shocks were not applied to the grid floor. Each mouse was again placed on the platform, and the SDL was recorded, with an upper cut off time of 300s [13,14] Step-through Passive Avoidance Test: The apparatus (BPT Co., Tehran) consisted of an illuminated chamber connected to dark chamber by a guillotine door. Electric shocks were delivered to the grid floor by an isolated stimulator. On the first and second day of testing, each rat was placed on the apparatus and left for 5 min to habituate to the apparatus. On the third day, an acquisition trial was performed. Rats were individually placed in the illuminated chamber. After a habituation period (5 min), the guillotine door was opened and after the rat entering the dark chamber, the door was closed and an inescapable scrambled electric shock (1 mA, 1 s once) was delivered. In this trial, the initial latency (IL) of entrance into the dark chamber was recorded and rats with ILs greater than 60 s were excluded from the study. Twenty-four hours later, each rat was placed in the illuminated chamber for retention trial. The interval between the placement in the illuminated chamber and the entry into the dark chamber was measured as step through latency (STL up to a maximum of 600 s as cut-off) [15] Active Avoidance The active avoidance task is a fear-motivated associative avoidance test based on electric current as a source of punishment. In this task the mouse has to learn to predict the occurrence of an aversive event based on the presentation of a specific stimulus, in order to avoid the aversive event by actively moving to a different compartment. The measures recorded, number of avoidances (the mouse crossing to the other compartment during the stimulus signal), number of non-responses (the mouse failing to cross to the other compartment during the trial), response latency (latency to avoid or escape), serve as an index of learning and allows memory to be assessed [16].

Shuttel Box Active Avoidance Test: Shuttle box avoidance is a more difficult task. Since the animal is not handeled between trials, the shuttle box can be easily automated [18]. In this apparatus consist of a rectangular chamber divided into 2 compartments. Both compartments are lighted by overhead stimulus lights. The two compartments are separated by an automatic guillotine door and each has a grid floor through which a foot shock can be delivered. On first day of experiment (habituation day) a mouse is placed in one of the two compartments and allowed to ambulate freely between the two compartments of the shuttle box for 10 minutes in order to become familiarized with the learning environment. On the next day (training day) a mouse is placed in one of the two compartments and allowed to ambulate freely between the two compartments of the shuttle box for 1 minute (lights are on in both compartments). After 1 minute the light, used as the conditioned stimulus (CS), is switched off in the compartment in which the mouse is in, and 5 seconds later, a foot shock is delivered (unconditioned stimulus (US), 0.3mA, 5 second duration). The shock and light co-terminate such that the light is on for 10 seconds. If the mouse fails to make a response, both CS and US are terminated after 5 seconds of foot shock. During inter trial intervals, mice are permitted to move freely and to cross back and forth between compartments. The next trial always starts in the compartment where the mouse was located at the end of the ITI.[17] Runway avoidance Mice or rats of either sex are used and maintain under standard conditions and handle for several days before the experiment. The same box as use in the step-through model can be use in this experiment. The apparatus is uniformly illuminated by an overhead light source. A loudspeaker, mount 50 cm above the start-box, serves for presenting the acoustic condition stimulus (CS; an 80 dB, 2000 Hz tone from an audio generator). The foot shock is employed by the same source as in the step-through avoidance. The animal is allowed to explore the whole apparatus for 5 min. The guillotine door is then close and the animal is place into the light starting area. After 10 s the acoustic CS is applied and the door is simultaneously open. Shock is turned on after 5 s. The CS continuous until the animal reaches the safe area. It is left there for 50-70 s (intertrial interval, ITI) before return to the same area again. The procedure starts again. The training is continued until the animal attains the criterion of 9 avoidances in 10 consecutive trials. On the next day the procedure is repeated until the same learning criterion is reached and finally the time need to reach the safe area is measured [18]

NUTRITIONAL SCREENING AND ASSESSMENT IN CANCER PATIENTS

Assessing weight loss in cancer patients has been used since long as the simplest and most effective way to determine malnutrition. Although BMI can be disturbed by ascites and body edema, many studies showed that BMI and unintended weight loss were the methods used to monitor malnutrition in patients and predict poor prognosis. Even though various nutritional assessment tools have been introduced and actively used, BMI still plays an important role. A study investigating 3,779 patients with colorectal cancer, between 1972 and 2017, revealed that the underweight group showed a significantly worse overall survival rate as compared to the normal weight group in stage III and IV cancer patients. More than 10% of weight reduction from pre-diagnosis to post-diagnosis showed a significant relation with poorer overall survival [34]. Moreover, in a prospective study analyzing 82 metastatic breast cancer patients from 2011 to 2012, overweight patients showed a significant association with lower rate of cancer mortality as compared to the normal weight patients [35]. Excessive nutrition is not recommended when considering the overall disease mortality including metabolic diseases. Furthermore, the prognosis is worse in overweight patients when there is accompanied muscle loss. Thus, it is obvious that simply maintaining the weight could play a protective role against cancer mortality.

Traditionally, serum concentrations of liver proteins, such as albumin, have been associated with the nutritional status of patients. Therefore, a lack of these proteins indicated undernourishment and was used as an indicator of active nutritional support [36]. However, since albumin has a long half-life and is inhibited by inflammatory cytokines including TNF-α and IL6, which are elevated in cancer patients, it cannot be an immediate and accurate indicator of malnutrition [37].

Nowadays, instead of using only 1 specific parameter to evaluate the patient, several factors are combined to assess the nutritional risk and evaluate the nutritional status. The Malnutrition Universal Screening Tool, Nutrition Risk Screening 2002, Mini Nutritional Assessment Short Form, and Malnutrition Screening Tool are validated and widely-used nutritional risk screening tools [38]. The purpose of nutritional risk screening is to emphasize the importance of nutritional support and promote early intervention to ultimately prevent poor outcomes due to malnutrition. Therefore, these screening tests should be easy to apply and interpret. Although they have different target patients, all the screening tools use parameters of BMI, weight change, accompanying disease, and degree of food intake [39]. The strategy for screening nutritional risk in cancer patients

should adopt an individualized strategy for each medical institution considering the applicability of each tool. Although there is a lack of clear evidence eliciting the clinical benefits of nutritional screening tools in cancer patients, no studies have proved the inefficacy of nutritional risk screening tools [40-42]. In fact, there are certain benefits of screening for nutritional risk depending on the type and treatment of cancers. Therefore, the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline recommends that there should be regular evaluation of nutritional intake, weight change, and BMI, that starts during cancer diagnosis and is repeated depending on the stability of the clinical situation [39].

If the patient is predisposed to have a nutritional risk, an assessment of the patient's nutritional status must be performed. Comprehensive nutritional assessment provides an objective goal for individualized nutritional care of the patients, ultimately improving the clinical outcomes by protecting the patients from treatment complications, and improving both the treatment outcomes and quality of life. Therefore, the nutritional assessment of cancer patients should be repeated periodically, and not just once. There are many nutritional assessment tools used in researches and clinical practice. Although each nutritional assessment tool varies slightly, most tools consist of the patient's medical history, food intake, physical activity level, weight change, other anthropometric measures, and laboratory test results [43]. Among the various tools available, the patient-generated-subjective global assessment (PG-SGA) has been developed specifically for cancer patients. PG-SAG is a tool that evaluates the clinical aspects, including physical examination and accompanying diseases, and confirms the change in the patient's weight or dietary intake, presence or absence of gastrointestinal symptoms that may affect the dietary intake, and expresses a numerical score [44]. The start and posttreatment follow-up of nutritional intervention are based on this score. PG-SGA is a valid and dependable tool that provides a reference to identify and classify the nutritional state of a cancer patient. Nutrition Risk Index is another commonly used assessment tools.

CONCLUSION

Optimal nutrition is an essential component of comprehensive cancer care, significantly influencing treatment tolerance, recovery, and survival outcomes. Early nutritional assessment and timely intervention can reduce complications, improve quality of life, and enhance overall therapeutic effectiveness. Integrating personalized nutritional strategies into routine oncology practice is vital for achieving better patient outcomes.

Acknowledgement

I would like thank each author for their contributions.

Conflict of Interest

No conflict of interest were found

Author's contribution

All the authors have contributed equally completing this manuscript.

REFRENCES:

1. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum S, Hudspeth AJ, Mack S, editors. Principles of neural science. New York: McGraw-hill; 2000 Jan.
2. Jewart RD, Green J, Lu CJ, Cellar J, Tune LE. Cognitive, behavioral, and physiological changes in Alzheimer disease patients as a function of incontinence medications. The American journal of geriatric psychiatry. 2005 Apr 1;13(4):324-8.
3. Crawford JG. Alzheimer's disease risk factors as related to cerebral blood flow: additional evidence. Medical hypotheses. 1998 Jan 1;50(1):25-36.

4. Okano H, Hirano T, Balaban E. Learning and memory. Proceedings of the National Academy of Sciences. 2000 Nov 7;97(23):12403-4.
5. Markowitsch HJ. Diencephalic amnesia: a reorientation towards tracts?. Brain Research Reviews. 1988 Dec 1;13(4):351-70.
6. Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. Psychological review. 1992 Apr;99(2):195.
7. White NM, McDonald RJ. Multiple parallel memory systems in the brain of the rat. Neurobiology of learning and memory. 2002 Mar 1;77(2):125-84.
8. Carroll ME, Overmier J. Animal research and human health: Advancing human welfare through behavioral science. American Psychological Association; 2001.
9. Parle, Milind, and Nirmal Singh. "Animal models for testing memory." (2004): 101-120.
10. Vyawahare NS, Nikam AP, Sharma RG, Deshpande MM, Tarnalli AD, Bodhankar SL. Effect of Clitoria ternatea extract on radial arm maze task performance and central cholinergic activity in rats.
11. Morris R. Developments of a water-maze procedure for studying spatial learning in the rat. Journal of neuroscience methods. 1984 May 1;11(1):47-60.
12. Netto CA, Izquierdo I. On how passive is inhibitory avoidance. Behavioral and Neural Biology. 1985 May 1;43(3):327-30.
13. Jaiswal AK, Upadhyay SN, Bhattacharya SK. Effect of dihydroergotoxine, a cerebral vasodilator, on cognitive deficits induced by prenatal undernutrition and environmental impoverishment in young rats. Indian journal of experimental biology. 1991 Jun 1;29(6):532-7.
14. Jaiswal AK, Upadhyay SN, Bhattacharya SK. Effect of pyritinol, a cerebral protector, on learning and memory deficits induced by prenatal undernutrition and environmental impoverishment in young rats. Indian journal of experimental biology. 1990 Jul 1;28(7):609-15.
15. Baluchnejadmojarad T, Roghani M. Chronic Rumex Patientia Seed Feeding Improves Passive Avoidance Learning and Memory in Streptozotocin-Diabetic Rats. Basic and Clinical Neuroscience. 2010 Jul 1;1(4):53.
16. Not refren….
17. Vogel HG, editor. Drug discovery and evaluation: pharmacological assays. Springer Science & Business Media; 2002 Jun 13.
18. Capaldi EJ, CAPALDI ED. Aversive learning situations: Apparatus and procedures. InMethods in psychobiology 1972 Jan 1 (pp. 59-81). Academic Press.
19. Essman WB. Electroshock-induced retrograde amnesia in seizure-protected mice. Psychological Reports. 1968 Jun;22(3):929-35.
20. Gozal D, Nair D, Goldbart AD. Physical activity attenuates intermittent hypoxia-induced spatial learning deficits and oxidative stress. American journal of respiratory and critical care medicine. 2010 Jul 1;182(1):104-12.
21. Drachman DA, Leavitt J Human memory and the cholinergic system. Arch Neurol;1974, 30:113–121.
22. Dilts SL, Berry CA Effects of cholinergic drugs on passive avoidance in the mouse. J Pharmacol Exper Ther;1976, 158:279–285.
23. Glick SD, Zimmerberg B. Amnesic effects of scopolamine. Behavioral biology. 1972 Apr 1;7(2):245-54.
24. Schindler U, Rush DK, Fielding S (1984) Nootropic drugs: Animal models for studying effects on cognition. Drug Devel Res;1972, 4:567–576.
25. Iversen SD Behavioural Pharmacology of Dementia. Naunyn Schmiedeberg's Arch Pharmacol;1998,2; 371
26. Gibson GE, Blass JP. Impaired synthesis of acetylcholine in brain accompanying mild hypoxia and hypoglycemia. Journal of neurochemistry. 1976 Jul;27(1):37-42.
27. Schindler U, Rush DK, Fielding S (1984) Nootropic drugs: Animal models for studying effects on cognition. Drug Devel Res;1972, 4:567–576.
28. Hock FJ. Effects of cromakalim on sodium nitrite intoxication. InGene, brain and behavior. Proceeding of 21st Gottingen Neurobiology Conference. Stuttgart: George Thieme Verlag 1993 (pp. 681-6).