Review Article

Revisiting Cancer Cachexia: Pathogenesis, Diagnosis, and Current Treatment Approaches

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ABSTRACT

The objective of this article is to group together various management strategies and to highlight the recent treatment modifications that attempt to target the multimodal etiological factors involved in cancer cachexia. The contemporary role of nursing fraternity in psychosocial and nutritional assessment of cancer patients is briefly discussed. Cachexia is a syndrome of metabolic disturbance, characterized by the inflammation and loss of muscle with or without loss of adipose tissue. In cancer cachexia, a multifaceted condition, patients suffer from loss of body weight that leads to a negative impact on the quality of life and survival of the patients. The main cancers associated with cachexia are that of pancreas, stomach, lung, esophagus, liver, and that of bowel. The changes include increased proteolysis, lipolysis, insulin resistance, high energy expenditure, and reduced intake of food, all leading to impaired response to different treatments. There is no standardized treatment for cancer cachexia that can stabilize or reverse this complex metabolic disorder at present. The mainstay of cancer cachexia therapy remains to be sufficient nutritional supplements with on-going efforts to explore the drugs that target heightened catabolic processes and complex inflammation. There is a need to develop a multimodal treatment approach combining pharmacology, exercise program, and nutritional support to target anorexia and the severe metabolic changes encountered in cancer cachexia.

Key words: Body weight, cancer cachexia, grehlin, lean body mass, muscle tissue, review

Introduction

The term "cachexia" derived from the Greek "kakos" (bad) and "hexis" (condition) is a syndrome of multiple organs associated with cancer and various systemic disorders and is characterized by the systemic inflammation and loss of body weight (at least 5%) because of extensive wasting of the skeletal muscle and adipose tissue.[1] Other than cancer, cachexia can also occur in other chronic conditions such as chronic obstructive pulmonary disease, congestive heart failure, chronic kidney disease, and the AIDS.[2,3] Cancer cachexia occurs in more than half of all the cancer cases. The various abnormalities associated with cancer cachexia include alterations in carbohydrate, protein, and lipid metabolism, and that of insulin resistance, anorexia, with overwhelming degradation of muscle proteins.[4] The sequelae of cachexia include muscle

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wasting, edema, anemia, fatigue, and gustatory changes, that result in compromised physical function, heightened treatment-associated toxicity, and a poor prognosis.[5] Cancer cachexia leads to progressive and irreversible functional impairment even in the presence of adequate nutritional support.[6] The loss of muscle mass in cancer cachexia occurs at a rapid rate in comparison to cachexia attributed to other disease states.[7] The highest affliction of cancer cachexia is seen in gastric and pancreatic cancer (up to 80%), and the least incidence is reported in leukemia and breast cancer (up to 40%).[8] However, palliative care studies have revealed that irrespective of the cancer site, cachexia rates are uniformly substantial in the number near the end of the life.[9] There is a lack of consensus as to the proportion of deaths due to cancer cachexia owing to the complexity of the disease, but it can have both direct and indirect contribution for the significant proportion of cancer-related deaths, besides causing a negative impact on quality of life (QOL), chemotherapy response, and overall survival.

Pathogenesis

The three factors that play a vital role in cancer cachexia syndrome include (1) negative energy balance secondary to metabolic dysregulation, (2) increased breakdown of fat and proteins due to very high catabolic drive, and (3) neurohormonal dysregulation [Figure 1].[10] The various disease-related states, such as pain, depression, impact of multimodal therapeutic modalities, uncertainty about various foods, and the burden of diseases *per se* can lead to inadequate intake of energy-protein foods.[11,12] However, reduced energy intake is not as significant a factor in ensuing cachexia as tumor and tumor microenvironment. There is evidence that proinflammatory cytokines are up regulated, altering patient's metabolism, especially their energy expenditure, along with the metabolism of muscle and adipose tissue.[4,13,14] Several proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-1 and-6 (IL-1/IL-6) play a vital role promoting cachexia.[15] TNF-α has been seen to hamper the differentiation of fat and muscle cells resulting in the insulin resistance.[16-18] It is probably the most talked about cytokine due to its role in the promotion of anorexia and wasting of skeletal muscle through nuclear factor-KB pathway.[19] TNF-α boosts gluconeogenesis, breakdown of fats and proteins, and thereby suppresses the synthesis of lipids, proteins, and glycogen.[20] Elevated levels of both the IL-1 and IL-6 are reported in cachexia associated with cancer. Increased IL-1 levels in cachectic state cause an increase in tryptophan concentrations, inducing feeling of fullness, and hunger suppression.[21] IL-6 has a direct effects on muscle and fat wasting in addition to effecting acute-phase response and metabolic remodeling of the liver.[22] The origin of IL-6 is both from the immune system and from the tumor itself,[23] pointing out at a direct role of tumor cells in the establishment of cachexia. IL-6 seemingly has a significant role in cachexia development, but it is not considered as the sole agent to induce such changes, working in an indirect fashion, shown by its failure to cause cachexia in animal model.[16] Similarly targeting TNF-α alone to prevent the development of cachexia did not reveal any benefits when neutralizing antibodies were used against it.[24] Therefore, it seems that a teamwork of these factors is important for the development of cachexia, rather than any one of them working alone.[25]

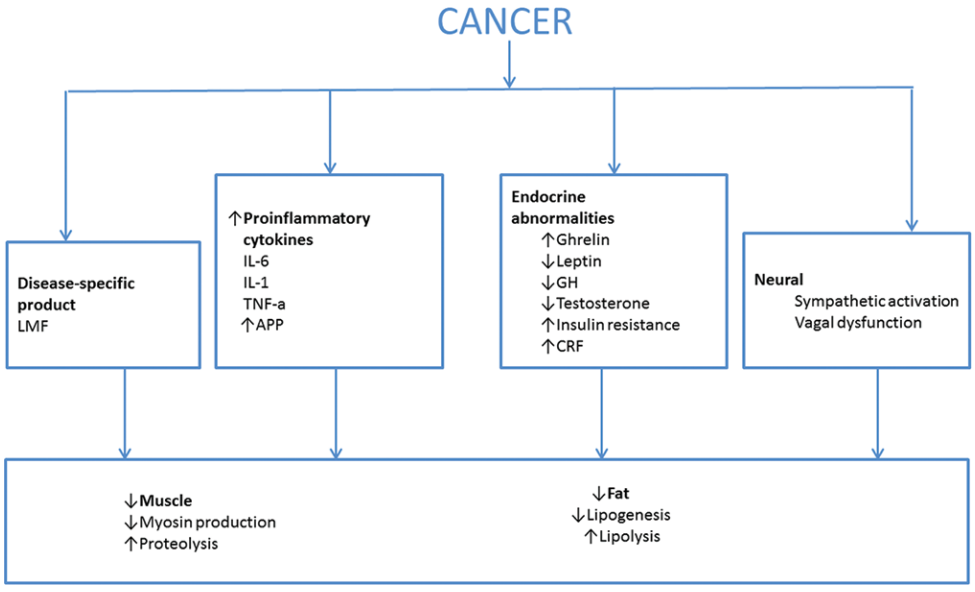

Figure 1: Pathophysiology of cancer cachexia. LMF: Lipid-mobilizing factor, IL-1: Interleukin 1; TNF-α: Tumor necrosis factor α; APP: Acute phase proteins' GH: Growth harmone, CRF: Corticotropin-releasing factor

Increased levels of proinflammatory cytokines (IL-1α, IL-6, and TNF-α) in participants with advanced cancer suggested a strong and collective network encouraging cachexia.[15] Systemic inflammation in cachectic models of mice and in patients with cachexia is a result of co-operation among numerous proinflammatory cytokines.[10] Various studies that established the role of proinflammatory cytokines in the pathogenesis of cachexia are shown in Table 1.[26-33]

Diagnosis of Cancer Cachexia

Body mass index (BMI) is not a defining factor for cancer cachexia. Patients who are obese may have adequate BMI but deficient lean body mass (sarcopenia), commonly seen in cancer patients.[34] Research has improved our knowledge of underlying features that lead to cancer cachexia, now known as a multifaceted syndrome associated with loss of muscle mass with or without loss of adipose tissue propelled by reduced energy intake and further changes in the metabolism.[35] As a result, the criteria used now to define cancer cachexia include loss of body weight, low skeletal muscle mass and BMI, reduced energy intake, proinflammatory markers, and metabolic alterations as shown in Table 2.[6,36,37]

Table 1: Cytokines mainly responsible in the pathogenesis of cachexia

Proinflammatory cytokines	Effect on cachexia
TNF-α	Promotes tissue proteolysis and NF-KB activation[26] Promotes anorexia and fatigue in cancer patients[27]
IL-1	Promotes anorexia[28] Genetic polymorphisms resulting in increased IL-1β levels are marker of poor prognosis[29]
IL-6	Increased circulating levels are poor prognosis markers[30,31] It can be produced directly by the tumor and trigger cachexia[32] Increased fat tissue browning[33]

IL: Interleukin; TNF-α: Tumor necrosis factor alpha; NF-KB: Nuclear factor-KB

Skeletal Muscle Wasting

Muscle wasting is a principal factor in cancer cachexia which leads to compromised life quality, disruption in normal functioning, and interferes with the prognosis. The weakness associated with muscle atrophy could result in reduced mobility, fatigue, and a chance of respiratory failure which accounts for the large number of cancer deaths.[38] In general, the process of muscle wasting is due to an imbalance between the synthesis of proteins and their degradation. Although it is suggested that both anabolic and catabolic reactions have a role in cachexia, most of the studies have stressed on the mechanism of induced proteolysis. The studies conducted on animal models have established the activation of ubiquitin proteasome pathway causing degradation of proteins leading to muscle wasting; however, it is not proven yet if such proteasomal degradation can have similar substantial effect in cachetic patients.[39,40]

Autophagy too has evoked a great interest in the process of skeletal muscle wasting in cancer cachexia.[41-43] Various studies carried out in animal models as well as in humans have contemplated the role of autophagy in the wasting disease in cachetic patients.[10,44] Autophagy mediators, LC3B (Protein) and BNIP3 (messenger RNA)[45] in lung cancer, and GABARAPL1 (lysosomal vesicles interactor and autophagy inducer)[46] in gastrointestinal cancer were found be upregulated. Another possible mechanism for skeletal muscle wasting has been attributed to calpain proteases,[47] although there is only little information about these proteases having any substantial role in muscle wasting.[48]

All these changes in cachexia are not restricted to skeletal muscle only and being a multiorgan syndrome involves other tissues as well; adipose, liver, kidneys, brain, and many more. The need of the hour is to decode the mediators of all the tissues involved, and to amplify our existing knowledge about causative factors in cancer cachexia.

Table 2: Cancer cachexia defining criteria

Cachexia associated with cancer	Defining factors	Diagnosis criteria
Consensus based[6]	Multifactorial syndrome: Existing skeletal muscle loss (with or without loss of adipose tissue) not fully reversed by conventional nutritional support leading to continuing functional deterioration. Manifested by negative protein and energy balance driven by a variable combination of reduced food intake and alterations in metabolism	Weight loss >5% over past 6 months Or BMI <20 kg/m^2 and any degree of weight loss >2% Or Muscle depletion and any degree of weight loss >2%
NCI CTCAE v4.0[36]	Overall loss of body weight	Grade 1: 5%-10% from baseline; intervention not indicated Grade 2: 10%-<20% from baseline; nutritional support indicated Grade 3: 20% from baseline; tube feeding or TPN indicated Grade 4: Not defined, life threatening Grade 5: Not defined, fatal
Cancer cachexia by three factors[37]	Multifactorial syndrome: Classified by in progress weight loss, reduced food intake, in the presence of systemic inflammation'	At least 2 of the following factors: Weight loss ≥10%, food intake <1500 kcal/day, CRP ≥10 mg/l

BMI: Body mass index; CRP: C-reactive protein; TPN: Total parenteral nutrition; CTCAE: Common terminology criteria for adverse events; NCI: National Cancer Institute's

Treatment of Cancer Cachexia

Despite its high clinical relevance, cancer cachexia is still an underrated and more often remains out of focus during the treatment of cancers. It has increasingly become clear that cancer cachexia being a multiorgan syndrome with multitude of factors involved in it, needs a combined approach (nutrient supply, exercise, drugs, etc.) for its management. Therefore, new cancer cachexia management protocols advise amalgamation of nutritional support, drugs and exercise therapy; the latter having additional benefit on QOL in cancer patients irrespective of cachexia.[49,50] Similarly, nutritional support is very important in cancer patients, as food intake is usually compromised secondary to anorexia, nausea, vomiting, and oral mucositis.[8] Therefore, immediately after the diagnosis of cancer, the patients should be monitored for any nutritional indices and administered nutritional and catabolic support.[51] In cancer cachetic patients, the average daily intake of proteins is about 0.7–1.0 g/kg of body weight.[52] An increase of 300–400 kcal and 50% of extraprotein is required daily for an effective anabolic resistance. A favorable effect in cachetic states was seen with some nutritional supplements such as β-hydroxy-β-methylbutyrate (HMB),[53,54] eico-sapentaenoic acid,[55,56] and with L-carnitine.[57,58] However, recent review pointed out at limited evidence in favor of using HMB and L-carnitine.[59] In the past, the beneficial effects of omega-3 fatty acids in cancer cachexia were not proven,[60-62] but the studies conducted recently with improved designs favor their use in cachetic patients.[63,64] The route of administration should be preferably enteral, only switching to parenteral route if maintaining adequate supplements becomes difficult through enteral route.[65]

Existing pharmacological agents for cancer cachexia

The pharmacological agents that target proinflammatory cytokines (or their associated receptors) have been widely studied due to a major role of systemic inflammation in the pathogenesis of cancer cachexia. Furthermore, other agents that stimulate appetite and help in weight gain also have enjoyed a greater role against cancer cachexia.

Proinflammatory cytokine inhibitors

Neither Etanercept[66] nor Infliximab,[24] both anti-TNF-α could prevent atrophy of skeletal muscle or improve appetite, in two randomized clinical trials in cachetic terminally ill patients. Similarly, Thalidomide[67-69] in three clinical trials and Pentoxifylline[70,71] in two showed only modest gain in muscle mass, but with aggravation of life or showed no noteworthy clinical effects. Clazakizumab, humanized anti-IL-6 monoclonal antibody in a phase I clinical trial led to an increase in hemoglobin and albumin levels and also relieved fatigue in patients with advanced cancer.[72] The monoclonal antibody caused reduction in the depletion of lean mass in patients with non-small cell lung carcinoma during a subsequent Phase II trial.[73] Xilonix, capable of down-regulating IL-1α was able to halt changes in body composition when used in a Phase I clinical trial in refractory cancer,[74] and in a Phase III clinical trial in patients with cachexia in advanced colorectal cancer.[75] Ruxolitinib, selective JAK1/2 inhibitor, used in patients with myelofibrosis, led to only a minimal increase in the size of the spleen and added on lean body mass increasing body weight in a significant proportion.[76] Ruxolitinib was included further in an open-label Phase II trial (NCT02072057) in 2014 to test its safety, efficacy, and its effect on overall survival, but the trial was ultimately aborted in 2019 due to unsuccessful recruitment.

Grehlin and anamorelin

Grehlin is a peptide hormone secreted mainly by the stomach and plays a vital role in hunger and maintains a balanced energy state. A high dose of subcutaneous 13 μg/kg or a low dose of 0.7 μg/kg Grehlin was administered to gastrointestinal cancer patients daily for 8 weeks.[77] There was improvement in appetite with reduced loss of fat in high dose group as compared to that of low dose group. Lean body mass showed an insignificant increase in the high dose group. In another study (Phase II randomized clinical trial), increased intake of food and appetite was seen in esophageal cancer patients during grehlin use (intravenous 3 μg/kg), and reduced nausea and anorexia reported during chemotherapy treatment.[78] Inconsistent results with grehlin were reported in few studies in which grehlin caused loss of appetite despite a state of hyper-grehlinemia.[79] This may be attributed to a short half-life (30 min) of grehlin.[80,81] This created a pursuit to find other agents that could efficiently target the grehlin axis. Anamorelin, a valid synthetic agonist of grehlin system mimics N-terminal active core of ghrelin. It qualifies for regulating the grehlin axis with an advantage of oral administration and having a half-life of 7 h.[82] In a Phase I trial, Anamorelin showed significant dose-dependent weight gain, with no notable adverse effects.[83] Similarly, several studies such as ROMANA[84,85] favored Anamorelin and reported increased appetite, lean body mass, but no benefits on hand grip strength and QOL; the reason US Food and Drug Administration (FDA) is yet to provide approval for its use. However, Anamorelin was approved for the use in Japan on December 11, 2020, based on the results of two studies[86,87] that showed increase in lean body mass, evaluated by dual-energy X-ray absorptiometry. One of the studies did show unfavorable results on muscle hand strength while the other did not account for functional endpoints such as muscle or physical strength.[88]

Progestins

US FDA allowed the use of megestrol acetate in 1993 for anorexia, unexplained weight loss, and cachexia associated with AIDS. Megestrol is derived from progesterone and is capable of stimulating appetite, thereby improving calorific intake and nutritional status. A meta-analysis incorporating 35 clinical trials studying the effect of megestrol in 3963 patients reported a dose-dependent increase in both the appetite and weight in cancer patients.[89] The megestrol probably has anti-inflammatory action because it is capable of down regulating the levels of proinflammatory cytokines or their associated receptors.[90,91] Medroxyprogesterone, another derivative of progesterone has also been seen to inhibit proinflammatory cytokines, particularly TNF-α, IL-1, and IL-6;[90,92] therefore, has been considered for the use in cancer-related anorexia and cachexia. It improves anorexia, QOL, and increases body weight, although the latter is due to its effects on adipose tissue rather than the actual lean body mass.

Corticosteroids

Different corticosteroids, dexamethasone (3–6 mg/day), methylprednisolone (12 mg/day), and prednisone (15 mg/day) leads to increased appetite and weight gain.[93] However, the effect is temporary and associated with adverse effects such as insulin resistance, adrenal insufficiency, myopathy, fluid retention, and sleep disorders.[94,95] Due to their long-term side effects, corticosteroids are restricted in use, only for rapid and short action and in few selected cases of cachexia only.[93]

Nonsteroidal anti-inflammatory drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) have been considered because of their effect on inflammation. Celecoxib or a placebo was randomly given to 11 patients with gastrointestinal or head and neck cancer for 21 days in a Phase II clinical pilot trial.[96] Body weight, BMI, and QOL showed significant increase in celecoxib group, while as all these parameters declined in the placebo group. In another Phase II trial, 300 mg/day of celecoxib was administered for 4 months in 24 advanced cancer patients.[97] The results showed a significant increase in lean body mass, down regulation of TNF-α increased hand grip strength, QOL and raised performance status. However, later two systematic reviews concluded that insufficient studies have been conducted to substantiate the effectiveness of NSAIDs in cancer cachexia,[98] also there is weak evidence to advocate use of NSAIDs despite no notable toxicity reports subsequent to their use in cancer cachexia.[99]

Cannabinoids

A class of heterogeneous compounds in marijuana, cannabinoids activate the receptors on certain cells that subdue release of neurotransmitters in brain. Cannabinoids occur naturally in cannabis plants and phytocannabinoid, tetrahydrocannabinol (THC) probably increases appetite, body fat level, nutritional intake, body weight, and improves QOL.[100] A Phase III clinical trial showed no significant changes in appetite and QOL when compared with a placebo.[101] However, a double-blind, placebo-controlled pilot trial with THC showed usefulness in abatement of chemosensory changes and it increased urge for high protein diet.[102] A recent pilot study carried on advanced cancer patients reported promising results with 5 mg/day or 10 mg/day in two divided doses of THC without any significant adverse reactions, justifying further large scale studies with regulated doses of cannabis in cancer cachexia.[103] Synthesized versions, nabilone and dronabinol have also been given potential considerations for use in cachexia.

Multimodal treatments

No multimodal treatment protocol for cachexia or extensive wasting has been standardized till date. The complexity of pathogenesis in cancer cachexia (multisystem syndrome) has led to growing considerations for multimodal treatment protocols. A critical review of the literature published between January 2008 and December 2019 was conducted to evaluate the multiple modal treatments for all types of cachexia.[104] A Phase II multimodal feasibility trial used resistance training, oral nutritional supplements, and celecoxib for cancer cachexia in patients with pancreatic or incurable lung cancer, undergoing chemotherapy.[105] No significant effects on physical activity or muscle gain were noticed probably due to sample size restrictions. The absence of any serious side effects during this trial possibly makes multimodal treatment safe and practicable; a Phase III trial was on going to evaluate the efficacy of the intervention.

A randomized controlled trial implementing nutritional support together with an exercise program (60 min exercise twice a week), did not show any improvement in QOL, but a good percentage (67%) of patients adhered to the intervention, showed reduction in nausea and vomiting and increase protein intake.[106] Larger trials are the need of the hour to assess the effect of combined nutrition and exercise in cancer cachexia.

A clinical study was conducted on two groups of cancer-related anorexia/cancer cachexia, the trial group was put under 160 mg per oral megestrol acetate bid plus 50 mg per oral thalidomide bid, whereas the patients in the control group were put only under megestrol acetate 50 mg per oral bid.[107] The trial group showed a significant increase from the baseline in body weight, appetite, QOL, and hand grip strength. A significant decrease was found in TNF-α and fatigue in this group. The trial group showed significantly

higher mean changes in the endpoints from baseline than that of the control group. Therefore, the combination of megestrol acetate and thalidomide had greater impact in cancer cachexia than single agent megestrol acetate. Both the groups showed negligible toxicity.

Psychosocial Consequences and their Intervention in Cancer Cachexia

Cancer patients face physical, psychological, social, and spiritual issues due to malnutrition.[108] The visible physical changes secondary to weight loss create emotional distress in cancer cachexia.[109,110] The loss of weight in cancer cachexia being involuntary and fast paced raises fear of imminent death among the patients.[111,112] The patients often stay recluse and get alienated from self as they feel uncomfortable meeting people due to disproportionate and severe bodily changes in them.[109,113]As the patients feel unfamiliar toward their own body image, it ensues in feelings of helplessness, abandonment, and loss of control[113] and a sense of being stigmatized.[114] As the burden of cancer and associated cachexia affect patients social interactions and relationships, it is justified to think that the families of the patients are affected as well. The family members can influence both the psychosocial support and patient compliance toward the treatment, but the role of family members and their impact has mostly been side-lined. Many studies have been conducted to evaluate the role of psychoeducational protocols and their effect in supporting the needs of the patients and their families. Only few of them have provided evidence-based results.

The Macmillan Approach to Weight and Eating (MAWE) was administered by a trained clinical nurse specialist in a Phase II trial to check its deliverability, acceptability, and patient-perceived effect on weight-related distress (WRD) and eating-related distress (ERD).[115] The various elements of MAWE are breaking through weight loss taboo, narrating healing stories, managing conflict, support for self-action, and support for eating well. Elements suitable to the patient's WRD and ERD were administered during home visits between trained nurse, patient, and the care taker. The trial showed that MAWE is both deliverable and acceptable to the patients in clinical practice and more importantly can be administered by a specialist community care nurse experienced in palliative care.

A mixed method qualitative research study was used to develop a family-oriented psychosocial intervention for eating and weight-related issues in patients with incurable cancer.[116] The mode of interaction was through a face to face deliberation between patient, caretaker (family), and a trained nurse: Family Approach to Weight and Eating (FAWE). Its aim was to reinforce the patient and family caretaker coping resources to get through the involuntary weight loss and reduced appetite. The nurse researcher found FAWE both acceptable and deliverable. 15 out of 16 patients–caretaker dyads acknowledged the advantages of the approach, improving QOL at the end stage of life.

A randomized controlled pilot trial (conducted in Australia and Hong Kong) in advanced cancer patients and carers, with family-oriented psychosocial-based nutritional intervention although faced difficulty during recruitment and even though only half of the participants completed the final assessment, showed potential in certain patient outcomes.[117] There were improvements in ERD in both Australian and in Hong Kong data. In addition, eating-related enjoyment increased in Hong Kong data, whereas Australian data showed increase in QOL. On the contrary, the data on carer, i.e., ERD, anxiety, depression, and burden on caregiving showed little or no change.

A protocol for a single arm feasibility trial (NCT04153019) utilising psychoeducational and rehabilitative intervention to manage cancer cachexia patients, and their caregivers were published recently on March 01, 2021.[118] The study involves two components: (1) Psychoeducational intervention: Face to face discussions between cancer patients (30 in number), their caregivers and trained nurses to help the dyads to go through the stage of weight loss (involuntary) and to strengthen coping resources of dyads: (2) Rehabilitation intervention: Three biweekly educating discussions between the trained physical therapists and the dyads concentrating on self-management, goal-setting exercises (three home exercises/week). Currently recruiting, the rehabilitation intervention adds novelty to the study and allegedly was the only study of this type having both psychoeducational and rehabilitation (physiotherapy).

Nursing Perspective

It is evident that the role of nursing staff becomes substantial during designing and administration of aforementioned studies and alike. Nurses deliver crucial psychological support to both the cancer patients and their families all along the course of the disease. Few of the activities that fall under the auspices of nursing practice include but not restricted to advice on nutrition, stress alleviation, management of associated symptoms, and reinforcing health-promoting behavior. All cancer patients probably interact with nurses more than they see other health-care workers including oncologists. This validates a convenient position for nurses to deliver support during prolonged care for the cachetic patients. As nutrition and exercise are strongholds of the multi-pronged treatment strategy in cancer cachexia, nurses ought to have ability in identifying and reporting

cancer patients who are in need of additional nutritional supplements and physical activity. However, there has been a lack of training for nurses to tackle the issues of nutritional inadequacy and physical inaction in cancer patients; therefore, they might consider themselves lacking in knowledge for delivering advice on such patient issues. A few studies have shown that nurses do feel having less knowledge for advocating nutritional and physical activity issues in cancer patients. A web-based questionnaire study involving 355 oncology nurses providing advice on nutrition and 327 out of these providing physical activity advice showed that 43% felt having inadequate knowledge to give advice on nutrition and 46% thought they had less understanding to provide advice on physical activity.[119] However, nutritional advice is seen within the purview of nursing practice as indicated by abundant literature across the Western countries. As for example, North American Nursing Diagnosis Association considers nutrition as one among the 13 domains of nursing, practiced in the region.[120] Similarly, the Nursing and Midwifery Council of UK (regulatory body for nursing) acknowledges the pivotal role of nutrition for productive care of patients.

A number of studies reveal, nurses appreciating the role of nutrition to prevent and manage the progression of diseases,[121,122] and appreciate nutritional care does fall under their jurisdiction.[123-125]

Limitations

This review is narrative and does not fulfil the criteria of a systematic study owing to the lack of methodological approaches.

The readers will have to refer to studies mentioned in this review to understand the methods employed and for any additional information as well.

Strengths

The compilation of the topics in the current review has been done in a streamlined fashion for easy comprehension.

The review attempts to put complete scale of issues including current advances in cancer cachexia in a concise fashion.

Conclusions

Recent in-depth understanding of cancer cachexia has made it one of the most sought-after research fields. The advancements have allowed for apt understanding of the multiple factors that modulate the onset and development of this multisystem syndrome. Due to intricate mechanisms involved in cachexia, the development of a multimodal treatment protocol comprising of pharmacological agents, different exercise regimes, and nutritional supplements is necessary. More importantly, the role of palliative care nurses needs to be upgraded in view of their close association with cancer patients' right from the diagnosis until the treatment lasts. Adequate nutritional intervention is fundamental to prevent depleting muscle mass in cancer cachexia. Advanced cancer patients rely more on nurses for support than any other health-care personnel during their long hospitalization. A nurse can take an important role of assessing nutritional requirements of patients that could pave way for targeted nutritional prescriptions (through studies) to either inhibit or reduce muscle mass depletion during treatment and increase anabolic muscle processes during patient recovery. Such actions can result in compliance toward treatment, good prognosis, and improve overall survival.

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Conflicts of interest

There are no conflicts of interest.

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