Published in final edited form as:

J Hosp Palliat Nurs. 2012 August ; 14(6): . doi:10.1097/NJH.0b013e31825f3470.

Management of Anorexia-Cachexia in Late Stage Lung Cancer Patients

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Abstract

Nutritional deficiencies are experienced by most adults with advanced lung cancer during the course of their disease and treatment. Well-nourished individuals tolerate cancer treatment with less morbidity, mortality, and increased response to treatment as compared to those who are malnourished. Novel anti-cancer therapies cause many deficits that impact nutritional and functional status during the treatment process. Nutritional deficits include weight loss, malnutrition, and anorexia-cachexia. Anorexia-Cachexia is complex, not well understood and seen in many solid tumors in late stage disease. Assessing adequate nutrition is one of the most challenging problems for nurses, their patients and patient's families. The purpose of this review is to define and describe cancer anorexia-cachexia in late stage lung cancer, through case presentation, and to describe palliative strategies for prevention, assessment, and management in the palliative care setting. Early assessment for nutritional imbalances must be done regularly with re-evaluation for intervention effectiveness and should continue throughout the illness trajectory. Management of adverse effects of cancer and cancer-related treatment is critical to improving quality of life. Palliative care and hospice nurses play a critical role in early assessment, education and prevention to support nutritional needs for patients and their families.

Keywords

Anorexia; Cachexia; Cachexia- Anorexia Syndrome

Introduction

In 2012, it is estimated there will be about 226,000 new cases of lung cancer (non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) combined) and more than 160,000 estimated related deaths will occur in the United States ¹. About 20% of the deaths will be caused by the effects of cancer related anorexia-cachexia syndrome ². Cancer anorexia-cachexia is a wasting syndrome that occurs in 80% of patients with incurable solid tumors ³. This syndrome is common in specific cancer types: gastric, 85%; pancreatic, 83%; non-

small cell lung, 61%; small cell lung, 57%; prostate, 57%; and colon, 54%⁴. It involves extreme weight loss and malnutrition. According to the data, 60% of patients with lung cancer have already experienced a significant weight loss at diagnosis^{3,5}. In addition, cancer itself may be complicated with metabolic disorders⁶. For example, paraneoplastic syndromes (PNPs) are rare metabolic disorders that are the result of remote clinical effects of cancer⁷. They are not due to the physical effects of the cancerous tumors but are caused by substances produced by the tumors acting on tissues in the body⁷.

Nutritional screening and assessment are recommended at initial diagnosis, before cancer treatment begins, and should continue throughout care⁵. Agreement exists among clinicians that cachexia related to cancer occurs in most patients with advanced lung cancer and cancer anorexia, the loss of appetite, is a common symptom of cachexia⁵. Assessing adequate nutrition is one of the most challenging problems for nurses and the interdisciplinary palliative care team. The purpose of this review is to describe cancer related anorexia-cachexia in late stage lung cancer, through a case presentation, and describe current and evolving strategies for prevention, assessment and management. Management strategies presented apply to other cancers and non-cancer illnesses in which effective treatment management for anorexia-cachexia is required.

Case Presentation

Mrs. AC is a 72-year-old elderly Latina woman, who is newly diagnosed with stage IV NSCLC with metastatic disease to the brain and liver. She initially presented when undergoing preoperative workup for bladder reconstruction one month ago. Chest x-ray and computerized axial tomography (CAT) scan revealed a 4 cm left upper lobe lung mass. Bronchoscopy with biopsy demonstrated atypical cells highly suspicious for bronchogenic carcinoma. She underwent a left upper lobectomy with lymph node dissection. Pathology confirmed a 4 cm poorly differentiated adenocarcinoma with clear margins, and positive lymph nodes, consistent with adenocarcinoma. She was referred to medical oncology for evaluation and an opinion of further treatment and care.

A comprehensive physical evaluation of the patient was done. Mrs. AC is a thin, elderly bilingual female in no acute distress, alert and oriented times three. She is 5'4" tall, weighs 115 pounds, with a body mass index (BMI) of 19.7. Her vital signs and oxygen saturation are within normal limits, and Karnofsky Performance Scale (KPS) is 70. Her comorbidities include osteoporosis, gastroesophageal reflux disease, and urinary incontinence. She is also status-post two bladder resuspension surgeries. Her current medications are Actonel and Prevacid. Her family cancer history includes a brother who died at age 80 of lung cancer, with a heavy smoking history. Her social history reveals that she is divorced, self-employed, college educated, and a lifetime non-smoker. She has 3 adult children. Mrs. AC lives at her younger son's home and he is her caregiver. She is Catholic and attends church regularly.

A complete blood count and comprehensive metabolic panel were normal. Her current complaints are moderate back pain, mild hoarse voice, mild hand tremors, moderate continual urinary incontinence, mild constipation, mild dyspnea on exertion, 3-pound weight loss within the last month, and mild fatigue.

After discussion of diagnosis, prognosis, treatment options, and goals of care with Mrs. AC and her family, she agreed to initiate palliative adjuvant therapy of oral erlotinib and whole brain radiation. Before initiation of treatment, the medical oncologist ordered a comprehensive nutritional screening and assessment based on Mrs. AC's complaints and exam noted above. The palliative care nurse conducted a comprehensive nutritional screening and assessment, assessing subjective and objective information. The Functional Assessment of Anorexia/Cachexia Treatment (FAACT) tool (Fig. 1) was utilized to further

assess concerns in Mrs. AC's appetite. The medical oncologist was notified and the findings were reviewed with Mrs. AC and her son.

A treatment plan was formulated with a multimodal approach consistent with the patient and family goals of care. Appropriate pharmacologic interventions were prescribed by the medical oncologist to stimulate appetite (megestrol acetate), control pain (oxycodone with acetaminophen), and constipation (sennosides). Non-pharmacologic interventions included referrals to the dietician for nutritional counseling and education, pulmonary rehabilitation to assess pulmonary function, physical therapy to increase strength, endurance and mobility, occupational therapy to address energy conservation needs for self-care, palliative care medicine for pain management, and radiation oncology for treatment evaluation. Before adjuvant treatment began, re-evaluation of the effectiveness of interventions was scheduled in one week. Re-evaluation noted a 1 pound increase in weight. Reports by the patient and family included an increased appetite and resolved pain. She continued to have mild constipation and admitted to “forgetting” to take her stool softener. She also stated that food was once again appetizing to eat especially foods she was culturally accustomed to cooking for lent. Treatment was initiated without delay.

Clinical Characteristics of Anorexia-Cachexia

Cancer malnutrition has been described as a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form, function, and clinical outcome⁸. Cancer-related anorexia and cancer-related cachexia are distinct syndromes but are often intertwined in progressive disease⁹. Cancer cachexia is unique but difficult to distinguish from other causes of weight or muscle loss such as malnutrition related to cancer anorexia or malabsorption related to impaired gastrointestinal function⁶. Therefore, because they are so closely related definitions of cancer-related anorexia and cachexia have been combined and referred to as the “anorexia-cachexia syndrome”^{6,10}.

Anorexia is the loss of appetite or desire to eat^{11,12}. In acute events, anorexia usually resolves with resolution of the illness, and any weight lost may be replaced with nutritional supplements or increased intake^{3,5}. In lung cancer patients anorexia may not be recognized and lead to insufficient caloric intake and protein-calorie malnutrition. Weight loss seen in this starvation phenomenon usually involves loss of fat, rather than muscle tissue³. The characteristics of anorexia are common among many patients with serious illnesses such as lung cancer, acquired immune deficiency syndrome (AIDS) and other chronic diseases^{3,5}. Anorexia is the most common cause of malnutrition in lung cancer patients and is a symptom that is associated with cachexia⁵.

Agreement exists that cachexia is a complex syndrome and not well understood^{3,6,8}. Cachexia has been recognized as a frequent problem in lung cancer patients and represents an unmet need⁶. Cachexia is a multi-factorial syndrome and may or may not be associated with anorexia, along with significant weight loss, loss of muscle tissue as well as adipose tissue, and generalized weakness^{6,13}. It is often complicated by other food intake problems such as impaired integrity and function of the gastrointestinal tract from mouth to anus and poorly controlled physical and psychosocial symptoms including pain, shortness of breath, depression, or severe fatigue^{3,6,13,14}.

The European Palliative Care Research Collaboration (EPCRC) is currently developing classification systems for pain, depression and cachexia in patients with advanced cancer^{6,15}. This process has been comprehensive involving expert and public consultations and literature reviews^{6,15}. The cachexia guideline expert group identified cancer cachexia as a continuum of three stages of clinical relevance: pre-cachexia, cachexia and refractory

cachexia⁶. It was noted that not all patients would move through the entire spectrum⁶. The stages of cachexia are defined on the basis of the patient's characteristics and circumstances^{6,15}. Diagnostic criteria for end stage cachexia have been defined by the EPCRC (Fig. 2)^{6,16}. In 2010, the cachexia guideline development group published European Clinical Guidelines on the management of cachexia in advanced cancer patients with a focus on refractory cachexia⁶.

Refractory cachexia is characterized by a low performance status and life expectancy of less than three months⁶. Refractory cachexia represents a stage where reversal of weight loss seems no longer possible due to very advanced or rapidly progressive cancer unresponsive to anti-cancer therapy⁶. In this stage the burden and risks of artificial nutritional support likely outweigh any potential benefit, and therapeutic interventions focus on alleviating the suffering associated with cachexia, such as symptom control with appetite stimulation and treatment of nausea or eating-related distress of patients and families⁶. The diagnostic criteria includes variable degrees of cachexia, cancer disease both pro-catabolic and not responsive anti-cancer treatment, low performance score, and , < 3 months expected survival⁶.

Lung cancer itself may be complicated by the PNPs of cachexia, which are often associated with anorexia¹⁷. Metabolic PNPs such as hypercalcemia or hyponatremia may also cause anorexia or symptoms such as fatigue that contribute to anorexia⁹. Overall, PNPs are rare and only 10%- 20% of the patients with cancer experience metabolic disorders of PNPs over the course of their illness¹⁸. PNPs occur more frequently in patients with lung cancer, particularly in small cell lung cancer (SCLC), occurring in 3%-5% of patients¹⁸. PNPs are the result of substances (hormones, growth factors, cytokines and antibodies) abnormally secreted by the primary tumor and its metastases¹⁹. These substances effect the endocrine, neurologic, hematologic, and musculoskeletal systems of the body¹⁸. The most common and best understood of the paraneoplastic syndromes are of the endocrine system²⁰. Endocrine PNPs seen in patients with lung cancer include humoral hypercalcemia of malignancy, ectopic adrenocorticotrophic hormone (ACTH) syndrome (also known as Cushing syndrome), and syndrome of inappropriate antidiuretic hormone (SIADH)²⁰.

Basic etiologies of the anorexia-cachexia syndrome are 1) decreased food intake; 2) metabolic abnormalities; 3) the actions of proinflammatory cytokines; 4) systemic inflammation; 5) neurohormonal dysregulation; 6) tumor by- products, and 7) the catabolic state²¹. Some of these mechanisms have a mutually reinforcing aspect; for example, anorexia leads to fatigue, fatigue increases anorexia, anorexia increases fatigue, and so forth⁹.

Assessment of Anorexia-Cachexia

Perhaps, the most important element of assessment involves patient and family goals of care^{3,5,6,9,22}. Nutritional screening and assessment are done before lung cancer treatment begins⁵. Specific recommendations include completing the a nutritional screening and assessment within 48 hours of admission or diagnosis of lung cancer, before initiation of cancer therapy, change in therapy or a weight change of 2%- 5%^{6,22,23}. A nutritional screening profile is the process of assessing characteristics (early satiety, weight loss, weakness, fatigue, impaired immune function, skeletal muscle wasting, and poor performance status) of malnutrition and risk factors that will predispose a patient to nutritional deficiencies¹⁷. Predisposing risk factors include: weight loss 5% in 1 month, 10% in 6 months, inadequate oral intake for 7 days, serum albumin , 3.5 g/dL, recent surgery, severe infection, recent radiation therapy or aggressive chemotherapy, persistent distress lasting > 2 weeks pain, nausea, vomiting, dysphagia, diarrhea, mucositis,

depression, anorexia, diminished self-care or lack of caretaker, dementia, poverty, and addiction (alcohol and or dugs) ^{17,22}. Currently there are no clearly accepted diagnostic criteria for identifying the specific cause of anorexia-cachexia seen in lung cancer, but anorexia from some etiologies is treatable and assessment of the possible presence of causes as mentioned above is vital to quality palliative care ^{6,9}. Early recognition of the etiologies followed by comprehensive assessments is recognized as imperative in the development of assessment guidelines ^{5,6,22}. Other areas of assessment include laboratory values, anthropometric measures (BMI), and tools to assess functioning and performance and prognosis such as the KPS, and the use of multidimensional standardized instruments, such as the FAACT tool (Fig. 2) ^{6,8,9}.

Management of Anorexia-Cachexia

The best way to treat anorexia-cachexia seen in lung cancer is obviously to cure lung cancer; this will normalize the metabolic abnormalities induced by the tumor and or tumor host interactions ^{6,21,24}. If cure cannot be achieved, the next option would be to increase nutritional intake by dietary counseling and education and oral nutritional supplements ^{5,6}. Early intervention to try to prevent malnutrition is easier than trying to reverse it after it occurs ²⁵. Therefore, management is multimodal with the focus of stabilizing weight, improving comfort, lowering the risk of infection, keeping up strength and energy, minimizing distress and improving QOL ^{5,9}. As previously stated management and recommendations for anorexia-cachexia seen in lung cancer applies to other advanced cancers and illnesses.

The National Comprehensive Cancer Network (NCCN) has published Guidelines for Supportive and Palliative Care Symptom Management for anorexia-cachexia (Fig. 3) ^{26,27}. The NCCN guidelines are a statement of evidence and consensus of the Palliative Care Panel Member authors regarding their views of currently accepted approaches to treatment ^{26,27}. These guidelines are defined as categories to evidence, and are based upon lower-level evidence where uniform NCCN consensus agrees that the strategies are appropriate ²⁷. These guidelines apply to all cancer diagnoses ^{26,27}. The guidelines are divided for patients whose life expectancy is years to months; months to weeks and weeks to days (dying patient) ²⁶.

When life expectancy is years to months the NCCN guidelines recommendations include assessments, medications and non-pharmacologic approaches. These are as follows: evaluate rate and severity of weight loss ²⁶. Treat readily reversible causes of anorexia for example early satiety (e.g. metoclopramide 10 mg before meals) and symptoms that interfere with intake such as dysgeusia, xerostomia, oral-pharyngeal candidiasis, mucositis, nausea and or vomiting, dyspnea, depression, constipation, and pain ²⁶. Review and or modify medications that interfere with intake ²⁶. Evaluate for endocrine abnormalities such as hypogonadism, thyroid dysfunction, and metabolic abnormalities (hypercalcemia and hyponatremia) ^{7,26}. Consider appetite stimulants for example progestational agents (e.g. megestrol acetate 160-180 mg BID), corticosteroids (e.g. decadron 4 mg/day or prednisone 10-20 mg/day), and cannabinoids (dronabinol 5-20 mg/day) ^{9,12,26}. Consider an exercise program ^{9,12}. Assess social and economic factors ^{9,26}. Consider a nutritional consultation ^{9,26}. Consider nutrition support, enteral and parental feeding (as appropriate) ²⁶. Reassess the effectiveness of intervention and continue to treat and monitor symptoms and QOL to determine whether status warrants change in strategies with ongoing assessments ²⁶. If the patient shows weight stabilization or gain, improvement in symptoms that interfere with intake, improved energy level, resolution of metabolic/endocrine abnormalities continue to treat and monitor symptoms and QOL to determine whether status warrants change in management ²⁶. If

unacceptable symptoms continue intensify palliative care interventions, provide dietary consultation and consider a clinical trial for anorexia-cachexia ²⁶.

When life expectancy is months to weeks or weeks to days the NCCN guidelines are as follows: assess importance of symptoms of anorexia and cachexia to patient and family, and if important consider short course of corticosteroids ²⁶. Focus on patient goals and preferences ^{9,26}. Provide family with alternative way of caring for the patient ²⁶. Provide emotional support and treat for depression (e.g. Mirtazapine 7.5-30 mg hs), if appropriate ²⁶. Provide education and support to patient and family regarding emotional aspects of withdrawal of nutritional support ²⁶. Recognize that discontinuation of nutrition is a value-laden issue and consider consultation with bioethicist or spiritual counselor ⁹. Educate the patient and family of the natural history of end-stage disease including the following points: absence of hunger and thirst is normal in the dying patient; nutritional support may not be metabolized in patients with advanced disease ²⁶; risks associated with artificial nutrition (e.g. fluid overload, infection, and hastened death) ²⁶; intravenous hydration may increase excretion of drug metabolites providing benefits to the patient ²⁶; symptoms like dry mouth should be treated with local measures (eg, mouthcare, and small amounts of liquids) ²⁶; Withholding or withdrawal of enteral or parenteral nutrition is ethically permissible in this setting and therefore it will not cause exacerbation of symptoms and may improve some symptoms ²⁶. Reassess the effectiveness of intervention. If acceptable continue to monitor, treat and reassess ²⁶. If unacceptable intensify palliative care efforts and involve specialized palliative services or hospice ²⁶. These guidelines provide current accepted practical approaches to the treatment and care ^{3, 9, 12, 26, 28}. The goal in palliative care is to minimize distress of symptoms and improve QOL ^{5,6}.

Impacts on Quality of Life

Quality of life (QOL) is influenced by nutritional status ^{17,27}. The anorexia-cachexia syndrome is the most common syndrome experienced by people with advanced stages of disease and seen in subset of cancers, led by pancreatic and gastric cancer, but also lung, esophageal, colorectal, and head and neck cancer ^{5,27}. The distress and disruption in daily activities, caused by anorexia-cachexia leaves patients frail and weak and their emaciated appearance is devastating for patients and their families ^{5, 6,27,28}.

QOL encompasses four dimensions of well-being: physical, psychological, social and spiritual ^{5,6,27,28}. In some ways, the dimensions are distinct, however there is tremendous overlap. The impact of anorexia-cachexia on QOL, seen in late stage lung cancer is illustrated in figure 4, adapted from the City of Hope Quality of Life model ²⁸. Whether physical, psychological, social or spiritual, a deficit that is identified in one domain impacts all other domains of QOL ^{27, 28}. The symptoms caused by anorexia-cachexia that impact physical well-being include weight loss, decrease in muscle mass and body in fat, fatigue weakness and dehydration ^{5,6,17,27,28}. Anorexia-Cachexia impacts psychological well-being with symptoms which include anxiety, depression worry and fear ^{5,6,17,27, 28}. Physical and psychological distress may also impact social well-being for patients and family caregivers ^{27,28}. Often family caregivers continue to try to help the patient by reminding and pleading with the patient to eat, in as eating/feeding have great cultural meanings ^{5,6, 17, 27,28}. The patient's inability to eat can lead to irritability and become a source of tension leading to family conflict and social isolation ^{5,6,17,27,28}. Food we eat is derived from our cultural heritage and in some cultures eating provides a way of socialization ^{5,6,17,27,28}. Increasing weight loss may lead to alteration in body image ^{5,6,17,27,28}. Spiritual well-being is impacted by helplessness, hopelessness, uncertainty and may cause one to reflect on meaning of their life and imminence of death ^{27,28}.

Nursing Implications

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with advanced illnesses such as lung cancer, through the prevention and relief of suffering by means of early identification and impeccable assessment. Palliative care nurses play a crucial role in ensuring that nutritional screening and assessments are conducted for all patients with lung cancer, regardless of where the patient is in the disease trajectory. It should be done early and should be tailored to the goals of the patient and family. Most importantly, continued reassessment is necessary to evaluate the effectiveness of the response of interventions throughout the care. Management strategies are multimodal therefore, collaborating with other specialists in the palliative care team is necessary to minimize suffering for patients and their families.

In conclusion, anorexia-cachexia is a challenging syndrome found in many cancers and other diseases. Further research is needed to continue testing of assessment and management approaches. Meanwhile nursing assessment and reassessment of nutritional status can be used to implement current strategies. Collaborating between palliative care clinicians and researchers will allow the development of effective and practical guidelines, which is long overdue. The European Palliative Research Collaborative currently is the primary source of evidence-based practice guidelines of cancer cachexia with the overall aim of improving the management of pain, depression and cachexia with translational research.

Acknowledgments

This work is supported by a grant from the National Cancer Institute (PO1 CA 136396 – Palliative Care for Quality of Life and Symptom Concerns in Lung Cancer; B. Ferrell, PI).

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FAACT (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

<u>ADDITIONAL CONCERNS</u>		Not at all	A little bit	Some- what	Quite a bit	Very much
C6	I have a good appetite.....	0	1	2	3	4
ACT1	The amount I eat is sufficient to meet my needs.....	0	1	2	3	4
ACT2	I am worried about my weight.....	0	1	2	3	4
ACT3	Most food tastes unpleasant to me.....	0	1	2	3	4
ACT4	I am concerned about how thin I look.....	0	1	2	3	4
ACT6	My interest in food drops as soon as I try to eat.....	0	1	2	3	4
ACT7	I have difficulty eating rich or "heavy" foods.....	0	1	2	3	4
ACT9	My family or friends are pressuring me to eat.....	0	1	2	3	4
O2	I have been vomiting.....	0	1	2	3	4
ACT1 0	When I eat, I seem to get full quickly.....	0	1	2	3	4
ACT1 1	I have pain in my stomach area.....	0	1	2	3	4
ACT1 3	My general health is improving.....	0	1	2	3	4

Figure 1.
Functional Assessment of Anorexia/Cachexia Treatment (facit.org)

Figure 2.
EPCR criteria for refractory cachexia ^{6, 16}

Years to Months:

- Assess severity and rate of weight loss.
- Treat reversible cause of anorexia:
 - ✓ Early satiety (e.g. metoclopramide 10 mg before meals).
 - ✓ Symptoms that interfere with intake (e.g. nausea, vomiting, pain, mucositis, etc).
- Review and modify medications that interfere with intake.
- Assess for endocrine/metabolic abnormalities (e.g. hypercalcemia or hyponatremia).
- Consider medication that improves/stimulates appetite:
 - ✓ Progestational agents (e.g. megestrol acetate 160-800 mg BID).
 - ✓ Corticosteroids (e.g. decadron 4 mg/day or prednisone 10-20 mg BID).
 - ✓ Cannabinoids (e.g. dronabinol 5-20 mg/day).
- Consider an exercise program.
- Assess possible social and economic factors (e.g. lack of care taker, poverty, or addiction)
- Consider/provide a nutrition consultation.
- Reassess at next visit:
 - ✓ If adequate: continue to treat and monitor symptoms and QOL.
 - ✓ If inadequate: Intensify palliative care interventions; consider clinical trial.
 - ✓ Ongoing reassessment.

Months to Weeks-Weeks to days (Dying patient):

- Evaluate importance of symptoms of anorexia and cachexia to patient and family.
 - ✓ If significant consider short course of corticosteroids.
- Focus on patient goals and preferences.
- Inform and provide family with alternate ways of caring for the patient.
- Provide emotional support and treat for depression, if appropriate (e.g. Mirtazapine 7.5-30 mg q hs).
- Provide education and support to patient and family regarding emotional aspects of withdrawal of nutritional support.
- Educate patient and family regarding the natural history of disease, including the following:
 - ✓ Absence of hunger and thirst is normal in patients with advanced disease.
 - ✓ Nutritional support may not be metabolized in patients with advanced disease.
 - ✓ The risks associated with artificial nutrition and hydration (e.g. fluid overload, infection, and hastened death).
 - ✓ IV hydration may increase excretion of drug metabolites providing benefit to the patient.
 - ✓ Symptoms like dry mouth should be treated with local measures (e.g. mouthcare).
 - ✓ Withholding or withdrawal of enteral or parenteral nutrition is ethically permissible in this setting and that it will not cause exacerbation of symptoms and may improve some symptoms.
- Reassess at next visit:
 - ✓ If adequate: continue to treat and monitor symptoms and QOL.
 - ✓ If inadequate: Intensify palliative care efforts; consult or refer to specialized palliative care services or hospice.
 - ✓ Ongoing reassessment.

Figure 3.
Management of Anorexia/Cachexia by Life Expectancy^{3, 9, 12, 26}

*Adapted from the City of Hope Quality of Life Model.

Figure 4.
Anorexia-Cachexia Impacts the Dimensions of Quality of Life^{28*}