


## INVITED REVIEW

# Updates on the pathogenesis of advanced lung cancer-induced cachexia

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Thoracic Cancer **10** (2019) 8–16**Abstract**

Advanced lung cancer is becoming a chronic disease threatening human life and health. Cachexia has been recognized as the most common problem associated with advanced lung cancer. Lung cancer-induced cachexia seriously affects patients' quality of life. The present article summarizes the pathogenesis of advanced lung cancer-induced cachexia from three aspects: anorexia, cytokines, and energy and metabolic abnormalities. In addition, the present article proposes corresponding nursing measures based on cachexia pathogenesis to improve the quality of life and survival rate of cachectic patients with advanced lung cancer by combining continuously advancing treatment regimens and effective nursing. The present article also provides references for healthcare professionals when administering related treatments and nursing care.

**Introduction**

Cachexia is a complex metabolic syndrome related to underlying disease, which is characterized by significantly decreased body weight and depleted muscle mass and adipose tissue over a short time.<sup>1</sup> Cachexia mainly manifests as anorexia; progressive emaciation; abnormal metabolism of sugar, fat, and protein; and functional impairment of multiple organs. According to the latest American Society of Clinical Oncology (ASCO) report on clinical research of cancer, there are now 15 million cancer survivors in the United States; that is, one in every 20 Americans has had or is living with cancer. One of the most common problems facing patients with advanced tumors is cancer cachexia.<sup>2</sup> Evidence suggests that more than half of the patients with malignant tumors could progress to the cancer cachexia stage.<sup>3</sup> One study showed that 45.6% of patients with advanced non-small cell lung cancer undergoing chemotherapy already had cancer cachexia at baseline.<sup>4</sup> Lung cancer and gastrointestinal tumors are the two

tumors most likely to cause cancer cachexia.<sup>5</sup> The occurrence of cachexia in patients with advanced lung cancer indicates that the patients are already at an extremely severe nutritional risk. Approximately 22% of lung cancer patient deaths are related to cachexia.<sup>1</sup> Sugar, fat, and protein metabolic disorders develop at the cachectic stage and severely degrade skeletal muscle proteins (the primary characteristic of cachexia). In addition, anorexia and a hypermetabolic state accelerate the depletion of patients' nutrient storage, seriously affecting their quality of life and leading to fatal consequences.<sup>6</sup> The cachectic status and its targeted therapy are of great clinical significance to cancer patients. The cachexia index has been used as a new index to evaluate the survival rate and quality of life of lung cancer patients.<sup>7</sup> In recent years, scholars have conducted many studies on advanced lung cancer-induced cachexia, searching for potential pathogenic mechanisms of cachexia and corresponding treatment strategies and attempting to improve the prognosis of patients with advanced cancer.

## Diagnosing advanced lung cancer-induced cachexia

As per the international consensus published in 2011, the following universal criteria are currently used to diagnose cancer cachexia: unintentional weight loss of > 5% in a tumor patient over the past six months; weight loss > 2% in a patient with a body mass index of < 20; or an appendicular skeletal muscle index (ASMI) consistent with sarcopenia (male ASMI < 7.26 kg/m<sup>2</sup>, female ASMI < 5.45 kg/m<sup>2</sup>), which is accompanied by weight loss of > 2%.<sup>8</sup> The causes and mechanisms of cancer cachexia are complicated and remain unclear. It is characterized by a marked negative protein and energy balance, which is generally believed to be caused by anorexia, reduced food intake, and increased energy expenditure. Current studies show that the occurrence of cachexia is related not only to high catabolic levels but also to the tumors and certain factors produced by the body. Inflammatory responses and the secretion of related cytokines, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 (IL-1), IL-6, and interferon gamma (IFN- $\gamma$ ), are considered to be associated with the hypercatabolic process.<sup>9</sup> In addition, food intake and energy balance are regulated by several mediators, including leptin (LEP) and resistin, secreted by the arcuate nucleus of the hypothalamus. Therefore, neuroendocrine effects contribute to the pathogenesis of cancer cachexia.<sup>10</sup> With advances in medical science, great progress has been made in determining the pathogenesis of cancer cachexia. The potential mechanisms of cancer cachexia are summarized within.

## Pathogenic mechanisms of advanced lung cancer-induced cachexia

### Anorexia

Patients with lung cancer cachexia are likely to develop symptoms such as anorexia and loss of appetite. Reports in the literature state that the prevalence of anorexia is as high as 66% in advanced lung cancer patients that have not been administered chemotherapy.<sup>11</sup> Anorexia mostly manifests as decreased appetite, accompanied by taste changes. Anorexia may have various causes, including gastrointestinal reactions induced by lung cancer and related treatments, olfactory and taste sensation abnormalities, psychological factors, and psychic anxiety. Malignant tumor-associated anorexia is mainly caused by central and peripheral factor-induced disorders in the food intake-related signaling pathways of the hypothalamus.<sup>12</sup> A recent study suggested that tumors with neuroendocrine activity secrete various substances during growth, resulting in

increased plasma tryptophan concentration. Increased tryptophan concentrations in the brain enhance serotonergic neuronal activity in the ventromedial nucleus of the hypothalamus, which plays an important role in anorexia pathogenesis.<sup>13</sup> Among the tumors with neuroendocrine activity, bronchial carcinoma is common, accounting for approximately 31% of all neuroendocrine tumors.<sup>14</sup> Neuropeptide Y (NPY)<sup>15</sup> and LEP<sup>16</sup> play important roles in regulating the hypothalamic feeding centers. LEP binds to the leptin receptor (LEPR) in the central nervous system (CNS), which activates the Janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathway, controls various hypothalamic neural pathways, and thus regulates the body feeding process and energy homeostasis.<sup>17</sup> In addition, inflammatory cytokines (such as TNF- $\alpha$ , IFN- $\gamma$ , IL-1, and IL-6) also promote the development and progression of anorexia.<sup>18</sup> The underlying mechanisms may be related to ability of these cytokines to pass directly through the blood-brain barrier. These cytokines enter the CNS and bind to their corresponding receptors in the hypothalamic region, thereby exerting their effects.<sup>19</sup>

### Cytokines

Currently, the well-recognized mechanism of cancer cachexia is that it is an integrated, systemic, physiological response involving inflammation-activated substrates.<sup>20</sup> Proinflammatory cytokine activities are enhanced during lung cancer progression, while a systemic inflammatory response is a distinctive feature of lung cancer-induced cachexia.<sup>21</sup> Among various proinflammatory factors, TNF- $\alpha$ , IL-1, IL-6, and IFN- $\gamma$  play apparent promotional roles in cachexia development and progression.<sup>22</sup> The above cytokines penetrate the blood-brain barrier into the brain and interact with epithelial cells on the ventricular surface. As a result, certain appetite-affecting substances are released, which induce anorexia and contribute to cachexia's occurrence.<sup>23</sup> TNF- $\alpha$  enhances gluconeogenesis; promotes the breakdown of fats and proteins; reduces the synthesis of proteins, lipids, and glycogen; and induces the production of other cytokines, such as IL-1.<sup>24</sup> TNF- $\alpha$  also inhibits adipocyte differentiation, resulting in decreased fat synthesis.<sup>25</sup> In addition, TNF- $\alpha$  enhances the production and activity of reactive oxygen species in tissues, thereby activating the nuclear factor-kappa B (NF- $\kappa$ B) pathway and subsequently the ubiquitin-proteasome pathway (UPP). The UPP is an important pathway responsible for protein degradation under physiological conditions, and UPP activation eventually results in degradation and depletion of skeletal muscle proteins.<sup>26</sup> By activating the NF- $\kappa$ B pathway, TNF- $\alpha$  induces degradation of the transcription factor MyoD, thereby inhibiting muscle formation.<sup>27</sup> Moreover, TNF- $\alpha$  in cachectic patients promotes UCP2 and

UCP3 expression in the skeletal muscles,<sup>28</sup> increases energy expenditure, and enhances catabolism. Intraperitoneal injection with a recombinant human TNF receptor antagonist consistently improved food intake and increased body weight in tumor-bearing rats, strongly indicating that TNF- $\alpha$  is closely related to cancer cachexia.<sup>29</sup>

IL-1 and TNF- $\alpha$  receptors are present in the hypothalamic regulatory region of the CNS. Once activated, the receptors regulate the organism's feeding behavior.<sup>30</sup> IL-1 and TNF- $\alpha$  act directly on the hypothalamus to induce anorexia. IL-1 concentration is increased under the cachectic state, resulting in a cachectic effect similar to that of TNF- $\alpha$ .<sup>31</sup> In patients with cachexia, IL-1 induces increased plasma tryptophan concentration, which in turn increases the plasma level of 5-hydroxytryptamine (serotonin). Increased serotonin levels lead to early satiety and inhibit hunger. Therefore, IL-1 is associated with anorexia and cachexia.<sup>32</sup> In addition, human IL-1 $\beta$  expression in transgenic mice promotes inflammatory responses and cancer cachexia.<sup>33</sup> Researchers established an animal model of serotonin production by stimulating the hypothalamus with IL-1 and found that gradually elevating the serotonin level continuously stimulated the appetite-suppressing pathways, eventually leading to anorexia symptoms.<sup>34</sup> Administering an IL-1 antibody or the IL-1 receptor antagonist slowed tumor growth, improved cancer patients' appetite, and reduced the breakdown of body fat. These findings further demonstrate the role of IL-1 in cachexia development in patients with malignant tumors.<sup>35</sup>

IL-6 is an important cytokine that regulates immune responses. Increased serum levels of IL-6 enhance transferin levels in tumor patients. IL-6 levels are significantly higher in patients with cachexia than in patients with relatively stable body weights.<sup>36</sup> One study showed that IL-6 enhanced heat production from brown adipose tissue, thereby increasing the breakdown and depletion of body fat.<sup>37</sup> Some scholars believe that IL-6 causes muscle atrophy, decreases body mass, and promotes protein degradation, thereby playing a role in cancer cachexia.<sup>38</sup> In addition, IL-6 stimulates the acute phase protein response in the liver, triggers tissue catabolism, and preferentially accelerates protein degradation in skeletal muscles, which are accompanied by increased levels of acute phase proteins, and 2–3-fold increases in fibrinogen and C-reactive protein levels.<sup>39</sup> IL-6 plays an important role in developing cachexia; however, because directly applying IL-6 alone failed to replicate the state of cachexia in animal models, some researchers believe that IL-6 only exerts an indirect effect.<sup>24</sup>

IFN- $\gamma$  inhibits lipoprotein lipase activity, increases fat breakdown, decreases protein synthesis, reduces food intake, and promotes tissue wasting, resulting in cachexia. IFN- $\gamma$  displays certain synergistic effects with TNF- $\alpha$ ,

leading to cancer cachexia.<sup>40</sup> Applying an IFN- $\gamma$  antibody alleviated weight loss under the cachectic state, indicating that IFN- $\gamma$  is directly or indirectly involved in tumor cachexia occurrence.<sup>41</sup>

Cytokines involved in cancer cachexia also include lipomobilizing factor (LMF) and proteolysis-inducing factor (PIF). A study found that LMF increases cyclic adenosine monophosphate levels by activating adenylate cyclase in adipocytes, thereby enhancing adipocyte catabolism. Moreover, tumor cells use catabolic products.<sup>42</sup> LMF enhances hepatic glycogenolysis and energy production to accommodate the metabolic needs of tumor patients, which is one reason for the increased energy expenditure in cancer cachexia.<sup>43</sup> Intravenous injection with PIF induced muscle wasting and cachexia in mice, accelerated muscle degradation, and reduced muscle formation.<sup>44</sup> PIF-induced muscle protein degradation may lead to muscle degradation via the NF- $\kappa$ B-mediated UPP.<sup>45</sup> Direct injection of PIF into healthy animals effectively simulated the muscle atrophy phenotype of cachexia and significantly enhanced the expression and secretion of acute phase proteins.<sup>46</sup>

## Matter and energy metabolism

The metabolic characteristics in the tumor-induced cachectic state include negative protein and energy balances, which differ from the negative metabolism of matter and energy caused by starvation. Starvation-induced weight loss is mainly related to reduced adipose tissue, whereas weight loss in cancer cachexia is caused by the loss of skeletal muscles and adipose tissue.<sup>47</sup>

## Abnormalities in glucose metabolism

Malignant tumor cells display increased glucose uptake and primarily resort to glycolysis to acquire energy, which is considered an important feature of malignant tumor cells. Malignant tumor cells consume much glucose and produce lactic acid, even under aerobic conditions. This phenomenon is termed the "Warburg effect."<sup>48</sup> Patients with cancer cachexia show an increased dependence on glycolysis. The reductive coenzyme II (NADPH) and protein kinase B (AKT) pathways are activated in patients with cancer cachexia, which manifests as increased cancer cell survivability under hypoxic conditions. These manifestations may be related to abnormal changes in mitochondrial function. Cellular DNA mutations in tumor cells prevent the tricarboxylic acid cycle (an essential part of aerobic metabolism).<sup>49</sup> In addition, gluconeogenesis is increased in cachectic patients. Tumor glycolytic metabolism produces a large amount of lactic acid. Lactic acid is transported to the liver and used as a precursor to resynthesize glucose, which again provides energy for the tumor tissues. The process described above consumes

much energy, mainly adenosine triphosphate (ATP). However, a very limited amount of ATP is regenerated, resulting in excessive energy consumption. This process is known as the Cori cycle.<sup>50</sup>

### Abnormalities in fat metabolism

Changes in fat metabolism mainly include increased fat hydrolysis, enhanced fatty acid oxidation, reduced fat production, and hypertriglyceridemia. Such changes result in decreased body fat storage and body mass loss. Free fatty acids in the serum are mainly derived from the breakdown of body fat, especially white adipose tissue. In the early stage of cachexia, the increase in serum free fatty acids is particularly apparent.<sup>51</sup> Hormone-sensitive lipase (HSL) is activated in adipose tissue, and increased lipolysis enhances the expression of the stimulatory protein Gas and downregulates expression of the inhibitory protein Gai. Expression levels of the HSL messenger RNA (mRNA) and protein are increased by 50% and 100%, respectively, and these increases promote fat breakdown.<sup>52</sup> LMF also significantly enhances the breakdown of fats, mainly via the classic adenylyl cyclase pathway, which is achieved via GTP-dependent stimulation of adenylyl cyclase and enhanced HSL activity.<sup>53</sup> Plasma concentrations of TNF- $\alpha$  and IL-6 are correlated with plasma free fatty acids. The effect of IL-6 is more significant. TNF- $\alpha$  and IL-6 likely accelerate the breakdown of adipose tissues, thereby causing weight loss under a cachectic state.<sup>51</sup>

### Abnormalities in protein metabolism

Abnormal protein metabolism includes elevated muscle catabolism, increased hepatic protein synthesis, decreased muscle protein synthesis, and hypoproteinemia. Organisms experiencing abnormal protein metabolism exhibit a negative nitrogen balance. Skeletal muscle groups are the main sites of endogenous nitrogen loss in tumor patients. Increased breakdown and depletion of skeletal muscle proteins are the main cause of cachexia in patients with malignant tumors.<sup>54</sup> Some scholars believe that skeletal muscle atrophy is mainly caused by reduced protein synthesis, and the breakdown of skeletal muscles represents a secondary change.<sup>55</sup> A recent study showed that increased UPP activity contributes significantly to muscle protein breakdown and weight loss in patients with cachexia. Under normal circumstances, the UPP mainly plays a role in eliminating intracellular proteins, which consume ATP energy.<sup>56</sup> The NF- $\kappa$ B pathway is involved in UPP-mediated muscle breakdown. NF- $\kappa$ B nuclear translocation causes high expression of the ubiquitin ligase E3, leading to enhanced ubiquitination of substrate proteins, accelerated protein degradation, and increased muscle depletion.<sup>57</sup> In addition, various cytokines are involved in abnormal protein metabolism. For example, IL-6 enhances ubiquitin mRNA levels

and increases 26S proteasome activity in the UPP.<sup>58</sup> TNF- $\alpha$  stimulates muscle proteolysis by directly activating the ATP-ubiquitin-dependent pathways.<sup>59</sup> In addition, patients suffering cancer cachexia synthesize an increased amount of acute phase reactants in the liver, which enhance the inflammatory response while promoting protein degradation.<sup>21</sup>

### Abnormalities in mitochondrial energy metabolism

Mitochondria are the main sites of intracellular oxidative phosphorylation and ATP synthesis. Mitochondria provide energy for cellular life and activity. Therefore, one study proposed that mitochondrial dysfunction is closely related to energy metabolic disorders.<sup>60</sup> In patients with cancer cachexia, overactivation of the oxidative phosphorylation-related UCPs in the mitochondria may destroy the mitochondrial proton electrochemical gradients. In addition, inflammatory responses in patients cause decreased mitochondrial membrane fluidity.<sup>61</sup> These changes lead to mitochondrial dysfunction, resulting in reduced energy production and increased catabolism in cachectic patients. A study found that UCP expression is upregulated in the muscle tissues of patients with cancer cachexia. Elevated expression of mitochondrial UCPs increases the total resting energy expenditure (REE) in patients with cancer cachexia. The underlying mechanism may involve increased heat production, which is achieved through UCP-induced promotion of proton flow in the mitochondrial inner membrane and reduction of proton electrochemical gradients.<sup>62</sup> The increased REE in the cachectic state results in energy waste. Moreover, most increased energy expenditure is wasted on useless metabolic cycles.<sup>63</sup> REE levels in tumor patients are closely related to tumor types. For example, the REE is significantly increased in patients with pancreatic and lung cancers compared to healthy individuals. In contrast, the REE may not increase in patients with other tumors.<sup>64</sup> In the cachectic state, expression of the proteins related to skeletal muscle energy metabolism, UCP2 and UCP3, is significantly upregulated, indicating that these two proteins participate in energy metabolic processes.<sup>28</sup> In addition, tumor-related weight loss increases the expression level of UCP-3 mRNA, while UCP-2 mRNA levels are unaffected by weight changes.<sup>65</sup> Therefore, elevated UCP3 mRNA levels may increase energy expenditure, thus contributing to tissue catabolism and promoting cancer cachexia.

In short, the pathogenesis of advanced lung cancer-induced cachexia is related to anorexia, cytokines, and energy and metabolic abnormalities. Experts on cancer cachexia syndrome agree that nursing care is an important component of multimodal intervention for cachexia throughout the course of cancer.<sup>66</sup> The aim is to protect

against adverse treatment outcomes, enhance treatment tolerance, and improve survival and quality of life.

## Nursing care for cachectic patients with advanced lung cancer

### Nursing care for patients with anorexia

Most cachectic patients with advanced lung cancer may develop symptoms of anorexia, such as appetite loss and taste alterations. In the pathogenesis of advanced lung cancer-induced cachexia, the occurrence of anorexia may be related to treatment-induced changes in gastrointestinal function, alterations in olfactory and taste sensation, and psychological factors. Therefore, proper nursing measures should be formulated based on the anorexia pathogenesis. Multifaceted nursing care (including oral, mental, food, and exercise nursing) should be provided to enhance patients' appetites, reduce their psychological burden, alleviate the continuous weight loss, and ensure better patient cooperation with medical staff. Proper nursing intervention for anorexia is important for improving the quality of life of cachectic patients with advanced lung cancer.

#### Oral care

A good oral environment promotes patients' food intake, stimulates their appetite, and effectively prevents oral diseases. Therefore, providing proper oral care to patients is crucial to encourage eating and alleviate anorexic symptoms. For patients with self-care ability, oral care includes assisting the patients in cleaning their oral cavity two to three times daily with a soft-bristled toothbrush and rinsing their mouth with mouthwash or normal saline after meals. Providing oral care to patients who are incapable of self-care and require assistance involves picking up cotton balls dipped in normal saline with a curved vascular clamp and sequentially cleaning the patient's lips, teeth, tongue, and palate two to three times daily. During the cleaning process, the patients' oral environments must be examined for oral mucosal hemorrhaging, sputum, or other secretions. Oral secretions must be cleared in a timely manner. If needed, drug or antibacterial solutions should be administered based on patients' oral environments.<sup>67</sup>

#### Mental care

Anorexia results in insufficient food intake and emaciation, which poses a great psychological burden to patients; however, insufficient attention is paid to psychological care. Therefore, the nursing staff should establish a good relationship with patients, communicate with them, listen actively to their demands, assist to adjust their moods in a timely manner, and perform individualized psychological interventions based on the patients' basic conditions,

educational attainments, and religious customs. The nursing staff should encourage patients to help each other, encourage each other, share their experiences, and build confidence. The nursing staff should share the details of cases of successful treatment to enhance patients' confidence in fighting the disease. Most patients lack knowledge of the disease, thus aggravating their anxiety. Therefore, the nursing staff should inform patients of the details of the disease to alleviate such anxiety. In addition, a good family support system is important, as it may help patients maintain a better mood and improve the quality of their diet.<sup>68</sup>

#### Dietary care

*Food choice:* The nursing staff should guide patients to eat small, frequent meals throughout the day and avoid overdrinking and overeating. Diet plans should be appropriately adjusted to patients' eating habits, individual backgrounds, and regional differences. When a patient is experiencing appetite loss, it may help to provide the patient with their favorite foods. A unitary diet should be avoided. If their condition permits, patients should be encouraged to try novel foods that may stimulate their appetite. Improving the visual appearance of foods and selecting bright-colored foods may also enhance their appetite. In addition, patients must be informed of the importance of diet in order to enhance their cooperation. The nursing staff should guide patients to eat scientifically. Patients should eat foods that are protein and vitamin-rich, plain, and easily digested; cold, greasy, spicy, and irritating foods should be avoided.

*Improving the eating environment:* Patients should be provided with a comfortable eating environment. If a patient does not feel like eating, playing food-focused films and pleasurable music may boost their appetite. In addition, nursing staff should provide patients with dietary guidance from a psychological aspect to consciously activate the patients' desire to eat.

#### Exercise nursing

Most cachectic patients suffer from fatigue and cannot exercise; however, proper exercise not only strengthens their immunity but also lifts their mood. Therefore, proper exercise can increase patients' appetites. Proper exercise programs should be designed according to patients' physical conditions. In general, the exercise programs mainly consist of walking and Tai Chi. In addition, patient tolerance should be closely monitored. Exercise duration and intensity should be adjusted based on tolerance. Patients suffering severe fatigue may undergo guided breathing exercises to relieve fatigue.

### **Nursing care for patients with systemic inflammatory response**

Patients living with advanced lung cancer-induced cachexia are particularly vulnerable to physical dysfunction.<sup>69</sup> Lung cancer patients experience increased proinflammatory cell activity during tumor progression, which causes systemic inflammatory responses, such as urinary tract, skin and respiratory infections. Closely monitoring changes in patients' vital signs and improved immunity may positively impact the prevention, treatment, outcome, and care of systemic inflammatory responses. Therefore, nursing care aimed at systemic inflammatory responses is vitally important for cachectic patients with advanced lung cancer.

### **Monitoring changes in patient vital signs**

Body temperature, pulse, respiration, and blood pressure in patients with systemic inflammatory reactions are prone to fluctuate. Therefore, changes in patient vital signs should be closely monitored to allow timely treatment.<sup>70</sup>

### **Preventing infection**

In patients with cachexia, urinary tract infections (UTIs) are more likely to cause symptoms of a systemic inflammatory response. Women are more likely to develop UTIs than men because of the physiological characteristics of their urinary tract. UTI occurrence must be prevented in cachectic patients. Patients with normal renal function should be advised to drink 2000 mL of water daily to flush the urinary tract. Patients should clean the perineal area and change their underwear when needed. For patients with indwelling urinary catheters, nurses should properly care for the urinary catheter in strict accordance with the operating specifications. In addition, nurses should replace the urinary catheter and drainage bag in a timely manner to prevent UTIs,<sup>71</sup> and the patients' skin must be well cleaned to prevent skin infection. Antibiotics should be prescribed based on the severity of the infection, and patients should take any antibiotics as directed.

### **Health propaganda and education**

Patients should be advised to keep their bodies warm to guard against respiratory infections. Patients should be supplemented with vitamins A and C to enhance immunity.<sup>71</sup> In addition, patients should be urged to maintain a regular lifestyle. Patients should control their sleep time during the day to ensure their sleep quality at night. If a patient sleeps poorly at night, the nursing staff may advise the patient to drink 200 mL of hot milk or soak their feet in warm water before going to bed. Adequate sleep must be ensured, as insufficient sleep can lead to a decline in the patient's immunity.

### **Nursing care for patients with abnormalities in matter and energy metabolism**

Cachectic patients with advanced lung cancer often exhibit a negative protein balance and abnormalities in sugar, fat, and protein metabolism. Metabolic abnormalities cause excessive depletion of skeletal muscle and fat, leading to weight loss. Nursing care should be provided based on the pathogenesis of cachexia-associated abnormal matter and energy metabolism. Nursing measures, such as monitoring changes in blood glucose levels, providing nutritional support, and encouraging patients to eat high-protein foods, are of positive significance for preventing progressive weight loss in patients.

### **Nursing care for patients with abnormal glucose metabolism**

Abnormal glucose metabolism mainly manifests as increased insulin resistance, which increases glucose synthesis, gluconeogenesis, and glucose-lactic acid cycle activity. In addition, glucose tolerance and turnover are decreased. Controlling blood sugar is important in cachectic patients with advanced lung cancer. Successfully controlling blood sugar levels not only reduces the incidence of cancer complicated with diabetes but also improves the quality of life of cancer patients. Because of the psychological and financial burden caused by the disease, many patients do not actively cooperate with medical treatments and display poor compliance. Additionally, most patients with cachexia suffer from anorexia, fatigue, and body wasting. Irregular eating and reduced exercise render it difficult to control blood glucose levels in these patients. Therefore, nursing staff should play an active role in improving patient compliance, thus successfully controlling blood glucose levels in patients.<sup>72</sup>

### **Nursing care for patients with abnormal fat metabolism**

Abnormal lipid metabolism is characterized by increased lipid mobilization, decreased lipogenesis and lipoprotein lipase activity, elevated triglyceride levels, reduced high-density lipoprotein levels, elevated venous glycerol levels, and decreased plasma glycerol clearance rates. Because adipose tissue depletion also causes weight loss, nutritional support therapy is very effective for cachectic patients with early lung cancer. Necessary nutritional support increases the amount of heat produced in a patient's body and the intake of various nutrients, as well as regulating metabolic disorders, thereby improving the patient's nutritional status and reversing their weight loss. For cachectic patients with advanced lung cancer, nutritional support therapy aims to improve their quality of life.<sup>73</sup> For various reasons,

cachectic patients with advanced lung cancer may be unable to eat or their food intake may not meet their bodies' needs. Under such circumstances, nutritional interventions should be applied.

*Enteral nutritional therapy:* If patients with normal gastrointestinal function cannot feed themselves or have difficulty swallowing, nutritional support can be provided through the stomach or jejunum. When selecting an enteral nutritional formula, both intestinal tolerance and energy/nutrient requirements must be considered.

*Parenteral nutritional therapy:* Patients suffering gastrointestinal dysfunction cannot undergo enteral feeding and will need parenteral nutritional support.

### Nursing care for patients with abnormal protein metabolism

Protein loss in patients with cachexia mainly manifests as skeletal muscle atrophy, hypoproteinemia, and reduced treatment tolerance.<sup>74</sup> Patients should be encouraged to eat more high-protein foods. If a patient develops hypoproteinemia, albumin infusion should be performed according to the patient's specific condition to supplement nutrients.

### Conclusion

Although the number of patients diagnosed with lung cancer has increased annually, the survival rate of lung cancer patients has also increased over the past decade. Reducing the controllable risk factors can prevent lung cancer cases and lung cancer-related deaths. Advanced lung cancer-induced cachexia is a syndrome that occurs in lung cancer patients and functionally impairs multiple systems. Various comprehensive factors jointly participate in the development of advanced lung cancer-induced cachexia, which is mainly characterized by weight loss. However, cancer cachexia is not simply weight loss. Bruggeman *et al.* explained that weight loss does not completely represent the pathophysiological changes and clinical impact of cachexia.<sup>75</sup> Assessing only body weight while ignoring other disease manifestations may account for patients having already entered the stage of refractory cachexia at diagnosis. Therefore, further investigation of the mechanisms underlying cancer cachexia development and progression is needed to improve treatments for cachexia. Medical personnel need to change their traditional views on treatment and not only treat the lung cancer site but also provide treatment regimens based on the cancer's pathogenesis and genetic characteristics. In addition, nursing staff should assist doctors during treatments. Nursing staff should formulate personalized nursing interventions that specifically target the cachexia pathogenesis to alleviate further progression and improve patient quality of life.

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