Original Research

CACHEXIA IN LUNG CANCER PATIENTS AT MILITARY HOSPITAL 103 AND SOME ASSOCIATED FACTORS

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ABSTRACT

Aims: The study aimed to evaluate the cachexia status and its associated factors in lung cancer patients.

Methods: The cross-sectional study was conducted on 97 lung cancer in patients at the Oncology Center, Military Hospital 103, between 2020 and 2021.

Results: The prevalence of cachexia in the lung cancer patients was 46.4%. In the multivariable regression models, the factors significantly associated with cachexia included age over 60 years (OR=3.3; p <0.05), nutrition impact symptoms (NIS) score (OR=1.26; p <0.01), and BMI <18.5 kg/m^2 (OR=11.4; p <0.01). The NIS score demonstrated the best ability to screen for cachexia (AUC=0.715; p <0.001) in the lung cancer patients. Among the models combining factors for classifying cachexia, the Model consisted of 4 factors: NIS, BMI < 18.5 kg/m^2, male gender, and age ≥ 60, yielding the best diagnostic value (AUC = 0.845; p < 0.001).

Conclusions: Malnutrition was common among lung cancer patients. Age, BMI, and NIS score were significantly associated with cachexia. The combination of the associated factors could improve the discrimination of cachexia in lung patients.

Keywords: *nutrition impact symptoms, cachexia, lung cancer, Military Hospital 103.*

I. INTRODUCTION

Cachexia is a complex syndrome related to pre-existing diseases, causing continuous muscle loss that cannot be fully restored through simple nutritional supplementation. This condition is characterized by rapid weight loss and changes in eating ability. Various different pathological conditions can lead to cachexia, including cancer, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic joint disease, and AIDS [1]. The prevalence of cachexia in cancer patients can reach 60-80% in advanced stages. Cachexia is associated with reduced quality of life and increased mortality rates in patients [2].

Lung cancer is a common type of cancer. Statistics show that there were approximately 2.2 million new cases of lung cancer in 2020, accounting for 11.4% of all new cancer cases. The standardized age-specific incidence rate of lung cancer globally is 36.6 per 100,000 population. However, it's worth noting that lung cancer has the highest mortality rate (18%) among all cancers [3]. In Vietnam, the incidence of lung cancer has been increasing in recent years. According to the Globocan 2020 report, an estimated 29,485 new cases of lung cancer occurred in Vietnam in 2020, representing 19.4% of all new cancer cases in the country.

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The standardized age-specific incidence rate of lung cancer in Vietnam is 33.2 per 100,000 population, ranking second after liver cancer [3]. Management and treatment of lung cancer depend on various factors, with nutritional therapy playing an important role [4, 5]. Malnutrition is a common condition in lung cancer patients and is related to nutrition impact symptoms (NIS) [6]. The lung cancer treatment process requires a multidisciplinary approach and close coordination [4, 5]. Military Hospital 103 is a first-class general hospital and serves as a practical base for the Military Medical University. The hospital has implemented a multidisciplinary treatment model, and group consultations ensure standardized quality. Assessing the cancer-related wasting status and analyzing its correlation with NIS scores will help clinicians detect early signs and provide timely nutritional interventions [7].

II. METHODS

2.1. Research design

The study was designed using the cross-sectional method on lung cancer patients diagnosed and treated inpatient at the Oncology Center, Military Hospital 103, during the period from October 2020 to December 2021. The research was approved by the scientific and ethical committee of the University of Public Health with decision number 40/QĐ-ĐHYTCC dated February 1, 2020.

2.2. Sample size

Sample size is calculated using a formula: $n = Z^2_{1-\alpha/2}\frac{p(1-p)}{d^2}$

Where: n is the minimum sample size; $Z^2_{1-\alpha/2}$= 1,96 is the reliability coefficient with α = 0.05; p= 0.744 is the proportion of people with lung cancer who are malnourished according to the PG-SGA method at the Central Lung Hospital [8]; d=0.10 is the absolute error. Substituting into the formula calculates *n* = 73.

2.3. Sampling method

Select a sample from all patients who were inpatients at the hospital during the study period and met the selection criteria and were selected for the study until the sample size was reached.

Criteria for selecting research subjects: adult age (≥ 18 years old), healthy enough to answer survey questions and completely voluntary to participate and research.

Exclusion criteria: medical records with incomplete information. The patient is unable to answer questions, not clear enough, and has difficulty communicating.

The study collected 102 patients with lung cancer, including 5 patients with cancer from other locations with lung metastases who were not included in the study. As a result, 97 primary lung cancer patients were selected who met the research criteria.

2.4. Data collection

Patients were clinically examined according to daily medical record form and routine laboratory tests. They were distributed questionnaires and instructions.

Information bias was controlled by carefully training investigators on how to collect data, especially the nutritional assessment method using the subjective global assessment (SGA) tool. Selection bias was controlled based on clear definition of research subjects with inclusion and exclusion criteria.

Blood samples were taken in the morning and transferred to the biochemistry and hematology department for tests according to hospital procedures. Biochemical tests were performed on the AU5800 Beckman Coulter machine, based on the principle of optical density measurement. Hematology tests were performed on the Sysmex XN-1000 machine, based on the principle of fluorescence flow cytometry.

The bench scale had a standard height measuring scale. Paper and electronic medical records were used together to collect patient information. Research variables were classified and the assessment tool set was tested before implementation.

2.5. Variables

Diagnostic criteria are based on Fearon's (2011) criteria, divided into 3 stages of pre-cachexia, cachexia, and irreversible cachexia based on the combination of body weight loss and body mass index (BMI). Cachexia is diagnosed when one of the following criteria is present: (1) weight loss over 5%; (2) weight loss over 2% and BMI<20 kg/m^2. Patients are not cachectic when (1) no weight loss or (2) weight loss is less than 5% but BMI ≥ 20 kg/m^2 [9]. Patients are classified malnutrition when BMI<18,5 kg/m^2 [10].

Nutrition impact symptoms (NIS) include 13 main symptoms: early feeling of fullness, nausea, vomiting, mouth ulcers, difficulty swallowing, food odor, dry mouth, pain, taste changes, fatigue, anorexia, diarrhea, constipation and other symptoms (anxiety, financial thoughts, toothache...) were asked according to the instructions of the patient-based subjective global assessment tool (PG-SGA) [11]. Specifically, patients answer 13 questions "I have decreased appetite and/or decreased food intake due to each symptom such as... changes in taste and smell by choosing one of four options: 1 = no, 2 = little, 3 = moderate, 4 = very much [12]. A threshold of three or more was chosen and considered significant for NIS symptom responses in this study.

2.6. Statistical analysis

The information collected on the questionnaire was be coded, entered and processed using SPSS 26.0 software.

Multivariable logistic regression model was used to evaluate the association between cachexia and the factors including age over 60 years, male gender, education above high school, job with stable income, rural residence, NIS score, advanced stage cancer, BMI <18.5, lymphoma <2 (G/L), and albumin <35 (g/L). The variables were checked for multicollinearity using the variance inflation factor (VIF) before being included in the regression model. The VIF values ≥ 5 were considered to have multicollinearity [13]. The final model included statistically significant variables. Results were presented as OR (95% CI). A *p*-value < 0.05 was considered statistically significant. The area under the curve (AUC) was used to examine the discrimination of cachexia for each statistically significant variable in the univariate analysis and the final model. AUC value > 0.7 means the model is applicable, > 0.8 is good and > 0.9 is very good.

III. RESULTS

Table 1. *General characteristics of lung cancer patients (n=97).*

Characteristics	*n* (%)
Age (years), mean±SD	61.0 ± 11.0
Age ≥ 60 years, n (%)	58 (59.8)
Gender (Male), n (%)	80 (82.5)
Education beyond high school, n (%)	68 (70.1)
Career with stable income, n (%)	76 (78.4)
Live in a rural area, n (%)	37 (38.1)
Advanced stage cancer, n (%)	88 (90.7)
BMI (kg/m^2), mean±SD	19.9 ± 2.9
Albumin (g/L), mean±SD	37.8 ± 4.7
Lympho (G/L), median (IQR)	1.73 (1.24–3.01)

Data are presented as mean±standard deviation (SD) or median(interquantil range (IQR); BMI: body mass index.

Table 1 shows the distribution of different cancer patient rates by age group, gender and education: group ≥ 60 years old (59.8%), male gender (82.5%), education above high school (High school) (70.1%). Advanced stage patients account for the majority (90.7%). Average hematological and biochemical values were within normal limits or slightly decreased.

Table 2. *Characteristics of cachexia symptoms in lung cancer patients (n=97).*

Symptoms	Non-cachexia (*n*=52)	Cachexia (*n* =45)	Total (*n*=97)	*p*-value
Weight loss ≥ 5%	0 (0)	42 (43.30)	42 (43.30)	<0.01
Weight loss 2–5%	9 (9.28)	3 (3.09)	12 (12.37)	<0.01
Anorexia	23 (23.71)	37 (38.14)	60 (61.86)	<0.01
Advanced stage cancer	45 (46.39)	43 (44.33)	88 (90.72)	>0.05
BMI < 18.5 kg/m^2	4 (4.12)	22 (22.68)	26 (26.80)	<0.01
BMI < 20 kg/m^2	19 (19.59)	33 (34.02)	52 (53.61)	<0.01

Data in the table are presented in n (%). P-value by Chi square test.
NIS, nutrition impact symptom; BMI, body mass index

As shown in Table 2, in the group with cachexia, the highest rate of cachexia symptoms is weight loss ≥ 5% (43.3%), followed by anorexia (38.1%), BMI < 20 kg/m^2 (34%). Symptoms of wasting and weight loss of 2-5% account for the lowest rate (3.1%). There was no statistically significant difference in disease stage between the 2 groups.

Table 3. *Some factors related to cachexia in multivariable logistic regression analysis (n=97).*

Variables	*p*-value	OR	95% CI
Model 1			
Age ≥ 60 years	0.035	5.10	1.12 – 23.1
Gender (male)	0.784	1.23	0.28 – 5.39
Education beyond high school	0.492	1.62	0.41 – 6.44
Career with stable income	0.886	1.13	0.22 – 5.87
Live in a rural area	0.784	1.22	0.29 – 5.12
NIS score	0.004	1.31	1.09 – 1.58
Advanced stage cancer	0.915	0.85	0.05 – 16.1
BMI < 18.5 kg/m^2	0.003	12.7	2.41 – 67.1
Lympho < 2 (G/L)	0.653	1.34	0.38 – 4.70
Albumin < 35 (g/L)	0.168	3.07	0.62 – 15.1
Constant	0.029	0.017	-
Model 2			
Age ≥ 60 years	0.033	3.30	1.10 – 9.90
Gender (male)	0.295	2.07	0.53 – 8.09
NIS score	0.001	1.26	1.10 – 1.45
BMI<18.5 kg/m^2	0	11.4	3.05 – 42.8
Constant	0	0.036	-

NIS: nutrition impact symptom; BMI: body mass index

In multivariable regression, Model 1 shows the factors that had a statistically significant influence on the cachexia of lung cancer patients included age (OR = 5.1; 95CI = 1.12–23.1), NIS score (OR = 1.31, 95CI = 1.09–1.58), BMI < 18.5 (OR = 12.7, 95CI = 2.41–67.1). In the Model 2, the significant factor for cachexia in the lung cancer patients were age (OR = 3.3; 95CI = 1.1–9.9), NIS symptoms score (OR = 1.26; 95CI = 1.1–1.45), BMI <18.5 (OR = 11.4, 95CI = 3.05–42.8).

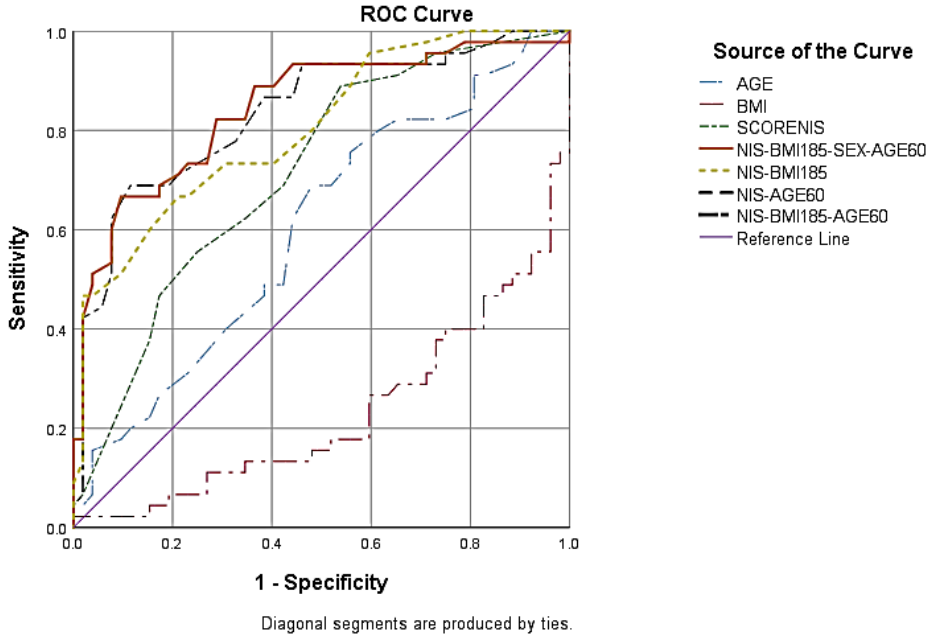

Figure 1. *Area under the curve for discnimination of cachexia (n=97).*

Table 4. *Comparison of the ability of indicators to identify cachexia via AUC (n=97).*

Factors	AUC	SE	*p*	95%CI
BMI	0.23	0.048	< 0.001	0.135 – 0.325
Age	0.601	0.058	0.086	0.488 – 0.714
NIS score	0.715	0.052	< 0.001	0.614 – 0.817
NIS-age ≥60	0.747	0.05	< 0.001	0.649 – 0.844
NIS-BMI <18.5	0.804	0.044	< 0.001	0.718 – 0.89
NIS-BMI <185-age≥60	0.834	0.042	< 0.001	0.752 – 0.916
NIS-BMI <18.5-gender-age≥60	0.845	0.041	< 0.001	0.765 – 0.925

AUC: Area Under the Curve; NIS: nutrition impact symptom; BMI: body mass index.
Model 1: NIS & age≥60; Model 2: NIS & BMI<18.5; Model 3: NIS & BMI<18.5 & age≥60; Model 4: NIS & BMI<18.5 & gender & age≥60.

Comparing the screening and detection ability of the factors shows that among separate factors (Fig.1 and Table.4), the NIS score has the highest discriminatory ability (AUC=0.715; p <0.001). Among the models combining factors to classify cachexia, model 4 including 4 factors NIS & BMI <18.5 & male gender & age ≥ 60 give the best diagnostic value (AUC=0.845; p < 0.001).

IV. DISCUSSION

4.1. Cachexia state of lung cancer patients

The mechanism of wasting is complex, not simply starvation. The pathological process uses energy from fat stores, in addition to muscle mass, to replace glucose as the main fuel for cells. Cancer causes changes in metabolism rather than simple energy deficiency, so conventional nutritional support is not enough to prevent wasting [14].

Research indicates that cancer cachexia is a poor prognostic sign for patients, with typical manifestations including significant muscle and fat loss. However, unlike weight loss due to reduced caloric intake, cachexia primarily leads to muscle wasting rather than fat loss. It occurs in chronic conditions such as late-stage cancer, chronic obstructive pulmonary disease, and chronic infections. Studies show an increase in pro-inflammatory factors characteristic of cachexia. Once a patient enters the cachexia stage, it is challenging to reverse solely through nutritional interventions. The consequences of cachexia include reduced quality of life, decreased tolerance for surgical or medical interventions, and ultimately, reduced survival time [15].

In this study, the evaluation results of cachexia status in lung cancer patients showed that the proportion of patients with cachexia was as high as 46.4%. These findings indicate that cachexia is more common in lung cancer patients compared to other types of cancer. The nutritional disorder status highlights the need for early screening, assessment, and regular monitoring to detect pre-cachexia and intervene promptly in all inpatient cancer cases [6], [16].

4.2. Cachexia and associated factors

The consequences of cancer-related wasting in patients result from various factors, primarily including cancer-related damage, adverse effects of treatment, and overall treatment strategies, which may also involve inadequate nutritional intake. A study applied a multivariable regression model to assess factors related to the wasting syndrome, considering both overall variables and statistically significant factors.

The limitation of BMI is that it cannot differentiate between body mass components, as it may conflate muscle mass, fat mass, and overall body water status. Consequently, BMI lacks true clinical value in predicting the severity of a patient's condition, especially in cases where patients experience early changes related to wasting. However, in this study, when the BMI indicates malnutrition (BMI < 18.5), it holds prognostic value for wasting (OR=11.4). Therefore, BMI should still be used due to its ease of implementation and assessment. It remains one of the initial indices that healthcare professionals use and document in patient records [10], and it serves as a prognostic indicator for wasting in lung cancer patients.

The symptoms affecting nutrition (NIS) significantly impact energy intake and the digestive capacity of patients. Data from this study (Table 2) show that during advanced stages of cancer, the prevalence of appetite loss in patients (38.14%) is nearly twice as high as in

early stages (23.71%). Appetite loss is consistently prominent, especially among lung cancer patients, and it significantly affects the overall condition of the patient [1]. Appetite dropping, along with fatigue and muscle weakness, leads to reduced eating activity, affecting swallowing reflex and resulting in decreased fluid secretion. Additionally, lack of taste sensation and side effects of certain medications can cause dry mouth. Consequently, the body fails to obtain sufficient nutrients from daily food intake to meet its needs. The combination of these symptoms exacerbates the situation, leading to reduced energy intake through oral feeding in patients [2]. If healthcare professionals do not promptly identify and proactively supplement energy (using oral nutritional supplements containing hydrolyzed protein, medium-chain triglycerides, omega-3 fatty acids, and/or artificial nutrition via enteral and/or parenteral routes), patients may rely on stored energy in the body, leading to muscle and fat loss, ultimately resulting in wasting [15, 17].

In clinical practice, a considerable number of patients have had to undergo nutritional tube placement when their oral intake is insufficient, especially in cases where patients experience loss of appetite and/or gastrointestinal damage. This situation often arises in patients with head and neck cancer or during cancer treatment. Early detection of key factors affecting the patient's nutritional status is crucial in clinical settings to assist physicians in devising treatment strategies and improving symptoms in patients [18].

The analysis of this study indicates that cachexia is not related to the cancer stage (p>0.05). This finding may be attributed to the small sample size and single-center nature of the study, which does not fully represent the lung cancer patient population. However, it's also possible that the lung's immune system plays a significant role in the early onset of cachexia, as the lungs are a major immune organ in the body, leading to earlier cachexia development compared to other cancer types [16]. Similarly, the multivariable correlation assessment reveals that living and working conditions, gender, albumin, and lymphocyte levels are not closely associated with cachexia in lung cancer patients (p>0.05).

The study has demonstrated the value of the Nutritional Index Score (NIS) in early monitoring and assessing the cachexia status of lung cancer patients. NIS assessment can be carried out by nurses and is an essential component of the Patient-Generated Subjective Global Assessment (PG-SGA), which provides an overall nutritional status evaluation based on patient input. Unlike the PG-SGA, which requires skilled nutrition experts, NIS symptoms are easily exploitable and assessable, even by patients themselves, making it more feasible in resource-constrained hospital settings

The novel aspect of this study lies in affirming the effectiveness of Nutritional Impact Symptoms (NIS) factors in screening for cachexia. This has practical applications in patient care, as rigorously assessing the factors influencing nutrition helps guide healthcare professionals in targeted interventions to improve the dietary intake and digestive status of cancer patients. To alleviate NIS symptoms, both non-pharmacological and pharmacological measures have been applied clinically, demonstrating efficacy in enhancing appetite [19]. The multidisciplinary team, including physicians, clinical pharmacists,

dysphagia and functional recovery experts, and nutrition specialists, has played a crucial role in cancer patient management model [20].

The study still has some limitations, including a small sample size, data from a single center, lack of monitoring of nutritional changes over time, and assessment of the impact of cancer treatment methods on cachexia status. Additional research is needed to address these points.

V. CONCLUSION

The research results indicate that cachexia was prevalent among lung cancer patients (46.4%). A multivariable logistic regression model revealed that age, BMI, and the Nutritional Impact Symptoms (NIS) were associated with the likelihood of malnutrition in lung cancer patients. The NIS score had the highest detectability ability for cachexia [AUC (95%CI) = 0.715 (0.614–0.817)] among separate factor. Combination of 4 factors, NIS & BMI<18.5 & male gender & age≥60 gave the best diagnostic value (AUC=0.845; p<0.001).

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