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ORIGINAL ARTICLE

Evaluation of Nutritional Status During Diagnosis, Treatment and Follow-up in Patients with Lung Cancer

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ÖZET

Amaç: Akciğer kanseri şu anda dünyada en sık görülen kanserdir. Tanı genellikle ileri evrede konulur. Bu nedenle mevcut sınırlı yaşam süresinde yaşam kalitesini artırmak oldukça önemlidir. Ortalama sağkalımı değiştirebilecek faktörlerden biri de kilo kaybıdır. Bu amaçla hastanede akciğer kanseri tedavisi gören popülasyonun Beslenme Risk Taraması (NRS-2002) ile kan biyokimyasal ve antropometrik ölçümleri ile akciğer kanseri malnütrisyon semptomlarının araştırılması ve akciğer kanseri hastalarının sağlık durumlarının araştırılması hedeflendi. **Yöntem:** Bu çalışma, 2020-2021 yılları arasında Adana Şehir Hastanesi Tıbbi Onkoloji Kliniğine başvuran, akciğer kanseri tanısı alan 18 yaş ve üzeri 216 erkek, 50 kadın olmak üzere toplam 266 gönüllü üzerinde gerçekleştirildi. **Bulgular:** 266 hasta dahil edildi: 216 erkek, 50 kadın, ortalama yaş 61,7±10,5, ortanca yaş 62 idi. BMI değeri 20'nin altında olan (p<0,001) ve son 3 ayda kilo kaybı olan hastalarda malnütrisyon riski (p<0,045) ikisi arasında pozitif bir ilişki vardı (p<0,005). Hastalarda albumin, antropometrik ölçümler, CRP ve NRS 2002 arasındaki ilişki incelendiğinde anlamlı pozitif ilişki olduğu görüldü. (p<0,005). Hastaların CRP değerleri ile BMI ve antropometrik ölçümleri arasında ters korelasyon mevcuttu (p<0,005). NRS 2002 ile hastanın kilosu ve antropometrik ölçümleri arasında ters korelasyon (p<0,005). Kemoterapi alan hastaların albümin, BMI ve antropometrik ölçümleri ile ters yön arasında, CRP değerleri ile son 3 aydaki kilo kaybı ile NRS 2002 arasında pozitif korelasyon bulundu. (p<0,005). Radyoterapi ile CRP arasında pozitif bir korelasyon. (p<0,005) Hastalarda metastaz ile albumin değerleri, antropometrik ölçümler ve BMI arasında ters ilişki varken; CRP ve NRS 2002 ile pozitif korelasyon bulundu (p<0,005). Yaş, albumin, BMI ve antropometrik ölçümlerle ters ilişki bulunurken, CRP ve NRS 2002 ile pozitif ilişki saptandı (p<0,005). Beslenme tedavisi alan hastalarda kemoterapi alma sıklığı (p=0,06) ve metastaz görülme sıklığı (p< 0,01) yüksek bulundu (p<0,005) **Sonuç:** Akciğer kanseri tanısı alan hastaların, tanı anından itibaren başka herhangi bir hastalık, yaşam kalitesi, malnütrisyon riski ve beslenme durumu açısından taranması gerektiğini, erken tıbbi tedavi ile birlikte beslenmeye yönelik önlemlerin alınmasıyla hastaların beklenen yaşam süresinin uzatılabileceğine inanıyoruz.

Anahtar kelimeler: Akciğer kanseri, beslenme, malnütrisyon, NRS 2002

ABSTRACT

Aim: Lung cancer is currently the most common cancer in the world. Diagnosis is usually made at an advanced stage. For this reason, it is very critical to enhance the standard of life during the current limited lifespan. One of the factors that can change the average survival is weight loss. For this purpose, the Nutritional Risk Screening (NRS-2002) of the population receiving lung cancer treatment in the hospital, blood biochemical and anthropometric measurements, and lung cancer malnutrition symptoms were targeted to explore the health status of lung cancer patients. **Methods:** This study was conducted on a total of 266 volunteers, 216 men and 50 women, aged 18 and over, who were diagnosed with lung cancer and admitted to Adana City Hospital Medical Oncology Clinic during the years 2020-2021. **Results:** Of the 266 patients included, 216 were men and 50 were women. The mean age was 61.7±10.5, and the median age was 62. There was a positive relationship between the risk of malnutrition in patients with BMI values below 20 (p<0.001) and weight loss in the last 3 months (p<0.045) (p<0.005). When the relationship between albumin, anthropometric measurements, CRP, and NRS-2002 in patients was examined, there was a significant positive relationship (p<0.005). There was an inverse correlation between the CRP values of the patients and their BMI and anthropometric measurements (p<0.005). An inverse correlation was also found between NRS-2002 and the patient's weight and anthropometric measurements (p<0.005). A positive correlation was found between the patients receiving chemotherapy and albumin, BMI, and anthropometric measurements, and an inverse correlation with CRP values and weight loss in the last 3 months and NRS-2002 (p<0.005).

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There was a positive correlation between radiotherapy and CRP (p<0.005). While there was an inverse relationship between metastases and albumin values, anthropometric measurements, and BMI in patients, a positive correlation was found with CRP and NRS-2002 (p<0.005). An inverse relationship was found between age, albumin, BMI, and anthropometric measurements, and a positive relationship with CRP and NRS-2002 (p<0.005). The frequency of receiving chemotherapy (p=0.06) and the incidence of metastasis (p<0.01) were found to be high in cases receiving nutritional therapy (p<0.005)

Conclusion: Cases diagnosed with lung cancer should be screened for any other diseases, quality of life, risk of malnutrition, and nutritional status from the time of diagnosis. We believe that the expected survival of patients can be extended by taking precautions for nutrition together with early medical treatment.

Keywords: Lung cancer, Nutrition, Malnutrition, NRS 2002

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INTRODUCTION

While the ratio of lung cancer has decreased all over the world in recent years, lung cancer remains the most common cause of cancer-related deaths in men and women. The vast majority of cases are detected at an advanced stage at the time of diagnosis. In lung cancer, whose average life span is limited to months even with the best treatment, new treatments developed in recent years, such as immunotherapy and targeted therapies, have significantly prolonged life expectancy in some patient groups with local, locally advanced, and metastatic disease. However, predicting the average life expectancy in lung cancer remains of great importance. One of the main factors that can change the average survival is weight loss, which is an indicator of malnutrition. Body mass index and nutritional parameters are other factors that can be used to determine the average life expectancy of lung cancer patients.

Among cancers, especially lung and gastrointestinal system cancers, one of the most common complications is malnutrition (1). Due to malnutrition, the response to chemotherapy and radiotherapy becomes difficult in cancer patients. It also increases the complications related to the disease, mortality, length of hospital stay, and cost. Malnutrition causes a significant decrease in the quality of life in patients since the diagnosis of cancer (2). For this reason, it is very important to evaluate cancer cases for the possibility of malnutrition from the time of diagnosis, to take the necessary precautions, and to treat them if necessary (3,4).

Cancer cachexia, which can be seen after malnutrition resulting from cancer, often causes loss of muscle mass and is responsible for a large portion of deaths due to cancer (5-6). In cancer cases, the feeling of quick satiety, changes in the functions of the gastrointestinal tract, pain, side effects of medications used for pain palliation (such as constipation, bowel movement disorders), side effects secondary to

chemotherapy (such as nausea, vomiting, loss of taste and smell in the mouth, dryness in the mouth) are various reasons that reduce oral intake and cause secondary weight loss (7-9).

Cancer cachexia, on the other hand, is characterized by the loss of skeletal muscle mass that cannot be fully recovered with current nutritional supplements, as well as the regression of physical activities, with or without fat loss (10). Cancer cachexia has an important place among the causes of death (11).

To show the decrease in skeletal muscle mass, it is necessary to define reference values according to gender and to make body composition measurements in accordance with certain standards. The commonly accepted rule is that absolute muscle mass should be below the 5th percentile. This is calculated as follows:

- By anthropometric measurement of middle upper arm muscle area: <32 cm^2 in men, <18 cm^2 in women
- Dual energy X-ray absorptiometry calculated extremity skeletal muscle mass index: <7.26 kg/m^2 in men, <5.45 kg/m^2 in women
- Lumbar skeletal muscle mass index determined by CT: <55 cm^2/m^2 in men, <39 cm^2/m^2 in women
- Total body mass index excluding adipose tissue as assessed by bioelectrical impedance: <14.6 kg/m^2 in men, <11.4 kg/m^2 in women

It has been recommended to measure direct muscle mass in cases such as diffuse edema in the body, the presence of a large tumor mass, and obesity (12).

Evaluating the nutritional status of patients diagnosed with lung cancer, identifying cases with malnutrition or those at risk of malnutrition, as well as cases needing nutritional support, evaluating body compositions, and observing the effect of nutritional support can lead to increased survival in patients diagnosed with lung cancer.

MATERIAL AND METHODS

This study was conducted on 266 volunteer patients, 216 men and 50 women, aged 18 and over, who were diagnosed with lung cancer and admitted to Adana City Training Hospital Medical Oncology Clinic between 2020-2021. Demographic information, laboratory results, nutritional risks according to NRS-2002 scoring, BMI values, body compositions, and treatments (chemotherapy, radiotherapy, immunotherapy, surgery) were recorded. A questionnaire consisting of five sections was applied to the patients. In the first part of the questionnaire, descriptive information of individuals, their existing diseases, whether they have habits such as smoking and alcohol, and the drugs they use were questioned. The second part of the questionnaire includes anthropometric measurements and body fat percentage analysis, while the fourth part includes the biochemical findings (CRP, albumin, etc.) of the patients. In the fifth part of the questionnaire, the malnutrition risk of

the patients was determined with the NRS-2002 screening tool.

Anthropometric measurements of individuals were made in accordance with standards. From anthropometric measurements, the weight (kg) and height (cm) of the individuals were measured according to the technique. The patient's body weight, body fat ratio, lean body mass, and body water ratio were measured with the Tanita MC 780 bioelectrical impedance device. Body mass index (BMI kg/m²) and the ratio of body weight to height (m²) were calculated.

The patients included in the research were evaluated according to the definition of Fearon cancer cachexia (10):

1. Involuntary loss of more than 5% of body weight in the last 6 months (without simple fasting); or
2. BMI below 20 kg/m² with any unintentional weight loss of more than 2%
3. FFMI (fat-free mass index) <14.6 kg/m² in men; <11.4 kg/m² in women

Among the blood findings evaluated were albumin and CRP. All measurements were made in Adana City Training and Research Hospital Central Laboratories.

The NRS-2002 screening tool was applied to the patients in order to evaluate their nutritional status and to determine the risks of malnutrition. The reason for choosing this screening tool is that it is recommended by ESPEN and is suitable for oncological patients.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) 23.0 was used for statistical analysis of the data. Categorical evaluations were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). Chi-square and Fisher's exact tests were used to compare categorical parameters. The Shapiro-Wilk test was used to determine whether the parameters in the study showed a normal distribution. The Mann-Whitney test was used in paired group analysis for parameters that did not show normal distribution, and the Kruskal-Wallis test was used in the analysis of more than two groups. The Bonferroni method, one of the post hoc analyses, was used to determine the source of the difference between the groups. Spearman correlation tests were used to determine the relationship between variables. The level of statistical significance was set at 0.05 in all tests. Our research was approved by the Adana City Hospital ethics committee (12.02.2020-714) and was performed in accordance with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Additionally, this research was produced from the internal medicine specialty thesis.

RESULTS

In this study, we evaluated 266 cases diagnosed with lung cancer. The mean age of the patients was 61.7±10.5 years, and the mean height was 167.2±7.9 cm. While there was no metastasis in 114 (42.9%) of the patients, it was determined that 152 (57.1%) of them were

metastatic. Accordingly, it was determined that 86.1% (n=229) of the patients received chemotherapy, 18.0% (n=48) received radiotherapy, 7.5% (n=20) received immunotherapy, and 13.5% (n=36) underwent surgical procedures (Table 1 and Table 2).

Table 1. General characteristics of individuals

	Frequency (n)	Percent (%)
Gender		
Male	216	81.2
Woman	50	18.8
Metastasis		
No	114	42.9
There is	152	57.1
Educational Status		
Primary school	127	47.7%
High school	84	31.5%
Degree	55	20.6%
Presence of Comorbid Disease		
No	105	23.4%
There is	161	60.5%
Comorbid Disease		
Hypertension	26	16.1%
COPD	23	14.28%
	Mean±sd	Median (Min-Max)
Age	61.7±10.5	62 (28-94)
Size	167.2±7.9	168 (142-190)

Table 2. Distribution of individuals according to their treatment status

	Frequency (n)	Percent (%)
Chemotherapy		
Not received	37	13.9
Has taken	229	86.1
Radiotherapy		
Not received	218	82.0
Has taken	48	18.0
Immunotherapy		
No	246	92.5
There is	20	7.5
Surgical procedure		
Not done	230	86.4
Made	36	13.5

The mean BMI of the individuals included in the study was 25.5±5.2. It was determined that 17.3% (n=46) had a BMI value of 20 and below, and 82.7% (n=220) had a BMI above 20. In patients at risk of malnutrition, the frequency of having a BMI of 20 and below ($p<0.001$) and the frequency of experiencing weight loss in the last 3 months ($p=0.045$) were found to be considerably higher ($p<0.05$).

The patients CRP value showed a weak inverse correlation with weight ($r=-0.234$), BMI ($r=-0.258$), fat mass ($r=-0.237$), abdominal muscle thickness ($r=-0.189$), upper middle arm muscle thickness ($r=-0.243$) and thigh thickness ($r=-0.246$) ($p<0.05$).

Weight (r=-0.301), BMI (r=-0.324), fat mass (r=-0.312), abdominal muscle thickness (r=-0.238), upper middle arm muscle thickness (r=-0.339), and thigh thickness (r=-0.340) showed a weak inverse correlation with the NRS-2002 value ($p<0.05$).

The patients' chemotherapy status showed a weak inverse correlation with albumin (r=-0.201), BMI (r=-0.141), and fat mass (r=-0.162), while showing a weak positive correlation with CRP (r=0.308), weight loss (r=0.168), and NRS-2002 (r=0.182) ($p<0.05$).

The presence of metastases showed a weak inverse correlation with albumin (r=-0.378), weight (r=-0.293), BMI (r=-0.280), fat mass (r=-0.275), abdominal muscle thickness (r=-0.218), upper middle arm muscle thickness (r=-0.315), and thigh thickness (r=-0.312), while showing a strong positive correlation with CRP (r=0.718) and NRS-2002 (r=0.811) values ($p<0.05$) (Table 3).

Table 3. Evaluation and distribution of anthropometric measurements of patients

	Mean±sd	Median (Min-Maks)
Weight	71,1±15,8	69,7 (40-118,4)
Size	167,1±7,9	168 (142-190)
BMI	25,45±5,19	25,7 (12,6-43,3)
Fat mass	16,76±9,38	15,8 (1,1-50)
Abdominal muscle thickness	98,7±59,4	94 (25-1001)
Upper middle arm muscle thickness	27,4±4,2	28 (9-40)
Thigh thickness	43,68±6,78	44 (23-68)

BMI: Body mass index

When the relationships between the patients' anthropometric measurements, albumin and CRP values, and NRS-2002 were examined, the patients albumin value showed a weak positive correlation with weight (r=0.307), BMI (r=0.289), fat mass (r=0.282), abdominal muscle thickness (r=0.246), upper middle arm muscle thickness (r=0.289), and thigh thickness (r=0.312) ($p<0.05$) (Table 4).

Table 4. Investigation of the relationship between anthropometric measurements, albumin and CRP values of patients and NRS 2002

	Albumin		CRP		NRS 2002	
	r	p	r	p	r	p
Weight	0.307**	<0.001	-0.234**	<0.001	-0.301	<0.001
Size	0.085	0.188	0.011	0.867	0.025	0.696
BMI	0.289**	<0.001	-0.258**	<0.001	-0.324	<0.001
Fat mass	0.282**	<0.001	-0.237**	<0.001	-0.312	<0.001
Abdominal muscle thickness	0.246**	<0.001	-0.189**	0.003	-0.238	<0.001
Upper middle arm muscle thickness	0.289**	<0.001	-0.243**	<0.001	-0.339	<0.001
Thigh thickness	0.312**	<0.001	-0.246**	<0.001	-0.340	<0.001

BMI: Body mass index * p<0.05, Spearman correlation test

DISCUSSION

Lung cancer is the most common cause of cancer-related deaths in men and women. Malnutrition causes an important decrease in the quality of life in patients starting from the diagnosis of cancer (13). Martin et al. (9) evaluated the percentage of BMI and weight loss in cancer cases (n=8160) . The mean BMI was 24.4±5.1 kg/m², and it was concluded that low weight loss and high BMI (≥25.0 kg/m²) increased the survival time independent of the cancer stage, the patient's performance and age. While the mean BMI of the individuals included in our study was 25.5±5.2 kg/m², it was determined that 17.3% (n=46) had a BMI value of 20 and below, and 82.7% (n=220) had a BMI above 20. Similarly, in our study, there was a significant correlation between those with BMI <20 and those with weight loss in the last 3 months, indicating that these patients are at higher risk of malnutrition (Figure 1)

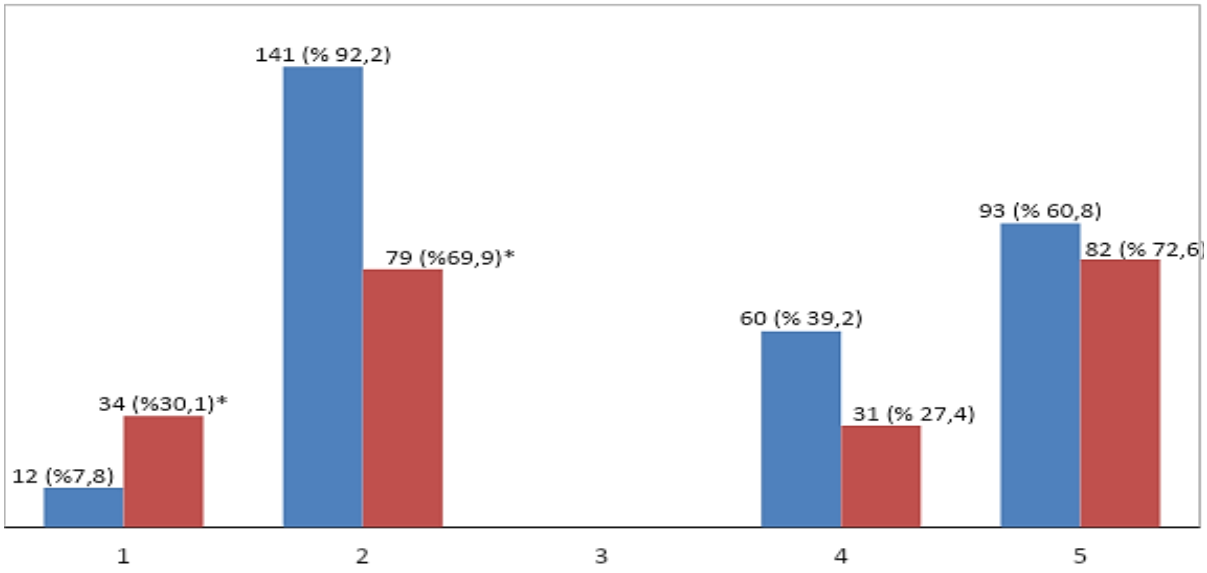

Figure 1. The relationship between malnutrition risk and BMI and weight loss findings in the last 3 months (blue column there is no risk of malnutrition, red there is a risk of malnutrition)

Muscle wasting in cancer is considered an indicator of poor quality of life, impaired functionality, and shortened survival (14). Jeejeebhoy (15) emphasized that muscle dysfunction secondary to malnutrition precedes changes in anthropometric measurements and laboratory parameters. There are many studies showing that it is related (16). In our study, although the UOCC was 27.4±4.2, malnourished cases were found to have statistically significantly lower calf circumference and upper middle arm muscle circumference than non-malnutrition cases. This is consistent with the results of studies by Christensen et al. (17) and Norman et al. (18)

Wu et al. (23) in a study on albumin values, identified individuals with normal nutritional status as having albumin values of 3.5 g/dL and above, mildly malnourished individuals as 3.1-3.4 g/dL, moderately malnourished individuals as 2.6-3.0 g/dL, and severely malnourished individuals as 2.5 g/dL and below. Ryu et al. (19) found the albumin value of well-nourished patients to be 3.86±0.3 g/dL in another study. The albumin value of cases with malnutrition was found to be 3.85±0.3 g/dL. In light of all this data, it is possible to detect the negative changes in the biochemical values of cancer cases whose nutritional status has deteriorated. Fanrong Zhang et al. emphasized that the CRP/albumin ratio was an independent predictor of disease progression and mortality in 617 patients with non-small cell lung cancer who were operated on in a retrospective clinical study (20). Ying Jin et al. conducted a meta-analysis that included 1,649 cases from eight clinical studies, emphasizing that CRP levels in patients with non-small cell lung cancer may be a determining factor in the prognosis of the disease and response to treatment (21). Similarly, in our study, CRP values were found to be higher in patients with metastatic lung disease, and the decrease in albumin values

and the decrease in BMI values were parallel with the increase in CRP values in an inverse proportion to these values.

Gavazzi et al. (4) found that the BMI rates of cases with NRS<3 were 26.1±3.2 kg/m², and the BMI rates of cases with NRS≥3 were 22.6±3.9 kg/m². There was a statistically significant distinction between the NRS 2002 groups in terms of mean body weight ratios ($p<0.001$). There was also a statistically significant distinction among the NRS 2002 groups in terms of mean weight loss values ($p<0.001$), with a statistically significant increase in mean weight loss as one goes towards NRS 4 (19). The weight loss rate of patients with NRS <3 was 0.89±1.4%, while the weight loss rate of patients with NRS ≥3 was 6.42±4.6%, which was statistically significant. Similar to our research, it was found that as the NRS 2002 score increased in cases with lung cancer, BMI decreased and weight loss in the last 3 months increased.

Tsai et al. (22) determined that there is a significant relationship between the MNA screening test, which is a screening method similar to NRS-2002, and MCQ and BMI values.

According to Vergara et al. (24) the malnutrition rate was reported as 40.21% in patients receiving chemotherapy. In another study, the malnutrition rate was found to be 86.3% in 74 adult lung and GIS cancer cases treated with chemotherapy, and it was determined that these cases were more prone to weight loss (25). Similarly, Ramos Chavez et al. (26) found that the risk of malnutrition was higher in lung and colorectal cancer cases. In two separate studies conducted on patients receiving radiotherapy treatment, malnutrition percentages were reported as 37.8% and 60%, respectively (27,28).

In our study, while the NRS 2002 score and CRP values increased in patients receiving chemotherapy, the susceptibility to hypoalbuminemia also increased. Additionally, it was determined that patients who received chemotherapy lost weight in the last 3 months. While there was no relationship between the status of receiving radiotherapy and NRS 2002, albumin values, and weight loss, there was a positive relationship with CRP values. If we evaluate in the light of these data, while the risk of malnutrition increases in patients receiving chemotherapy, the risk is also present in radiotherapy, but it is more pronounced in chemotherapy.

According to a study conducted in France, the presence of lung cancer and metastases had a direct effect on the risk of malnutrition as a result of records obtained from 154 hospitals (29). In our study, 57.1% of cases diagnosed with lung cancer were found to be metastatic. While the NRS 2002 score was higher in cases with metastatic lung cancer, a similar increase in CRP values was observed ($p<0.005$). In the follow-up of patients with metastatic lung cancer, significant weight loss was observed in the last 3 months, and it is noteworthy that the upper arm muscle thickness decreased. The significant determination of these parameters used in the evaluation of nutritional status indicates that metastasis status significantly increases the risk of malnutrition.

CONCLUSION

The incidence of lung cancer has tended to decrease significantly with the reduction of modifiable etiological factors such as smoking. However, lung cancer is still the most widespread cause of death in men and women worldwide. In advanced, locally advanced, or localized lung cancer, with newly developed systemic therapies such as targeted therapies and immunotherapy, the success of treatment seems to increase significantly in cases with locally advanced and localized disease, where the survival of some cancer patients with advanced disease is significantly prolonged.

Malnutrition, on the other hand, is very common in patients with lung cancer and is a factor that directly affects life expectancy and quality of life. For this reason, detecting malnutrition, which is very common in all cancer patients, especially lung cancer patients, using many parameters and screening methods, especially in the early period, is crucial. Early detection and treatment of malnutrition will significantly increase the success of treatment and quality of life in cases with lung cancer.

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Ethical Statement: This article was produced from the thesis titled "Akciğer Kanserli Hastalarda Tanı Tedavi Takip Esnasında Beslenme Durumunun Değerlendirilmesi," which was conducted with the approval of the Scientific Research Ethics Committee of Adana City Hospital (Approval Number: 12/02/2020-714)

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