Low prognostic nutrition index predicts poorer quality of life in late-stage lung cancer

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Background: Quality of life (QOL) is one of the most important endpoints in lung cancer care. Both nutritional and immune status reportedly correlate with QOL, so we investigated whether the prognostic nutritional index (PNI), a reliable marker of nutritional and immune status, can predict QOL in late-stage lung cancer.

Methods: We enrolled 80 lung cancer patients and their clinical data including PNI were obtained. The FACT-L questionnaire in Chinese version 4 was administered to every patient.

Results: Of the 80 lung cancer patients, 16 were stage III and 64 were stage IV. The average PNI value was 44.24±5.53. The average FACT-L score was 99.58±21.84, indicating impaired QOL. The FACT-L score in the stage IV group was significantly lower than that in the stage III group (P=0.001), especially for the four subscales of physical, social/family, emotional, and functioning well-being. In the stage IV group, the FACT-L score in the high PNI group was significantly higher than that in the low PNI group (P=0.042), with especially higher score for the physical well-being subscale. PNI was significantly related to both the FACT-L score (r=0.3265, P=0.0085) and physical well-being subscale (r=0.4746, P<0.0001).

Conclusions: PNI is a simple but valuable biomarker of QOL in stage IV lung cancer patients. A lower PNI may indicate the need for detailed QOL evaluation and intervention.

Keywords: Lung cancer; prognostic nutrition index (PNI); quality of life (QOL)

Introduction

For decades, lung cancer has remained the most prevalent cancer worldwide with high morbidity and mortality rate (1,2). In GLOBOCAN 2018, lung cancer was estimated to account for 11.6% of all new cancer cases, and 18.4% of the total cancer deaths (3). In China, the prevalence of lung cancer is still rising, but the mortality rate is decreasing because of advances in medical treatment and diagnosis in the past decade (4). Nevertheless, most lung cancer patients

have a high burden of psychological suffering leading to poor quality of life (QOL), which is related to unfavorable outcomes (5,6). Although it has been proved that high QOL is a positive predictor of prognosis in lung cancer (7,8), the complex physical and psychological consequences of the disease that typically affect patients are still overlooked in the common disease-centered approach (9,10). Consequently, QOL is an issue of importance for lung cancer patients, but its evaluation requires administration of tedious questionnaires such as EORTC QLQ-C30 and so

is not routinely performed in daily clinical practice (11,12). Thus, a simple but reliable biomarker of QOL in lung cancer patients would be helpful.

Nutritional status is related to QOL in lung cancer patients (13), and several parameters for evaluating nutritional status have been proposed, such as serum albumin, the prognostic nutritional index (PNI), body mass index (BMI) and the subjective global assessment (SGA) (14-16). The calculation of the PNI is based on the concentration of albumin and the lymphocyte count [10 × albumin (g/dL) + 0.005 × lymphocyte count (/mm^3)]. Thus, the PNI comprehensively reflects both the nutritional and immune status of the patient and has proven reliable in predicting survival of lung cancer patients (17,18). However, the predictive value of the PNI for the QOL of late-stage lung cancer patients is unclear, so we investigated the relationships among PNI, the clinicopathological characteristics and QOL in late-stage lung cancer patients.

We present the following article in accordance with the MDAR reporting checklist (available at http://dx.doi.org/10.21037/apm-20-1892).

Methods

Study design and patients

From January 2019 to December 2019, 80 patients with newly diagnosed lung cancer in the Department of Pulmonary and Critical Medicine of the First Affiliated Hospital of Sun Yat-sen University were included in the study. Inclusion criteria were as follows: diagnosis of histopathologically confirmed stage III or IV lung cancer; age 18–80 years; and Eastern Cooperative Oncology Group (ECOG) score ≤2. Exclusion criteria included patients with poor functional performance status, who refused to take part in the study, who had received previous systemic treatment such as radiotherapy and/or chemotherapy, and patients with signs of acute infection. Clinical data were obtained after the patient's first admission to the Department, including medical history, blood cytology and chemistry, definitive histopathological diagnosis, and clinical tumor-node-metastasis (TNM) stage (19), as well as ECOG score determined by the clinical oncologist.

All subjects gave written consent after they were fully informed of the study's objectives and methods. The study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University. All subjects were required to be able to

independently complete a questionnaire. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

QOL evaluation

The QOL evaluation was performed at baseline, which was 7 days prior to initiation of systemic therapy. We used the Chinese version 4 of the FACT-L questionnaire, which has five domains (subscales): physical well-being (PWB, 7 items), social/family well-being (SFWB, 7 items), emotional well-being (EWB, 6 items), functioning well-being (FWB, 7 items) and additional concerns-lung (LCS, 9 items). The details of this questionnaire were described in a previous study (20).

Statistical analysis

All data analyses were performed using SPSS software (version 18.0) (SPSS Inc., Chicago, IL, USA). Continuous variables are shown as average means with standard deviation or median with range. Differences between groups were analyzed by the Student's t-test for those that were normally distributed, and by the Mann-Whitney U test for those that were not. Multivariate analysis of factors associated with QOL used the linear multiple regression model. $P<0.05$ was considered statistically significant. Statistical analyses were performed using GraphPad Prism5.

Results

Characteristics of the study subjects

The majority of the 80 late-stage lung cancer patients were male (68.8%), with an average age of 61.20± 11.01 years, mean BMI of 22.03±2.84 kg/m^2, mean serum albumin of 37.62±5.02 g/L, mean blood lymphocyte count of (1.32±0.48)×10^3/mm^3 and mean hemoglobin of 118.34±21.56 g/L. The most common pathological type was adenocarcinoma (66.3%). Most of the patients had an ECOG score 0–1 (84.09%). The average PNI value was 44.24±5.53, and the average FACT-L score was 99.58±21.84, which indicated impaired QOL. Details are shown in *Table 1*.

PNI and stage of lung cancer

The patients were divided according to clinical stage into

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Table 1 Clinical characteristics of the lung cancer patients

Parameter	N=80
Gender	
Male	55
Female	25
Age (years)	61.20±11.01
Height (m)	1.65±0.08
Weight (kg)	60.06±9.85
BMI (kg/m²)	22.03±2.84
Histology	
Adenocarcinoma	53
Squamous cell carcinoma	19
Small-cell carcinoma	6
Other	2
TNM stage	
III	16
IV	64
ECOG	
0	44
1	30
≥2	6
Albumin (g/L)	37.62±5.02
Lymphocytes (×10³/mm³)	1.32±0.48
Hemoglobin (g/L)	118.34±21.56
PNI	44.24±5.53
FACT-L score	99.58±21.84
Physical well-being	20.79±6.38
Social/family well-being	20.80±4.37
Emotional well-being	16.45±6.34
Functioning well-being	17.13±7.06
Additional concerns-lung	24.16±5.75

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group performance status; PNI, prognostic nutritional index.

stage III (n=16) and stage IV (n=64). There were more male patients in the stage III group, but no significant differences were observed between the two groups with regard to age, sex, height, weight, and BMI. The pathological types and ECOG scores were similar between groups. There were
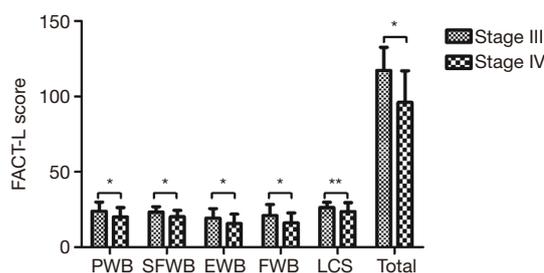

Figure 1 Comparison of FACT-L total score and each scale in stage III and stage IV lung cancer patients. *, P<0.05; **, P>0.05. PWB, physical well-being; SFWB, social/family well-being; EWB, emotional well-being; FWB, functioning well-being; LCS, additional concerns-lung; PNI, prognostic nutritional index.

no significant differences in serum album, hemoglobin, lymphocyte count or PNI. However, the FACT-L score in the stage IV group was significantly lower than that in the stage III group (P=0.001). The stage IV group had lower scores for the subscales of PWB, SFWB, EWB, and FWB; however, no significant differences were found for the subscale of LCS (*Figure 1*, *Table 2*).

PNI and QOL in stage IV lung cancer

All stage IV lung cancer patients were divided into low PNI (≤44, n=28) and high PNI (>44, n=36). The high PNI group had higher levels of serum album, hemoglobin and lymphocytes (*Figure 2*). The FACT-L score in the high PNI group was significantly higher than that in the low PNI group (P=0.042), with an especially higher score for the PWB subscale. However, no significant differences were observed for the other four subscales (*Figure 3*, *Table 3*).

Correlation between PNI and FACT-L in stage IV lung cancer

In the stage IV group of lung cancer patients, PNI was significantly related to FACT-L (r=0.3265, P=0.0085). Further correlation analysis showed that PNI was positively related to the subscale of PWB (r=0.4746, P<0.0001), but there was no statistical significance observed between PNI and SFWB, EWB, FWB or LCS (*Figure 4*).

Determinants of QOL

Variables including age, sex, BMI, hemoglobin, and PNI were analyzed in a regression equation: FACT-L score =

Table 2 Clinical characteristics of stage III and IV lung cancer patients

Parameter	Stage III (N=16)	Stage IV (N=64)	P
Gender			0.016
Male	15	40	
Female	1	24	
Age (years)	65.06±9.92	60.23±11.12	0.117
Height (m)	1.68±0.06	1.64±0.08	0.078
Weight (kg)	60.41±9.27	59.98±10.06	0.877
BMI (kg/m^2)	21.38±2.72	22.20±2.87	0.305
Histology			0.013
Adenocarcinoma	7	46	
Squamous cell carcinoma	6	13	
Small-cell carcinoma	1	5	
Other	2	0	
ECOG			0.578
0	9	35	
1	7	23	
≥2	0	6	
Albumin (g/L)	36.13±6.44	37.99±4.59	0.187
Lymphocytes (×10^3/mm^3)	1.37±0.47	1.31±0.48	0.653
Hemoglobin (g/L)	121.06±24.08	117.66±21.04	0.575
PNI	42.99±6.79	44.55±5.19	0.316
FACT-L score	117.35±15.34	96.02±21.01	0.001
Physical well-being	23.88±6.04	20.02±6.27	0.030
Social/family well-being	23.31±3.61	20.17±4.34	0.0009
Emotional well-being	19.31±6.43	15.73±6.17	0.043
Functioning well-being	21.06±7.29	16.14±6.70	0.012
Additional concerns-lung	26.25±4.86	23.64±5.87	0.105

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group performance status; PNI, prognostic nutritional index.
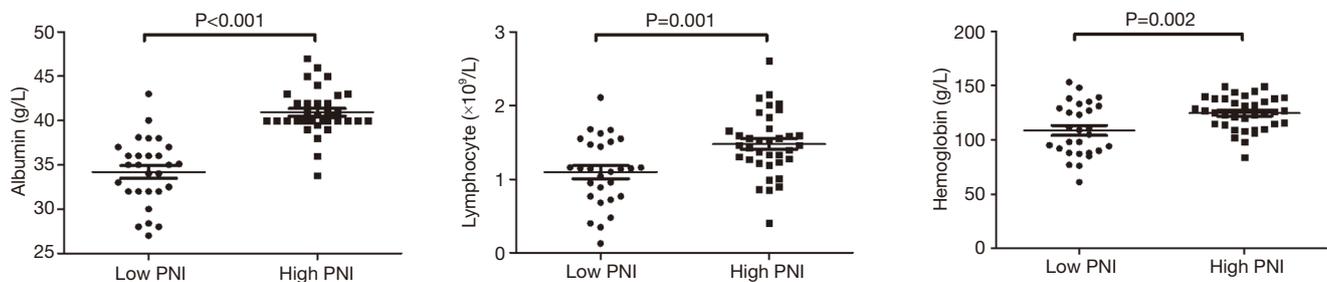
Figure 2 Comparison of nutritional parameters in lung cancer patients with low PNI and high PNI. PNI, prognostic nutritional index.
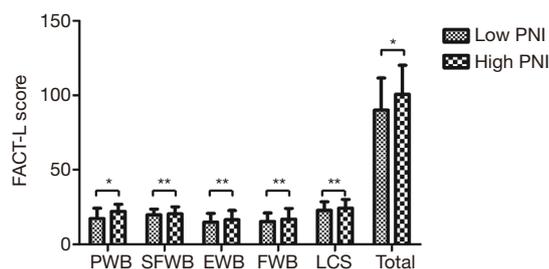
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Figure 3 Comparison of FACT-L total score and each scale in lung cancer patients with low PNI and high PNI. *, P<0.05; **, P>0.05. PNI, prognostic nutritional index; PWB, physical well-being; SFWB, social/family well-being; EWB, emotional well-being; FWB, functioning well-being; LCS, additional concerns-lung; PNI, prognostic nutritional index.

37.128 + 1.322 × PNI. PNI was an independent determinant of FACT-L score (P=0.008).

Discussion

In this study, we analyzed the clinical characteristics and QOL of late-stage lung cancer patients. In particular, we evaluated the relationship of PNI and QOL. The stage IV lung cancer patients had a lower FACT-L score than the stage III patients, and their PNI correlated with their FACT-L scores. Therefore, a low PNI could be a predictor of poorer QOL in this group of lung cancer patients.

QOL is defined as an individual's self-reported sense of well-being, and is measured by several scales such

Table 3 Clinical characteristics of stage IV lung cancer patients with low and high PNI

Parameter	Low PNI (N=28)	High PNI (N=36)	P
Gender			0.802
Male	18	22	
Female	10	14	
Age (years)	60.18±9.54	60.28±12.35	0.972
Height (m)	1.65±0.08	1.63±0.08	0.502
Weight (kg)	58.73±10.74	60.94±9.53	0.387
BMI (kg/m^2)	21.48±2.94	22.75±2.72	0.079
Histology			0.592
Adenocarcinoma	21	25	
Squamous cell carcinoma	6	7	
Small-cell carcinoma	1	4	
ECOG			0.372
0	13	22	
1	11	12	
≥2	4	2	
Albumin (g/L)	34.22±3.80	40.93±2.55	<0.001
Lymphocytes (×10^9/L)	1.10±0.46	1.48±0.43	0.001
Hemoglobin (g/L)	108.79±24.19	124.56±15.27	0.002
FACT-L score	90.00±21.74	100.69±19.45	0.042
Physical well-being	17.32±6.94	22.11±4.82	0.002
Social/family well-being	19.79±3.88	20.47±4.70	0.535
Emotional well-being	14.82±5.98	16.44±6.30	0.300
Functioning well-being	15.32±5.69	16.78±7.41	0.393
Additional concerns-lung	22.75±5.85	24.33±5.87	0.288

PNI, prognostic nutritional index; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group performance status.
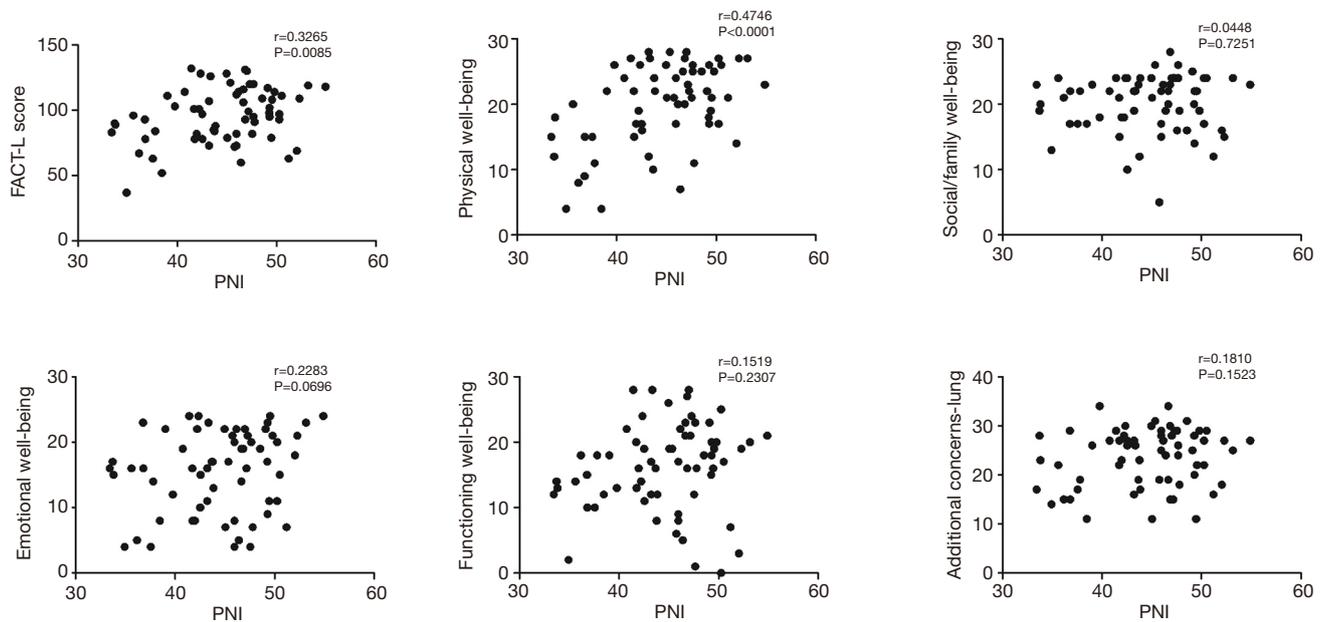
Figure 4 Correlation of PNI and FACT-L score including all subscales in stage IV lung cancer patients. PNI, prognostic nutritional index.

as physical, social, functional, and emotional well-being (21,22). Studies have shown that higher baseline/pretreatment QOL is associated with longer overall survival (23,24), so to some extent improving QOL by effective palliation of cancer-related symptoms is as important as curing the cancer (25).

It has been proposed that QOL should be a routine evaluation in lung cancer care and many instruments have been developed for this purpose (26). However, in daily clinical practice the evaluation is not always performed for every patient because administering and completing questionnaires can be time consuming, which suggests the need for a simple means of identifying patients at high risk of low QOL.

In our study, we found the stage IV lung cancer patients had lower FACT-L scores than the stage III patients, especially for the subscales of PWB, SFWB, EWB, and FWB, which can be explained by distant metastasis of the lung cancer. The most common metastatic sites of lung cancer include the brain, bone and pleura (19), and the fatigue and pain from the cancer lesions, as well as psychological symptoms and comorbidities lead to a decrease in QOL (27).

Malnutrition is common in lung cancer patients because of the tumor itself and the systemic therapy (28,29). It has

been reported that approximately 34–69% of lung cancer patients are malnourished, and the percentage of patients at risk of malnutrition might be even higher (30). Cancer-related symptoms such as loss of appetite, pain, coughing and fatigue can lead to insufficient energy intake, while abnormal protein and energy metabolism by the cancer cells and aberrant systemic inflammatory reactions result in energy overconsumption.

The PNI was first introduced by Onodera *et al.* in 1984 to evaluate the risk of postoperative complications according to baseline nutritional status in gastric cancer patients (31). The PNI reflects the nutritional and immune status of patients and has proved to be a reliable predictor of survival in several malignancies including lung cancer (32).

In our study, the average PNI of the late-stage lung cancer patients was 44.24±5.31, reflecting impaired nutritional and immune status. The PNI correlated with QOL in stage IV lung cancer patients, especially in the subscale of PWB, which suggests that improving both nutritional and immune status might be beneficial for improving QOL, but further research is needed to confirm this. A possible reason for the correlation between low PNI and poor QOL in stage IV lung cancer patients is that they more frequently develop the cachexia syndrome due to disease severity, which contributes to the state

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of malnutrition through increased fatigue and pain, psychological symptoms and comorbidities, eventually leading to decreased QOL (33,34). Another important factor is immune status: a lower PNI correlates with impaired immune status, which leads to treatment failure and increased comorbidities (35).

However, no statistically significant correlation between the PNI and QOL was observed in stage III lung cancer patients, and a possible explanation would be the difference in disease severity. Greater severity of disease symptoms correlates with lower QOL (36). Stage III lung cancer patients may have less severe symptoms, so the PNI was less able to predict QOL in this group of patients.

There are several limitations in our study. First, this was an observational study with a relatively small number of patients. Second, we focused on the baseline PNI and QOL of late-stage lung cancer patients. A large, prospective study is needed to confirm the relationship of nutrition and immune interventions and QOL.

Conclusions

PNI was a marker of QOL in stage IV lung cancer patients. Lower PNI may indicate the need for QOL interventions, making it a simple biomarker for use in lung cancer management. However, further study is needed to clarify the exact role of PNI in lung cancer.

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Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at http://dx.doi.org/10.21037/apm-20-1892

Data Sharing Statement: Available at http://dx.doi.org/10.21037/apm-20-1892

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-20-1892). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All subjects gave written consent after they were fully informed of the study's objectives and methods. The study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University. All subjects were required to be able to independently complete a questionnaire. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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