

Original Article

Effects of overall enteral nutrition management overall on nutritional condition and life quality of NSCLC patients treated by apatinib combined with chemoradiotherapy

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Abstract: Objective: In this study, the effects of enteral nutrition nursing care intervention under overall nutrition management on nutritional condition and life quality of NSCLC patients treated by Apatinib combined with chemoradiotherapy were discussed and analyzed. Methods: Totally 86 inoperable stage-III NSCLC patients hospitalized from April 2018 to January 2020 were recruited and divided into two groups, the control group and the observation group (n=43 for each group), based on the date of admission. The two groups of patients both received Apatinib combined with chemoradiotherapy. Based on chemoradiotherapy, the control group received routine enteral nutrition intervention while the observation group received enteral nutrition nursing care intervention under overall nutrition management. The nutritional indices, changes in nutritional knowledge level, changes in T-lymphocyte subsets and incidences of adverse reactions to chemotherapy in each group of patients were compared before and after intervention. Results: After intervention, the patients in the observation group had remarkably higher nutritional indices ($P<0.05$), as well as higher nutritional knowledge level than those of the control group. In addition, the percentages of CD_3^+ , CD_4^+ cells, values of CD_4^+/CD_8^+ , and SF-36 scores in the observation group were significantly higher than those in the control group ($P<0.05$); while the incidence of grade III-IV adverse reactions in the observation group was significantly lower than that in the control group (13.95% vs. 32.56%, $P<0.05$). Conclusion: For those patients with inoperable stage III NSCLC treated by Apatinib combined with chemoradiotherapy, nursing intervention of enteral nutrition under full nutrition management overall can effectively improve their nutritional condition and knowledge level, enhance their life quality, protect their immune function, and reduce the incidence of serious adverse reactions to chemoradiotherapy. Therefore, this method is worthy of clinical promotion.

Keywords: Overall nutrition management, apatinib, chemoradiotherapy, non-small cell lung cancer, nutritional condition

Introduction

Clinically, radiotherapy combined with chemotherapy is mainly used as the first-line treatment for inoperable NSCLC patients in stage III to effectively alleviate and delay the development of the disease. However, due to local recurrence or distant metastasis, patients are generally in poor physical condition with decreased physiological functions [1, 2]. With the prolonged duration of chemotherapy, the drug resistance of patients continues to rise, and the drug strength is gradually decreased. The obvious toxic and side effects of chemo-

therapy and poor treatment compliance lead to poor overall clinical treatment effects. The clinical healing of patients is poor after the failure of standardized treatment [3, 4]. In recent years, with the advances of the research on tumor molecular biology, targeted therapy has received extensive attention by scholars. It can inhibit angiogenesis, tumor development and metastasis, thus contributing to the improvement of the clinical prognosis [5-7]. As a new small-molecule targeted drug against angiogenesis, Apatinib has been confirmed as the first safe and effective targeted drug with few clinical effects after the failure of standard chemo-

therapy, which can greatly extent the survival period of patients. Moreover, Apatinib is currently the only oral preparation of targeted drugs, which can effectively improve patients' treatment compliance [8, 9]. Apatinib combined with chemoradiotherapy in our hospital has a certain effect on patients with inoperable NSCLC in stage III. For patients treated with chemoradiotherapy, on the one hand, chemoradiotherapy increases their energy protein metabolism and water metabolism of patients; on the other hand, it can cause nausea, vomiting, bone marrow suppression and other adverse reactions, thus leading to different degrees of malnutrition in patients [10, 11].

Studies have shown [12, 13] that the consumption of NSCLC disease itself and adverse reactions during treatment may lead to malnutrition in patients, which will then lead to the decline in both clinical therapeutic efficacy and the patients' life quality. Therefore, nutritional support is essential for patients in the treatment process. The Committee of Cancer Nutrition and Supportive Therapy of China Anti-cancer Association recommends the use of enteral nutrition for nutritional interventions in cancer patients treated with chemotherapy. However, the complexity of condition of NSCLC patients treated with chemotherapy has led to unsatisfactory clinical effects of enteral nutrition intervention [14-16]. Therefore, how to effectively implement enteral nutrition support in clinical work to achieve better nutritional support effect has become the focus of scholars. This study is to discuss and analyze the outcome of enteral nutrition nursing care intervention under overall nutrition management on the nutritional condition and life quality of NSCLC patients treated by Apatinib combined with chemoradiotherapy.

Materials and methods

Clinical materials

Totally 86 inoperable NSCLC patients in stage III admitted to our hospital from April 2018 to January 2020 were recruited as the research objects, including 52 males and 34 females. The patients were aged 30 to 82, with an average age of 58.90 ± 13.97 . Pathological type: 53 patients with squamous cell carcinoma, 33 patients of adenocarcinoma; clinical classification: 23 cases at stage III A, 63 cases at stage

III B. The patients were divided into the control group and the observation group (n=43 for each group) based on the date of admission. The study was approved by the ethics committee of the principal investigating hospital.

The inclusive and exclusive criteria

Inclusive criteria: (1) All patients were diagnosed as NSCLC by histopathological biopsy; (2) KPS score ≥ 70 points; (3) Estimated survival period ≥ 3 months; (4) TNM stages were all in stage III; (5) All patients involved voluntarily signed the informed consents.

Exclusive criteria: (1) Patients that complicated with severe infection and severe anemia; (2) Patients whose leukocyte and platelet levels were below the normal range; (3) Patients who could not tolerate chemoradiotherapy; (4) Patients complicated with severe dysfunction of vital organs, such as heart, liver, kidney and lung.

Treatment methods

The two groups of patients were both treated by Apatinib combined with chemoradiotherapy with details as follows: (1) Radiotherapy: Adopted overall 3D-CRT by Siemens ONCOR linear accelerator. The patients were in supine position and fixed with vacuum body membrane and wing plate. Adopted simulated CT positioning, Lantis network data transmission system, Pinnacle planning system for conventional fractionated radiotherapy. (2) Chemotherapy: cisplatin (Jiangsu Hansoh Pharmaceutical Group Co., Ltd., H20040813, specification: 6 ml, 30 mg) chemotherapy, 25 mg/m² intravenous drip in d1~d3; vinorelbine (Hangzhou Minsheng Pharmaceutical Co., Ltd., H20051605, specification: 1 ml, 10 mg), 25 mg/m² intravenous drip in d1. (3) Targeted therapy: Oral ingested Apatinib Mesylate Tablets (Jiangsu Hengrui Medicine Co., Ltd., H20140103, specification: 0.25 g) with initial dose of 250 mg/d. If the patients had no obvious adverse reactions, the dose would be increased to 500 mg/d after two weeks later. All patients completed 4 courses of treatment, with each course of 28 days.

Intervention of nutritional support

The control group received independent oral enteral nutrition and routine nutritional health

guidance. The nurse in charge distributed nutrition publicity materials and relevant treatment information to the patients, conducted the publicity and education of nutritional knowledge, and timely answered the questions about nutrition raised by the patients and their families. Patients were advised to eat more frequently but less food at each time and take enteral nutrition preparations as a nutritional supplement in accordance with their preferences every day, such as Intacted Protein Enteral Nutrition Powder. There was no limit on the dosage.

The patients in the observation group took normal diet combined with enteral nutrition as energy supplement. They were also implemented with the overall nutrition management measures with details as follows: Both groups were taken care of by the same group of nurses, who received the training of health and nutrition knowledge before the implementation of overall nutrition management. The first nutrition assessment and nutritional grade assessment were carried out to estimate the nutritional energy and the corresponding nutrition management files were established for the patients after their admission; the NSCLC nutrition education publicity materials were distributed, and the individualized nutrition health education guidance was carried out for the patients; the individualized nutrition diet plan was drawn up based on the patients' own nutritional status, and the patients and their families were instructed to strictly implement with; the patients' food intake and compliance were evaluated on a weekly basis and the nutrition intervention plan was adjusted in time; during the intermission of chemotherapy, patients were given an out-of-hospital diet plan and followed up by calls and adjust if necessary. Enteral nutrition intervention under nutritional management was used throughout the treatment. The above-mentioned processes were drawn up into tables, and the existing problems were discussed and adjusted in time, therefore it can develop into a spiral upward management measures to continuously improve the management treatment.

Observational indexes

(1) The changes in nutritional indices before and after intervention between the two groups were compared, including hemoglobin, total

serum protein, and serum prealbumin. (2) The patients' nutrition knowledge levels before and after intervention were evaluated by the self-prepared *Nutrition Knowledge Level Questionnaire* of our hospital. The content of the questionnaire covered nutrients in food; sources of calories; nutritional differences between meat and soup; optimal sources of foods, such as protein, trace elements, dietary fiber and vitamins; knowledge of various nutrients in vegetables; effects of food on specific diseases and stimulation and protection of food on gastrointestinal tract. The scale had a total score of 100 points and contained a total of 20 items. The questionnaire scoring was based on a 0-5 point scoring method, and the higher scores indicated the better nutritional knowledge of the patient. (3) The venous blood of the two groups of patients was drawn before and after intervention, and the level of T-lymphocyte subsets of the patients' venous blood, including the proportions of CD_3^+ , CD_4^+ , CD_8^+ cells, was determined by flow cytometer, and the value of CD_4^+/CD_8^+ was calculated. (4) The questionnaire of SF-36 scale was used to survey and analyze the quality of life of the two groups of patients before and after treatment, which included social function (SF), mental health (MH), role physical (RP), role emotional (RE), physical functioning (PF), body pain (BP), vitality (VT), and general health (GH). The questionnaire was distributed by the trained nursing staff and collected by them on the spot. (5) The two groups' incidences of side effect on grade III to IV were compared in accordance with WHO classification criteria for toxic and side effects of chemotherapy.

Statistical analyses

The test was analyzed by software SPSS 22.0; ($\bar{x} \pm sd$) represented as the measuring data and *t*-test for comparison; Using percentage to describe the enumeration data and χ^2 test for comparison; $P < 0.05$, indicated that there is statistical significance of the difference.

Results

Clinical data

The differences in the clinical data between the two groups regarding gender, age, pathological type, and clinical stage were not statistically significant ($p > 0.05$), as shown in **Table 1**.

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Table 1. Comparison of the clinical data between the two groups of patients

Clinical data	The observation group (n=43)	The control group (n=43)	t/X ²	P
Gender				
Male	25	27	0.195	0.659
Female	18	16		
Age (years old, $\bar{x} \pm sd$)	58.47 \pm 13.27	59.64 \pm 15.22	0.380	0.705
Pathological type				
Squamous cell carcinoma	28	25	0.443	0.506
Adenocarcinoma	15	18		
Clinical stages				
Stage III A	13	10	0.534	0.465
Stage III B	30	33		

Table 2. Comparison of nutritional indexes before and after intervention ($\bar{x} \pm sd$)

Group	Time	Hemoglobin (g/L)	Albumin (g/L)	Total protein (g/L)
The observation group (n=43)	Before intervention	7.18 \pm 1.75	24.85 \pm 1.27	42.17 \pm 3.42
	After intervention	9.20 \pm 2.84*	28.59 \pm 2.10*	46.83 \pm 3.51*
	t	3.971	9.993	6.235
	P	0.000	0.000	0.000
The control group (n=43)	Before intervention	7.21 \pm 1.64	24.52 \pm 1.33	41.97 \pm 2.75
	After intervention	7.55 \pm 1.83	25.01 \pm 1.85	42.64 \pm 3.06
	t	0.907	1.410	1.068
	P	0.367	0.162	0.289

Note: Comparison with the control group in the same period, * $P < 0.05$

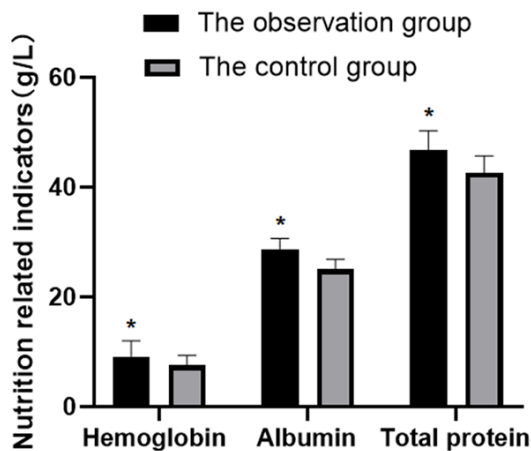


Figure 1. Comparison of nutritional indexes between the two groups after intervention. Note: * $P < 0.05$, comparison with the control group.

Comparison of nutritional indices pre- and post-intervention

The difference was statistically insignificant in nutritional indices (hemoglobin, total protein,

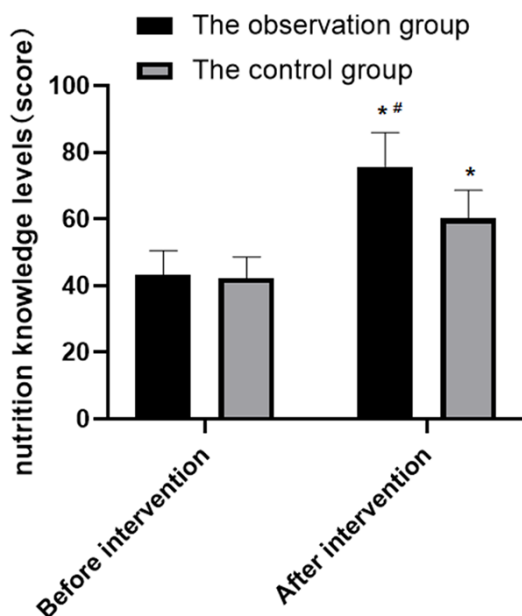
albumin) for the pre-intervention of the two groups ($P > 0.05$). The difference was statistically insignificant in the changes of nutritional indices of the control-group patients pre-and-post-intervention ($P > 0.05$). The nutritional indices after intervention were remarkably higher than those before the intervention ($P < 0.05$), and the nutritional indices of the observation-group patients after intervention were noticeably higher than those of the control-group patients ($P < 0.05$), as shown in **Table 2** and **Figure 1**.

Comparison of nutritional knowledge levels pre-and-post intervention

The difference was statistically insignificant for scores of nutritional knowledge level between the control and observation group of patients before the intervention ($P > 0.05$); After intervention, the nutritional knowledge level scores of patients in the two groups of patients were remarkably higher than those before intervention ($P < 0.05$), and the nutritional knowledge level scores of the observation-group patients

Table 3. Comparison of nutritional knowledge levels before and after intervention (score, $\bar{x} \pm s$)

Group	Number of cases	Before intervention	After intervention	t	P
The observation group	43	43.20 \pm 7.38	75.69 \pm 10.25	16.868	0.000
The control group	43	42.17 \pm 6.42	60.22 \pm 8.43	11.170	0.000
t	-	0.691	7.644	-	-
P	-	0.492	0.000	-	-

**Figure 2.** Comparison of nutritional knowledge levels before and after intervention. Note: * $P < 0.05$ Comparison with this group before treatment; # $P < 0.05$, comparison with the control group in the same period.

were notably higher than those of the control-group patients ($P < 0.05$), as shown in **Table 3** and **Figure 2**.

Comparison of T-lymphocyte subsets pre-and-post intervention

The difference was statistically insignificant in T-lymphocyte subsets for the control and observation group of patients before the intervention ($P > 0.05$); After intervention, the percentages of CD_3^+ , CD_4^+ cells and the value of CD_4^+/CD_8^+ in both groups of patients were lower than those before intervention ($P < 0.05$), and the percent of CD_8^+ cells was not significantly changed ($P > 0.05$). Besides, the percentages of CD_3^+ , CD_4^+ cells and the value of CD_4^+/CD_8^+ of the observation-group-patients were notably higher than those of the patients in the control group ($P < 0.05$), as shown in **Table 4**.

Comparison of life quality of the two groups of patients pre- and -after intervention

Before intervention, the difference was statistically insignificant of the dimensions of SF-36 scale for both groups of patients ($P > 0.05$); After intervention, the scores of the dimensions of SF-36 scale of the observation-group patients were increased compared to those before intervention ($P < 0.05$), while the scores of the dimensions of SF-36 scale of the control-group patients were not remarkable different compared with those before intervention ($P > 0.05$). In addition, the scores of the dimensions of SF-36 scale of the observation-group patients were notably increased compared to those of the control-group patients after intervention ($P < 0.05$), as shown in **Table 5**.

Comparison of incidences of grade III-IV adverse reactions to chemoradiotherapy between the two groups

The incidences of grade III-IV adverse reactions to chemoradiotherapy in the observation group were notably lower than those in the control group ($P < 0.05$), as shown in **Table 6**.

Discussion

A great number of studies have shown that enteral nutrition intervention can effectively help NSCLC patients treated with chemoradiotherapy to recover their gastrointestinal function, and to avoid bacterial translocation thus reducing the incidence of enterogenous infection [17, 18]. The process of enteral nutrient absorption is active absorption, which effectively regulates the synthesis and metabolism of visceral protein. The enteral nutrition does not affect the cardiac output and visceral blood flow. In addition, it also has the characteristics of simple clinical application, economical efficiency and high safety. Therefore, it is currently recommended as a nutritional support method for NSCLC sufferers to give consent to concurrent radiochemotherapy. The study adopted

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Table 4. Comparison of T-lymphocyte subsets before and after intervention ($\bar{x} \pm sd$)

Group	Time	CD ₃ ⁺ (%)	CD ₄ ⁺ (%)	CD ₈ ⁺ (%)	CD ₄ ⁺ /CD ₈ ⁺
The observation group (n=43)	Before intervention	50.28±6.38	31.48±2.37	23.17±3.75	1.39±0.27
	After intervention	45.62±4.72*	29.01±2.16*	23.81±3.89	1.22±0.19*
	t	3.850	5.051	0.777	3.377
	P	0.000	0.000	0.440	0.001
The control group (n=43)	Before intervention	50.97±5.02	32.04±2.67	23.52±3.96	1.36±0.25
	After intervention	41.21±4.84	26.85±2.35	23.93±3.10	1.09±0.17
	t	9.178	9.568	0.535	5.856
	P	0.000	0.000	0.594	0.000

Table 5. Comparison of quality of life between the two groups of patients

SF-36	The observation group (n=43)		t	P	The control group (n=43)		t	P
	Before intervention	After intervention			Before intervention	After intervention		
SF	71.83±10.28	79.27±8.95*	3.579	0.001	70.92±9.57	72.13±8.39	0.623	0.535
MH	69.82±7.21	76.29±8.04*	3.929	0.000	68.34±8.35	67.92±7.69	0.243	0.809
RP	64.27±6.44	69.22±5.96*	3.699	0.000	65.01±7.03	65.39±7.20	0.248	0.805
RE	67.85±9.15	73.85±6.07*	3.583	0.001	67.12±7.23	68.02±5.96	0.630	0.531
PF	64.31±8.30	69.22±5.73*	3.192	0.002	64.95±7.94	65.04±4.27	0.065	0.948
BP	67.72±6.49	73.29±6.20	4.069	0.000	66.36±9.52	67.39±7.92	0.545	0.587
VT	65.44±7.83	71.26±5.96	3.878	0.000	64.95±8.32	65.22±6.39	0.169	0.866
GH	66.21±6.02	73.21±5.84	5.473	0.000	65.74±5.83	66.29±7.32	0.385	0.701

Table 6. Comparison of incidences of grade III to IV adverse reactions to chemoradiotherapy between the two groups [n (%)]

Group	n	Blood system	Gastrointestinal tract	Kidney	Nervous system	Total
The observation group	43	1 (2.33)	3 (6.98)	1 (2.33)	1 (2.33)	6 (13.95)
The control group	43	4 (9.30)	7 (16.28)	1 (2.33)	2 (4.65)	14 (32.56)
X ²		-	-	-	-	3.943
P		-	-	-	-	0.047

overall management for enteral nutrition support in NSCLC sufferers treated with concurrent radiochemotherapy, including their dietary habits and body weight assessment before admission, overall supervision in the hospital, and guidance and feedback after discharge. Besides, the management process was reflected in the form of tables, which can also help to implement nutrition support programs.

The study results indicated that the nutritional indexes of the patients in the observation group improved after the intervention, but did not change apparently in the control group; furthermore, the patients in the observation group have seen their nutrition knowledge level increased significantly than the other group of

patients. Through the pattern of overall nutrition management, the continuous understanding of nutritional knowledge under the supervision and management of family members, medical staff and patients themselves is conducive to strengthening the management of patients' body condition. On the premise that the treatment staffs fully understand the patient's physical condition, reasonable intervention of enteral nutrition can be more helpful to the improvement of the patient's nutritional indicators. After intervention, the percents of CD₃⁺, CD₄⁺ cells and the value of CD₄⁺/CD₈⁺ in both groups of patients decreased compared with those pre-intervention ($P < 0.05$), and the percentages of CD₃⁺, CD₄⁺ cells and the value of CD₄⁺/CD₈⁺ of the patients in the observation

group were significantly higher than those of the patients in the control group. Similar to the research results reported by scholars [19, 20], the patients' cellular immune function may be reduced due to the consumption of tumor and the damage of chemoradiotherapy. Effective nutritional interventions, however, can help to protect sufferers' immune function while improving their basic body nutrition. Therefore, it has a positive significance for improving the prognosis of patients. In addition, the scores of the dimensions of SF-36 scale of the observation-group patients were increased post-intervention, while the scores of the dimensions of SF-36 scale of the control-group patients were not significantly modified after intervention compared with those before intervention, and the scores of the dimensions of SF-36 scale of the observation-group patients were remarkably increased than the control-group patients after intervention. It is likely that the enteral nutrition management is helpful to improve the nutritional indexes of patients and the protection of immune function; therefore the patients' physical condition and tolerance are improved. Through the participation of family members, medical staff and patients themselves in disease management, patients can feel more social support, so as to enhance the quality of their life [21]. Besides, the incidences of grade III-IV adverse reactions to chemoradiotherapy of the observation-group patients were notably lower than those in the control-group patients. Similar to the findings of other scholars [22], effective nutritional management measures are conducive to more reasonable nutritional interventions in line with the patients' own specific conditions, thereby maximizing the protection of their body's immune function, and the improvement of the body status will then help improve the life quality of the patients and reduce the adverse reactions of chemoradiotherapy.

However, due to the limited size of samples included and lack of follow-up analysis for long-term treatment prognosis of patients, it is suggested that the sample size can be expanded, and the influence of effective nutrition management on the long-term survival of patients can be studied and analyzed in depth in further researches.

In conclusion, for stage III inoperable NSCLC patients gave consent to Apatinib combined

with concurrent radiochemotherapy, enteral nutrition nursing care intervention under overall nutrition management can effectively improve the nutritional status of their bodies, increase their nutrition knowledge level, enhance their quality of life, protect their immune function, and reduce the incidence of serious adverse reactions to chemoradiotherapy. Therefore, the method is worthy of clinically promotion.

Disclosure of conflict of interest

None.

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References

- [1] Herbst RS, Morgensztern D and Boshoff C. The biology and management of non-small cell lung cancer. *Nature* 2018; 553: 446-454.
- [2] Holt GE and Daftarian P. Non-small-cell lung cancer homing peptide-labeled dendrimers selectively transfect lung cancer cells. *Immunotherapy* 2018; 10: 1349-1360.
- [3] Kelly R and Houseknecht S. Considerations in the care of non-small-cell lung cancer: the value imperative. *Oncology (Williston Park)* 2018; 32: 534-540.
- [4] Powell B and Bolton WD. Management of lung cancer with concomitant cardiac disease. *Thorac Surg Clin* 2018; 28: 69-79.
- [5] Julka PK, Sharma DN, Madan R, Mallick S, Benson R, Kunhi PH, Gupta S and Rath GK. Patterns of care and survival among small cell lung cancer patients: experience from a tertiary center in India. *J Egypt Natl Canc Inst* 2017; 29: 47-51.
- [6] Li W, Lin X, Wang R, Wang F, Xie S and Tse LA. Hormone therapy and lung cancer mortality in women: systematic review and meta-analysis. *Steroids* 2017; 118: 47-54.
- [7] Sheehan DF, Criss SD, Chen Y, Eckel A, Palazzo L, Tramontano AC, Hur C, Cipriano LE and Kong CY. Lung cancer costs by treatment strategy and phase of care among patients enrolled in Medicare. *Cancer Med* 2019; 8: 94-103.
- [8] Sears CR. DNA repair as an emerging target for COPD-lung cancer overlap. *Respir Investig* 2019; 57: 111-121.
- [9] Kyte K, Ekstedt M, Rustoen T and Oksholm T. Longing to get back on track: patients' experiences and supportive care needs after lung

- cancer surgery. *J Clin Nurs* 2019; 28: 1546-1554.
- [10] Dhanasopon AP and Kim AW. Lung cancer screening and its impact on surgical volume. *Surg Clin North Am* 2017; 97: 751-762.
 - [11] Naylor EC, Desani JK and Chung PK. Targeted therapy and immunotherapy for lung cancer. *Surg Oncol Clin N Am* 2016; 25: 601-609.
 - [12] Presley CJ, Reynolds CH and Langer CJ. Caring for the older population with advanced lung cancer. *Am Soc Clin Oncol Educ Book* 2017; 37: 587-596.
 - [13] Jacobsen MM, Silverstein SC, Quinn M, Waterston LB, Thomas CA, Benneyan JC and Han PKJ. Timeliness of access to lung cancer diagnosis and treatment: a scoping literature review. *Lung Cancer* 2017; 112: 156-164.
 - [14] Biswas A, Mehta HJ and Folch EE. Chronic obstructive pulmonary disease and lung cancer: inter-relationships. *Curr Opin Pulm Med* 2018; 24: 152-160.
 - [15] Berman AT, DeCesaris CM, Simone CB, Vachani C, DiLullo G, Hampshire MK, Metz J and Hill-Kayser C. Use of survivorship care plans and analysis of patient-reported outcomes in multinational patients with lung cancer. *J Oncol Pract* 2016; 12: 527-535.
 - [16] Hamann HA, Ver Hoeve ES, Carter-Harris L, Studts JL and Ostroff JS. Multilevel opportunities to address lung cancer stigma across the cancer control continuum. *J Thorac Oncol* 2018; 13: 1062-1075.
 - [17] Ha D, Mazzone PJ, Ries AL, Malhotra A and Fuster M. The utility of exercise testing in patients with lung cancer. *J Thorac Oncol* 2016; 19: 1397-1410.
 - [18] Ashinuma H, Shingyoji M, Yoshida Y, Itakura M, Iizasa T, Sakashita Y and Sekine I. Retrospective analysis of lung cancer patients treated with supportive care alone. *Int J Clin Oncol* 2017; 22: 455-460.
 - [19] Dan T and Williams NL. Management of stage I lung cancer with stereotactic ablative radiation therapy. *Surg Oncol Clin N Am* 2017; 26: 393-403.
 - [20] Nair CK, Mathew AP and George PS. Lung cancer: presentation and pattern of care in a cancer center in South India. *Indian J Cancer* 2017; 54: 164-168.
 - [21] Zhang X, Liu Y, Shao H and Zheng X. Obesity paradox in lung cancer prognosis: evolving biological insights and clinical implications. *J Thorac Oncol* 2017; 12: 1478-1488.
 - [22] Rosenblum AM and Chasen M. Comprehensive metastatic lung cancer care must include palliative care. *Curr Oncol* 2018; 25: 192-193.