Original Article Influence of respiratory function training under the mode of mutual-assisted patients on postoperative pulmonary infection and immune function on lung cancer

Ruiling He*, Qunying Zhu*, Yixia Wang, Guini Chen, Shaoli Chen, Yuechan Wang

Department of Cardiothoracic Surgery, The First Affiliated Hospital of Hainan Medical University, Haikou 570102, Hainan, China. *Equal contributors.

Received December 13, 2020; Accepted March 29, 2021; Epub August 15, 2021; Published August 30, 2021

Abstract: Objective: This study explored the effect of respiratory function training under the mode of mutual-help of patients to the postoperative pulmonary infection and immune function on lung cancer. Methods: 116 lung cancer patients who received surgical treatment from June 2018 to June 2019 were enrolled as the object. Patients were categorized into a control or observation group, according to the admission time of patients. Each group contained 58 subjects. The control-group was given regular nursing intervention, and the observation-group received respiratory function training under the mode of mutual assist between patients. Subsequently, the postoperative pulmonary infection, pulmonary function, and the changes of immune function before and after surgery were compared between the two groups. Result: The pulmonary infection rate of the group for observation was much lower than that of the control-group. The difference was statistically significant (5.17%, 17.24%, = 0.0394). The postoperative pulmonary function indexes in the observation-group were conspicuously better than those in control-group, the difference was statistically conspicuous (P<0.05). After nursing intervention, the cellular immune factors TNF- α , IL-8, and IL-6 of the two groups were conspicuously lower than those before the nursing intervention, and the decrease in the observation-group was remarkably greater than that in control-group, with the difference of statistical significance (P<0.05). In addition, the T cell subsets CD4⁺ and CD4⁺/CD8⁺ in the observation-group were conspicuously higher than those in the control-group. CD8⁺ in the observation-group was conspicuously lower than that in the group of control, with statistical significance (P<0.05). Conclusion: The respiratory function training under the mode of mutual-assist of patients can effectively reduce the incidence of postoperative pulmonary infection, improve the postoperative pulmonary function index, and improve the immune function, which is worthy of clinical promotion.

Keywords: The mode of mutual-assist between patients, lung cancer, respiratory function training, postoperative pulmonary infection, immune function

Introduction

Lung cancer, which originated from the mucosa and glands of trachea or bronchus, is one of the most common primary malignant lung tumors [1, 2]. In recent years, factors such as environmental pollution and heavy smoking, show the appearance of lung cancer in China is on the rise. According to statistical data, the mortality of lung cancer reaches 25.8%, which is a primary cause of cancer-induced death in China [3]. In 2018, global statistics showed that lung cancer incidence rate ranked third in female population, and has the second highest mortality rate after breast cancer. In male population, both incidence and death of the lung cancer ranked first among the malignant tumors [4, 5]. Currently, surgical resection of lung lobes and peripheral lymphoid tissue is often used in clinical treatment. During the operation, the use of narcotic drugs and traumatic injury would cause a certain degree of damage in the respiratory function of patients, especially for those elderly sufferers [6, 7]. After surgery, patients often have chest pain, cough weakness, and increased respiratory secretion. These symptoms will affect postoperative recovery. Therefore, it is of great necessity to enhance

the training of respiratory function. According to the literature reports, due to the single form of respiratory exercise, coupled with the disease itself and other factors, the training compliance of patients is poor [8]. The respiratory function training under the mode of mutual-assist of patients is a new intervention mode formed in recent years. It is conducted through the mutual support and encouragement among patients to improve the compliance with respiratory function training, to improve the postoperative recovery level of patients. Current researches stated that cancer is a disease closely related to immune function. T lymphocytes is a type of the most important cell groups in immune system, which can be divided into CD4⁺ and CD8⁺ T cells by its different phenotypes. To understand the changes of T lymphocytes in patients with lung cancer is of grand value for realizing the disease and its prognosis. This study investigated the effect of the training of respiratory function on postoperative pulmonary infection and immune function in patients with lung cancer.

Data and methods

Research object

One hundred sixteen lung cancer patients that underwent/surgical treatment from June 2018 to June 2019 were chosen as research objects, including 75 men and 41 women with an average age of (61.37±4.25) years. TNM staging: 51 cases in stage I, 49 cases in stage II, 16 cases in stage III; 62 cases had smoking experience and 54 cases were non-smokers. In addition, the objects were categorized into an observation-group and a control-group according to the admission time of patients, with each group containing 58 cases. The study was approved by the hospital ethics committee.

Standard for admission and exclusion

Inclusion criteria: (1) All subjects enrolled met the diagnostic criteria for lung cancer after pathological and imaging examinations; (2) Patients that met the indications for radical surgery and undergoing the surgical treatment; (3) Patients that were conscious and had normal communicating ability; (4) Patients who voluntarily participated in the study and signed the informed consent. Exclusion criteria: (1) Patients with other malignant tumor(s); (2) Patients that complicated with other diseases affecting respiratory function; (3) Patients with abnormal function of important organs like heart, liver, and kidney; (4) Patients with cognitive impairment and inability to communicate normally.

Method

The control-group received routine nursing intervention, including smoking cessation requirements for patients, routine preoperative health education, the formation of a diet plan in accordance with the patient's; instructed the patients on taking take deep breaths, turning over and patting the back after operation and effective coughing; informed of the postoperative attention items and carried out exercise and diet intervention to patients to promote their recovery.

The observation-group, in addition to the conventional measures above, were further adopted the respiratory function training under the mode of mutual-help of patients. The specific methods were as follows: (1) Set up an intervention group, including one attending physician, one supervisor nurse, and two nurses. The members of the intervention group participated in the formulation of respiratory function training. The nurse in charge was responsible for the implementation of respiratory function training, and supervision and guidance of patients. (2) Implementation and methods of respiratory function training: the hospitalized patients were studied by on-site observation of respiratory function demonstration and scene simulation, and the nurse gave corresponding guidance for the patients. The methods were as follows: first, the patient closed the mouth and inhaled through the nose, contracted the lips to whistles, and slowly exhaled. The intensity of exhalation would be kept to be able to blow the candle flame 20 cm in front of the lip to tilt but not extinguish. This prolonged the time of exhalation as much as possible. The best ratio of inhalation to exhalation time was 1:2 or 1:3. The patients were trained for 15-20 minutes each time, and 2-3 times per day. Abdominal breathing: patients chose supine, semi-decubitus or sitting position according to their own state, placed palms of hands on their abdomen and chest respectively, and breathed slowly

| 0 | Gender | Age $(\overline{x} \pm s)$ | TNM phases | | | Smoking history | |
|----------------------------------|---------------|----------------------------|-------------|----------|-----------|-----------------|------------|
| Group | (male/female) | years old) | Phase I | Phase II | Stage III | Smoke | No smoking |
| Control-group (n = 58) | 36/22 | 60.66±4.38 | 29 | 22 | 7 | 35 | 23 |
| observation group for $(n = 58)$ | 39/19 | 62.17±3.94 | 22 | 27 | 9 | 27 | 31 |
| <i>X</i> ² /t | 0.3395 | 1.9520 | | 1.7210 | | 2.2174 | |
| Р | 0.5601 | 0.0534 | 0.4230 0.13 | | .1365 | | |

 Table 1. Comparison of general information

 Table 2. Comparison of postoperative pulmonary infection between the two groups

| Group | Number of cases of infection | Infection rate (%) | X ² | Р |
|-------------------------------|------------------------------|-----------------------|----------------|--------|
| Control-group (n = 58) | 10 | 17.24 | 4.2450 | 0.0394 |
| Observation-group (n = 58) | 3 | 5.17 | | |

Table 3. Comparison of postoperative pulmonary function between the two groups

| Group | PaO ₂ (mm Hg, | Sp0 ₂ (%, | PaCO ₂ (mm Hg, | |
|-------------------------------|--------------------------|----------------------|---------------------------|--|
| Gloup | x±s) | ∓±́s) | $\overline{x} \pm s$) | |
| Control-group (n = 58) | 69.29±3.36 | 88.15±2.47 | 34.85±2.66 | |
| Observation-group (n = 58) | 79.44±3.12 | 97.76±1.13 | 45.61±2.58 | |
| Т | 16.8586 | 26.9447 | 22.1136 | |
| Р | 0.0000 | 0.0000 | 0.0000 | |

and deeply through nasal inhalation and oral exhalation. When breathing in, the hand on the abdomen was raised, while the hand on the chest was not moved. The patient kept it for 3~5 s, then exhaled slowly. When exhaling, the abdominal muscles contracted, the hand at abdomen position turned lower, and the one on chest kept still. The training lasted for 15-20 minutes, and 2-3 times a day. Effective cough and expectoration: The patient took deep breaths in supine position and closed the larynx. By prolonging the breath hold, the patient's diaphragm was raised, which increased the pressure in chest, and then to perform an effective cough. When coughing, both hands could be pressed on the abdomen so as to discharge the deep sputum or gas. The training was conducted several times a day. (3) Mutual-assist exercise of patients. After admission, 4-6 patients with close admission time were arranged in same ward. The patients introduced themselves in turn under the guidance of the nurse to strengthen the communication between patients as well as between nurses and patients and cultivate the sense of a team. After learning the method of respiratory function training, the patients carried out the exercise in groups. During the exercise, mutual communication among team members was used to increase the recognition between team members. A patient was selected by self-recommendation as the group leader, who was responsible for the supervision of training. The patients were encouraged to express their inner doubts and ideas during the training. These doubts were eliminated through various strategies su-

ch as question answering guidance of medical staff or discussion within the group. The intervention team conducted preoperative education for group members to further improve their self-awareness. After the operation, the patients were encouraged to communicate with each other and share their feelings. When the vital signs of the patients were stable, the patients were instructed to carry out appropriate respiratory function training.

Observation index

The incidence of postoperative pulmonary infection and the postoperative pulmonary function of the two groups were compared: PaO_2 , SpO_2 . $PaCO_2$ were detected on the 1st day after operation; The changes of immune function before and after nursing intervention were compared between the two groups: The fasting venous blood of the patient was extracted at admission and 7 d after operation to detect the tumor necrosis factor- α (TNF- α), interleukin-8 (IL-8), interleukin-6 (IL-6), and other immune cytokines (ELISA method), and CD4⁺ and CD8⁺ levels of T cell subsets (by Bricyte E6 flow

Effect of respiratory function training on postoperative lung cancer

| Cell factor | | Control-group (n = 58) | Observation-group (n = 58) | Т | Р | |
|-------------|-----------------------------|---------------------------|----------------------------|---------|--------|--|
| TNF-α | Before nursing intervention | 35.87±3.17 | 36.62±3.55 | 1.2001 | 0.2326 | |
| | After nursing intervention | 18.69±1.24 | 12.41±1.13 | 28.5084 | 0.0000 | |
| IL-8 | Before nursing intervention | 48.55±3.79 | 47.49±3.65 | 1.5342 | 0.1277 | |
| | After nursing intervention | 33.73±2.07 | 25.65±1.83 | 22.2718 | 0.0000 | |
| IL-6 | Before nursing intervention | 465.33±44.31 | 469.94±41.58 | 0.57878 | 0.5645 | |
| | After nursing intervention | 257.67±31.26 | 201.17±30.46 | 9.8586 | 0.0000 | |

Table 4. Changes of immune cytokines in the two groups after nursing intervention $(x \pm s)$



Figure 1. Comparison of TNF- α between the two groups. Note: Compare with before nursing intervention, *P<0.05; Compare with the control-group, #P<0.05.

cytometer), and then calculated $\text{CD4}^{\text{+}}/\text{CD8}^{\text{+}}$ value.

Statistical methods

We carried out statistical analysis and processing through Spss19.0 statistical software. The measurement data were expressed by ($\bar{x} \pm s$), the comparison within the group was conducted by paired sample t-test, the comparison between groups was conducted by independent sample t-test, the count data were expressed by percentage, and the comparison was conducted by X^2 test. *P*<0.05 referred as the difference was statistically significant. The graphic software was by Graphpad prism9.



Figure 2. Comparison of IL-8 between the two groups. Note: Compare with before nursing intervention, *P<0.05; Compare with the control-group, #P<0.05.

Results

Clinical data

The two groups of patients had insignificant difference in general information of gender, age, TNM stage, and smoking experience (P>0.05), as shown in **Table 1**.

Situation of postoperative pulmonary infection between the two groups

The incidence of pulmonary infection was 17.24% in the observation-group and 5.17% in the control-group. The pulmonary infection rate of the group for observation was conspicuously lower than that of the group of control, and the



Figure 3. Comparison of IL-6 between the two groups. Note: Compare with before nursing intervention, *P<0.05; Compare with the control-group, #P<0.05.

difference was statistically conspicuous (*P*< 0.05), as shown in **Table 2**.

Comparison of postoperative pulmonary function between two groups

The postoperative PaO_2 and SpO_2 in the observation-group were significantly higher than those in the control-group (*P*<0.05). Postoperative $PaCO_2$ in observation-group was critically lower than that in control-group (*P*<0.05) (**Table 3**).

Comparison of changes of immune cytokines between two groups before and after nursing intervention

The levels of IL-8 and TNF- α in the two groups were conspicuously lower than those in the control-group (P<0.05), as shown in **Table 4** and **Figures 1-3**.

Comparison of the changes of T cell subsets between the two groups before and after nursing intervention

After nursing intervention, $CD4^+$ and $CD4^+/$ CD8⁺ in observation-group were dramatically higher than that in the group of control, while the CD8⁺ in the observation-group was conspicuously lower than that in control-group, and there was statistical significance (P<0.05), as shown in **Table 5** and **Figures 4**, **5**.

Discussion

In the surgical treatment of lung cancer, the lung function is often affected by the traumatic stimulation caused to the body during operation. This leads to the decline of d ventilation function, and the temporary damage to the respiratory function [10, 11]. In addition, the local severe pain after the operation limits the effective cough and expectoration of the patients, leading to the failure of patients to completely exclude the respiratory secretions from the body, further affecting the ventilation function of the lung. The use of anesthetic drugs during operation and the local bandage after the operation can also cause a certain degree of respiratory dysfunction, and has a certain impact on recovery of postoperative lung recruitment and pulmonary function [12, 13]. Lung cancer patients have usually had poor immunity and physical function. Surgical treatments would impose great impacts on them. Patients are prone to disorders of pulmonary function and immune function. Some patients may even fail to discharge sputum normally after surgery, which seriously affects their quality of life and physical and mental health. According to clinical research, respiratory function training for lung cancer patients can effectively reduce the incidence of postoperative pulmonary infection, improve lung and immune function, and improve the prognosis of treatment effect [14, 15]. However, it is undeniable that the patient's compliance with respiratory function training is poor, leading to difficulty in achieving the desired therapeutic effect.

The respiratory function training under the mode of mutual-assist of patients is based on the theory of mutual help. It can improve the patients' confidence in treatment by improving the communication between patients and medical staff, patients and social environment, and between patients themselves [16]. During the mutual-assist period, the patients' compliance with treatment and respiratory function training can be improved by setting an example for each other. The results of this study

Effect of respiratory function training on postoperative lung cancer

Table 5. Comparison of changes of T cell subsets between the two groups before and after nursing

| intervention $(\bar{x} \pm s)$ | | | | | | |
|--------------------------------|-----------------------------|---------------------------|-------------------------------|---------|--------|--|
| Cell factor | | Control-group (n = 58) | Observation-group (n = 58) | Т | Р | |
| CD4+ (%) | Before nursing intervention | 37.48±4.21 | 37.52±4.33 | 0.0504 | 0.9599 | |
| | After nursing intervention | 28.97±4.25 | 41.37±4.01 | 16.1617 | 0.0000 | |
| CD8+ (%) | Before nursing intervention | 28.22±4.33 | 28.55±4.95 | 0.3821 | 0.7031 | |
| | After nursing intervention | 27.67±4.34 | 25.05±4.77 | 3.0941 | 0.0025 | |
| $CD4^{+}/CD8^{+}$ | Before nursing intervention | 1.33±0.95 | 1.34±0.87 | 0.0591 | 0.9530 | |
| | After nursing intervention | 1.05+0.98 | 1.65+0.84 | 3.5402 | 0.0006 | |

В A 1.0M 1.0M 800K 800K SSC-A :: SSC-A SSC-A :: SSC-A 600K 600K 35.7% 36.8% 400K 400K 200K 200K 0 0 1.111 10⁴ 10⁵ 10⁵ 10⁰ 10⁰ 104 . 10² . 10³ 10⁶ . 10² . 10³ 10⁶ 10¹ 10 BL4-A :: PE-vio770-CD4-A BL4-A :: PE-vio770-CD4-A С D 1.0M 1.0M 800K 800K SSC-A :: SSC-A SSC-A :: SSC-A 600K 600K 26.0% 40.9% 400K 400K 200K 200K 0 0 T 11111 щ P 1.111 10⁵ 10⁴ 10⁶ 10⁰ 10² 10³ 10⁵ 106 10⁰ . 10² . 10³ -10⁴ 10¹ 10¹ BL4-A :: PE-vio770-CD4-A BL4-A :: PE-vio770-CD4-A

Figure 4. Comparison of changes of CD4⁺ cell between the two groups before and after nursing intervention. A: Control-group of before nursing intervention; B: Observation-group of after nursing intervention; C: Control-group of before nursing intervention; D: Observation-group of after nursing intervention.

showed that the pulmonary infection rate of the observation-group was conspicuously lower

than that of the control-group (P<0.05). The postoperative pulmonary function indexes of

Am J Transl Res 2021;13(8):9260-9268



Figure 5. Comparison of changes of CD8⁺ cell between the two groups before and after nursing intervention. A: Control-group of before nursing intervention; B: Observation-group of after nursing intervention; C: Control-group of before nursing intervention; D: Observation-group of after nursing intervention.

the observation-group were conspicuously better than those of control-group. The difference was statistically conspicuous (P<0.05). This may be due to the respiratory function training under mutual-assist which can improve the lung function of patients with lung cancer through interventions of multi-angles, so that the incidence of infection could be reduced. By strengthening communication and improving the attention to the perioperative matters of patients, the adverse situations can be avoided during the period, which is beneficial for postoperative recovery.

Tumor necrosis factor- α (TNF- α), interleukin-8 (IL-8), interleukin-6 (IL-6), and other cellular immune factors are important inflammatory mediators, which play a role in the whole body or locally by binding with their specific receptors [17, 18]. TNF- α , IL-8, and IL-6 can not only effectively promote the release of inflammatory mediators and the aggregation of inflam-

matory cells, but also chemotactic neutrophils to the inflammatory site of patients, thus aggravating the inflammation [19]. The results showed that after nursing intervention, the levels of cellular immune factors TNF- α , IL-8, IL-6 in the two groups were conspicuously lower than those before the nursing intervention, and the decrease in observation-group was conspicuously greater than that in the controlgroup (P<0.05). This indicates that the respiratory function training under the mode of mutual-assist of patients can effectively improve the level of immune cytokines on lung cancer, thereby enhancing the defense ability in the body.

T lymphocyte is one of the most important cell groups in immune system, which can be divided into CD4⁺ and CD8⁺ T cells according to their different phenotypes. CD4+ T cells are induced T cells, which can release a lot of cytokines. CD8⁺ T cells are cytotoxic inhibitory T cells, which play the role of virus clearance [20]. The ratio of CD4⁺ and CD8⁺ T cells reflects the immune balance of the body. The normal ratio of CD4⁺/CD8⁺ is generally between 1.2~2, and the decrease of the ratio indicates the immune function of the body is in disorder [21]. The results showed that after nursing intervention, CD4⁺ and CD4⁺/CD8⁺ of observation-group were notably higher than those of the controlgroup, while CD8⁺ was conspicuously lower than that of the control-group (P<0.05). This refers that the respiratory function training under the mode of mutual-assist of patients can improve the immune function of cancer patients by reducing the release of inflammatory factors and the immunosuppression.

Due to the small sample size of this study, the research results may be biased. The follow-up study will further expand the sample size to provide a more reliable basis for clinical work.

In brief, the respiratory function training under the mode of mutual-assist of patients can effectively reduce the incidence of postoperative pulmonary infection, and improve the postoperative pulmonary function index and immune function, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Qunying Zhu, Department of Cardiothoracic Surgery, The First Affiliated Hospital of Hainan Medical University, No. 31 Longhua Road, Haikou 570102, Hainan, China. Tel: +86-0898-66528186; E-mail: bettyzqy@163.com

References

- Lim RB. End-of-life care in patients with advanced lung cancer. Ther Adv Respir Dis 2016; 10: 455-67.
- [2] Tandberg DJ, Tong BC, Ackerson BG and Kelsey CR. Surgery versus stereotactic body radiation therapy for stage I non-small cell lung cancer: a comprehensive review. Cancer 2018; 124: 667-678.
- [3] Zhang T, He H, Liu Q, Lv X, Song Y and Hong J. Supportive care needs of patients with lung cancer in mainland china: a cross-sectional study. J Nurs Res 2019; 27: e52.
- [4] 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.
- [5] Pedersen JH, Saghir Z, Wille MM, Thomsen LH, Skov BG and Ashraf H. Ground-glass opacity lung nodules in the era of lung cancer ct screening: radiology, pathology, and clinical management. Oncology (Williston Park) 2016; 30: 266-274.
- [6] Heineman DJ, Hoeijmakers F, Beck N, Dickhoff C, Daniels JM, Schreurs WH and Jakobsen E. Impact of health care organization on surgical lung cancer care. Lung Cancer 2019; 135: 181-187.
- [7] Ashinuma H, Shingyoji M, Yoshida Y, Itakura M, lizasa 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.
- [8] Bradley SH, Kennedy MPT and Neal RD. Recognising lung cancer in primary care. Adv Ther 2019; 36: 19-30.
- [9] He Y, Yu XQ, Luo Q, Xu X, Wang Y, Li S and Shan B. Patterns of care of nonsmall cell lung cancer patients in China and implications for survival. J Cancer Res Ther 2018; 14: 410-415.
- [10] Nwagbara UI, Ginindza TG and Hlongwana KW. Lung cancer awareness and palliative care interventions implemented in low-and middleincome countries: a scoping review. BMC Public 2020; 20: 1466.
- [11] Cope DG, Reb A, Schwartz R and Simon J. Older adults with lung cancer: assessment, treatment options, survivorship issues, and palliative care strategies. Clin J Oncol Nurs 2018; 22: 26-35.
- [12] Hamann HA, Ver Hoeve ES, Carter-Harris L, Studts JL and Ostroff JS. Multilevel opportuni-

ties to address lung cancer stigma across the cancer control continuum. J Thorac Oncol 2018; 13: 1062-1075.

- [13] Rosenblum AM and Chasen M. Comprehensive metastatic lung cancer care must include palliative care. Curr Oncol 2018; 25: 192-193.
- [14] 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.
- [15] Brooks GA, Bergquist SL, Landrum MB, Rose S and Keating NL. Classifying stage IV lung cancer from health care claims: a comparison of multiple analytic approaches. JCO Clin Cancer Inform 2019; 3: 1-19.
- [16] 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.
- [17] Kelly R and Houseknecht S. Considerations in the care of non-small-cell lung cancer: the value imperative. Oncology (Williston Park) 2018; 32: 534-40.

- [18] Ganti AK, Hirsch FR, Wynes MW, Ravelo A, Ramalingam SS, Ionescu-Ittu R, Pivneva I and Borghaei H. Access to cancer specialist care and treatment in patients with advanced stage lung cancer. Clin Lung Cancer 2017; 18: 640-650.
- [19] McDermott CL, Bansal A, Ramsey SD, Lyman GH and Sullivan SD. Depression and health care utilization at end of life among older adults with advanced non-small-cell lung cancer. J Pain Symptom Manage 2018; 56: 699-708.
- [20] Collett GK, Durcinoska I, Rankin NM, Blinman P, Barnes DJ, Anderiesz C and Young JM. Patients' experience of lung cancer care coordination: a quantitative exploration. Support Care Cancer 2019; 27: 485-493.
- [21] Weller DP, Peake MD and Field JK. Presentation of lung cancer in primary care. NPJ Prim Care Respir Med 2019; 29: 21.