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The incidence of chronic obstructive pulmonary disease in advanced non-small cell lung cancer patients

Abstract

Background and aim. Lung cancer is one of the most common tumours and the cause of cancer-related deaths in European countries. In the past few years, a significant morbidity of chronic obstructive pulmonary disease (COPD) has been noticed in this group of patients. Cigarette smoking is the strongest risk factor for both conditions. The palliative care of lung cancer patients is often based solely on the tumour symptoms' management, whereas some patients would benefit from the combined treatment including the treatment for COPD. The aim of this study was to evaluate the incidence of COPD in advanced (TNM = IIIB and IV) non-small cell lung cancer (NSCLC) patients.

Material and methods. The study was a retrospective analysis. One hundred four patients (28 women and 76 men, aged from 47 to 74 years, mean: 63.2 years) with advanced NSCLC were included in the study.

Results. Chronic obstructive pulmonary disease (according to GOLD criteria) was diagnosed in 26 cases (25%), including 1 mild, 17 moderate and 8 with severe or very severe disease. Chronic obstructive pulmonary disease was significantly more frequent in squamous cell lung carcinoma in comparison to other types ($p = 0.009$).

Conclusions. Coexistence of lung cancer and COPD is frequent. Therefore, it is important to consider the treatment for COPD in palliative care of advanced lung cancer patients.

Key words: advanced lung cancer, NSCLC, chronic obstructive pulmonary disease, pulmonary function tests, spirometry

Introduction

Lung cancer is the most common tumour in adults in Europe. Although the trends of lung cancer mortality in the European Union for the next years estimate a reduction in mortality between 2000 and 2015 by 11% [1], the problem still remains widespread and the mean age of the patients gradually decreases. Smoking is one of the best-documented risk factors in lung cancer. Moreover, it is also the

strongest risk factor for chronic obstructive pulmonary disease (COPD). The symptoms of advanced stages of both conditions may be very similar: dyspnoea, chronic cough, weakness, gradual decline in general health and quality of life. The treatment of chronic dyspnoea, however, may differ in both conditions. The results of recent studies demonstrate, that COPD is underdiagnosed in Poland [2]. Thus, it is likely that the proportion of patients treated for advanced lung cancer may also require the proper treatment for

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COPD. The aim of this analysis was to assess the frequency of simultaneous occurrence of advanced non-small cell lung cancer (NSCLC) and COPD.

Material and methods

The study was a retrospective analysis of the medical records of 104 patients with advanced (stage IIIB and IV) NSCLC hospitalised between 2003 and 2004 at the Department of Pneumology, Medical University in Gdansk, Poland. According to WHO classification, 62 (59.6%) patients had stage IIIB and 42 (40.4%) had stage IV of the disease. The following inclusion criteria to the study were used:

- relevant medical history;
- complete case record together with the results of diagnostic imaging results;
- histopathological documentation of malignancy;
- documented pulmonary function tests documented.

Gender ratio was 2,71:1 (men vs. women) with 76 (73%) male and 28 (27%) female patients. Age ranged between 42 and 80 years with the mean age of 63.8 years (SD = 9.26). Histological examination confirmed NSCLC in all cases. Histological type was defined as squamous cell carcinoma (SCC) in 44.2% (n = 46), adenocarcinoma (AC) in 9.6% (n = 10), and mixed type in 1% (n = 1). A diagnosis of unspecified NSCLC was established in 45.2% (n = 47) of all patients.

Pulmonary function tests were performed with the "Lungtest 1000" spirometer, MES, Krakow, Poland. Staging of the COPD was based on GOLD 2006 guidelines [3]. Computer software "Statistica 7.0 PL" StatSoft, Krakow, Poland, was used for Statistical analysis.

Results

Chronic obstructive pulmonary disease was found in every fourth of the NSCLC patients (n = 26). There were 22 (84.6%) male and 4 (15.4%) female patients in this group. Mean age was 63.2 years (range 47–74 years, SD = 7.55). Eight (31%) of these patients had severe and very severe COPD, whereas moderate and mild COPD was found in 17 (65%) of COPD patients. In 19 out of 26 patients (73%) COPD coexisted with the SCC (correlation coefficient $r = 0.25$, $p = 0.009$). Histological type was not defined in 7 remaining cases.

Mean FEV₁ was 66.9% and ranged between 25% and 117% with SD = 18.49. In patients with coexisting COPD mean FEV₁ value was 55.9% (range 25–

–95%, SD = 16.82) and in patients without COPD mean FEV₁ was significantly higher at the level of 70.6% (range 34–117%, SD = 17.64); $p = 0.003$. Mean FEV₁/FVC ratio for the whole population was 0.798 (range 0.47–1.23, SD = 0.1489), while in patients with and without COPD it was 0.61 (range 0.47–0.70, SD = 0.06) and 0.86 (range 0.70–1.23, SD = 0.113); respectively; $p < 0.00001$.

MEF < 50% was found in 70% (n = 73) of all patients, in 96% (n = 25) of COPD patients and in 61.5% (n = 48) of no-COPD patients; $p = 0.027$. At the same time the correlation between MEF < 50% and simultaneous existence of the COPD and NSCLC was found (correlation $r = 0.33$, $p = 0.001$).

Eighty four (81%) patients admitted to be smokers: 20 (77%) patients from the COPD group and 64 (82%) among the remaining patients; $p = 0.03$. Mean number of the pack-years for the whole population was 39.5; 41.2 for COPD group and 38.9 for no-COPD patients (correlation $r = 0.03$, $p = 0.76$).

The level of haemoglobin was comparable in both groups — with and without COPD (**Table 1**).

Discussion

The results of our study demonstrate that every forth patient with advanced NSCLC cancer may additionally suffer from COPD. These results are in concordance with a large Dutch analysis, which assessed the frequency of COPD in the consecutive cancer patients registered in the Eindhoven Cancer Registry between 1995 and 2004. Twelve percent of all cancer patients had COPD at the time of diagnosis. In the group of lung cancer the frequency was even higher — 30% [4]. In this study a multivariate Cox-regression model showed that, COPD was associated with a significantly worse survival and NSCLC patients with COPD less frequently underwent surgery, and chemotherapy, whereas radiotherapy was used more frequently [4]. Another study found COPD as a predictive factor for severe postradiation pneumonitis in patients with locally advanced NSCLC treated with three-dimensional conformal chemoradiotherapy [5]. Furthermore, COPD was related to perioperative complications after pneumonectomy for primary lung cancer in Polish series [6].

Coexistence of COPD is an important issue in every stage of lung cancer. Even in as early stage as IA the coexistence of COPD is associated with poorer prognosis and the higher risk of recurrence after the complete surgical resection [7]. Recent Serbian study in patients with resectable tumour showed that, lung function measured by FEV₁ was signifi-

Table 1. Patients' characteristics in relation to coexistence of Chronic obstructive pulmonary disease (COPD)

	All patients (n = 104)	COPD patients (n = 26)	No COPD patients (n = 78)	p value*
Age				p = 0.8
> 60 years	70 (67.3%)	18 (69.2%)	52 (66.7%)	
< 60 years	34 (32.7%)	8 (30.8%)	26 (33.3%)	
Gender				r = -0.15
Female	28 (27%)	4 (15.4%)	24 (30.8%)	p = 0.13
Male	76 (73%)	22 (84.6%)	54 (69.2%)	
Stage				r = 0.07
IIIB	62 (59.6%)	17 (65.4%)	45 (57.7%)	p = 0.49
IV	42 (40.4%)	9 (34.6%)	33 (42.3%)	
Histology				r = 0.25
Squamous cell carcinoma	46 (44.2%)	19 (73.1%)	27 (34.6%)	p = 0.009
Adenocarcinoma	10 (9.6%)	0	10 (12.8%)	
Mixed type	1 (1%)	0	1 (1.3%)	
Histological type not defined, non small cell	47 (45.2%)	7 (26.9%)	40 (51.3%)	
Smoking				p = 0.03
Yes	84 (81%)	20 (77%)	64 (82%)	
No	20 (19%)	6 (23%)	14 (18%)	
Mean number of the pack-years	39.5	41.2	38.9	r = 0.03 p = 0.76
Hypertension				r = -0.1 p = 0.27
Yes	33 (31.7%)	6 (23.1%)	27 (34.6%)	
No	71 (68.3%)	20 (76.9%)	51 (65.4%)	
Haemoglobin [mg/dL]	13.78	13.3	12.8	r = 0.03 p = 0.75

*t-student test (double-sided); p — p value; r — correlation coefficient

cantly worse in those with COPD. In addition, operative morbidity in this group occurred in 50% of cases [8]. Interestingly, this finding indicates the necessity of proper diagnosis, because preoperative bronchodilator therapy may significantly improve small airways function and postoperative outcomes in some patients [8].

Dyspnoea is a leading and devastating symptom in advanced lung cancer [9, 10]. The choice of palliative treatment is related to underlying causes. Chronic pleural effusion is usually managed with pleurodesis [11], central bronchial obstruction may be relieved with the use of chest irradiation [12], or — in selected patients — with brachytherapy or other endobronchial strategies [13, 14]. Three cycles of chemotherapy in patients with relatively good performance status may also be an option [15, 16]. At the end of life opioids are usually used to palliate chronic dyspnoea [17]. On the contrary, the use of oxygen in patients with advanced lung cancer is still a matter of controversy [18, 19].

Patients with coexisting COPD and advanced lung cancer may benefit from the bronchodilator treatment, prolonged oxygen therapy (in cases with decreased oxygen saturation) and pulmonary rehabilitation [3].

The results of our study (according to our knowledge it is the first assessment of the frequency of COPD in the advanced lung cancer patients in Poland) indicate that the thorough diagnosis of other respiratory tract diseases, including COPD, may be of high importance in advanced lung cancer patients, since the frequency of both diseases is common in Polish population.

References

1. Levi F, Lucchini F, Negri E, La Vecchia C. Continuing declines in cancer mortality in the European Union. *Ann Oncol.* 2007; 18: 593–595.
2. Zielinski J, Bednarek M, Gorecka D et al. Increasing COPD awareness. *Eur Respir J* 2006; 27: 833–852.
3. http://www.goldcopd.dk/index_uk.htm
4. Van de Schans SA, Janssen-Heijnen ML, Biesma B et al. COPD in cancer patients: Higher prevalence in the elderly, a different treatment strategy in case of primary tumours above the diaphragm, and a worse overall survival in the elderly patient. *Eur J Cancer* 2007; 43: 2194–2202.
5. Moreno M, Aristu J, Ramos LI et al. Predictive factors for radiation-induced pulmonary toxicity after three-dimensional conformal chemoradiation in locally advanced non small cell lung cancer. *Clin Transl Oncol* 2007; 9: 596–602.
6. Dancewicz M, Kowalewski J, Peplinski J. Factors associated with perioperative complications after pneumonectomy for primary carcinoma of the lung. *Interact Cardiovasc Thorac Surg* 2006; 5: 97–100.

7. Sekine Y, Yamada Y, Chivo M et al. Association of chronic obstructive pulmonary disease and tumor recurrence in patients with stage IA lung cancer after complete resection. *Ann Thorac Surg* 2007; 84: 946–950.
8. Subotic DR, Mandaric DV, Eminovic TM et al. Influence of chronic obstructive pulmonary disease on postoperative lung function and complications in patients undergoing operations for primary non small cell lung cancer. *J Thorac Cardiovasc Surg* 2007; 134: 1292–1299.
9. Dudgeon DJ. Dyspnoea in cancer patients: prevalence and associated factors. *J Pain Symptom Manage* 2001; 21: 95–102.
10. Bruera E, Schmitz B, Pither J et al. The frequency and correlates of dyspnoea in patients with advanced cancer. *J Pain Symptom Manage* 2000; 19: 357–362.
11. Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. *Cochrane Database Syst Rev* 2004; CD002916.
12. Duisters C, Beusken H, Nijsten S et al. Palliative chest irradiation in sitting position in patients with bulky advanced lung cancer. *Radiother Oncol* 2006; 79: 285–287.
13. Mallick I, Sharma SC, Behera D. Endobronchial brachytherapy for symptom palliation in non-small cell lung cancer — analysis of symptom response, endoscopic improvement and quality of life. *Lung Cancer* 2007; 55: 313–318.
14. Maiwand O, Glynne-Jones R, Chambers J, Asimakopoulos G. Direct cryosurgery for inoperable metastatic disease of the lung. *Ann Thorac Surg*. 2006; 81: 718–721.
15. Von Plessen C, Bergman B, Andresen O et al. Palliative chemotherapy beyond three courses conveys no survival or consistent quality of life benefits in advanced non small cell lung cancer. *Br J Cancer* 2006; 95: 966–973.
16. Camps C, Caballero C, Blasco A et al. Weekly paclitaxel as second/third-line treatment in advanced non small cell lung cancer patients: efficacy and tolerability. *Anticancer Res* 2005; 25: 4611–4614.
17. Kvale PA, Selecky PA, Prakash UBS. Palliative Care in Lung Cancer. ACCP Evidence-Based Clinical Practice Guidelines. *Chest* 2007; 132: 389–403.
18. Bruera E, Sweeney C, Willey J et al. A randomized controlled trial of supplemental oxygen versus air in cancer patients with dyspnoea. *Palliat Med* 2003; 17: 659–663.
19. Philip J, Gold M, Milner A et al. A randomized, double-blind, crossover trial of the effect of oxygen on dyspnoea in patients with advanced cancer. *J Pain Symptom Manage* 2006; 32: 541–550.