ORIGINAL RESEARCH

Histological subtype of lung cancer affects acceptance of illness, severity of pain, and quality of life

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Introduction: Histologic classification of lung cancer plays an important role in clinical practice. Two main histological subtype of lung cancer: small-cell lung cancer (SCLC) and nonsmall-cell lung cancer (NSCLC) differ in terms of invasiveness, response to treatment, and risk factors, among others.

Aims: To evaluate differences in acceptance of illness, level of perceived pain, and quality of life (QoL) between patients with SCLC and NSCLC.

Materials and methods: Two hundred and fifty-seven lung cancer patients, who were treated in 2015, completed Acceptance of Illness Scale, Visual Analog Scale for pain, and European Organization for Research and Treatment of Cancer 30-item Core Quality of Life Questionnaire and European Organization for Research and Treatment of Cancer 13-item Lung Cancer specific Quality of Life Questionnaire. Clinical and sociodemographic data were collected. For statistical analysis, the Student t-test and the Mann–Whitney U test were used. For comparisons among three or more groups, analysis of variance was employed.

Results: Patients with SCLC had significantly worse health as measured with the presence of metastases, parameters of lung function, comorbidities, and number of previous hospitalizations. The Acceptance of Illness Scale score and Visual Analog Scale score were significantly worse in patients with SCLC than in those with NSCLC (24.58 ± 8.73 vs 27.05 ± 9.06; $p=0.046$ and 4.81 ± 2.01 vs 4.17 ± 1.97; $p=0.003$). Patients with SCLC achieved worse scores of all aspects of QoL than patients with NSCLC. Comparison with the reference values showed that all dimensions of functioning are impaired in patients with lung cancer regardless of its type; only the role functioning in patients with NSCLC remains unaffected.

Conclusion: Monitoring of QoL, personalized approach to treatment, and interventions for symptom management should be conducted in a tailored manner. Socioeconomic status in lung cancer patients, especially those suffering from SCLC, needs to be addressed.

Keywords: Acceptance of Illness Scale, Visual Analog Scale for pain, lung cancer, quality of life, QLQ-C30 and QLQ-LC13

Introduction

Histologic classification of lung cancer plays an important role in clinical practice. Determining histologic subtype of lung cancer helps to personalize treatment strategies and determine prognosis more precisely. Since 1967, when the first edition of histological classification was published by the World Health Organization, efforts have been made to improve the knowledge about associations between cancer histology and response to treatment options, underlying genetic disorders, risk factors, and survival, among others.[1,2]

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The histological characteristic of cancer is based on architectural or cytological features of cancer cells and includes mitotic count, cell differentiation, and the presence of necrosis. There are two main histological subtypes of lung cancer: small-cell lung cancer (SCLC), which has an incidence of 15%–17% of all diagnosed lung cancers, and nonsmall-cell lung cancer (NSCLC), which has an incidence exceeding 85%.[3,4] Despite their origin in the lung tissue, many differences exist between these two subtypes such as invasiveness, response to treatment options, and risk factors.

SCLC is diagnosed about nine times less often than NSCLC, but this subtype of cancer is responsible for high mortality due to its invasiveness and ease of metastasis. The median survival of patients with this cancer is about 6 months and the 1-year relative survival rate about 33%.[5] Low survival rates are a consequence of 70% of SCLC being diagnosed at extensive disease stage with hematogenous metastases, which limits the use of radical surgery. However, sensitivity to initial chemotherapy and radiotherapy does not improve outcomes due to frequent recurrence.[6]

The natural history of the disease is different for NSCLC. First, about one-third of patients present with limited-stage disease at the time of diagnosis. However, the median survival of patients with NSCLC based on National Lung Cancer Audit is 6.3 months, and prognosis is better for patients with good performance status and early stage of the disease.[7] There are differences in outcomes between males and females, partly due to exposure to tobacco smoke. According to Visbal et al,[8] estimated crude survival in men is 51% and 15% at 1 and 5 years, whereas in women, it is 60% and 19%, respectively.

The differences in the natural course of the disease between SCLC and NSCLC may translate into severity of perceived symptoms and adaptation to the disease; therefore, the aim of the study was to evaluate differences in acceptance of illness, the level of perceived pain, and quality of life (QoL) between patients with SCLC and NSCLC.

Materials and methods

For the study, 257 lung cancer patients (115 women and 142 men) treated in the Lower Silesian Center of Lung Diseases in Wroclaw in 2015 were enrolled. Two hundred and eighty patients at admission to hospital were asked to complete Acceptance of Illness Scale (AIS), Visual Analog Scale for pain (VAS), and European Organization for Research and Treatment of Cancer 30-item Core Quality of Life Questionnaire (QLQ-C30) and European Organization for Research and Treatment of Cancer 13-item Lung Cancer specific Quality of Life Questionnaire (QLQ-LC13) questionnaires for

the assessment of QoL. Twenty-three patients were excluded due to incompletely or incorrectly filled in questionnaires. Clinical data were collected from medical records. Sociodemographic data were sourced from the survey. The study was conducted after obtaining approval from the local Bioethics Committee at Wroclaw Medical University (No 507/2015). Each enrolled patient gave his/her written informed consent prior to entering the study.

In the study, the AIS questionnaire developed by Felton et al[10] and adapted to Polish conditions was used.[9] This scale can be used to evaluate acceptance of any illness among adult patients. The scale consists of 8 items—answers are measured with a 5-point Likert scale. The total score is from 8 to 40. A total score below 20 indicates poor acceptance of illness translating into psychological discomfort. Scores between 20 and 30 indicate a moderate level of acceptance, whereas above 30 indicates high acceptance of the disease. The scale showed high reliability in Polish population (Cronbach's α=0.85; test–retest reliability=0.64).[9]

The intensity of pain was measured with the VAS for pain. It is one of the most common tools for assessment of pain, because it is simple and intuitive. It includes only 1 item in the form of a 10 cm horizontal line with the two endpoints labeled: "no pain" and "maximum pain" on which patients mark a point corresponding to the severity of pain they feel. The result ranges from 0 to 10, with higher score indicating greater intensity of pain.[11,12]

For the measurement of QoL, two questionnaires were used: the European Organization for Research and Treatment of Cancer QLQ-C30 and a supplementary module for lung cancer patients.[13–15] The QLQ-C30 is a 30-item questionnaire that includes questions about global health status, functioning (physical, role, cognition, emotional, and social), and symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial problems). In the first module of the scale, higher scores indicate better QoL, whereas in the second, higher scores indicate greater symptom burden, thus worse QoL. The QLQ-LC13 module is used to evaluate lung cancer-specific symptoms such as dyspnea; coughing; hemoptysis; sore mouth and tongue; dysphagia; peripheral neuropathy; hair loss; pain in the chest, arm, or other sites; and using analgesics. Items in both QoL scales are scaled to range from 0 to 100. The results of QLQ-C30 were compared with reference values calculated separately for SCLC and NSCLC.[16] The QLQ-C30 was validated among the Polish cancer population. The interclass correlations ranged from 0.82 to 0.91 and Cronbach's α was 0.62.[17]

Data were statistically analyzed. Descriptive statistics were calculated. The Shapiro–Wilk test was used to analyze the distribution of the data. For comparisons between two groups with normal distribution, Student *t*-test was used, whereas for comparisons between two groups with distribution other than normal, the Mann–Whitney *U* test was used. For comparisons of quantities variables among three or more groups, analysis of variance was performed, that is, the Kruskal–Wallis test for variables with distribution other than normal. If such a comparison revealed significant differences, analysis of variance was followed by post hoc test: LSD Fisher test for variables with normal distribution and Dunn test for variables with distribution other than normal. Correlations were described as Pearson's correlation coefficient and Spearman's rank correlation coefficient depending on the distribution of variables. Data were considered to be statistically significant at a value of *p*<0.05. Statistical analysis was carried out with the R Project for Statistical Computing v. 3.4.1.

Results

Two hundred and fifty-seven lung cancer patients with mean age of 63.2 (9.4) were recruited for the study. Of this group, 72 were diagnosed with SCLC and 185 with NSCLC. No significant differences were found between the group with SCLC and NSCLC in age (62.8±9.6 vs 64.1±8.8; *p*=0.358), sex (*p*=0.841), marital status (*p*=0.701), education (*p*=0.054), employment status (*p*=0.279), performance status (*p*=0.325), and the number of reported symptoms (*p*=0.353). Patients with SCLC had significantly more comorbidities (*p*<0.001), more metastases (*p*=0.036), and were more often admitted to the hospital (*p*<0.001). Significantly greater number of patients with NSCLC than with SCLC was treated with surgery as the only type of treatment (40.54% vs 6.94%; *p*<0.001). Over 93% of patients with SCLC were offered other types of treatment including combined treatment. Additionally, patients with SCLC had lower values of forced expiratory volume in 1 second (2.1±0.6 vs 2.4±0.8; *p*=0.014) and forced vital capacity (2.8±0.9 vs 3.1±1; *p*=0.005), but the difference in forced expiratory volume in 1 second/forced vital capacity (%) was insignificant (79.2±15.879.4±20.6; *p*=0.219). Demographic and clinical characteristics by the type of the cancer histology are presented in Table 1.

AIS score was significantly lower in patients with SCLC than in those with NSCLC (24.58±8.73 vs 27.05±9.06; *p*=0.046). This result showed worse acceptance of illness in the group of SCLC patients. Similarly, patients with SCLC experienced significantly more pain measured with VAS than patients with NSCLC (4.81±2.01 vs 4.17±1.97; *p*=0.003).

For both groups, AIS score was significantly negatively correlated with VAS score (*R*=–0.517; *p*<0.001), which means that less pain is associated with better acceptance of illness.

Patients with SCLC had lower QoL than patients with NSCLC. Nearly all of the aspects of QoL were affected by the disease to the greater degree in patients with SCLC than in those with NSCLC. Comparison with the reference values showed that all dimensions of functioning are impaired in patients with lung cancer regardless of its type; only the role functioning in patients with NSCLC remains unaffected. Scores of QLQ-C30 with respective reference values and scores of QLQ-LC13 scale are presented in Table 2.

The level of acceptance of illness correlates with QoL. There was a significant correlation between AIS score and all functioning scores measured with QLQ-C30 in both study groups. Severity of greater number of symptoms was significantly correlated with AIS score in the group of patients with NSCLC than in the group of patients with SCLC. Correlation coefficients are presented in Table 3.

Discussion

Our study revealed that patients with SCLC had significantly worse health condition, lower acceptance of illness, and experienced significantly more pain, which was associated with worse QoL in comparison with patients with NSCLC; however, comparison with reference values revealed that lung cancer patients reported reduced QoL regardless of the cancer subtype in all QLQ-C30 items except for role functioning in NSCLC patients.[16]

Patient-reported QoL is an important aspect of treatment in oncology. The Food and Drug Administration included QoL into patient-reported outcomes and defined them as a measurement of any aspect of a patient's health status that comes directly from the patient (ie, without the interpretation of the patient's responses by a physician or anyone else).[18] First of all, QoL has an impact on prognosis. Montazeri et al[19] confirmed that general health measured with the Nottingham Health Profile and functioning scores and global QoL assessed with QLQ-C30 are significant predictors of survival in the population of lung cancer patients. Efficace et al,[20] using the same tools as we used in our study (QLQ-C30 and QLQ-LC13), showed that among patients with NSCLC stage IIIB and stage IV, pain and dysphagia translated into significant increase in the likelihood of death with an HR of 1.11 (95% CI 1.07–1.16; *p*<0.001) and 1.12 (95% CI: 1.04–1.21; *p*=0.003), respectively. Similar results were reported by Herndon et al[21] who studied a group of patients with advanced metastatic NSCLC. After adjustment for clinical factors, perceived pain

Table 1 Demographic and clinical characteristics of the study group

Variables	SCLC; n=72, n (%)	NSCLC; n=185, n (%)	Total; n=257, n (%)	*p*-value
Sex				
Woman	31 (43.06%)	84 (45.41%)	115 (44.75%)	0.841
Men	41 (56.94%)	101 (54.59%)	142 (55.25%)	
Marital status				
In a relationship	45 (62.50%)	109 (58.92%)	154 (59.92%)	0.701
Alone	27 (37.50%)	76 (41.08%)	103 (40.08%)	
Education				
Primary	14 (19.44%)	15 (8.11%)	29 (11.28%)	
Vocational	28 (38.89%)	90 (48.65%)	118 (45.91%)	0.054
Secondary	25 (34.72%)	61 (32.97%)	86 (33.46%)	
Higher	5 (6.94%)	19 (10.27%)	24 (9.34%)	
Employment status				
Employed	14 (19.44%)	54 (29.19%)	68 (26.46%)	
Pensioner	56 (77.78%)	125 (67.57%)	181 (70.43%)	0.279
Supported by relatives	2 (2.78%)	6 (3.24%)	8 (3.11%)	
Comorbidities				
No comorbidities	12 (16.67%)	62 (33.51%)	74 (28.79%)	
One disease	28 (38.89%)	82 (44.32%)	110 (42.80%)	
Two diseases	25 (34.72%)	39 (21.08%)	64 (24.90%)	<0.001
Three diseases	7 (9.72%)	2 (1.08%)	9 (3.50%)	
Metastases				
No metastases	35 (48.61%)	121 (65.41%)	156 (60.70%)	
To one organ	23 (31.94%)	44 (23.78%)	67 (26.07%)	**0.036**
Multiorgan	14 (19.44%)	20 (10.81%)	34 (13.23%)	
Treatment				
Surgery alone	5 (6.94%)	75 (40.54%)	80 (31.13%)	**<0.001**
Other	67 (93.06%)	110 (59.46%)	177 (68.87%)	
WHO performance status				
Grade 0	13 (18.06%)	34 (18.38%)	47 (18.29%)	
Grade 1	27 (37.50%)	80 (43.24%)	107 (41.63%)	
Grade 2	26 (36.11%)	61 (32.97%)	87 (33.85%)	0.325
Grade 3	3 (4.17%)	9 (4.86%)	12 (4.67%)	
Grade 4	3 (4.17%)	1 (0.54%)	4 (1.56%)	

Note: Significant differences are marked in bold.
Abbreviations: NSCLC, nonsmall-cell lung cancer; SCLC, small-cell lung cancer; WHO, World Health Organization.

had the greatest prognostic importance for survival with an HR of 1.006.[21] The level of QoL should be monitored even before the diagnosis because many cancer patients experience nonspecific symptoms such as pain or couching much earlier, thus it is important to establish a prediagnosis status of QoL. Additionally, a prediagnosis level of QoL was proved to be an important predictor of survival.[19–22] However, measuring a prediagnosis level of QoL in all patients suffering from non-specific symptoms is difficult and challenging, but it would give valuable information; therefore, it essential to establish the level of QoL at least at the time of diagnosis.

Our study showed that patients with SCLC presented with lower levels of QoL and acceptance of illness than patients with NSCLC. This condition may be rooted in many factors. Primarily, SCLC patients reported worse well-being. The comparison between the groups revealed that SCLC patients had more advanced disease in terms of metastases and were more treated with combined treatment, which also reflects greater progression of metastatic disease. Disease origin, histology, treatment, and prognosis for those groups of patients add to the differences found between patients with SCLC and NSCLC. Reports from the literature show that despite the differences, there are also many similarities between those groups of patients.[23–27] Therefore, we believe that comparison between SCLC and NSCLC patients can help to improve treatment strategies, especially since comparison in QoL and acceptance of illness are scarce in the literature.

QoL and symptom burden is important for lung cancer patients. Due to the severity of the disease, in most cases, treatment is aggressive, associated with treatment-induced toxicity, and often conducted with the aim to palliate symptoms, which affects patients with SCLC to a greater degree. Also, current research into lung cancer therapy is largely focused on molecular therapies for NSCLC which may improve

Table 2 Comparison of QoL between patients with NSCLC and SCLC

Variables	NSCLC	SCLC	*p*-value	Reference values NSCLC[a]	Reference values SCLC[a]
QLQ-C30 functioning area					
Global	47.12±23.21	38.31±20.25	0.009	58.8±22.5	67.1±20.4
Physical	72.32±17.96	61.02±21.13	**<0.001**	78.4±19.3	78.7±18.7
Role	65.95±27.41	51.62±28.96	**<0.001**	60.7±33.1	73.9±29.8
Emotional	57.97±28.76	52.43±25.46	0.171	68.1±24.2	75.9±21.7
Cognitive	76.13±21.12	68.06±24.35	**0.018**	84.0±21.1	85.7±19.7
Social	65.77±32.4	59.49±23.21	**0.038**	73.6±28.9	76.0±26.1
QLQ-C30 symptom area					
Fatigue	42.64±26.51	51.23±25.4	**0.016**	40.4±27	36.4±25.3
Nausea/vomiting	12.61±18.23	30.32±26.88	**<0.001**	9.7±18.3	9.9±17.6
Pain	36.94±23.8	44.44±27.69	**0.033**	29.7±30.3	18.4±24.8
Dyspnea	41.62±24.4	48.61±27.37	0.057	38.5±31.7	31.8±29.8
Sleep disturbance	41.98±31.43	50.46±29.6	0.054	32.4±32.7	23.1±27.8
Appetite loss	31.17±28.36	43.52±31.47	**0.004**	27.9±33.5	24.3±30.4
Constipation	17.48±26.25	27.78±28.53	**0.002**	17.4±27.9	15.6±26.1
Diarrhea	9.19±22.65	11.57±19.51	0.065	6.8±17.4	7.3±16
Financial problems	33.33±31.85	53.7±28.83	**<0.001**	12.8±25.8	17.0±28.8
QLQ-LC13					
Dyspnea	34.17±22.83	47.99±23.58	**<0.001**		
Coughing	50.09±24.11	54.63±27.01	0.256		
Hemoptysis	14.59±20.78	19.91±24.17	0.105		
Sore mouth and tongue	7.57±15.63	23.15±27.2	**<0.001**		
Dysphagia	12.79±19.93	25.93±29.19	**<0.001**		
Peripheral neuropathy	11.89±18.79	29.63±28.28	**<0.001**		
Hair loss	12.07±23.92	30.56±37.42	**<0.001**		
Chest pain	23.24±25.19	41.2±29.86	**<0.001**		
Pain in arm or shoulder	12.79±22.49	21.76±28.61	**0.009**		
Other pain sites	23.78±27.56	29.17±34.46	0.451		
Taking analgesics	50.41±37	49.31±31.67	0.477		

Notes: Significant differences are marked in bold. [a]According to the EORTC QLQ-C30 reference values.[16]
Abbreviations: NSCLC, nonsmall-cell lung cancer; SCLC, small-cell lung cancer; QoL, quality of life; QLQ-C30, European Organization for Research and Treatment of Cancer 30-item Core Quality of Life Questionnaire; QLQ-LC13, European Organization for Research and Treatment of Cancer 13-item Lung Cancer specific Quality of Life Questionnaire.

future outcomes, but only in this group of patients. Studies revealed deficits in QoL dimensions with no improvement after introduced treatment and shorted survival in patients with SCLC.[28] Our study also confirmed that QoL is worse in SCLC than in NSCLC. However, interventions with the aim to alleviate symptoms of the disease have significant impact of QoL. Pain management and cessation of smoking are associated with reduction in perceived pain, dyspnea, and fatigue.[29]

Studies assessing acceptance of illness in lung cancer patients are scarce. Religioni et al[30] reported that patients with lung cancer had significantly lower level of acceptance of illness than patients with breast, colorectal, and prostate carcinoma. The mean AIS score for lung cancer patients was 23.17. They also found a correlation between income and AIS score, which was significant only in lung cancer patients.[30] Patients from our study had slightly higher level of acceptance (27.05 for NSCLC and 24.58 for SCLC), but interestingly, in the group with SCLC, financial problems scale score was

over threefold worse than reference values. Such discrepancy is alarming. It draws attention to the fact that patients with advanced lung cancer may live in poverty, which in turn decreases their QoL and chances for optimal treatment.

Our study draws attention to the fact that intensity of symptoms and QoL may vary among patients with the same diagnosis; therefore, there is a need for collection of patient-reported outcomes data with standardized tools and tailored approach to treatment. In clinical practice, patient's perspective differs from physician's assessment, which can lead to underestimating symptom severity or health condition. Efficace et al[31] showed that agreement on symptom ratings between patients with chronic myeloid leukemia and their treating physicians ranges from 34% for muscle cramps to 66% for nausea. All symptoms were more severe from patient's perspective than from physician's perspective.[31] Also, attitudes to treatment options and outcomes expectations may not be the same. As reported

Table 3 Correlations between acceptance of illness and dimensions of QoL in patients with NSCLC and SCLC

Variables	AIS score in NSCLC patients		AIS score in SCLC patients	
	Correlation coefficient	*p*-value	Correlation coefficient	*p*-value
QLQ-C30 functioning area				
Global	0.754	**<0.001**	0.577	**<0.001**
Physical	0.495	**<0.001**	0.62	**<0.001**
Role	0.629	**<0.001**	0.666	**<0.001**
Emotional	0.742	**<0.001**	0.593	**<0.001**
Cognitive	0.595	**<0.001**	0.537	**<0.001**
Social	0.723	**<0.001**	0.642	**<0.001**
QLQ-C30 symptom area				
Fatigue	0.723	**<0.001**	−0.658	**<0.001**
Nausea/vomiting	−0.648	**<0.001**	−0.229	0.053
Pain	−0.396	**<0.001**	−0.617	**<0.001**
Dyspnea	−0.648	**<0.001**	−0.525	**<0.001**
Sleep disturbance	−0.324	**<0.001**	−0.453	**<0.001**
Appetite loss	−0.47	**<0.001**	−0.366	**0.002**
Constipation	−0.443	**<0.001**	−0.09	0.453
Diarrhea	−0.154	**0.037**	−0.069	0.565
Financial problems	−0.187	**0.011**	−0.182	0.125
QLQ-LC13				
Dyspnea	−0.598	**<0.001**	−0.554	**<0.001**
Coughing	−0.409	**<0.001**	−0.336	**0.004**
Hemoptysis	0.158	**0.032**	−0.173	0.147
Sore mouth and tongue	−0.205	**0.005**	−0.357	**0.002**
Dysphagia	−0.394	**<0.001**	−0.048	0.687
Peripheral neuropathy	−0.328	**<0.001**	−0.206	0.083
Hair loss	−0.022	0.765	−0.125	0.294
Chest pain	−0.339	**<0.001**	−0.254	**0.031**
Pain in arm or shoulder	−0.251	**0.001**	−0.225	0.057
Other pain sites	−0.441	**<0.001**	−0.339	**0.004**
Taking analgesics	−0.049	0.509	−0.123	0.302

Note: Bold text represents a statistically significant value of *p*<0.05.
Abbreviations: AIS, Acceptance of Illness Scale; NSCLC, nonsmall-cell lung cancer; SCLC, small-cell lung cancer; QoL, quality of life; QLQ-C30, Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QLQ-LC13, Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 13.

by Chu et al,[32] physicians were more inclined to set smaller goals such as relief of symptoms, whereas patients with advanced NSCLC more likely opted for extended survival with acceptance of high toxicity due to chemotherapy. These examples emphasize the role of proper dialogue between patients and their treating physicians to enable taking into consideration patients reported outcomes and using tools for their assessment broadly in clinical practice.

Conclusion

Patients with SCLC reported lower level of QoL, lower acceptance of illness, and higher intensity of pain than patients with NSCLC. Monitoring of QoL, personalized approach to treatment, goal of treatment based on mutual expectations, and interventions for symptom management may improve prognosis in this group of patients. Socioeconomic status of lung cancer patients, especially those suffering from SCLC, needs to be addressed.

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Disclosure

The authors report no conflicts of interest in this work.

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