VIA MEDICA

NOWOTWORY Journal of Oncology
2023, volume 73, number 6, 338–346
DOI: 10.5603/njo.97368

ISSN: 0029–540X, e-ISSN: 2300-2115
www.nowotwory.edu.pl

Original article

Lung cancer

Analysis of the clinical and pathological characteristics of patients with the squamous-cell lung carcinoma including group survival rates and the occurrence of symptoms depending on the extent of the tumor

Weronika Targosz[1], Julia Świerczek[1], Błażej Ochman[1], Paweł Kiczmer[2], Paweł Ziora[2], Mateusz Rydel[3], Damian Czyżewski[3], Maciej Borowiecki[1], Bogna Drozdowska[2]

[1]*Medical University of Silesia, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland*
[2]*Department of Pathomorphology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland*
[3]*Department of Thoracic Surgery, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland*

Introduction. Non-small-cell lung carcinoma (NSCLC) constitutes 80% of all lung cancer cases, of which 25–30% are squamous-cell carcinoma (SCC). We investigated the impact of comorbidities and other risk factors on the survival of patients with SCC, including the correlation between symptoms and the maximum tumor size.

Materials and methods. The study cohort included 417 patients. The Kaplan-Meier method, the Log-rank test, Gehan's generalized Wilcoxon test, the Mann-Whitney U test, the t-test and Cox's model of proportionality of hazards were applied.

Results. The maximum tumor size exhibited a significant correlation with the presence of symptoms such as cough, hemoptysis, and weight loss. Patients who presented with a positive family history of cancer, a prior history of cancer, respiratory diseases, or hypertension experienced a notably reduced survival time.

Conclusions. Patient's symptoms and their medical history are important in predicting survival.

Key words: lung, carcinoma, squamous-cell, survival analysis

Introduction

According to the GLOBOCAN data for the year 2020, lung cancer constitutes 11.4% of all malignant tumors in terms of morbidity, and it is responsible for 18% of deaths caused by malignant tumors worldwide. Non-small-cell lung carcinoma (NSCLC) constitutes 80% of all lung carcinoma cases, of which 25–30% are squamous-cell carcinoma. The prognosis for patients diagnosed with lung cancer is unfavorable and is closely associated with the cancer's stage at the time of diagnosis, and the specific subtype of NSCLC. Men demonstrate a higher incidence of lung cancer compared to women, a discrepancy probably linked to lifestyle and genetic factors [1–5].

Among NSCLC, squamous-cell lung carcinoma (SCC) is the cancer most strongly associated with smoking. The role of classic or electronic cigarette fumes in the pathogenesis of SCC may be related to a decreased DNA methylation in regions strictly responsible for the proper functioning

How to cite:

Targosz W, Świerczek J, Ochman B, Kiczmer P, Ziora P, Rydel M, Czyżewski D, Borowiecki M, Drozdowska B. ***Analysis of the clinical and pathological characteristics of patients with the squamous-cell lung carcinoma including group survival rates and the occurrence of symptoms depending on the extent of the tumor.*** *NOWOTWORY J Oncol* 2023; 73: 338–346.

of the respiratory epithelium. In addition to active smoking, it is important to consider the role of passive smoking, which significantly influences the occurrence of lung cancer. There is substantial evidence suggesting that passive smoking has a greater impact on the development of adenocarcinoma than on the development of SCC. The SCC is also associated with environmental factors, genetic predisposition, i.e. a positive family history of cancer, positive cancer history, and also comorbidities – especially lung diseases [6–9].

Symptoms of centrally located tumors are most often a cough, as well as symptoms resulting from atelectasis or obstructive pneumonia, i.e. shortness of breath. Haemoptysis, which is often associated with lung cancer, may occur in SCC due to the extravasation of blood from the bronchial artery within the tumor or less often, from the pulmonary artery [4, 6].

The aim of the study was to determine the characteristics of patients with SCC and the characteristics of tumors such as size, TNM grade, and histopathological grade. The study also aimed to detect a possible relationship between exposure to risk factors and patient survival, so as to detect a correlation between patients' symptoms and maximum tumor size.

Materials and methods

The study included a cohort of 417 patients diagnosed with SCC who underwent radical anatomical resection of the lung tissue (segmentectomy, lobectomy, bilobectomy or pneumonectomy) due to lung cancer between May 2012 and December 2021. A dedicated database was established to compile the medical records of all patients who underwent surgery for lung cancer. Patients were observed for five years from the day of surgery. Data about patients' survival was collected up to 1st May 2022. All further outcomes were considered incomplete. Inclusion criteria: primary SCC confirmed histologically, lobectomy or pneumonectomy, age over 18. Exclusion criteria: histopathologically confirmed adenocarcinoma, histopathologically confirmed secondary lung cancer, the presence of more than one histologically different tumor in the specimen. Limits of our study: lack of information about patients after the end of the 5-year follow-up, lack of exact information about death, lack of exact data about chemotherapy. The detailed study design is presented in figure 1.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the Medical University of Silesia (No PCN/0022/KB/27/21).

Statistical analysis

Data is presented as the number of cases with percentage and for quantative variables as mean +/– SD or median with Q1 and Q3. The normality assumption was tested for each quantitative variable based on a graphical interpretation of the Q-Q plots and histograms. Odds ratios with 95% confidence intervals were calculated for categorical variables.

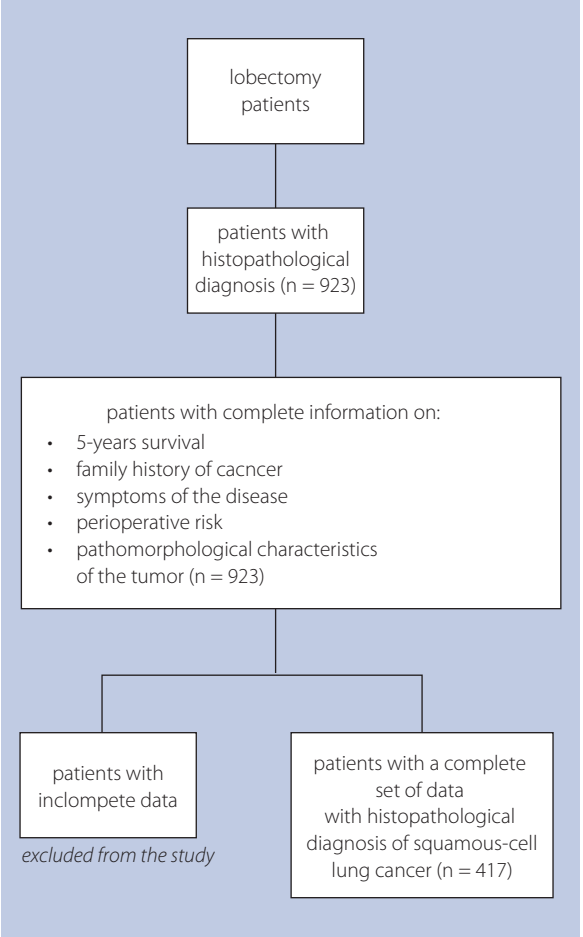

Figure 1. Study design flowchart

Pearson's chi-square test, the t-test and the Wilcoxon test were used to determine the significance of differences between groups with different selected characteristics. The Kaplan–Meier method was used to determine the probabilities of survival among the groups. The comparison of survival was performed using the Mantel-corrected log-rank test during which more than two groups were compared. To assess the impact of variables on patient survival, the Cox proportional hazards model was used. P-values less than 0.05 were considered significant. The analysis was carried out using the Rlanguage in the Rstudio software.

Results

The study encompassed 281 male and 136 female participants. Among the study participants, 81.5% were active cigarette smokers, while 73.4% had been exposed to second-hand smoke. Complications during the surgical procedure affected 33.3% of patients. The predominant T classifications for the cancer cases were T2 (36.1%) and T1 (33.6%). The majority of patients showed no neoplastic involvement in their lymph nodes (61.3%). Most patients presented with a histopathological malignancy of grade G2. A total of 1.4% of patients died during hospitalization. The mean age of the participants

in the study was approximately 68 years. The median pack-years for smokers was approximately 40 years. The median maximum tumor size was 40.00 mm, and the median survival duration was 1321 days (approximately 3.5 years). Notably, no statistically significant differences were observed between the groups ($p > 0.05$) (tab. I).

Symptoms indicative of neoplastic disease were reported by 54.9% of the patients. A cough was the most frequently reported symptom, accounting for 41.0% of the total cases and prevalent among both smokers and non-smokers. The median of weight loss was 8.00 kg in the smoking group and 6.50 kg in the non-smoking group. The median of percentage weight loss was 10.00% in the smoking group and 9.00% in the non-smokers group. There were no significant differences observed between these groups ($p > 0.05$) (tab. I).

A positive cancer history concerned 15.8% of patients, while a positive family history of cancer was noted in 14.9% of patients. Surgical risk factors were identified in 58.3%

Table I. Characteristics of patients grouped by smoking status (n = 417)

Characteristic	Overall	Smoker		p-value
		No	Yes	
	n (%)	n (%)	n (%)	
smoking cigarettes	340 (81.5%)	–	–	–
second-hand smoking	306 (73.4%)	–	–	–
gender				
male	281 (67.4%)	54 (70.1%)	227 (66.8%)	0.664
female	136 (32.6%)	23 (29.9%)	113 (33.2%)	
surgery complication	139 (33.3%)	25 (32.5%)	114 (33.5%)	0.964
hemothorax requiring re-surgery	15 (3.6%)	4 (5.2%)	11 (3.2%)	0.621
blood tranfusion during or after surgery	36 (8.6%)	5 (6.5%)	31 (9.1%)	0.606
drainage	40 (9.6%)	12 (15.6%)	28 (8.2%)	0.078
disease symptoms	229 (54.9%)	35 (45.5%)	194 (57.1%)	0.085
pain	15 (3.6%)	1 (1.3%)	14 (4.1%)	0.389
hemoptysis	48 (11.5%)	6 (7.8%)	42 (12.4%)	0.350
dyspnoea	17 (4.1%)	3 (3.9%)	14 (4.1%)	1.000
cough	171 (41.0%)	30 (39.0%)	141 (41.5%)	0.783
weight loss	21 (5.0%)	2 (2.6%)	19 (5.6%)	0.427
TNM scale				
T feature				
I	135 (33.6%)	23 (30.7%)	112 (34.3%)	0.860
II	145 (36.1%)	27 (36.0%)	118 (36.1%)	
III	80 (19.9%)	18 (24.0%)	62 (19.0%)	
IV	41 (10.2%)	7 (9.3%)	34 (10.4%)	
x	1 (0.2%)	0 (0.0%)	1 (0.3%)	
N feature				
0	253 (61.3%)	44 (57.1%)	209 (62.2%)	0.719
I	87 (21.1%)	16 (20.8%)	71 (21.1%)	
II	5 (1.2%)	1 (1.3%)	4 (1.2%)	
x	68 (16.5%)	16 (20.8%)	52 (15.5%)	
M feature = x	410 (100.0%)	77 (100.0%)	333 (100.0%)	

→

Table I cont. Characteristics of patients grouped by smoking status (n = 417)

Characteristic	Overall	Smoker		p-value
		No	Yes	
	n (%)	n (%)	n (%)	
grade				
I	27 (6.5%)	3 (3.9%)	24 (7.1%)	0.301
II	222 (53.2%)	48 (62.3%)	174 (51.2%)	
III	141 (33.8%)	24 (31.2%)	117 (34.4%)	
IV	1 (0.2%)	0 (0.0%)	1 (0.3%)	
x	26 (6.2%)	2 (2.6%)	24 (7.1%)	
death during hospitalization	6 (1.4%)	1 (1.3%)	5 (1.5%)	1.000
quantitative characteristics				
pack-years				
median	30.00	–	–	–
q1	20.00	–	–	–
q3	45.00	–	–	–
age during surgery				
mean	67.77	68.44	67.62	0.387
stabilization of the disease (SD)	7.11	7.63	6.99	
weight loss (kg)				
median	8.00	6.50	8.00	0.586
q1	4.00	4.75	4.50	
q3	10.00	8.25	11.00	
weight loss (%)				
median	10.00	9.00	10.00	0.809
q1	5.00	6.00	6.50	
q3	15.00	12.00	16.50	
maximum tumor size (mm)				
median	40.00	40.00	40.00	0.987
q1	25.00	25.00	25.00	
q3	55.00	55.00	60.00	
5-year survival (days)				
median	1321.00	1251.00	1358.00	0.731
q1	623.00	684.00	622.00	
q3	1825.00	1825.00	1825.00	

x – feature cannot be assessed

of patients, with hypertension (60.2%), non-insulin-dependent diabetes mellitus (24.9%), respiratory system diseases (24.5%), and coronary artery disease (24.2%) being the prevailing factors. Statistically significant differences were observed between smokers and non-smokers who had experienced a myocardial infarction more than six months prior and those diagnosed with coronary artery disease. A higher percentage of patients who had a myocardial infarction six months earlier ($p = 0.022$) and a greater proportion of patients diagnosed with coronary artery disease ($p = 0.044$) were non-smokers (tab. II).

The median of the maximum tumor size was higher among patients who reported disease symptoms. The Wilcoxon test analysis revealed that these differences were highly significant

Table II. Overall medical history and depending on smoking status (n = 417)

Characteristic	Overall	Smoker		p-value
		No	Yes	
	n (%)	n (%)	n (%)	
positive cancer history	66 (15.8%)	17 (22.1%)	49 (14.4%)	0.136
positive family history of cancer	62 (14.9%)	10 (13.0%)	52 (15.3%)	0.737
surgery risk factors and comorbidities	243 (58.3%)	49 (63.6%)	194 (57.1%)	0.353
insulin-dependent diabetes	2 (0.5%)	1 (1.3%)	1 (0.3%)	0.811
insulin-independent diabetes	104 (24.9%)	26 (33.8%)	78 (22.9%)	0.066
cardiac infarction ≤6 months	2 (0.5%)	1 (1.3%)	1 (0.3%)	0.811
cardiac infarction >6 months	35 (8.4%)	12 (15.6%)	23 (6.8%)	0.022
epilepsy	1 (0.2%)	0 (0.0%)	1 (0.3%)	1.000
circulatory failure	8 (1.9%)	2 (2.6%)	6 (1.8%)	0.983
kidney failure	2 (0.5%)	1 (1.3%)	1 (0.3%)	0.811
COPD	83 (19.9%)	13 (16.9%)	70 (20.6%)	0.564
varicose veins and lower extremity venous insufficiency	10 (2.4%)	0 (0.0%)	10 (2.9%)	0.267
hypertension	251 (60.2%)	50 (64.9%)	201 (59.1%)	0.416
coronary artery disease	101 (24.2%)	26 (33.8%)	75 (22.1%)	0.044
respiratory system diseases	102 (24.5%)	17 (22.1%)	85 (25.0%)	0.695
chronic bronchitis	2 (0.5%)	0 (0.0%)	2 (0.6%)	1.000
bronchial asthma	18 (4.3%)	5 (6.5%)	13 (3.8%)	0.465
post-tuberculosis changes in the lungs	4 (1.0%)	0 (0.0%)	4 (1.2%)	0.757

COPD – chronic obstructive pulmonary disease

($p < 0.001$). The median of the maximum tumor size was significantly larger in the group of patients who reported hemoptysis ($p = 0.023$), a cough ($p = 0.0012$) and weight loss ($p = 0.002$) as disease symptoms (tab. S–I [supplementary files], fig. 2).

The median of the maximum tumor size was higher in the group of patients who reported pain ($p = 0.47$) and dyspnoea ($p = 0.054$) as disease symptoms. It is essential to note that these differences were not statistically significant (tab. S–I, fig. S–1 [supplementary files]). There were no statistically significant differences in survival duration observed between women and men ($p = 0.060$) (tab. III, fig. S–2 [supplementary files]). Patients with a positive cancer history were almost twice as likely to experience mortality compared to those with a negative cancer history ($p = 0.008$) (tab. III, fig. S–3 [supplementary files]). Likewise, patients with a positive family history of cancer had twice the risk of mortality in comparison to those with a negative family history of cancer ($p = 0.002$) (tab. III, fig. S–4 [supplementary files]). The group of patients exposed to second-hand smoking exhibited an almost sixfold higher risk of mortality compared to those who were not exposed to second-hand smoking ($p < 0.001$) (tab. III). Patients with surgical risk factors had a fivefold higher risk of death compared to patients without surgical risk factors ($p < 0.001$) (tab. III, fig. S–5 [supplementary files]).

Patients with hypertension had an approximately twofold higher risk of death compared to those without hypertension ($p = 0.011$) (tab. III–IV, fig. 3). The division of the patients by gender revealed a significant impact of hypertension on survival exclusively within the male group. There were no significant differences in survival between women with hypertension compared to the group of women without hypertension (fig. 4, S–6 [supplementary files]). Patients with respiratory system diseases had a mortality risk nearly twice as high as those without this group of comorbidities ($p = 0.035$) (tab. III, fig. 5).

Compared to patients with T1 cancer, patients with T2 had a twofold higher risk of death ($p = 0.006$), while T3 patients had an almost threefold higher risk ($p < 0.001$), and T4 patients had an almost fourfold higher risk of death ($p < 0.001$). Patients with the N feature at the N2 level had an approximately sevenfold higher risk of death compared to patients with N0 ($p < 0.001$) (tab. III, fig. S–7, S–8 [supplementary files]).

Patients with a tumor grade at G3 had an approximately threefold higher risk of death than patients with G1 ($p = 0.047$), while patients with G4 had a more than 100-times higher risk of death than patients with G1 ($p < 0.001$). Furthermore, patients with a larger maximum tumor size had a higher risk of death (tab. III, fig. S–9 [supplementary files]).

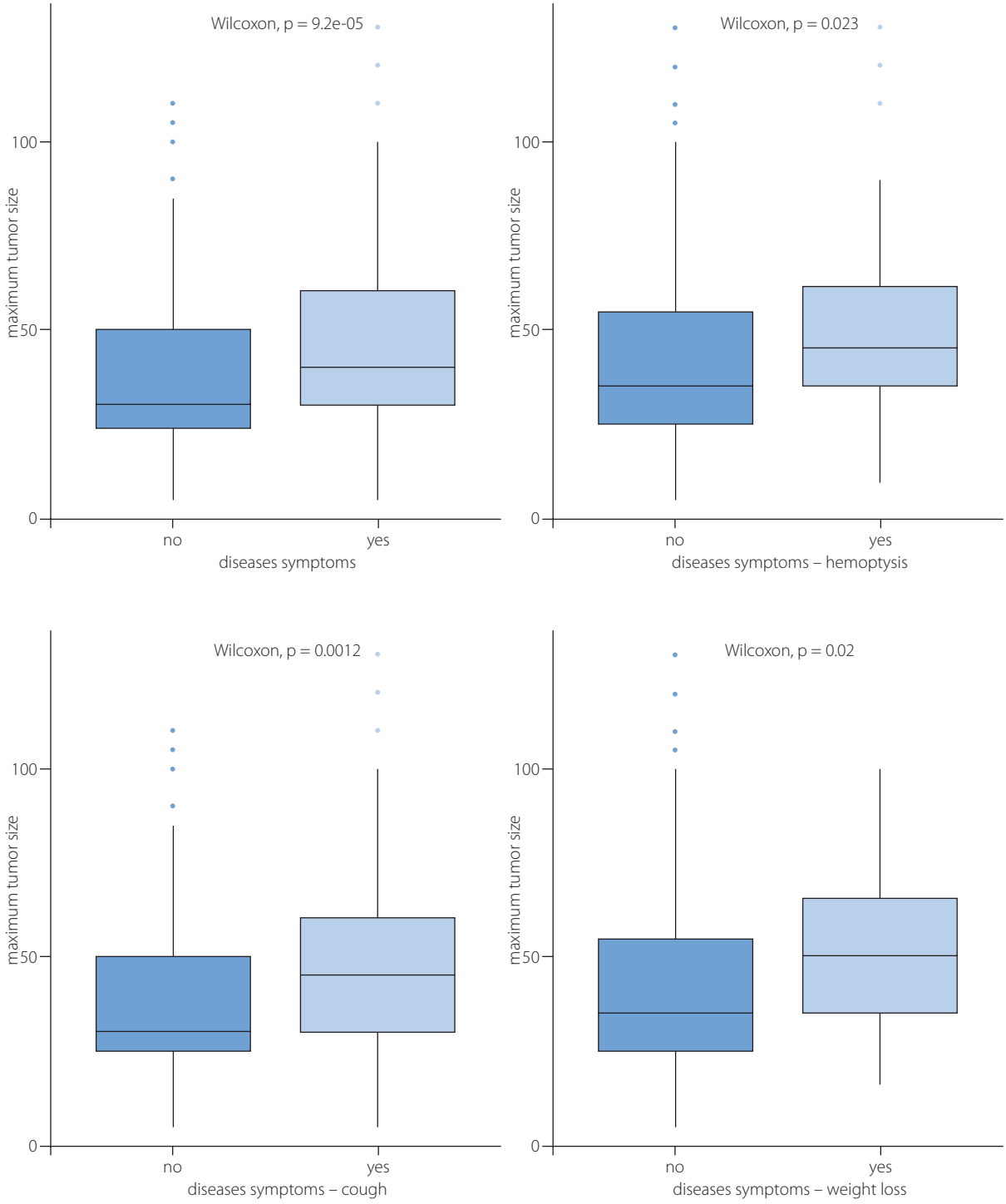

Figure 2. Disease symptoms such as hemoptysis, coughing, and weight loss depending on the maximum tumor size (n = 417), boxplot

Discussion

Our study focused on patients with SCC. However, given that the majority of previous studies in this field have been predominantly based on NSCLC studies in general, and considering the similarities between squamous and non-squamous tumors concerning factors influencing postoperative survival, we have concentrated on discussing studies primarily grounded in NSCLC research.

The article by Iachin et al. [10] from 2014 presented the conclusions that patients with cardiovascular disease presented higher mortality rates. The conclusions also show that patients with lung diseases have a higher mortality rate. In our work, we also highlighted different survival rates in these groups of patients. Another study showed that patients with congestive heart failure (CHD) had a higher mortality rate. Likewise, our research revealed varying survival rates among

Table III. Survival probability depending on specific features (n = 417)

Variable	Beta	HR (95% CI)	Wald. test	p-value
gender – female	–0.43	0.65 (0.42–1.00)	3.60	0.060
smoking cigarettes	–0.13	0.87 (0.54–1.40)	0.30	0.590
second-hand smoking	1.00	6.20 (2.90–13.00)	22.00	<0.001
positive cancer history	0.64	1.90 (1.20–3.00)	7.20	0.008
surgery risk factors and comorbidities	1.00	5.00 (2.90–8.40)	36.00	<0.001
hypertension	0.55	1.70 (1.10–2.70)	6.50	0.011
respiratory system disease	0.45	1.60 (1.00–2.40)	4.40	0.035
disease symptoms	–0.11	0.89 (0.6–1.30)	0.33	0.560
weight loss	-0.4×10^{-3}	1.00 (0.41–2.40)	0.00	0.990
positive family history of cancer	0.71	2.00 (1.30–3.20)	9.40	0.002
pack-years	–0.01	0.99 (0.99–1.00)	1.10	0.290
maximum tumor size	0.01	1.00 (1.00–1.00)	21.00	<0.001
T feature				
II	0.79	2.19 (1.25–3.84)	20.86	0.006
III	1.16	3.18 (1.76–5.76)		<0.001
IV	1.38	3.98 (2.07–7.65)		<0.001
x	–13.39	1.53×10^{-6} (0–Inf)		0.995
N feature				
I	0.06	1.06 (0.95–0.65)	15.56	0.822
II	1.99	7.34 (0.14–2.65)		<0.001
x	–0.15	0.86 (1.17–0.49)		0.594
grade				
II	0.48	1.61 (0.62–0.58)	23.40	0.360
III	1.04	2.82 (0.35–1.01)		0.047
IV	4.62	101.24 (0.01–10.22)		<0.001
x	0.35	1.42 (0.71–0.38)		0.604

x – feature cannot be assessed

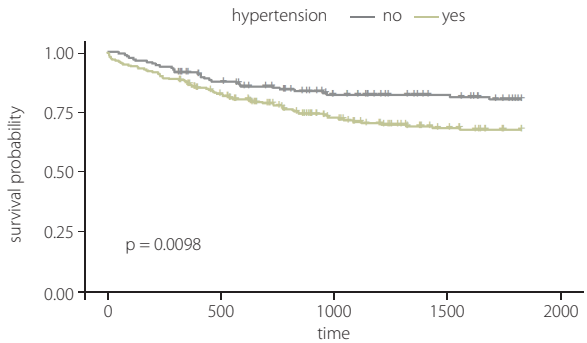

Figure 3. Survival probability depending on hypertension appearance, the Kaplan–Meier curve (n = 417)

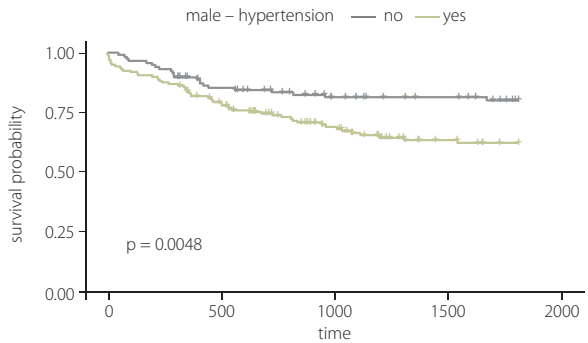

Figure 4. Survival probability for men depending on hypertension appearance, the Kaplan–Meier curve (n = 417)

groups of patients with similar comorbidities. Another study showed that patients with congestive heart failure (CHD) exhibited higher mortality rates. However, it was not possible to delve into this topic extensively in our work due to the limited

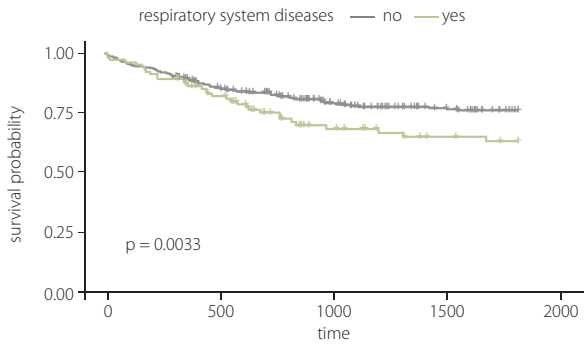

Figure 5. Survival probability depending on respiratory system disease appearance, the Kaplan–Meier curve (n = 417)

number of patients suffering from this condition. However, the assumption that cardiovascular diseases are a significantly negative prognostic factor in patients with lung cancer was clarify. A study by Tammemagi [12] showed that the presence of comorbidities negatively affects the survival of patients with lung cancer both in early and late stages of the disease. This observation presents an intriguing avenue for future investigations into the prevention of lung cancer, particularly regarding the prevention of diseases that frequently coexist with this condition [10–12]. Agarwal's study revealed a significant correlation between gender and survival outcome of patients with SCC. This conclusion could not be drawn from our work [13].

A subsequent study, conducted in 1999, presents valuable information, some of which is reflected in our work. This study examined aspects such as quality of life before the onset of lung cancer, the manifestation of disease symptoms, and their impact on survival. The findings from this study indicated that the onset of >5% weight loss and the presence of dyspnea were unfavorable prognostic factors. Despite the passage of time, this study remains a relevant up-to-date analysis of information on how we can predict the course of patients' disease [14].

A study conducted by Montazeri focused on the quality of life of lung cancer patients in relation to survival time. In the study, deceased patients were more likely to report symptoms such as fatigue, loss of appetite, a cough, shortness of breath and haemoptysis. This is reflected in our study, especially weight loss symptoms, shortness of breath and haemoptysis. Additionally, the author emphasizes that the quality of life before the cancer diagnosis significantly impacts survival after diagnosis. This is a relevant topic for future research [15].

A study conducted by Osowiecka, Rucińska, Każarnowicz et al. [16] focused on the influence of gender, T and N features. According to the presented analysis results, gender and T feature had no significant impact on the survival of patients with non-small-cell lung carcinoma treated with radiation. That said, the N feature turned out to have a significant impact on the survival of these patients. Compared to the results of our study, there was no significant effect of gender on the survival of patients with NSCLC but the N feature was significant. Unlike the presented study, the T feature was significant as well. Nevertheless, the similarity of survival depending on N feature despite treatment method is worth to be pointed out, which creates an interesting area of future research [16].

Conclusions

The maximum tumor size significantly influences specific symptoms of patients suffering from squamous-cell lung carcinoma including hemoptysis, weight loss, and coughing. Moreover, patients with a positive family history of cancer and respiratory diseases exhibit reduced survival time following lobectomy. The 5-year survival rate is comparable between women and men. As regards the prediction of patient survival in cases of squamous-cell lung carcinoma, the relationships should be properly considered.

Article information and declarations

Data availability statement

The data presented in this study are available in this article.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Medical University of Silesia (No PCN/0022/KB/27/21).

Author contributions

Weronika Targosz – data curation, funding acquisition, project administration, supervision.
Julia Świerczek – data curation, funding acquisition, project administration, supervision.
Błażej Ochman – formal analysis, methodology, writing – original draft.
Paweł Kiczmer – data curation, formal analysis, funding acquisition, investigation, methodology, project administration, supervision, writing—review & editing.
Paweł Ziora – data curation, resources, writing – review & editing.
Mateusz Rydel – resources, software.
Damian Czyżewski – resources, writing – original draft, validation.
Maciej Borowiecki – software.
Bogna Drozdowska – investigation, resources, validation, writing – review & editing.
All authors have read and agreed to the published version of the manuscript.

Funding

None declared

Conflict of interest

None declared

Weronika Targosz
Medical University of Silesia
Faculty of Medical Sciences in Zabrze
ul. Poniatowskiego 15
40-055 Katowice, Poland
e-mail: s81421@365.sum.edu.pl

Received: 11 Sep 2023
Accepted: 30 Nov 2023

References

1. 39-All-Cancers-Fact-Sheet.Pdf.
2. Zarogoulidis K, Zarogoulidis P, Darwiche K, et al. Treatment of non-small cell lung cancer (NSCLC). J Thorac Dis. 2013; 5 Suppl 4(Suppl 4): S389–S396, doi: 10.3978/j.issn.2072-1439.2013.07.10, indexed in Pubmed: 24102012.
3. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021; 71(3): 209–249, doi: 10.3322/caac.21660, indexed in Pubmed: 33538338.
4. Jackson SS, Marks MA, Katki HA, et al. Sex disparities in the incidence of 21 cancer types: Quantification of the contribution of risk factors. Cancer. 2022; 128(19): 3531–3540, doi: 10.1002/cncr.34390, indexed in Pubmed: 35934938.
5. Green J, Cairns BJ, Casabonne D, et al. Million Women Study collaborators. Height and cancer incidence in the Million Women Study: prospective cohort, and meta-analysis of prospective studies of height and total cancer risk. Lancet Oncol. 2011; 12(8): 785–794, doi: 10.1016/S1470-2045(11)70154-1, indexed in Pubmed: 21782509.
6. Drilon A, Rekhtman N, Ladanyi M, et al. Squamous-cell carcinomas of the lung: emerging biology, controversies, and the promise of targeted therapy. Lancet Oncol. 2012; 13(10): e418–e426, doi: 10.1016/S1470-2045(12)70291-7, indexed in Pubmed: 23026827.
7. Tsai JC, Saad OA, Magesh S, et al. Tobacco Smoke and Electronic Cigarette Vapor Alter Enhancer RNA Expression That Can Regulate the Pathogenesis of Lung Squamous Cell Carcinoma. Cancers (Basel). 2021; 13(16), doi: 10.3390/cancers13164225, indexed in Pubmed: 34439379.
8. Kim AS, Ko HJ, Kwon JH, et al. Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. Int J Environ Res Public Health. 2018; 15(9), doi: 10.3390/ijerph15091981, indexed in Pubmed: 30208628.
9. Barta JA, Powell CA, Wisnivesky JP. Global Epidemiology of Lung Cancer. Ann Glob Health. 2019; 85(1), doi: 10.5334/aogh.2419, indexed in Pubmed: 30741509.
10. Iachina M, Jakobsen E, Møller H, et al. The effect of different comorbidities on survival of non-small cells lung cancer patients. Lung. 2015; 193(2): 291–297, doi: 10.1007/s00408-014-9675-5, indexed in Pubmed: 25516286.
11. Islam KM, Jiang X, Anggondowati T, et al. Comorbidity and Survival in Lung Cancer Patients. Cancer Epidemiol Biomarkers Prev. 2015; 24(7): 1079–1085, doi: 10.1158/1055-9965.EPI-15-0036, indexed in Pubmed: 26065838.
12. Tammemagi CM, Neslund-Dudas C, Simoff M, et al. Impact of comorbidity on lung cancer survival. Int J Cancer. 2003; 103(6): 792–802, doi: 10.1002/ijc.10882, indexed in Pubmed: 12516101.
13. Agarwal M, Brahmanday G, Chmielewski GW, et al. Age, tumor size, type of surgery, and gender predict survival in early stage (stage I and II) non-small cell lung cancer after surgical resection. Lung Cancer. 2010; 68(3): 398–402, doi: 10.1016/j.lungcan.2009.08.008, indexed in Pubmed: 19762109.
14. Herndon J, Fleishman S, Kornblith A, et al. Is quality of life predictive of the survival of patients with advanced nonsmall cell lung carcinoma? Cancer. 1999; 85(2): 333–340, doi: 10.1002/(sici)1097-0142(19990115)85:2<333::aid-cncr10>3.0.co;2-q.
15. Montazeri A, Milroy R, Hole D, et al. Quality of life in lung cancer patients: as an important prognostic factor. Lung Cancer. 2001; 31(2-3): 233–240, doi: 10.1016/s0169-5002(00)00179-3, indexed in Pubmed: 11165402.
16. Osowiecka K, Rucińska M, Każarnowicz A, et al. Przeżycia chorych na niedrobnokomórkowego raka płuca leczonych napromienianiem w latach 2003–2006 w Samodzielnym Publicznym Zakładzie Opieki Zdrowotnej Ministerstwa Spraw Wewnętrznych z Warmińsko-Mazurskim Centrum Onkologii w Olsztynie. Nowotwory. Journal of Oncology. 2015; 65(1): 14–22, doi: 10.5603/njo.2015.0003.