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Risk Factors of Lung Cancer

RESEARCH ARTICLE

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Risk Factors for the Diagnosis of Lung Cancer in Poland: A Large-Scale, Population-Based Case-Control Study

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Abstract

Objective: Lung cancer is one of the most common and deadly malignant neoplasms. Currently, it is one of the main causes of cancer deaths worldwide. The study aimed to identify and evaluate patient characteristics, demographic and lifestyle factors that are associated with lung cancer at diagnosis. **Methods:** The study included 400 patients diagnosed with lung cancer and 400 within the control group. The research was based on a clinical, direct, individual, structured, in-depth and focused interview. Assessment of activity and BMI was used according to WHO recommendations, as well as the expert system. **Results:** The mean age of the patients was 74.53 ± 7.86 years, while in the control group 59.5 (7.93). There was a strong positive relationship between the incidence of tuberculosis and chronic obstructive pulmonary disease and the risk of lung cancer ($p < 0.001$). The risk of lung cancer was significant in the case of smoking 20 or more than 20 cigarettes a day and smoking for more than 20 years ($p = 0.01$). **Conclusions:** Active and passive smoking, are a leading risk factor for lung cancer, which shows that understanding of the long-term and fatal effects of smoking is still very low in society. No significant correlation has been found between lifestyle and risk of lung cancer. However, there was a strong positive correlation between tuberculosis and chronic obstructive pulmonary disease and the risk of lung cancer. Occupation is a predisposing factor for lung cancer occurrence.

Keywords: lung cancer- risk factors- demographic factors- lifestyle factors

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Introduction

Lung cancer in Poland in the first decade of the 21st century was diagnosed annually in approximately 16,000 men and over 5,500 women. Most patients who develop lung cancer die. The 5-year survival rates remain around 12% and do not differ significantly between the sexes (11% for men and 16% for women). Lung cancer causes one in three cancer deaths in men and one in eight in women. The incidence of lung cancer is 3-4 times higher in men than in women (Polish Oncology Union, 2020; Cancer Statistics Center, 2020). In the US, lung cancer is the second most common cancer in both men and women. The American Cancer Society estimate for lung cancer in the United States for 2020 is approximately 228,820 new cases of lung cancer (11,6,300 men and 112,520 women) and approximately 135,720 deaths from lung cancer (72,500 men and 63,220 women) (American Cancer Society, 2020; US Department of Health and Human Services, 2015). Lung cancer mainly occurs in the elderly. Most people diagnosed with lung cancer are 65 years of age or older; a very small number of people diagnosed are under 45 years of age. The average age of diagnosed people is approx. 70 years (International Agency for Research on Cancer, 2020; World Cancer Research Fund, 2021).

The most important risk factor for lung cancer is active smoking. Tobacco smoke contains several thousand chemical compounds, many of which are substances with proven strong carcinogenic properties. About 80% of lung cancer deaths are thought to be caused by smoking, and the number is likely even higher in small cell lung cancer. The risk of developing the disease is proportional to the length of time you smoke, the number of cigarettes you smoke and the age at which you start smoking. In smokers, the risk is higher than in non-smokers, where, for example, for one packet of cigarettes smoked a day for over 30

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years, it increases 20-60 times in men and 14-20 times in women. Smoking cigars and pipes can cause lung cancer, almost in the same way as cigarette smoking. Smoking low tar cigarettes increases the risk of lung cancer as much as regular cigarettes. Smoking menthol cigarettes can increase the risk even more, as menthol allows smokers to inhale more smoke. Passive smoking is also associated with a higher risk of lung cancer compared with people not exposed to tobacco smoke. It is estimated that about 20-50% of "non-smokers" who suffer from lung cancer are passive smokers. The remaining lung cancer risk factors are of much less importance on the population scale. These include exposure to ionizing radiation, exposure to asbestos, cadmium, lead, nickel, arsenic. It has also been proven that long-term exposure to coal and liquid fuel fumes increase the risk of lung cancer. So far, the role of genetic factors is relatively poorly understood. Frequent occurrence of lung cancer in some families is associated with a genetically determined tendency to over-activate carcinogenic compounds contained in tobacco smoke or to remove these compounds too slowly from the body (Jung, 2021; Luo et al., 2021).

We did not find many similar studies in the literature. We wanted to compare the results obtained in the group of patients with lung cancer with those of patients without cancer diagnosis. We need data on differences in levels and trends in lung cancer to understand the impact of individual risk factors.

Objective of the work

The study aims to identify and evaluate patient characteristics, demographic and lifestyle factors that are associated with lung cancer at diagnosis. Our hypothesis is that among the risk factors for cancer in general, there are those specific to lung cancer. Knowledge of these factors can influence targeted preventive actions.

Materials and Methods

Study design

A population-based, multi-area cross-sectional study conducted among patients of the Cancer Center of the Provincial Hospital in Rzeszow. Patients diagnosed with histopathologically confirmed lung cancer were invited to participate in the study. Patients in the control group without a diagnosis of lung cancer were invited to participate in the study. The research was conducted in the Provincial Hospital of the Podkarpackie Province. The period of recruitment and research with data collection took place in 2019 and 2020. Due to the small sample size, the proportion of patients with fairly consistent characteristics was important. The predictors are age, gender, education, residence. The confounding factors are the inability to conduct a face-to-face interview and patients choosing to complete the interview online. Lack of the face-to-face contact with the patient poses a higher risk of misunderstanding the question or leaving questions unanswered. In our study, all patients chose direct contact.

Eligible patients received an information pack from the research group. The information package consisted of a letter describing the objectives of the study and its course, a consent form to participate in the study, which should be completed if patients are interested in the study, and a refusal sheet. After providing informed consent, the patient chose to participate in a face-to-face interview conducted in the clinic by an interviewer who was a member of the research group or to fill in the interview form on-line. The paper survey was filled out by 800 patients. The interview lasted approximately 40 minutes. The interview in the case of patient fatigue was divided into parts. The on-line interview could be completed at any time by the patient.

Participant recruitment, inclusion and exclusion criteria

All types of histopathologically confirmed lung cancer cases, regardless of their stage, were included in the study. The main indicators of participation in the study were the diagnosis of cancer at least three months before the study, life expectancy> 6 months (life expectancy exceeding half a year), age over 18 and awareness of the diagnosis. The study excluded patients who did not want to participate in the study, who were subject to palliative care, and also if the diagnosis of cancer was shorter than three months, because the initial period of diagnosis and treatment is associated with a psychological burden, which could possibly introduce errors in the results. Patients who were too physically ill, too emotionally stressed, under the age of 18 or unable to read Polish were also excluded.

Patients without the cancer diagnosis were selected for control group. They were patients of the internal medicine ward of the Provincial Hospital. There was one control per one case. All patients recruited for the research, who agreed to participate in the study, took part in it. No one withdrew during the study.

Sample

The study included 400 patients diagnosed with lung cancer and 400 within the control group. The average age of the patients was 74.53 ± 8.86 years, the control group 59.5 (7.93).

Questionnaire for the Patient

The method used in the research was clinical, direct, individual, structured interview, which was in-depth and focused. The qualitative interview questionnaire was a standardized measuring tool and was verified by testing a group of 30 patients during the month. The questionnaire contained open-ended, single and multiple-choice questions to obtain demographic, epidemiological, lifestyle and risk behaviour information as well as risk factors.

Body mass index assessment

Body mass index (BMI) expressed in kg/m^2 was calculated from the baseline height and weight and divided into three categories according to the WHO standard: normal (<25 kg/m^2), overweight (25-29.9 kg/m^2) and obesity (≥ 30 kg/m^2).

Assessment of physical activity

Assessment of activity according to WHO recommendations was used: undertaking at least moderate activity for about 30 minutes five times a week, moderate

or intense physical effort performed for at least 45 minutes on at least five days a week, undertaking 18-27 hours of metabolic effort MET effort equivalent per week (hour of jogging, cycling, tennis, swimming - 7 METs, hour of aerobics, lawn mowing - 6 METs, walking for an hour 6 days a week - 18 METs).

Assessment of covariates

Potential confounders of lung cancer risk were selected based on published evidence from European Prospective Investigation into Cancer and Nutrition (EPIC), the International Agency for Research on Cancer (IARC), and the World Cancer Research Fund (WCRF), which included: smoking status (never smoking, passive smoking, active smoking, age at which they started and stopped smoking, number of cigarettes smoked), weekly alcohol consumption based on a relatively safe portion of pure alcohol per day for women (10 g) and for men (20 g), i.e. one glass of wine, a glass beer or a small glass of strong alcohol. A portion is 30 ml of vodka (40% / vol.), 100 ml of wine (12% / vol.), 285 ml of strong beer (4.9% / vol.) Or 375 ml of light beer (3.5% / vol.), adherence to fruit and vegetable guidelines defined as eating more than 2 portions of fruit and 5 portions of vegetables per day or 400-800 g per day, consuming 600-800 g of fibre per day, eating less than 80 g per day or 500 g per week.

Expert system

The research method was an individual analysis of cancer risk performed with the use of a computer application based on an expert system. The tools included a skeleton expert system Jess, allowing formation of decision rules and conclusions. The graphic interface was created with the use of a programming language JavaFx, which allows creation of advanced forms using the CSS styles. Placing the patient's data in a constructed survey of the expert system allows the generation of a database of risk factors. On this basis, with a sufficiently large sample, it will be possible to build a system allowing a percentage assessment of cancer risk for an individual patient. The system will be available for primary health care workers as a form of quick interview and verification possible before a medical assessment.

Ethical considerations

The study was approved by the Ethics Committee (Resolution No. 1/12/2019). Participation in the study was voluntary and anonymous, and the respondents were informed of their right to refuse or withdraw from the study at any time. Each participant was informed about the study objective and the time of study termination.

Data analysis

Data analysis was performed with the SPSS statistical package version 15.0 for Windows.

Descriptive analysis, bivariate, and multivariate logistic regression models were carried out. The adjusted odds ratio (AOR) was used to determine the association between the dependent variable and independent variables with a statistically significant level at a 95% confidence interval (CI). The data were tested for the distribution and the homogeneity of variance was validated before applying the parameter tests. Comparison of quantitative variables between groups was performed using ANOVA / Kruskal-Wallis Test. Quantitative comparison of the variables between the groups was done using the unpaired t / Mann-Whitney test. The comparison of qualitative variables between the groups was performed using the exact Chi-square / Fisher test. Statistical significance was used at the conventional 5% level ($p < 0.05$.

It was assumed that only interviews with complete data would be analysed - otherwise, they would be excluded. During the analysis of the collected data, no interview cards were excluded, as all elements of the interview cards were filled out properly. The reason for this is that the interviews were conducted by the members of the research group who participated in the research team from the very beginning.

Results

Demographic data

The study included 400 patients diagnosed with lung cancer and 400 within the control group. The mean age of the patients was 74.53 ± 7.86 years, while in the control group 59.5 (7.93). Increasing age was strongly associated with the risk of developing lung cancer. The incidence of lung cancer correlated with both sex ($p < 0.0001$) and occupation ($p < 0.0001$). Multivariate logistic regression showed that the overall incidence of lung cancer was significantly higher in men (AOR = 1.78; 95% CI: 1.36; 2.85) and in the driving profession (AOR = 0.46; 95% CI : 0.30). 0.68) compared with the corresponding groups. Other descriptive statistics identifying the studied group are presented in Table 1.

Family history of neoplastic diseases

When assessing the incidence of neoplastic diseases in the families of the respondents, it was shown that 55% (95% CI: 52-59) of patients reported cancer and 31% (95% CI: 29-39) in control group. Family history of neoplastic diseases was not significantly associated with the risk of lung cancer (Table 2,3).

Personal medical history

An important element of the analysis was the assessment of the presence of diseases that increase the risk of lung cancer among the examined diseases. The most common disease entities in the control group are arterial hypertension (45%, 95% CI: 42-50) and diabetes (29%, 95% CI: 22-30) (Table 4). There was a strong positive relationship between the incidence of tuberculosis and chronic obstructive pulmonary disease and the risk of lung cancer ($p < 0.001$) (Table 4).

Bodyweight, physical activity

45% (95% CI: 43-47) of patients had BMI greater than 25 kg / m2 and 35% (95% CI: 32-36) in control group. Increasing BMI was associated with an increased risk of lung cancer ($p < 0.01$). Among obese subjects, the risk of developing lung cancer was 1.36 (AOR = 1,36; 95% CI, 1.07-1.55) compared with non-obese subjects. Of the

Table 1. Descriptive Statistics of the Examined Group of Patiens

Demographic Information	Cases (n=400)	Control group (n=400)	P
Characteristics % (N)			
Sex			
Women	12% (48)	88% (352)	0.01
Men	88% (352)	12% (48)	
The age of the study group			
SD	74.53 (7.86)	59,5 (7,93)	0.12
95%CI	<63; 80>	<35; 85>	
Place of residence			
City	55% (220)	36% (144)	0.21
Village	45% (180)	64% (256)	
Financial situation			
Very good	5% (20)	20% (80)	0.19
Good	17% (68)	51% (204)	
Average	56% (224)	20% (80)	
Bad	22% (88)	9% (36)	
Age groups			
34-44	0% (0)	15% (60)	0.07
45-55	0% (0)	12% (48)	
56-66	22% (88)	27% (108)	
67-77	66% (264)	23% (92)	
78-88	12% (48)	23% (92)	
Education of the study group			
higher education	11% (44)	20% (80)	0.21
Secondary education	45% (180)	71% (284)	
Vocational education	33% (132)	5% (20)	
Primary education	11% (44)	4% (16)	
Marital status			
Married	89% (356)	65% (260)	0.62
Widowed	11% (44)	11% (44)	
Unmarried	0% (0)	24% (96)	
Source of income			
Professionally active	55% (220)	65% (260)	0.59
Annuity	22% (88)	12% (96)	
Unemployed	0% (0)	9% (36)	
Retirement	23% (92)	14% (56)	
Profession			
Professional driver	12% (48)	44% (260)	0.01
Teacher	22% (88)	4% (16)	
Factory worker	5% (20)	12% (48)	
Mechanic	5% (20)	5% (20)	
Farmer	11% (44)	32% (36)	
Clerk	45% (180)	3% (12)	

patients, 41% (95% CI: 40-43) declared moderate physical activity, 47% (95% CI: 43-49) did not meet the guidelines for vigorous activity, while subjects in control group were more likely to follow them. Patients with cancer spent more hours a day in a sitting position. A strong positive relationship was found between low physical activity converted to metabolic equivalent of MET effort per week and the risk of lung cancer (p <0.001) (Table 5).

Table 2. The Occurrence of Neoplasms in the Respondents' Family

Family history of diseases	Cases (n=400)"	Control group (n=400)	P
Characteristics /% (N)			
Family history of respiratory diseases			
No	82% (328)	100% (400)	
Yes	18% (72)	0% (0)	0.19
Cancer family history			
No	45% (180)	69% (276)	0.71
Yes	55% (220)	31% (124)	0.21

Drugs

Active smokers among patients constitute 45% (95% CI: 42-47), in the control group 37% (95% CI: 32-39). The group of patients did not declare chewing tobacco leaves. The lowest age at the start of smoking was 16 years

Table 3. The Occurrence of Neoplasms in the Respondents' Family

Type of cancer	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
Nervous system	2% (8)	3% (12)	0.55
Lung	10% (40)	24% (96)	0.41
Colorectal	5% (20)	15% (60)	0.71
Oral cancer	8% (32)	1% (4)	0.91
Breast	19% (76)	20% (80)	0.88
Ovary	8% (32)	10% (40)	0.54
Prostate	16% (64)	5% (20)	0.91
Pancreas	10% (40)	0% (0)	0.44
Liver	10% (40)	0% (0)	0.91
Skin	1% (4)	2% (8)	0.74

Table 4. History of Illness among the Respondents

Recognized diseases	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
Diabetes	11% (44)	29% (116)	0.99
Ulcerative colitis	1% (4)	4% (16)	0.56
Crohn's disease	0% (0)	0% (0)	0.41
Intestinal polyps	1% (4)	0% (0)	0.55
Hypertension	49% (196)	45% (180)	0.88
Heart arythmia	8% (32)	18% (72)	0.74
Rheumatic disease	0% (0)	4% (16)	0.99
Tuberculosis	15% (60)	0% (0)	0.01
Asthma	8% (32)	10% (20)	0.99
Chronic obstructive pulmonary disease	42% (168)	2% (8)	0.01
Emphysema	17% (68)	0% (0)	0.74

Table 5. Life Style of the Respondents

Variables	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
BMI			
< 25	55% (180)	65% (260)	0.71
25,0 – 29,9	34% (176)	23% (92)	0.59
≥ 30	11% (44)	12% (48)	0.59
Metabolic equivalent of MET effort per week			
< 10 MET	72% (288)	51% (204)	0.59
10 – 17 MET	19% (76)	29% (116)	0.59
18 – 27 MET	9% (36)	20% (80)	0.14
Weekly activity time			
Lack of activity	22% (88)	9% (36)	0.53
5 days a week for 30 minutes	41% (164)	67% (268)	0.16
5 days a week for 1 hour	45% (180)	15% (60)	0.16
7 days a week for 30 minutes	3% (12)	9% (36)	0.32
Seating hours / day			
1-Feb	8% (32)	72% (288)	0.53
3-May	42% (168)	22% (88)	0.53
6-Aug	21% (84)	4% (16)	0.1
> 8	29% (116)	2% (8)	0.53
Stress			
Acute	45% (180)	27% (108)	0.73
Chronic	21% (84)	53% (212)	0.88

in the group of patients (11%, 95% CI: 8-13). Patients were significantly more likely to smoke (p <0.0001) and smoking started at an early age significantly more often (p = 0.01). There was a strong association between cigarette smoking and the risk of lung cancer (p = 0.01). The risk of lung cancer was significant in the case of smoking 20 or more than 20 cigarettes a day and smoking for more than 20 years (p = 0.01). Patients who started smoking at an early age (AOR = 2.65; 95% CI: 2.55, 5.35) and smoked more than 30 cigarettes a day (AOR = 2.42; 95% CI: 1.21, 2, 98) had a 2.8 and 2.1 times greater risk of developing cancer (Table 6).

Diet

Daily consumption of fat in the diet was declared by as many as 89% (95% CI: 82-93) of patients and in the control group 51% (95% CI: 48-57). There were no significant associations between diet and lung cancer risk (Table 7).

Other factors

44% (95% CI: 42-47)of the surveyed patients had professional contact with pesticides, 11% (95% CI: 9-12) with asbestos, and 33% with paints and varnishes. There was a strong correlation between occupational exposure to varnishes and paints and the risk of lung cancer (p = 0.01) (Table 8).

Discussion

Lung cancer is the leading cause of morbidity and mortality worldwide, accounting for 2094 million cases

Table 6. Life Style of the Respondents

Variables	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
Smoking			
Never	33% (64)	29% (116)	0.94
Passive smoking	67% (160)	7% (28)	0.94
An active smoker	45% (120)	37% (148)	0.01
Former smoker	22% (188)	27% (108)	0.94
Age at the start of regular smoking			
10-14 years	0% (0)	0% (0)	0
15-20 years	44% (132)	4% (16)	0.01
21-25 years	56% (28)	8% (32)	0.01
> 25 years	0% (0)	88% (352)	0.94
Burning time			
< 10 years	0% (0)	25% (100)	0.62
10-20 years	33% (80)	64% (256)	0.65
> 20 years	67% (292)	11% (44)	0.01
Number of cigarettes smoked			
up to 10 cigarettes a day	0% (0)	12% (48)	0.12
20 a day	67% (80)	70% (280)	0.59
Over 30 a day	33% (292)	18% (72)	0.01
Consuming alcohol			
Abstinent	45% (132)	39% (156)	0.94
30 ml of vodka daily	12% (56)	4% (16)	0.12
100 ml of wine daily	22% (56)	7% (28)	0.52
380 ml of beer a day	11% (0)	10% (40)	0.94
60 ml of vodka daily	11% (0)	2% (8)	0.94
200 ml of wine a day	15% (56)	24% (96)	0.59
700 ml of beer a day	17% (56)	6% (24)	0.12
More	11% (44)	8% (32)	0.59

Table 7. Eating Habits among the Respondents

Variables	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
Fresh vegetables, fruits			
Several times every day	11% (44)	41% (164)	0.18
Daily once a day	33% (132)	29% (116)	0.21
Often several times a week	56% (224)	30% (120)	0.17
Preparation of dishes			
Boiled / steamed	66% (264)	57% (228)	0.2
Fried	22% (88)	18% (72)	0.55
Baked	23% (92)	26% (104)	0.73
Grilled	20% (80)	5% (20)	0.71
Fatty meals			
Daily	89% (356)	51% (204)	0.01
A few times a week	11% (44)	33% (132)	0.41
Several times a month	0% (0)	16% (64)	0.37
Consumption of salt			
< 6 g/day	31% (124)	27% (108)	0.91
> 6 g/day	69% (276)	73% (292)	0.01
Consumption of red meat			
< 80 g/ day or 500 g/week	33% (132)	66% (264)	0.82
> 80 g/ day or > 500g/week	67% (268)	34% (136)	0.01

Table 8. Occupational Risk Factors among the Respondents

Variables	Cases (n=400)	Control group (n=400)	P
Characteristics /% (N)			
Harmful factors			
Occasional contact			
pesticides	44% (44)	14% (56)	0.18
asbestos	33% (132)	0% (0)	0.21
paints, varnishes	53% (224)	50% (200)	0.17
Professional contact			
pesticides	44% (44)	14% (56)	0.18
asbestos	11% (132)	0% (0)	0.21
paints, varnishes	33% (224)	10% (40)	0.17

and 1.8 million deaths annually. Lung cancer has become a global problem, from a rare disease to an emerging public health problem. The current GLOBOCAN data indicate that this disease has the highest mortality rate among all types of cancer. The aetiological factors of lung cancer have become more complex, including features related to demographics, morbidity, environmental and occupational exposure (Shankar et al., 2019; Adamek et al., 2016).

The conducted studies have shown that cigarette smoke is an unquestionable risk factor for lung cancer. It is known that active and passive smoking is carcinogenic to humans, and the risk of dying from lung cancer increases with the increase in the length of smoking and the increase in the number of cigarettes smoked (National Toxicology Program, 2019; Butler et al., 2017; Sun et al., 2017; Das et al., 2017). Many epidemiological studies, including the case-control study by Avino et al. (2018) have shown an increased risk of developing lung cancer following long-term exposure to environmental tobacco smoke, whether from tobacco aerosol or electronic cigarettes. According to studies by Rapiti et al. (1999) childhood exposure to environmental tobacco smoke is strongly associated with lung cancer (OR 3.9; 95% CI: 1.9–8.2). According to numerous reports, there is no safe number of cigarettes. From Norwegian research conducted on 600,000 men and 500,000 women, smoking only four cigarettes a day increases the risk of dying from lung cancer threefold. The likelihood of developing cancer depends much more on the length of the addiction period than on the intensity of the addiction. However, the course of the neoplastic disease may depend on the intensity of the addiction. A US study found that people who smoked more cigarettes were more likely to die from cancer than people who smoked lightly. From the scientific analysis of data, 600 thousand. In Norway, it appears that smoking is a greater risk to the health of a woman than a man (Chapman and Wu, 2014; Diethelm and Farley, 2015; Leon et al., 2015). Numerous prospective studies have shown that there is a quantitative relationship between the development of lung cancer and the degree of exposure to tobacco smoke, showing that the incidence of lung cancer increases 4.5 times in correlation with duration of smoking, compared to 1.5 times in correlation with daily consumption (Aberle et al., 2011; Nair and Hansell, 2011; Shlomi et al., 2014). Our studies have shown that patients were significantly more likely to smoke ($p < 0.0001$) and that the respondents started smoking at a young age significantly more often ($p = 0.01$). The risk of lung cancer was significant in the case of smoking 20 or more than 20 cigarettes a day and smoking for more than 20 years ($p = 0.01$).

Age is another key risk factor for lung cancer. Only 5-10% of lung cancer cases occur under the age of 50, approximately 53% of cases occur in those aged 55 to 74 years, and 37% in those over the age of 75. The mean age of lung cancer diagnosis is 70 years for both men and women (Alberg et al., 2013; Torre et al., 2016). This relationship is also confirmed by our research, where 66% of patients were in the 67-77 age group, the mean age of the patients was 74 years, and the increasing age was strongly associated with the risk of developing lung cancer.

The undertaken research also assessed lifestyle factors in terms of their potential role in influencing the risk of lung cancer (Alberg et al., 2013). High consumption of meat, especially fried or well-baked red meat may increase the risk of lung cancer and it can be connected to the formation of nitrosamines during cooking (Sinha et al., 2000; Smith-Warner et al., 2002). There is also evidence that low vitamin D levels are associated with lung cancer risk (Herr et al., 2011), and drinking coffee over 6 cups a day has been linked to lung cancer in the NIH-AARP report (HR 95% CI: 4.56 (4, 08–5,10) (Guertin et al., 2015). A pooled study of eight cohorts found no evidence of an increased risk of lung cancer with high fat intake (Smith-Warner et al., 2002), and no association with high BMI has been shown (Thun et al., 2009; Olson et al., 2002). However, meta-analyzes indicated an increased risk of lung cancer among alcoholics (Bagnardi et al., 2011; Bandera et al., 2001; Korte et al., 2002; Freudenheim et al., 2005). In our studies, no significant correlation was found between diet, alcohol consumption and physical activity and the risk of lung cancer, but there was a link to a higher BMI.

The risk factors also include a history of lung diseases before lung cancer was diagnosed. Chronic obstructive pulmonary disease patients are at increased risk of lung cancer and studies suggest that this is independent of smoking (Malhorta et al., 2016; McWilliams et al., 2013; Sanchez-Salcedo et al., 2015; Sverzellati et al., 2012). It has also been found that patients with pulmonary tuberculosis are at increased risk of lung cancer by up to 50% (Malhorta et al., 2016). One study that examined the risk of lung cancer among smokers and never-smokers with TB found that women who never smoked with TB had an approximately eight-fold increase in lung cancer risk (Samet et al., 2009). Asthma has also been studied frequently in relation to the risk of lung cancer. Most of the studies have shown an increased risk of lung cancer in never-smokers with asthma. A meta-analysis of lung cancer and asthma studies in non-smokers showed a relative risk of 1.8 (95% CI 1.3–2.3) (Rosenberger et al., 2012). Moreover, it has been shown that emphysema is identified as an independent risk factor for lung cancer. A Danish study showed that the incidence of lung cancer in

current smokers without emphysema was 1.1% compared with 2.3% in people with emphysema (odds ratio 1.8) (Henschke et al., 2015). The above data confirm our research, which found a strong positive relationship between the incidence of tuberculosis and chronic obstructive pulmonary disease and the risk of lung cancer ($p < 0.001$).

Many studies have drawn attention to the relationship between lung cancer and the profession. We found that the overall incidence of lung cancer was significantly higher among drivers (44%). Similar results were obtained by Steenland et al., (1998) Garshick et al. (2008). This shows that employees of the transport industry are regularly exposed to the effects of exhaust gases from diesel engines, and according to IARC they are considered a probable carcinogen for humans (International Agency for Research on Cancer, 2020). Most studies focused on the link between diesel exhaust gas exposure and lung cancer suggest a consistent increased risk. SYNERGY collected information on occupation and smoking from 13,304 lung cancer cases and 16,282 controls from 11 case-control studies conducted in Europe and Canada. Cumulative exposure to diesel fuel was associated with an increased risk of lung cancer, with an odds ratio of 1.31 and a significant exposure-response relationship (p-value <0.01) (Silverman et al., 2012; Olsson et al., 2011). Other occupations related to lung cancer, according to other reports, include bartenders, workers exposed to tar, soot, workers in the ceramics, construction and rubber industries (Shankar et al., 2019). The research also shows other evidence pointing to chemical compounds as carcinogenic factors, which are very often related to the profession. All forms of asbestos are lung carcinogens, as are chromium compounds and radon (Meguid et al., 2010; Wakelee et al., 2007). An increased risk of cancer was also noted among workers in the production of cadmium-based batteries (IARC 2020; Malhotra et al., 2016). Moreover, a high level of exposure to inorganic arsenic, mainly in steel, fur, sheep paste and pesticide workers, shows an increased risk of lung cancer. An increased risk of lung cancer has also been reported among people exposed to a high level of arsenic in their drinking water (Hayes 1997). Some studies indicate a carcinogenic effect of crystalline silica in foundries, pottery, ceramics, and mining (Steenland et al., 2001). In our study of lung cancer patients 44% had occupational contact with pesticides and 33% with paints and varnishes.

The studies also tried to demonstrate the role of familial disease in patients with lung cancer. Strong evidence from previous analyses showed that these associations were specific to a family history of lung cancer, while a family history of any cancer was not significantly associated with lung cancer risk (Lissowska et al., 2010). Our research also confirms the importance of the family history of lung cancer as a clinically useful risk indicator.

Numerous scientific reports also indicate exposure to ionizing radiation as a factor increasing the risk of lung cancer. This increased risk has been proven among people who had survived a nuclear bomb attack, as well as those treated with radiotherapy (RR 1,5-2 for cumulative exposure over 100 cGy) (IARC 2020; Malhotra et al., 2016; Boice 1996). Also, people exposed to radioactive radon and its decay products emitting α particles consistently show an increased risk of lung cancer (IARC 2020; Lubin 1994). Currently, the main concern related to the lung cancer risk caused by radon and its decay products comes from exposure at the residence rather than in the workplace. A pooled analysis of 13 European case-control studies showed a relative risk of 1.16 (95% CI 1.05–1.31). The US Environmental Protection Agency estimates it is the second most common cause of lung cancer in the US. Thus, indoor radon exposure may be an important cause of lung cancer (Malhotra et al., 2016; Darby et al., 2005; Krewski et al., 2006). In our studies, patients did not identify this factor as aggravating their health history.

Our study included patients diagnosed with lung cancer. The obtained results complement the evidence from studies that both passive and active smoking increase the risk of lung cancer, especially prolonged smoking started at an early age. However, there are some limitations to consider. We did not perform an environmental exposure analysis due to the lack of data. Our research should be interpreted as exploratory.

Conclusions

1. Active and passive smoking, are a leading risk factor for lung cancer, which shows that understanding of the long-term and fatal effects of smoking is still very low in society.

2. No significant associations between lifestyle (diet, alcohol consumption, physical activity) and lung cancer have been proven, which suggests that these are not strong risk factors for lung cancer. However, there was a strong positive association between tuberculosis and chronic obstructive pulmonary disease and the risk of lung cancer.

3. The profession, especially the contact with chemical substances with proven carcinogenic effects, is a factor predisposing to the occurrence of lung cancer.

4. Preventive public health strategies should focus in particular on preventing exposure to passive smoking and the initiation of smoking by children and adolescents, as long-term smoking and the initiation of smoking at an early age constitute the most aggravating risk factor.

5. A better understanding of lung cancer risk factors helps prevent lung cancer. Identification of people from the highest risk group, i.e. smokers, ex-smokers, selected professional groups, family burden allows for the implementation of preventive and detection measures aimed at people most at risk.

Author Contribution Statement

Conceptualization, A.L.; K.P.; D.Z; S.E.A; data curation, A.L., formal analysis, A.L. and T.L.; funding acquisition, A.L.;T.L.; K.P.; D.Z; S.E.A; B.Z; M.N; investigation, A.L.; B.Z; M.N; methodology, A.L.; K.P.; D.Z; project administration, A.L., and T.L.; resources, T.L.; software, T.L. ; supervision, A.L.; validation, A.L; K.P.; D.Z; S.E.A; B.Z; M.N; visualization, T.L.; writing—original draft, A.L.; writing—review and editing, A.L. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by The Bioethics Committee at the University of Rzeszow (Resolution No. 1/12/2019).

Data Availability Statement

The data are not publicly available due to privacy and ethical restrictions. The data presented in this study may be available conditionally from the corresponding author.

Conflicts of Interest

The authors declare no conflict of interest.

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