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Familial lung cancer risk among women in Poland

Jadwiga Rachtan[a,*], Andrzej Sokołowski[a,b], Stanisław Niepsuj[c], Brunon Zemła[d], Maria Zwierko[e]

[a] Epidemiology Unit, Centre of Oncology, M. Skłodowska-Curie Memorial Institute, Garncarska 11, 31-115 Cracow, Poland
[b] Department of Statistics, Cracow University of Economics, Rakowicka 27, 31-510 Cracow, Poland
[c] Pulmonology and Oncology Centre, Jagiellońska 78, 10-357 Olsztyn, Poland
[d] Cancer Epidemiology Department, Centre of Oncology, M. Skłodowska-Curie Memorial Institute, Wybrzeże Armii Krajowej 15, 44-101 Gliwice, Poland
[e] Independent Unit-Warsaw Cancer Registry, Centre of Oncology M. Skłodowska-Curie Memorial Institute, W.K. Roentgena 5, 02-781 Warsaw, Poland

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ABSTRACT

A case–control study involving 1058 women with histologically confirmed lung cancer and 2116 healthy controls, was conducted in Poland between 2004 and 2007. The aim of this study was to examine of the role of familial aggregation of lung cancer in women. Multivariate analysis has shown that family history of lung cancer in a first-degree relative significantly increases the risk of lung cancer (OR = 1.61, $p = 0.0003$). For cases with early onset of the disease (<55 years) we observed significantly elevated risk of lung cancer (OR = 2.48, $p = 0.0001$). Results of our analysis confirmed synergistic influence of smoking and family history of lung cancer (OR = 12.91, $p = 0.0000$).

1. Introduction

In Poland, lung cancer is responsible for the biggest part of total cancer incidence and mortality. In 2005, lung cancer was diagnosed in 15,248 men and 4797 women. The number of deaths was 16,522 in men and 4933 in women. It accounts for 15.9% of all cancers and 23.7% of cancer deaths in both men and women [1].

Tobacco smoking is the predominant cause of lung cancer in both men and women, but 10–15% of all lung cancer cases diagnosed are non-smokers [2]. Although tobacco smoking is well-established causal factor for lung cancer, there is an accumulating evidence that genetic factors also a play role in lung cancer development. In 1963, Tokuhata and Lilienfeld [3] provided the first epidemiologic evidence of familial aggregation of lung cancer. Later, case–control and cohort studies have shown an increased lung cancer risk for relatives of lung cancer cases. In case–control studies, lung cancer risk for relatives of lung cancer cases ranged between 1.8 and 2.8 and in cohort studies it was similar from 1.7 to 2.0 [4–12].

Familial aggregation may be due to inheritance of a cancer causing genetic abnormality (genetic predisposition), inheritance of alteration in carcinogen handling (genetic susceptibility) or other unidentified mechanisms. Segregation analysis of lung cancer families suggests a genetic model of co-dominant inheritance, implying the existence of rare autosomal dominant cancer causing gene [13].

Women appear to have increased susceptibility to tobacco carcinogen when compared to men. A number of cohort studies have suggested that females are more susceptible to the carcinogenic effects of tobacco smoke than men [14,15]. Results of case–control studies also reported elevated risk for all major lung cancer types in women as compared to men, at every level of exposure to cigarette smoke [14,16].

We conducted the case–control study to further examine the role of familial aggregation of lung cancer in women. This is the first study in Poland, reporting familial risk of lung cancer in women, based on the data of 1058 lung cancer cases and 2116 controls.

The study is being undertaken with the approval of the local ethical committee in accordance with the principles of the Helsinki Declaration.

2. Materials and methods

Case subjects were 1058 women with newly diagnosed and histologically confirmed primary lung cancer (10th Revision ICD code 34) who were admitted to the three oncological centres (M. Skłodowska-Curie Memorial Institute, Cracow Branch, M. Skłodowska-Curie Memorial Institute, Gliwice Branch and

* Corresponding author. Tel.: +48 12 429 3753; fax: +48 12 426 1370.
E-mail address: z5rachta@cyf-kr.edu.pl (J. Rachtan).

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M. Skłodowska-Curie Memorial Institute in Warsaw), and one oncological hospital (Pulmonology and Oncology Centre in Olsztyn) in Poland, between 1 January 2004 and 31 September 2007.

Controls were 2116 healthy women randomly selected from among patients of outpatient clinics providing general medical care for the communities in the areas covered by the study. Controls, according to the files of the Cracow Cancer Registry, Silesia Cancer Registry, Warsaw Cancer Registry and Warmian-Masurian Cancer Registry, at the time of study had no previous cancer diagnosis registered.

Controls were matched to lung cancer cases (2:1 ratio) on age (±5 years) and area of living (rural/urban). After obtaining oral consent, all cases and controls were interviewed in the hospital (cases) and outpatient clinic (controls) by a trained interviewer. Interviews we conducted using a structured questionnaire including information (among other items) on demographic characteristics, active smoking and passive smoking history, family history of lung cancer in first-degree relatives, smoking in first-degree relatives.

Questions on smoking included the age when smoking started, the age when smoking stopped (for ex-smokers), the average number of cigarettes smoked per day, duration of smoking, smoked filter versus non-filter cigarettes and inhalation.

Exposure to passive smoking was assessed by the question about domestic exposure before and after the age of 18. Women who ever smoked at least one cigarette a day were defined as smokers. Women were considered ex-smokers if they stopped smoking at least 3 years before the interview. Statistical analysis has been performed using STATISTICA version 8.0 software. Groups were compared with Student's *t*-test with respect to quantitative variables. Qualitative variables were tested with chi-square test for independence. Univariate logistic models were used to calculate odds ratio (OR) together with 95% confidence intervals (CI) [17]. Final multivariate model was obtained through stepwise regression (backwards approach). A *p*-value less then 0.05 was considered as indicating statistical significance in all analyses.

3. Results

Table 1 describes the demographic characteristics of 1058 cases and 2116 controls. Cases and controls were well matched on age. The mean age for cases was 59.0 years, for controls 58.7. Approximately one-third of cases and controls were under 55 years. There were no differences between cases and controls by place of residence. A higher proportion of urban lifetime residence was observed for cases and controls (82.4% vs. 83.0%). There was significant difference between cases and controls by education structure. University and secondary education were less common among cases (53.1%) than controls (60.2%).

Table 1
Demographic characteristics of cases and controls.

	Cases $n = 1058$ (%)	Controls $n = 2116$ (%)	p
Age			
Mean age	59.0	58.7	0.4461
<55 years	364 (34.4)	752 (35.5)	
≥55 years	694 (65.6)	1364 (64.5)	0.5281
Place of residence			
Urban	872 (82.4)	1756 (83.0)	
Rural	186 (17.6)	360 (17.0)	0.6898
Education			
Incomplete elementary	12 (1.1)	24 (1.1)	0.0028
Elementary	261 (24.7)	461 (21.8)	
Vocational	223 (21.1)	358 (16.9)	
Secondary	437 (41.3)	964 (45.6)	
University	125 (11.8)	309 (14.6)	

Table 2
Characteristics of cases and controls according to smoking habits.

	Cases $n = 1058$ (%)	Controls $n = 2116$ (%)	p
Cigarette smoking			
Non-smokers	147 (13.9)	1070 (50.6)	0.0000
Ex-smokers	238 (22.5)	440 (20.8)	
Current smokers	673 (63.6)	606 (28.6)	
Mean years smoked			
All ever smokers	33.3	26.2	0.0000
Ex-smokers	27.2	19.0	0.0000
Current smokers	35.4	31.5	0.0000
Pack-years			
0	147 (13.9)	1070 (50.6)	0.0000
[1–20)	209 (19.7)	583 (27.5)	
[20–30)	202 (19.1)	173 (8.2)	
≥30	500 (47.3)	290 (13.7)	
Mean pack-years			
All ever smokers	32.6	20.6	0.0000
Ex-smokers	25.5	14.8	
Current smokers	35.2	24.9	
Type of cigarettes			
Filter	795 (87.3)	912 (87.3)	0.7028
Non-filter	21 (2.3)	30 (2.9)	
Both	95 (10.4)	104 (9.9)	
Inhalation			
No	25 (2.7)	74 (7.1)	
Yes	886 (97.3)	972 (92.9)	0.0000

Smoking habits of cases and controls are summarized in Table 2. Percentage of non-smokers was significantly lower among cases (13.9%) than controls (50.6%). The proportion of current smokers was significantly higher for cases than controls (63.6% vs. 28.6%). Mean years smoked were also significantly higher among ever smoking, currently smoking and ex-smoking cases, compared with controls. It has also been observed that pack-years of smoking and mean pack-years of smoking were significantly higher for cases than controls.

Type of cigarettes was equally distributed between cases and controls. In the material, percentage of inhalation during smoking was significantly higher among cases compared to controls (97.3% vs. 92.9%). Passive exposure before and after the age 18 was significantly higher in case group compared to control group (56.6% vs. 45.7%, $p = 0.0000$, 64.7% vs. 49.2%, $p = 0.0000$).

The distribution of histological types of lung cancer observed in our study is summarized in Table 3. Among smoker cases, the most common histological type observed in both the younger (<55 years) and older (≥55 years) age groups was small cell carcinoma (37.3% vs. 33.1%). The majority (46.9%) of non-smoker cases were diagnosed with adenocarcinoma. This histological type dominates in both the younger (41.2%) and the older (48.7%) age groups.

The characteristics of the family members for both groups are summarized in Table 4. There were no significant differences in year of birth of first-degree relatives (father, mother, siblings) between the two studied groups.

The mean number of siblings was similar (2.7 vs. 2.6). No significant differences in the distribution of number of siblings were noted between the studied groups.

Generally, all first-degree relatives of cases reported significantly higher frequency of smoking habits than first-degree relatives of controls. It has been also observed that mean years smoked were significantly higher among fathers and siblings of cases than fathers and siblings of controls.

The comparison of family history of lung cancer in first-degree relatives of cases and controls revealed significantly higher percentage of history of lung cancer among relatives of cases. Lung cancer