HISTOLOGICAL TYPES OF LUNG CANCER IN URANIUM MINERS

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INTRODUCTION

Long term exposure to radon and its progeny is one of the most important health problems. Epidemiological studies have demonstrated that exposure of miners to radon in a mine atmosphere can cause lung cancer. It has been recognized that lung cancer risk in uranium miners is associated with increased incidence of certain histological types, especially epidermoid and small cell type (1, 2). Previous results showed that the basic dependence of the relative risk for the two main histological types is linear with cumulative exposure (3). However, there is a suggestion that time and age modifiers of the dependence may be different for the two types. The aim of the study was firstly to verify the assumed differences in incidence of histological types of lung cancer for the studied cohort and general population and secondly to characterize the relation of histological types specific incidence to different exposure patterns.

The study is based on data of the oldest Czechoslovak cohort, which belongs among the largest ones with the longest follow-up. The cohort includes 4320 former uranium miners who started working in uranium mines in West Bohemia in the period 1948-59, the work lasted more than 4 years (4, 5). The study method is long-term prospective follow-up. The cohort was divided in two groups according to exposure rate pattern in order analyze the impact of exposure conditions on main histological types incidence. The exposure rate never exceeded the level of 5 WL since the third year of exposure in the group 1 while the exposure rate exceeded at least once the level of 5 WL in group 2. The first two years of exposure had not been taken into consideration in order to confirm the hypothesis about the inhibitory effect of high exposure rate levels. Consequently, it could influence lung cancer risk level caused by previous exposures.

The basic method of the study is an analysis of observed frequencies of lung cancer and their histological type specification in relation to expected standardized frequencies (age and time period). In accordance to WHO classification and from previous data analysis (6), lung cancer cases were divided into four groups:

1 - epidermoid
2 - small cell
3 - adenocarcinoma
4 - other histological types

RESULTS

A total of 705 lung cancer cases were recorded by 31 December 1990. The ratio of observed and expected numbers was 5.11. Morphological diagnoses were available in 458 cases. This represents histological type specification in 65% of lung cancer cases in the cohort as shown in Table 1.

Tab. 1: Distribution by histological types

Histological type	Code	Cases	%
no information	0	201	28.5
epidermoid	1	173	24.5
small cell	2	185	26.2
adenocarcinoma	3	31	4.4
other types	4	29	4.1
unspecified	5	40	5.7
no material	9	46	6.5
Total	-	705	100.0

Tab. 2: Age and histological type specific mortality

Age	Small cell		Epidermoid	
	O	O/E	O	O/E
- 44	24	35.02	7	10.64
45 - 54	71	11.97	39	7.20
55 - 64	65	4.27	81	5.39
65 - 84	25	2.65	46	3.79
Total	185	5.91	173	5.20

Histological types could not been specified in 41% of cases. In 40 cases the morphological findings are available (code 5), but it is impossible to specify any reliably histological type from these. In 46 cases, no material is available to specify the histological type (code 9),althought the diagnosis of lung cancer is correct.

Table 2 summarizes observed (O) and expected (E) death frequencies in dependence on attained age for both main histological types. The decrease of relative risk with age is apparent in both histological types. A more detailed analysis shows that decrease of relative risk in epidermoid type is less rapid than in small cell type. From this fact follows that risk of lung cancer death will be significantly lower in small cell carcinoma than in epidermoid one in higher age of former miners. This is the contrary of situation in younger age groups of miners.

Table 3 demonstrates dependence of relative risk on cumulated exposure (lagged by 5 years) for the two types. The relative risks show similar values in corresponding exposure categories.

Tab. 3: Exposure and histological type specific relative risk

Exposure WLM	Small cell		Epidermoid	
	O	O/E	O	O/E
0 - 99	18	2.72	17	2.42
100 - 199	69	5.03	62	4.26
200 - 299	48	8.36	42	6.98
300 - 399	21	7.72	21	7.07
400 -	29	11.68	31	11.52

RISK MODELS

Epidemiological studies have demonstrated that time since exposure and attained age considerably influence excess relative risk of lung cancer (7). In this study, the modifying effect of three factors on exposure - risk relationship was examined (Table 4):

(1) time since exposure (TSE),
(2) age at exposure (AM),
(3) time pattern (TP).

Tab. 4: Relative risk models for histological types

ERR/WLM	Epidermoid	Small cell
	0.066	0.329
TSE		
5 - 14	1	1
15 - 21	0.926	0.110
25 - 34	0.150	0.014
35 -	-0.016	0.008
AM	-0.0338	-0.0878
TP	0.708	0.534

The estimated values of model parameters for the two histological types show important differences (Tab.4). The ERR/WLM was 6.6% in epidermoid and 32.9% in small cell type (5 times higher). The effect of time pattern was found significant in small cell type and not in epidermoid type, which confirm hypothesis about parallel inhibitory effect of alpha radiation on small cell type of lung cancer. Significant negative values of the AM parameter confirm the assumed decrease of lung cancer risk with age at exposure. This trend is more pronounced in small cell type.

SUMMARY

The recent results of the study confirme the linear dependence of exposure and relative risk, decrease of alpha radiation effect with time since exposure and decrease of effect in older age categories.

More detailed analysis of exposure - effect relationship in main histological types of lung cancer confirmes hypothesis formulated by J. Ševc about parallel inhibitory effect of alpha radiation in higher exposure rates which followed after period of initiation of malignant process of bronchial epithelium cells. This phenomenon is observed in small cell type of lung cancer. These conclusions are based on application of proportional risk model.

REFERENCES

1. J. Ševc, E. Kunz, V. Plaček, *Health Phys.* 30: 433 - 437(1976).

2. J. Horáček, V. Plaček , *Cancer* 77; 40: 832 - 835 (1977).

3. J. Ševc, E. Kunz, L Tomášek ,V. Plaček, J. Horáček, *Health Phys.* 54:27-46 (1988)

4. L Tomášek, S. C. Darby , T. Fearn , A. J. Swerdlow, V. Plaček , E. Kunz, *Radiation Research* 137:251-261 (1994).

5. L Tomášek , A. J. Swerdlow, S. C. Darby, V. Plaček, E. Kunz, . Occup. Environ. Medicine 51:308-315 (1994).

6. J. Ševc, V. Plaček , L Tomášek , E. Kunz,J. Horáček, Pracov. Lék. 41:415-423 (in Czech) (1989)

7. National Research Council. Committee on Biological Effects of Ionizing Radiation (BEIR IV). Washington, DC, National Academy Press, 1988.